United States
Environmental Protection Agency

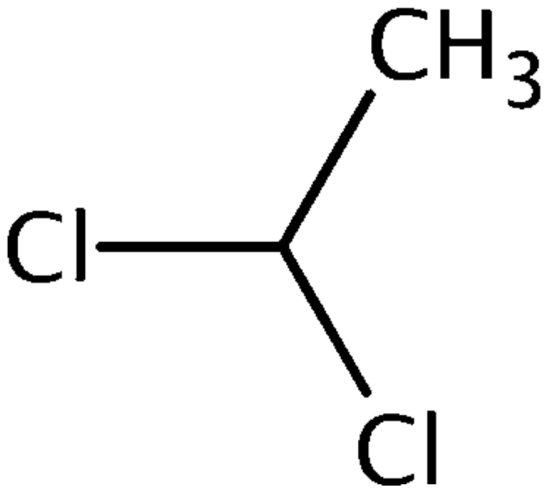
July 2024
Office of Chemical Safety and
Pollution Prevention

Draft Risk Evaluation for 1,1-Dichloroethane

Systematic Review Supplemental File:

Data Quality Evaluation Information for Human Health Hazard Epidemiology

CASRN: 75-34-3



July 2024

This supplemental file contains information regarding the data quality evaluation results for data sources that met the PECO screening criteria for the *Draft Risk Evaluation for 1,1-Dichloroethane* and were used to characterize human health hazard. EPA conducted data quality evaluation based on author-reported descriptions and results; additional analyses (*e.g.*, statistical analyses performed during data integration into the risk evaluation) potentially conducted by EPA are not contained in this supplemental file. EPA used the TSCA systematic review process described in the *Draft Systematic Review Protocol Supporting TSCA Risk Evaluations for Chemical Substances* (also referred to as '2021 Draft Systematic Review Protocol'). Any updated steps in the systematic review process since the publication of the 2021 Draft Systematic Review Protocol are described in *Draft Risk Evaluation for 1,1-Dichloroethane - Systematic Review Protocol*.Within the contents of this document, 1,1-dichloroethane may be referred to as the acronyms 1,1-DCA and 1,1-DCE. The acronyms 1,2-DCA, 1,2-DCE, and DCE refer to the chemical 1,2-dichloroethane. The acronyms 1,1,2-TCE, 1,1,2-TCA, and TCE refer to the chemical 1,1,2-trichloroethane. The acronym trans-1,2-DCE refers to the chemical trans-1,2-dichloroethylene. The acronym 1,2-DCP refers to the chemical 1,2-dichloropropane.

Table of Contents

200241	Bowler, R.M., Gysens, S., Hartney, C. (2003). Neuropsychological effects of ethylene dichloride exposure. NeuroToxicology 24(4-5):553-562.	**1393**
2799700	Brender, J.D., Shinde, M.U., Zhan, F.B., Gong, X., Langlois, P.H. (2014). Maternal residential proximity to chlorinated solvent emissions and birth defects in offspring: A case-control study. Environmental Health: A Global Access Science Source 13(1):96.	**1396**
5451581	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.	**1398**
200266	Cheng, T.J., Huang, M.L., You, N.C., Du, C.L., Chau, T.T. (1999). Abnormal liver function in workers exposed to low levels of ethylene dichloride and vinyl chloride monomer. Journal of Occupational and Environmental Medicine 41(12):1128-1133.	**1406**
4697224	Dosemeci, M., Cocco, P., Chow, W.H. (1999). Gender differences in risk of renal cell carcinoma and occupational exposures to chlorinated aliphatic hydrocarbons. American Journal of Industrial Medicine 36(1):54-59.	**1409**
3014082	Garcia, E., Hurley, S., Nelson, D.O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health: A Global Access Science Source 14(1):14.	**1415**
1938385	Guo, P., Yokoyama, K., Piao, F., Sakai, K., Khalequzzaman, M., Kamijima, M., Nakajima, T., Kitamura, F. (2013). Sick building syndrome by indoor air pollution in Dalian, China. International Journal of Environmental Research and Public Health 10(4):1489-1504.	**1420**
194820	Kernan, G.J., Ji, B.T., Dosemeci, M., Silverman, D.T., Balbus, J., Zahm, S.H. (1999). Occupational risk factors for pancreatic cancer: A case-control study based on death certificates from 24 U.S. states. American Journal of Industrial Medicine 36(2):260-270.	**1423**
5440630	Niehoff, N.M., Gammon, M.D., Keil, A.P., Nichols, H.B., Engel, L.S., Sandler, D.P., White, A.J. (2019). Airborne mammary carcinogens and breast cancer risk in the Sister Study. Environment International 130:104897.	**1427**
1357737	Sobel, W., Bond, G.G., Skowronski, B.J., Brownson, P.J., Cook, R.R. (1987). A soft tissue sarcoma case control study in a large multi-chemical manufacturing facility. Chemosphere 16(8-9):2095-2099.	**1430**
200633	Teta, M. J., Ott, M. G., Schnatter, A. R. (1991). An update of mortality due to brain neoplasms and other causes among employees of a petrochemical facility. Journal of Occupational Medicine 33(1):45-51.	**1435**

Study Citation:	Brender, J.D., Shinde, M.U., Zhan, F.B., Gong, X., Langlois, P.H. (2014). Maternal residential proximity to chlorinated solvent emissions and birth defects in offspring: A case-control study. Environmental Health: A Global Access Science Source 13(1):96.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	birth defects (neural tube defects, limbs deficiencies, oral cleft defects, heart defects, spina bifida, anencephaly)
Chemical:	1,1-Dichloroethane- Parent compound
Linked HERO ID(s):	No linked references.
HERO ID:	2799700

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Participants were drawn from the Texas Birth Defects Registry (TBDR) for years 1996-2008. Controls were frequency matched from the same registry. Study authors state that neural tube cases were more likely to not be successfully geocoded which may introduce selection bias, however, the authors note that both cases and controls with addresses that could not be geocoded were similar. In spite of that, the inclusion criteria, methods of participant selection, and frequency match were reported.
	Metric 2:	Attrition	Medium	13.3% case mother addresses and 12.8% control mother addresses were unable to be geocoded, however this most likely only lowered the precision of the study and most likely does not vary based on exposure level.
	Metric 3:	Comparison Group	Medium	Controls were matched to cases and pulled from the same eligible population by year of delivery and public health service region. Other demographic factors, e.g., race was not matched in population selection. However, statistical analyses were adjusted for year of delivery, maternal age, race/ethnicity, education, and public health region of residence.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Used Emission Weighted Proximity Model to estimate exposure at a given address based on proximity to emission sources and the specific amount or type of pollutant emitted. There may be some exposure misclassification due to mothers moving away from geocoded addresses. Previous studies indicate ~67% of mothers do not move between conception and delivery.
	Metric 5:	Exposure Levels	Medium	Reports exposure as "exposure risk value" and groups the risk values into quartiles, with exposure risk values < 0 being the referent group
	Metric 6:	Temporality	Medium	The study authors estimated exposure based on residence during pregnancy and evaluated birth outcomes. Temporality is established. Previous studies indicate ~67% mothers don't move between trimester and delivery. For mothers who moved during the pregnancy, the temporality is unknown.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Outcomes determined by Texas Birth Defect Registry, checking for birth defect diagnosis. Birth certificates came from Center for Health Statistics at Texas Department of State Health Services
	Metric 8:	Reporting Bias	High	Outcome data measured and reported clearly, stratified by specific type of birth defect
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Brender, J.D., Shinde, M.U., Zhan, F.B., Gong, X., Langlois, P.H. (2014). Maternal residential proximity to chlorinated solvent emissions and birth defects in offspring: A case-control study. Environmental Health: A Global Access Science Source 13(1):96.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	birth defects (neural tube defects, limbs deficiencies, oral cleft defects, heart defects, spina bifida, anencephaly)
Chemical:	1,1-Dichloroethane- Parent compound
Linked HERO ID(s):	No linked references.
HERO ID:	2799700

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	High	Cases were frequency matched by year of delivery and public health service region. Final models were adjusted for year of delivery, public health region, maternal age (<20, 20-24, 25-29, 30-34, 35-39, >39 years), education (<12 years, 12 years, >12 years), and race/ethnicity (Whit non-Hispanic, Black non-Hispanic, Hispanic, other non-Hispanic).
	Metric 10:	Covariate Characterization	High	Used birth and death certificates for demographic information
	Metric 11:	Co-exposure Counfounding	Medium	other co-exposures were not described
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	study used logistic regression to measure association between exposure and birth defects
	Metric 13:	Statistical Power	Medium	Overall adequate number of cases and controls - some effects have low cell counts, but at least one health effect has sufficient statistical power.
	Metric 14:	Reproducibility of Analyses	Medium	Methods sufficiently detailed for reproducibility
	Metric 15:	Statistical Analysis	High	No logistic regression model assumption violations were identified.

Additional Comments: This study examined the association between proximity to several point sources of chlorinated solvents and birth defects. Exposure was assessed using EPA's Toxic Release Inventory, and birth defects were assessed using Texas birth registries. The geocoded address of mothers on day of delivery and the amount of solvent was plugged into the Emission Weighted Probability model to assign each mother an exposure risk value. Limitations include limited evidence of temporality. Additionally, elective terminations lacked a vital record, which meant only 69% of mothers with neural tube defects were geocoded.Mothers highly exposed to 1,1-dichloroethane were 2.14 times more likely to have the spina bifida birth defect than mothers who were not significantly exposed.

Overall Quality Determination High

* No biomarkers were identified for this evaluation.

Study Citation:	Garcia, E., Hurley, S., Nelson, D.O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health: A Global Access Science Source 14(1):14.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	breast cancer in females
Chemical:	1,1-Dichloroethane- Parent compound
Linked HERO ID(s):	No linked references.
HERO ID:	3014082

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	A total of 112,378 women were included in this study out of 133,479 eligible female participants from the California Teacher Study cohort. A full description of the cohort is provided in Bernstein et al. 2002 (HERO ID 808446). Reasons for exclusion were provided. The reported information indicates that participant selection in or out of the study and participation was not likely to be biased.
	Metric 2:	Attrition	High	112,378/133,479 participants were included in the study. Exclusions were for the purpose of the study and analysis. Exclusion criteria were documented. Included participants had completed questionnaires. The California Cancer Registry is estimated to be 99% complete.
	Metric 3:	Comparison Group	Medium	There is only indirect evidence that groups are similar. Participants were recruited from the same eligible population with the same method of ascertainment. Comparisons were provided for participants with and without breast cancer. Characteristics between these two groups were generally similar. 5 Quintiles of exposure were used, and Q2-5 were compared with Q1.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	High	The Assessment System for Population Exposure Nationwide and the Human Exposure Model are used as part of the National-Scale Air Toxics Assessment produced by the EPA and was used to estimate ambient HAP concentrations for geographic locations. Methods are described online through the US EPA Assessment Methods.
	Metric 5:	Exposure Levels	Medium	The distribution of the NATA annual ambient concentration for each compound was plotted in Figure 1 using a box plot, and 5 Quintiles were used in the analyses.
	Metric 6:	Temporality	Medium	The follow-up period was from 1995-2011, and the NATA estimates were made in 2002 because it was approximately half way between the start and end of the follow-up period. However, it is unclear whether exposures fall within relevant exposure windows for the outcome of interest.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Annual linkage between the CTS cohort and the California Cancer Registry (CCR) was used to identify cases of invasive breast cancer. The CCR is estimated to be 99% complete. The case of invasive breast cancer was defined by ICD codes.

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Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	breast cancer in females
Chemical:	1,1-Dichloroethane- Parent compound
Linked HERO ID(s):	No linked references.
HERO ID:	3014082

Domain	Metric		Rating	Comments
	Metric 8:	Reporting Bias	High	A description of measured outcome is reported for adjustments by age and race, and effect estimates are reported with a 95% confidence interval. The measured outcomes using multiple comparisons were generally described in the text, but non-significant results were excluded from Table 3. Several significant results for ethylidene dichloride were provided in Table 3.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	The models were stratified by age and race. Additionally, adjustments were made for multiple comparisons among subsets of the participants (significant results reported in Table 3). Socioeconomic status (SES) of each participant was not evaluated, however, cohort SES characteristics were thought to be similar by study authors.
	Metric 10:	Covariate Characterization	Medium	Information about baseline characteristics for each participant was collected through a questionnaire. It is unknown if the questionnaire was validated.
	Metric 11:	Co-exposure Counfounding	Medium	A total of 37 compounds were identified as mammary gland carcinogens, but 13 were not included in this analysis. Thirteen compounds were excluded from the analysis due to insufficient variability (nine because they had the same value for all census tracts in the state of California; and four because they had less than 25% non-zero values). Ethylidene dichloride (1,1-dichloroethane) was among the 24 compounds evaluated in this assessment, and evaluations for breast cancer were conducted for each of these 24 individual compounds.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen (prospective cohort) was appropriate for the research question (incidence of breast cancer). Cox proportional hazard models and SAS 9.3 were used in this assessment. Data analysis was described.
	Metric 13:	Statistical Power	Medium	Statistical power calculations were not provided. No significant effects were observed with ethylidene dichloride (1,1-dichloroethane), however, this study utilized a large cohort, approximately 112,000 individuals. Distributions of chemicals of interest suggest there were sufficient numbers of participants in exposure subgroups.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to understand precisely what has been done and to be conceptually reproducible with access to the analytic data.
	Metric 15:	Statistical Analysis	High	The statistical models that were used were identified and described. ”No apparent violation of the underlying assumption of proportional hazards was detected”.

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Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	breast cancer in females
Chemical:	1,1-Dichloroethane- Parent compound
Linked HERO ID(s):	No linked references.
HERO ID:	3014082

Domain	Metric	Rating	Comments
Additional Comments:	A group of 112,378 female participants from the California Teacher Study cohort were assessed for their estimated exposure to ambient air pollutants, including ethylidene dichloride (1,1-dichloroethane), and the incidence of invasive breast cancer. Air contaminant concentrations were estimated using the US EPA NATA and the ASPEN and HEM models. The approximate median concentration of 1,1-dichloroethane is between 1E-4 and 1E-2 (estimated from Figure 1). Exposures were categorized into 5 Quintiles, and compared against Quintile 1. An increase in the hazard risk for breast cancer was observed for Quintile 3 when compared with Quintile 1 (OR 1.09, 95% CI 1.00-1.18) and results were adjusted for age and race; however, this increase was not observed in Quintiles 4 or 5, and the p(trend) for Quintiles 2-5 was not significant (0.19). An increase in tumor hormone responsiveness to estrogen-receptor positive or progesterone receptor positive risk compared with all tumor types and the risk among past or never hormone therapy users were also associated with 1,1-dichloroethane exposure.		

Overall Quality Determination High

* No biomarkers were identified for this evaluation.

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	Metric 2:	Attrition	High	112,378/133,479 participants were included in the study. Exclusions were for the purpose of the study and analysis. Exclusion criteria were documented. Included participants had completed questionnaires. The California Cancer Registry is estimated to be 99% complete.
	Metric 3:	Comparison Group	Medium	There is only indirect evidence that groups are similar. Participants were recruited from the same eligible population with the same method of ascertainment. Comparisons were provided for participants with and without breast cancer. Characteristics between these two groups were generally similar. 5 Quintiles of exposure were used, and Q2-5 were compared with Q1.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	High	The Assessment System for Population Exposure Nationwide and the Human Exposure Model are used as part of the National-Scale Air Toxics Assessment produced by the EPA and was used to estimate ambient HAP concentrations for geographic locations. Methods are described online through the US EPA Assessment Methods.
	Metric 5:	Exposure Levels	Medium	The distribution of the NATA annual ambient concentration for each compound was plotted in Figure 1 using a box plot, and 5 Quintiles were used in the analyses.
	Metric 6:	Temporality	Medium	The follow-up period was from 1995-2011, and the NATA estimates were made in 2002 because it was approximately half way between the start and end of the follow-up period. However, it is unclear whether exposures fall within relevant exposure windows for the outcome of interest.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Annual linkage between the CTS cohort and the California Cancer Registry (CCR) was used to identify cases of invasive breast cancer. The CCR is estimated to be 99% complete. The case of invasive breast cancer was defined by ICD codes.
	Metric 8:	Reporting Bias	High	A description of measured outcome is reported for adjustments by age and race, and effect estimates are reported with a 95% confidence interval. The measured outcomes using multiple comparisons were generally described in the text, but non-significant results were excluded from Table 3. Several significant results for ethylidene dichloride were provided in Table 3.

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Chemical:	1,1-Dichloroethane- Parent compound
Linked HERO ID(s):	No linked references.
HERO ID:	3014082

Domain	Metric		Rating	Comments
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	The models were stratified by age and race. Additionally, adjustments were made for multiple comparisons among subsets of the participants (significant results reported in Table 3). Socioeconomic status (SES) of each participant was not evaluated, however, cohort SES characteristics were thought to be similar by study authors.
	Metric 10:	Covariate Characterization	Medium	Information about baseline characteristics for each participant was collected through a questionnaire. It is unknown if the questionnaire was validated.
	Metric 11:	Co-exposure Counfounding	Medium	A total of 37 compounds were identified as mammary gland carcinogens, but 13 were not included in this analysis. Thirteen compounds were excluded from the analysis due to insufficient variability (nine because they had the same value for all census tracts in the state of California; and four because they had less than 25% non-zero values). Ethylidene dichloride (1,1-dichloroethane) was among the 24 compounds evaluated in this assessment, and evaluations for breast cancer were conducted for each of these 24 individual compounds.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen (prospective cohort) was appropriate for the research question (incidence of breast cancer). Cox proportional hazard models and SAS 9.3 were used in this assessment. Data analysis was described.
	Metric 13:	Statistical Power	Medium	Statistical power calculations were not provided. No significant effects were observed with ethylidene dichloride (1,1-dichloroethane), however, this study utilized a large cohort, approximately 112,000 individuals. Distributions of chemicals of interest suggest there were sufficient numbers of participants in exposure subgroups.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to understand precisely what has been done and to be conceptually reproducible with access to the analytic data.
	Metric 15:	Statistical Analysis	High	The statistical models that were used were identified and described. ”No apparent violation of the underlying assumption of proportional hazards was detected”.

Additional Comments: A group of 112,378 female participants from the California Teacher Study cohort were assessed for their estimated exposure to ambient air pollutants, including ethylidene dichloride (1,1-dichloroethane), and the incidence of invasive breast cancer. Air contaminant concentrations were estimated using the US EPA NATA and the ASPEN and HEM models. The approximate median concentration of 1,1-dichloroethane is between 1E-4 and 1E-2 (estimated from Figure 1). Exposures were categorized into 5 Quintiles, and compared against Quintile 1. An increase in the hazard risk for breast cancer was observed for Quintile 3 when compared with Quintile 1 (OR 1.09, 95% CI 1.00-1.18) and results were adjusted for age and race; however, this increase was not observed in Quintiles 4 or 5, and the p(trend) for Quintiles 2-5 was not significant (0.19). An increase in tumor hormone responsiveness to estrogen-receptor positive or progesterone receptor positive risk compared with all tumor types and the risk among past or never hormone therapy users were also associated with 1,1-dichloroethane exposure.

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Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	breast cancer in females
Chemical:	1,1-Dichloroethane- Parent compound
Linked HERO ID(s):	No linked references.
HERO ID:	3014082

Domain	Metric	Rating	Comments
Overall Quality Determination		**High**	

* No biomarkers were identified for this evaluation.

Study Citation:	Niehoff, N.M., Gammon, M.D., Keil, A.P., Nichols, H.B., Engel, L.S., Sandler, D.P., White, A.J. (2019). Airborne mammary carcinogens and breast cancer risk in the Sister Study. Environment International 130:104897.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Breast cancer diagnosis (overall), tumor characteristics, and estrogen receptor positive (ER+) invasive breast cancer
Chemical:	1,1-Dichloroethane- Parent compound
Linked HERO ID(s):	No linked references.
HERO ID:	5440630

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	Data from the Sister Study were used. The Sister Study is "a prospective cohort of 50,884 women from across the US who were ages 35–74 at enrollment (Sandler et al., 2017). Participants were recruited from 2003 to 2009 using a national advertising campaign in English and Spanish. Women were eligible for the Sister Study if they had a sister who had been diagnosed with breast cancer, but no prior breast cancer themselves."Exclusions from the study occurred for the following reasons:-breast cancer diagnosed before enrollment was complete, or did not have follow-up information (n = 163)-Residential address couldn't be geocoded (n = 1003, < 2%) - This is a small perecentage, but all of those who were excluded for this reason were from Puerto Rico, West Virginia, Missouri, or Oklahoma.Key elements of the study design are reported. There is some potential for selection bias, but based on the small percentage of those eligible who were excluded, participation was not likely to be substantially biased.
	Metric 2:	Attrition	High	Response rates in the overall Sister study remained over 91% over follow-up. Reasons for non-response were not reported, and characteristics of those lost to follow up were not reported or compared with those included, but 9% loss to follow-up is minimal.
	Metric 3:	Comparison Group	High	Differences in baseline characteristics of groups were considered as potential confounding variables.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	The EPA NATA database of census-tract level modeled air toxics data was used. The study authors note the potential for exposure misclassification: "Concentrations at the census tract level do not fully account for variation in an individual's daily activities that could lead to higher or lower exposure, and all women within a census tract are assigned the same concentration."
	Metric 5:	Exposure Levels	Medium	There were five quintiles of exposure, so there was a sufficient range and distribution of exposure.
	Metric 6:	Temporality	Medium	This is a prospective cohort study.Exposure data from 2005 were chosen because they represented the middle of the enrollment period (2003-2009).The study reported that "94% of women enrolled in 2005 or later, and thus the exposure assessment primarily predated enrollment for the majority of Sister Study participants."The six percent of women who had the potential to have the outcome before exposure was measured in 2005 are a concern. But sensitivity analyses were used to assess whether the associations changed when restricted to those who enrolled in 2005 or later.The authors note that the study is making assumptions about the relevant exposure windows - therefore the exposure window is not certain.

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Domain	Metric		Rating	Comments
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Women who reported a breast cancer diagnosis on the annual health updates or follow-up questionnaires were asked to provide additional diagnosis information, and to grant permission for the study to obtain medical records and pathology reports. Medical records were obtained for 81% of breast cancer diagnoses. Agreement between self-reported breast cancers and medical records was high (positive predictive value > 99%) (Sandler et al., 2017), so self-report was used when medical records were not available. Tumor characteristics (stage; histology; and estrogen receptor (ER) status) were abstracted from medical records, or self-reported.
	Metric 8:	Reporting Bias	High	A description of measured outcomes is reported. Effect estimates are reported with confidence intervals.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Covariates considered included age, race, BMI, residence type, education, and smoking status. Potential confounders were identified using DAGs and literature review. Appropriate considerations were made for potential confounders.
	Metric 10:	Covariate Characterization	Medium	”Most covariates were assessed by self-report at the baseline interview.””At baseline, women completed a computer-assisted telephone interview and written questionnaires.”Previous publications might describe whether the questionnaires were validated, but validation was not specified in this publication.
	Metric 11:	Co-exposure Counfounding	Medium	Co-exposures to other air pollutants were assessed, but at the census tract level.Multipollutant classification trees were used, which might provide useful qualitative information.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design (large prospective cohort) and analysis method (Cox proportional hazard single and multi-pollutant models accounting for potential confounders) were appropriate to assess the association between exposure and disease.
	Metric 13:	Statistical Power	Medium	The study had an adequate sample size (1975 cancer cases) and follow-up time (mean=8.4 years).
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to be conceptually reproducible.

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Domain	Metric	Rating	Comments
	Metric 15: Statistical Analysis	High	Hazard ratios and 95% confidence intervals (CIs) are reported "comparing index categories of exposure to exposures below the first quintile using Cox proportional hazards regression, with age as the time scale." The method of calculating the hazard ratios is transparent. The authors reported that "the proportional hazards assumption was evaluated by conducting a Wald test for an interaction between the continuous form of the air toxic measure and time." Censoring times and times at-risk are described.

Additional Comments: This was a well-conducted study of a large prospective cohort, but the measurement of exposure at the census-tract rather than the individual level is a limitation.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Brender, J.D., Shinde, M.U., Zhan, F.B., Gong, X., Langlois, P.H. (2014). Maternal residential proximity to chlorinated solvent emissions and birth defects in offspring: A case-control study. Environmental Health: A Global Access Science Source 13(1):96.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	birth defects (neural tube defects, limbs deficiencies, oral cleft defects, heart defects, spina bifida, anencephaly)
Chemical:	1,1-Dichloroethane- Parent compound
Linked HERO ID(s):	No linked references.
HERO ID:	2799700

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Participants were drawn from the Texas Birth Defects Registry (TBDR) for years 1996-2008. Controls were frequency matched from the same registry. Study authors state that neural tube cases were more likely to not be successfully geocoded which may introduce selection bias, however, the authors note that both cases and controls with addresses that could not be geocoded were similar. In spite of that, the inclusion criteria, methods of participant selection, and frequency match were reported.
	Metric 2:	Attrition	Medium	13.3% case mother addresses and 12.8% control mother addresses were unable to be geocoded, however this most likely only lowered the precision of the study and most likely does not vary based on exposure level.
	Metric 3:	Comparison Group	Medium	Controls were matched to cases and pulled from the same eligible population by year of delivery and public health service region. Other demographic factors, e.g., race was not matched in population selection. However, statistical analyses were adjusted for year of delivery, maternal age, race/ethnicity, education, and public health region of residence.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Used Emission Weighted Proximity Model to estimate exposure at a given address based on proximity to emission sources and the specific amount or type of pollutant emitted. There may be some exposure misclassification due to mothers moving away from geocoded addresses. Previous studies indicate ~67% of mothers do not move between conception and delivery.
	Metric 5:	Exposure Levels	Medium	Reports exposure as "exposure risk value" and groups the risk values into quartiles, with exposure risk values < 0 being the referent group
	Metric 6:	Temporality	Medium	The study authors estimated exposure based on residence during pregnancy and evaluated birth outcomes. Temporality is established. Previous studies indicate ~67% mothers don't move between trimester and delivery. For mothers who moved during the pregnancy, the temporality is unknown.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Outcomes determined by Texas Birth Defect Registry, checking for birth defect diagnosis. Birth certificates came from Center for Health Statistics at Texas Department of State Health Services
	Metric 8:	Reporting Bias	High	Outcome data measured and reported clearly, stratified by specific type of birth defect
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Brender, J.D., Shinde, M.U., Zhan, F.B., Gong, X., Langlois, P.H. (2014). Maternal residential proximity to chlorinated solvent emissions and birth defects in offspring: A case-control study. Environmental Health: A Global Access Science Source 13(1):96.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	birth defects (neural tube defects, limbs deficiencies, oral cleft defects, heart defects, spina bifida, anencephaly)
Chemical:	1,1-Dichloroethane- Parent compound
Linked HERO ID(s):	No linked references.
HERO ID:	2799700

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	High	Cases were frequency matched by year of delivery and public health service region. Final models were adjusted for year of delivery, public health region, maternal age (<20, 20-24, 25-29, 30-34, 35-39, >39 years), education (<12 years, 12 years, >12 years), and race/ethnicity (Whit non-Hispanic, Black non-Hispanic, Hispanic, other non-Hispanic).
	Metric 10:	Covariate Characterization	High	Used birth and death certificates for demographic information
	Metric 11:	Co-exposure Counfounding	Medium	other co-exposures were not described
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	study used logistic regression to measure association between exposure and birth defects
	Metric 13:	Statistical Power	Medium	Overall adequate number of cases and controls - some effects have low cell counts, but at least one health effect has sufficient statistical power.
	Metric 14:	Reproducibility of Analyses	Medium	Methods sufficiently detailed for reproducibility
	Metric 15:	Statistical Analysis	High	No logistic regression model assumption violations were identified.

Additional Comments: This study examined the association between proximity to several point sources of chlorinated solvents and birth defects. Exposure was assessed using EPA's Toxic Release Inventory, and birth defects were assessed using Texas birth registries. The geocoded address of mothers on day of delivery and the amount of solvent was plugged into the Emission Weighted Probability model to assign each mother an exposure risk value. Limitations include limited evidence of temporality. Additionally, elective terminations lacked a vital record, which meant only 69% of mothers with neural tube defects were geocoded.Mothers highly exposed to 1,1-dichloroethane were 2.14 times more likely to have the spina bifida birth defect than mothers who were not significantly exposed.

Overall Quality Determination High

* No biomarkers were identified for this evaluation.

Study Citation:	Garcia, E., Hurley, S., Nelson, D.O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health: A Global Access Science Source 14(1):14.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	breast cancer in females
Chemical:	1,1-Dichloroethane- Parent compound
Linked HERO ID(s):	No linked references.
HERO ID:	3014082

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	A total of 112,378 women were included in this study out of 133,479 eligible female participants from the California Teacher Study cohort. A full description of the cohort is provided in Bernstein et al. 2002 (HERO ID 808446). Reasons for exclusion were provided. The reported information indicates that participant selection in or out of the study and participation was not likely to be biased.
	Metric 2:	Attrition	High	112,378/133,479 participants were included in the study. Exclusions were for the purpose of the study and analysis. Exclusion criteria were documented. Included participants had completed questionnaires. The California Cancer Registry is estimated to be 99% complete.
	Metric 3:	Comparison Group	Medium	There is only indirect evidence that groups are similar. Participants were recruited from the same eligible population with the same method of ascertainment. Comparisons were provided for participants with and without breast cancer. Characteristics between these two groups were generally similar. 5 Quintiles of exposure were used, and Q2-5 were compared with Q1.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	High	The Assessment System for Population Exposure Nationwide and the Human Exposure Model are used as part of the National-Scale Air Toxics Assessment produced by the EPA and was used to estimate ambient HAP concentrations for geographic locations. Methods are described online through the US EPA Assessment Methods.
	Metric 5:	Exposure Levels	Medium	The distribution of the NATA annual ambient concentration for each compound was plotted in Figure 1 using a box plot, and 5 Quintiles were used in the analyses.
	Metric 6:	Temporality	Medium	The follow-up period was from 1995-2011, and the NATA estimates were made in 2002 because it was approximately half way between the start and end of the follow-up period. However, it is unclear whether exposures fall within relevant exposure windows for the outcome of interest.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Annual linkage between the CTS cohort and the California Cancer Registry (CCR) was used to identify cases of invasive breast cancer. The CCR is estimated to be 99% complete. The case of invasive breast cancer was defined by ICD codes.

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Study Citation:	Garcia, E., Hurley, S., Nelson, D.O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health: A Global Access Science Source 14(1):14.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	breast cancer in females
Chemical:	1,1-Dichloroethane- Parent compound
Linked HERO ID(s):	No linked references.
HERO ID:	3014082

Domain	Metric		Rating	Comments
	Metric 8:	Reporting Bias	High	A description of measured outcome is reported for adjustments by age and race, and effect estimates are reported with a 95% confidence interval. The measured outcomes using multiple comparisons were generally described in the text, but non-significant results were excluded from Table 3. Several significant results for ethylidene dichloride were provided in Table 3.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	The models were stratified by age and race. Additionally, adjustments were made for multiple comparisons among subsets of the participants (significant results reported in Table 3). Socioeconomic status (SES) of each participant was not evaluated, however, cohort SES characteristics were thought to be similar by study authors.
	Metric 10:	Covariate Characterization	Medium	Information about baseline characteristics for each participant was collected through a questionnaire. It is unknown if the questionnaire was validated.
	Metric 11:	Co-exposure Counfounding	Medium	A total of 37 compounds were identified as mammary gland carcinogens, but 13 were not included in this analysis. Thirteen compounds were excluded from the analysis due to insufficient variability (nine because they had the same value for all census tracts in the state of California; and four because they had less than 25% non-zero values). Ethylidene dichloride (1,1-dichloroethane) was among the 24 compounds evaluated in this assessment, and evaluations for breast cancer were conducted for each of these 24 individual compounds.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen (prospective cohort) was appropriate for the research question (incidence of breast cancer). Cox proportional hazard models and SAS 9.3 were used in this assessment. Data analysis was described.
	Metric 13:	Statistical Power	Medium	Statistical power calculations were not provided. No significant effects were observed with ethylidene dichloride (1,1-dichloroethane), however, this study utilized a large cohort, approximately 112,000 individuals. Distributions of chemicals of interest suggest there were sufficient numbers of participants in exposure subgroups.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to understand precisely what has been done and to be conceptually reproducible with access to the analytic data.
	Metric 15:	Statistical Analysis	High	The statistical models that were used were identified and described. ”No apparent violation of the underlying assumption of proportional hazards was detected”.

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Study Citation:	Garcia, E., Hurley, S., Nelson, D.O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health: A Global Access Science Source 14(1):14.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	breast cancer in females
Chemical:	1,1-Dichloroethane- Parent compound
Linked HERO ID(s):	No linked references.
HERO ID:	3014082

Domain	Metric	Rating	Comments
Additional Comments:	A group of 112,378 female participants from the California Teacher Study cohort were assessed for their estimated exposure to ambient air pollutants, including ethylidene dichloride (1,1-dichloroethane), and the incidence of invasive breast cancer. Air contaminant concentrations were estimated using the US EPA NATA and the ASPEN and HEM models. The approximate median concentration of 1,1-dichloroethane is between 1E-4 and 1E-2 (estimated from Figure 1). Exposures were categorized into 5 Quintiles, and compared against Quintile 1. An increase in the hazard risk for breast cancer was observed for Quintile 3 when compared with Quintile 1 (OR 1.09, 95% CI 1.00-1.18) and results were adjusted for age and race; however, this increase was not observed in Quintiles 4 or 5, and the p(trend) for Quintiles 2-5 was not significant (0.19). An increase in tumor hormone responsiveness to estrogen-receptor positive or progesterone receptor positive risk compared with all tumor types and the risk among past or never hormone therapy users were also associated with 1,1-dichloroethane exposure.		

Overall Quality Determination High

* No biomarkers were identified for this evaluation.

Study Citation:	Garcia, E., Hurley, S., Nelson, D.O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health: A Global Access Science Source 14(1):14.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	breast cancer in females
Chemical:	1,1-Dichloroethane- Parent compound
Linked HERO ID(s):	No linked references.
HERO ID:	3014082

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	A total of 112,378 women were included in this study out of 133,479 eligible female participants from the California Teacher Study cohort. A full description of the cohort is provided in Bernstein et al. 2002 (HERO ID 808446). Reasons for exclusion were provided. The reported information indicates that participant selection in or out of the study and participation was not likely to be biased.
	Metric 2:	Attrition	High	112,378/133,479 participants were included in the study. Exclusions were for the purpose of the study and analysis. Exclusion criteria were documented. Included participants had completed questionnaires. The California Cancer Registry is estimated to be 99% complete.
	Metric 3:	Comparison Group	Medium	There is only indirect evidence that groups are similar. Participants were recruited from the same eligible population with the same method of ascertainment. Comparisons were provided for participants with and without breast cancer. Characteristics between these two groups were generally similar. 5 Quintiles of exposure were used, and Q2-5 were compared with Q1.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	High	The Assessment System for Population Exposure Nationwide and the Human Exposure Model are used as part of the National-Scale Air Toxics Assessment produced by the EPA and was used to estimate ambient HAP concentrations for geographic locations. Methods are described online through the US EPA Assessment Methods.
	Metric 5:	Exposure Levels	Medium	The distribution of the NATA annual ambient concentration for each compound was plotted in Figure 1 using a box plot, and 5 Quintiles were used in the analyses.
	Metric 6:	Temporality	Medium	The follow-up period was from 1995-2011, and the NATA estimates were made in 2002 because it was approximately half way between the start and end of the follow-up period. However, it is unclear whether exposures fall within relevant exposure windows for the outcome of interest.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Annual linkage between the CTS cohort and the California Cancer Registry (CCR) was used to identify cases of invasive breast cancer. The CCR is estimated to be 99% complete. The case of invasive breast cancer was defined by ICD codes.
	Metric 8:	Reporting Bias	High	A description of measured outcome is reported for adjustments by age and race, and effect estimates are reported with a 95% confidence interval. The measured outcomes using multiple comparisons were generally described in the text, but non-significant results were excluded from Table 3. Several significant results for ethylidene dichloride were provided in Table 3.

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Study Citation:	Garcia, E., Hurley, S., Nelson, D.O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health: A Global Access Science Source 14(1):14.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	breast cancer in females
Chemical:	1,1-Dichloroethane- Parent compound
Linked HERO ID(s):	No linked references.
HERO ID:	3014082

Domain	Metric		Rating	Comments
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	The models were stratified by age and race. Additionally, adjustments were made for multiple comparisons among subsets of the participants (significant results reported in Table 3). Socioeconomic status (SES) of each participant was not evaluated, however, cohort SES characteristics were thought to be similar by study authors.
	Metric 10:	Covariate Characterization	Medium	Information about baseline characteristics for each participant was collected through a questionnaire. It is unknown if the questionnaire was validated.
	Metric 11:	Co-exposure Counfounding	Medium	A total of 37 compounds were identified as mammary gland carcinogens, but 13 were not included in this analysis. Thirteen compounds were excluded from the analysis due to insufficient variability (nine because they had the same value for all census tracts in the state of California; and four because they had less than 25% non-zero values). Ethylidene dichloride (1,1-dichloroethane) was among the 24 compounds evaluated in this assessment, and evaluations for breast cancer were conducted for each of these 24 individual compounds.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen (prospective cohort) was appropriate for the research question (incidence of breast cancer). Cox proportional hazard models and SAS 9.3 were used in this assessment. Data analysis was described.
	Metric 13:	Statistical Power	Medium	Statistical power calculations were not provided. No significant effects were observed with ethylidene dichloride (1,1-dichloroethane), however, this study utilized a large cohort, approximately 112,000 individuals. Distributions of chemicals of interest suggest there were sufficient numbers of participants in exposure subgroups.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to understand precisely what has been done and to be conceptually reproducible with access to the analytic data.
	Metric 15:	Statistical Analysis	High	The statistical models that were used were identified and described. ”No apparent violation of the underlying assumption of proportional hazards was detected”.

Additional Comments: A group of 112,378 female participants from the California Teacher Study cohort were assessed for their estimated exposure to ambient air pollutants, including ethylidene dichloride (1,1-dichloroethane), and the incidence of invasive breast cancer. Air contaminant concentrations were estimated using the US EPA NATA and the ASPEN and HEM models. The approximate median concentration of 1,1-dichloroethane is between 1E-4 and 1E-2 (estimated from Figure 1). Exposures were categorized into 5 Quintiles, and compared against Quintile 1. An increase in the hazard risk for breast cancer was observed for Quintile 3 when compared with Quintile 1 (OR 1.09, 95% CI 1.00-1.18) and results were adjusted for age and race; however, this increase was not observed in Quintiles 4 or 5, and the p(trend) for Quintiles 2-5 was not significant (0.19). An increase in tumor hormone responsiveness to estrogen-receptor positive or progesterone receptor positive risk compared with all tumor types and the risk among past or never hormone therapy users were also associated with 1,1-dichloroethane exposure.

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Study Citation:	Garcia, E., Hurley, S., Nelson, D.O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health: A Global Access Science Source 14(1):14.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	breast cancer in females
Chemical:	1,1-Dichloroethane- Parent compound
Linked HERO ID(s):	No linked references.
HERO ID:	3014082

Domain	Metric	Rating	Comments
Overall Quality Determination		**High**	

* No biomarkers were identified for this evaluation.

Study Citation:	Niehoff, N.M., Gammon, M.D., Keil, A.P., Nichols, H.B., Engel, L.S., Sandler, D.P., White, A.J. (2019). Airborne mammary carcinogens and breast cancer risk in the Sister Study. Environment International 130:104897.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Breast cancer diagnosis (overall), tumor characteristics, and estrogen receptor positive (ER+) invasive breast cancer
Chemical:	1,1-Dichloroethane- Parent compound
Linked HERO ID(s):	No linked references.
HERO ID:	5440630

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	Data from the Sister Study were used. The Sister Study is "a prospective cohort of 50,884 women from across the US who were ages 35–74 at enrollment (Sandler et al., 2017). Participants were recruited from 2003 to 2009 using a national advertising campaign in English and Spanish. Women were eligible for the Sister Study if they had a sister who had been diagnosed with breast cancer, but no prior breast cancer themselves."Exclusions from the study occurred for the following reasons:-breast cancer diagnosed before enrollment was complete, or did not have follow-up information (n = 163)-Residential address couldn't be geocoded (n = 1003, < 2%) - This is a small perecentage, but all of those who were excluded for this reason were from Puerto Rico, West Virginia, Missouri, or Oklahoma.Key elements of the study design are reported. There is some potential for selection bias, but based on the small percentage of those eligible who were excluded, participation was not likely to be substantially biased.
	Metric 2:	Attrition	High	Response rates in the overall Sister study remained over 91% over follow-up. Reasons for non-response were not reported, and characteristics of those lost to follow up were not reported or compared with those included, but 9% loss to follow-up is minimal.
	Metric 3:	Comparison Group	High	Differences in baseline characteristics of groups were considered as potential confounding variables.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	The EPA NATA database of census-tract level modeled air toxics data was used. The study authors note the potential for exposure misclassification: "Concentrations at the census tract level do not fully account for variation in an individual's daily activities that could lead to higher or lower exposure, and all women within a census tract are assigned the same concentration."
	Metric 5:	Exposure Levels	Medium	There were five quintiles of exposure, so there was a sufficient range and distribution of exposure.
	Metric 6:	Temporality	Medium	This is a prospective cohort study.Exposure data from 2005 were chosen because they represented the middle of the enrollment period (2003-2009).The study reported that "94% of women enrolled in 2005 or later, and thus the exposure assessment primarily predated enrollment for the majority of Sister Study participants."The six percent of women who had the potential to have the outcome before exposure was measured in 2005 are a concern. But sensitivity analyses were used to assess whether the associations changed when restricted to those who enrolled in 2005 or later.The authors note that the study is making assumptions about the relevant exposure windows - therefore the exposure window is not certain.

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Study Citation:	Niehoff, N.M., Gammon, M.D., Keil, A.P., Nichols, H.B., Engel, L.S., Sandler, D.P., White, A.J. (2019). Airborne mammary carcinogens and breast cancer risk in the Sister Study. Environment International 130:104897.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Breast cancer diagnosis (overall), tumor characteristics, and estrogen receptor positive (ER+) invasive breast cancer
Chemical:	1,1-Dichloroethane- Parent compound
Linked HERO ID(s):	No linked references.
HERO ID:	5440630

Domain	Metric		Rating	Comments
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Women who reported a breast cancer diagnosis on the annual health updates or follow-up questionnaires were asked to provide additional diagnosis information, and to grant permission for the study to obtain medical records and pathology reports. Medical records were obtained for 81% of breast cancer diagnoses. Agreement between self-reported breast cancers and medical records was high (positive predictive value > 99%) (Sandler et al., 2017), so self-report was used when medical records were not available. Tumor characteristics (stage; histology; and estrogen receptor (ER) status) were abstracted from medical records, or self-reported.
	Metric 8:	Reporting Bias	High	A description of measured outcomes is reported. Effect estimates are reported with confidence intervals.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Covariates considered included age, race, BMI, residence type, education, and smoking status. Potential confounders were identified using DAGs and literature review. Appropriate considerations were made for potential confounders.
	Metric 10:	Covariate Characterization	Medium	”Most covariates were assessed by self-report at the baseline interview.””At baseline, women completed a computer-assisted telephone interview and written questionnaires.”Previous publications might describe whether the questionnaires were validated, but validation was not specified in this publication.
	Metric 11:	Co-exposure Counfounding	Medium	Co-exposures to other air pollutants were assessed, but at the census tract level.Multipollutant classification trees were used, which might provide useful qualitative information.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design (large prospective cohort) and analysis method (Cox proportional hazard single and multi-pollutant models accounting for potential confounders) were appropriate to assess the association between exposure and disease.
	Metric 13:	Statistical Power	Medium	The study had an adequate sample size (1975 cancer cases) and follow-up time (mean=8.4 years).
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to be conceptually reproducible.

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Study Citation:	Niehoff, N.M., Gammon, M.D., Keil, A.P., Nichols, H.B., Engel, L.S., Sandler, D.P., White, A.J. (2019). Airborne mammary carcinogens and breast cancer risk in the Sister Study. Environment International 130:104897.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Breast cancer diagnosis (overall), tumor characteristics, and estrogen receptor positive (ER+) invasive breast cancer
Chemical:	1,1-Dichloroethane- Parent compound
Linked HERO ID(s):	No linked references.
HERO ID:	5440630

Domain	Metric	Rating	Comments
	Metric 15: Statistical Analysis	High	Hazard ratios and 95% confidence intervals (CIs) are reported "comparing index categories of exposure to exposures below the first quintile using Cox proportional hazards regression, with age as the time scale." The method of calculating the hazard ratios is transparent. The authors reported that "the proportional hazards assumption was evaluated by conducting a Wald test for an interaction between the continuous form of the air toxic measure and time." Censoring times and times at-risk are described.

Additional Comments: This was a well-conducted study of a large prospective cohort, but the measurement of exposure at the census-tract rather than the individual level is a limitation.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	visual-motor reaction (simple, complex), changes in the function of the motor apparatus in the upper extremities, neuritis and radiculitis, diseases of the muscles, tendons, and ganglia.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Occupational cohort study in Russian aircraft manufacturing plant. The study focuses on the soft tank shop. The participation of all workers in the aircraft plant shops (including the soft tank shop and controls from the mechanical shop) is implied, however numbers of eligible participants and the total number of included participants across analyses are not reported. 17 gluers represented the exposed and were compared to 10 mechanical shop machinists.
	Metric 2:	Attrition	Medium	Rates of attrition cannot be determined based on the limited information provided. The study solely reports those included in analyses of visual-motor function and changes in the functions of motor apparatus in upper extremities.
	Metric 3:	Comparison Group	Low	Mechanical shop machinists (n=10) served as the controls. Though the controls were also workers in the same plant as those exposed, the dichloroethane levels in air in the mechanical shop are not provided; thus, the similarity between cases and controls is not clear. Additionally, authors note that controls did not perform work that strained the hands, which is distinct from the gluers (exposed).
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Authors report quantitative measures of dichloroethane in air, but do not provide any information on the method used to quantify exposure levels.
	Metric 5:	Exposure Levels	Low	Neurological health outcomes are reported for two groups: gluers (exposed) and mechanical shop mechanists (controls). A range of exposure levels are provided based on activities conducted by gluers. "The highest concentrations of dichloroethane (0.08 - 0.158 mg/L) occurred when the rubber sheets were coated with glue. These concentrations were maintained for only 5-6 min; they subsequently decreased to 0.062 - 0.082 mg/L as the glue dried, and at the end of the drying period 15 min later, they had decreased to 0.03 - 0.04 mg/L. The concentration of dichloroethane remains at the level of 0.05 mg/L and lower during most of the shift."
	Metric 6:	Temporality	Medium	The study reports visual-motor reaction at the end of the working day after exposure, establishing temporality, though it is unclear if exposure fell during relevant exposure windows for neuritis and radiculitis.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Uninformative	No information on outcome measurement and diagnostic criteria is provided for visual-motor reaction, neuritis, radiculitis, or changes in motor function of upper extremities.

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Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	visual-motor reaction (simple, complex), changes in the function of the motor apparatus in the upper extremities, neuritis and radiculitis, diseases of the muscles, tendons, and ganglia.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
	Metric 8:	Reporting Bias	Medium	Results are reported for visual-motor reactions (occurrence of errors for exposed and unexposed), but results for other outcomes are reported qualitatively (changes in motor function of upper extremities), and only case numbers are reported for neuritis and radiculitis. These results would not be useful for detailed extraction.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	There is no discussion of confounders or analysis of differing characteristics.
	Metric 10:	Covariate Characterization	N/A	No confounders were measured.
	Metric 11:	Co-exposure Counfounding	Low	There is no indication that co-exposures of concern were assessed, though the study was conducted in an occupational setting with higher potential for chemical co-exposures.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Exposure levels and common chronic disease over time are appropriately measured with a cohort design.
	Metric 13:	Statistical Power	Low	It is unclear how many study participants are included in the measures of cases throughout the plant. Additionally, n=17 workers are included in the exposed group and n=10 in the unexposed control group.
	Metric 14:	Reproducibility of Analyses	Medium	The analyses are reproducible, as the study only reports number of cases, and number of disabled days in the shop and plant. Further analyses of these case numbers were not conducted.
	Metric 15:	Statistical Analysis	N/A	No statistical modeling was conducted.

Additional Comments: Occupational study of aircraft plant workers exposed to dichloroethane via air. Study reports number of cases of a variety of neurological conditions and provides one crude comparison of prevalence of visual-motor reaction impairment with a control group. Otherwise, statistical analyses and comparisons are not provided for outcomes and only case numbers are reported, limiting the informativeness of the study. Study refers only to dichloroethane, thus, 1,1 and 1,2 dichloroethane cannot be separated in this review. Both chemicals have been included in evaluations.

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Musculoskeletal
Reported Health Effect(s):	changes in the function of the motor apparatus in the upper extremities, diseases of the muscles, tendons, and ganglia.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Occupational cohort study in Russian aircraft manufacturing plant. The study focuses on the soft tank shop. The participation of all workers in the aircraft plant shops (including the soft tank shop and controls from the mechanical shop) is implied, however numbers of eligible participants and the total number of included participants across analyses are not reported. 17 gluers represented the exposed and were compared to 10 mechanical shop machinists.
	Metric 2:	Attrition	Medium	Rates of attrition cannot be determined based on the limited information provided. The study solely reports those included in assessment of changes in the functions of motor apparatus in upper extremities.
	Metric 3:	Comparison Group	Low	Mechanical shop machinists (n=10) served as the controls. Though the controls were also workers in the same plant as those exposed, the dichloroethane levels in air in the mechanical shop are not provided; thus, the similarity between cases and controls is not clear. Additionally, authors note that controls did not perform work that strained the hands, which is distinct from the gluers (exposed).
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Authors report quantitative measures of dichloroethane in air, but do not provide any information on the method used to quantify exposure levels.
	Metric 5:	Exposure Levels	Low	Musculoskeletal health outcomes are reported for two groups: gluers (exposed) and mechanical shop mechanists (controls). A range of exposure levels are provided based on activities conducted by gluers. "The highest concentrations of dichloroethane (0.08 - 0.158 mg/L) occurred when the rubber sheets were coated with glue. These concentrations were maintained for only 5-6 min; they subsequently decreased to 0.062 - 0.082 mg/L as the glue dried, and at the end of the drying period 15 min later, they had decreased to 0.03 - 0.04 mg/L. The concentration of dichloroethane remains at the level of 0.05 mg/L and lower during most of the shift."
	Metric 6:	Temporality	Medium	The study reports musculoskeletal outcomes at the end of the working day after exposure, establishing temporality, though specific details about measurement of exposure and outcome timings are not provided.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Uninformative	No information on outcome measurement and diagnostic criteria is provided for changes in motor function of upper extremities or diseases of the muscles, tendons, and ganglia.
	Metric 8:	Reporting Bias	Medium	Results are reported qualitatively (changes in motor function of upper extremities), and only case numbers are reported for diseases of the muscles, tendons, and ganglia. These results would not be useful for detailed extraction.

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Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Musculoskeletal
Reported Health Effect(s):	changes in the function of the motor apparatus in the upper extremities, diseases of the muscles, tendons, and ganglia.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	There is no discussion of confounders or analysis of differing characteristics.
	Metric 10:	Covariate Characterization	N/A	No confounders were measured.
	Metric 11:	Co-exposure Counfounding	Low	There is no indication that co-exposures of concern were assessed, though the study was conducted in an occupational setting with higher potential for chemical co-exposures.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Exposure levels and common chronic disease over time are appropriately measured with a cohort design.
	Metric 13:	Statistical Power	Low	It is unclear how many study participants are included in the measures of cases throughout the plant. Additionally, n=17 workers are included in the exposed group and n=10 in the unexposed control group.
	Metric 14:	Reproducibility of Analyses	Medium	The analyses are reproducible, as the study only reports number of cases, and number of disabled days in the shop and plant. Further analyses of these case numbers were not conducted.
	Metric 15:	Statistical Analysis	N/A	No statistical modeling was conducted.

Additional Comments: Occupational study of aircraft plant workers exposed to dichloroethane via air. Study reports number of cases of muscle, tendon, and ganglia disease and provides qualitative information on decreased motor function of upper extremities. Statistical analyses and comparisons are not provided for outcomes and only case numbers are reported, limiting the informativeness of the study. Study refers only to dichloroethane, thus, 1,1 and 1,2 dichloroethane cannot be separated in this review. Both chemicals have been included in evaluations.

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	liver and gall bladder diseases.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Occupational cohort study in Russian aircraft manufacturing plant. The study focuses on the soft tank shop. The participation of all workers in the aircraft plant shops (including the soft tank shop and controls from the mechanical shop) is implied, however numbers of eligible participants and the total number of included participants across analyses are not reported. 17 gluers represented the exposed and were compared to 10 mechanical shop machinists.
	Metric 2:	Attrition	Medium	Rates of attrition cannot be determined based on the limited information provided. The study solely reports those included in assessment of changes in the functions of motor apparatus in upper extremities, but not of liver disease.
	Metric 3:	Comparison Group	Uninformative	Solely case numbers are reported for liver and gall bladder disease. Case numbers among those unexposed are not clear.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Authors report quantitative measures of dichloroethane in air, but do not provide any information on the method used to quantify exposure levels.
	Metric 5:	Exposure Levels	Uninformative	Liver and gall bladder disease are reported as case numbers only, with no indication of likely exposure.
	Metric 6:	Temporality	Low	Temporality is unclear, as limited information is provided about the measurement of exposure and outcome.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Uninformative	No information on outcome measurement and diagnostic criteria is provided for liver and gall bladder diseases.
	Metric 8:	Reporting Bias	Medium	Only case numbers are reported for liver and gall bladder disease with no information about their relationship to exposure. These results would not be useful for detailed extraction.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	There is no discussion of confounders or analysis of differing characteristics.
	Metric 10:	Covariate Characterization	N/A	No confounders were measured.
	Metric 11:	Co-exposure Counfounding	Low	There is no indication that co-exposures of concern were assessed, though the study was conducted in an occupational setting with higher potential for chemical co-exposures.
Domain 5: Analysis				

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Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	liver and gall bladder diseases.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Exposure levels and common chronic disease over time are appropriately measured with a cohort design.
	Metric 13:	Statistical Power	Low	It is unclear how many study participants are included in the measures of cases throughout the plant.
	Metric 14:	Reproducibility of Analyses	Medium	The analyses are reproducible, as the study only reports number of cases, and number of disabled days per 100 workers. Further analyses of these case numbers were not conducted.
	Metric 15:	Statistical Analysis	N/A	No statistical modeling was conducted.

Additional Comments: Occupational study of aircraft plant workers exposed to dichloroethane via air. Study reports number of cases of liver and gall bladder diseases. Statistical analyses and comparisons are not provided for outcomes and only case numbers are reported, limiting the informativeness of the study. Study refers only to dichloroethane, thus, 1,1 and 1,2 dichloroethane cannot be separated in this review. Both chemicals have been included in evaluations.

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Gastrointestinal
Reported Health Effect(s):	acute gastrointestinal diseases, acute gastritis, and chronic gastritis.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Occupational cohort study in Russian aircraft manufacturing plant. The study focuses on the soft tank shop. The participation of all workers in the aircraft plant shops (including the soft tank shop and controls from the mechanical shop) is implied, however numbers of eligible participants and the total number of included participants across analyses are not reported. 17 gluers represented the exposed and were compared to 10 mechanical shop machinists.
	Metric 2:	Attrition	Medium	Rates of attrition cannot be determined based on the limited information provided. The study solely reports those included in assessment of changes in the functions of motor apparatus in upper extremities, but not of gastrointestinal outcomes.
	Metric 3:	Comparison Group	Low	Case numbers per 100 workers are reported for those exposed (working in the shop) and those unexposed (working in the plant) for acute gastrointestinal diseases. Solely case numbers per 100 workers are reported for other gastrointestinal outcomes (acute and chronic gastritis, acute gastrointestinal diseases).
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Authors report quantitative measures of dichloroethane in air, but do not provide any information on the method used to quantify exposure levels.
	Metric 5:	Exposure Levels	Uninformative	No description is provided on the levels or range of exposure for those in the shop compared to the plant. The exposure difference between groups is unclear.
	Metric 6:	Temporality	Low	Temporality is unclear, as limited information is provided about the measurement of exposure and outcome.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Uninformative	No information on outcome measurement and diagnostic criteria is provided for gastrointestinal outcomes.
	Metric 8:	Reporting Bias	Medium	Case numbers are reported for gastrointestinal outcomes for the shop and the plant, but there is no clear information about their relationship to exposure levels. These results would not be useful for detailed extraction.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	There is no discussion of confounders or analysis of differing characteristics.
	Metric 10:	Covariate Characterization	N/A	No confounders were measured.
	Metric 11:	Co-exposure Counfounding	Low	There is no indication that co-exposures of concern were assessed, though the study was conducted in an occupational setting with higher potential for chemical co-exposures.
Domain 5: Analysis				

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Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Gastrointestinal
Reported Health Effect(s):	acute gastrointestinal diseases, acute gastritis, and chronic gastritis.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Exposure levels and common chronic disease over time are appropriately measured with a cohort design.
	Metric 13:	Statistical Power	Low	It is unclear how many study participants are included in the measures of cases throughout the plant.
	Metric 14:	Reproducibility of Analyses	Medium	The analyses are reproducible, as the study only reports number of cases and number of disabled days per 100 workers. Further analyses of these case numbers were not conducted.
	Metric 15:	Statistical Analysis	N/A	No statistical modeling was conducted.

Additional Comments: Occupational study of aircraft plant workers exposed to dichloroethane via air. Study reports number of cases of gastrointestinal diseases per 100 workers in the plant and in the shop (likely exposed). No information is provided on the dichloroethane levels in the plant. Statistical analyses and comparisons are not provided for outcomes and only case numbers are reported, limiting the informativeness of the study. Study refers only to dichloroethane, thus, 1,1 and 1,2 dichloroethane cannot be separated in this review. Both chemicals have been included in evaluations.

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Morbidity
Reported Health Effect(s):	Overall morbidity, and other diseases.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Occupational cohort study in Russian aircraft manufacturing plant. The study focuses on the soft tank shop. The participation of all workers in the aircraft plant shops (including the soft tank shop and controls from the mechanical shop) is implied, however numbers of eligible participants and the total number of included participants across analyses are not reported. 17 gluers represented the exposed and were compared to 10 mechanical shop machinists.
	Metric 2:	Attrition	Medium	Rates of attrition cannot be determined based on the limited information provided. The study solely reports those included in assessment of changes in the functions of motor apparatus in upper extremities, but not of other diseases/overall morbidity.
	Metric 3:	Comparison Group	Low	Case numbers per 100 workers are reported for those exposed (working in the shop) and those unexposed (working in the plant) for overall morbidity and other diseases.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Authors report quantitative measures of dichloroethane in air, but do not provide any information on the method used to quantify exposure levels.
	Metric 5:	Exposure Levels	Uninformative	No description is provided on the levels or range of exposure for those in the shop compared to the plant. The exposure difference between groups is unclear.
	Metric 6:	Temporality	Low	Temporality is unclear, as limited information is provided about the measurement of exposure and outcome.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Uninformative	No information on outcome measurement and diagnostic criteria is provided for overall morbidity or other diseases.
	Metric 8:	Reporting Bias	Medium	Case numbers are reported for overall morbidity and other diseases for the shop and the plant, but there is no clear information about their relationship to exposure levels. These results would not be useful for detailed extraction.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	There is no discussion of confounders or analysis of differing characteristics.
	Metric 10:	Covariate Characterization	N/A	No confounders measured.
	Metric 11:	Co-exposure Counfounding	Low	There is no indication that co-exposures of concern were assessed, though the study was conducted in an occupational setting with higher potential for chemical co-exposures.
Domain 5: Analysis				

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Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Morbidity
Reported Health Effect(s):	Overall morbidity, and other diseases.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Exposure levels and common chronic disease over time are appropriately measured with a cohort design.
	Metric 13:	Statistical Power	Low	It is unclear how many study participants are included in the measures of cases throughout the plant.
	Metric 14:	Reproducibility of Analyses	Medium	The analyses are reproducible, as the study only reports number of cases and number of disabled days per 100 workers. Further analyses of these case numbers were not conducted.
	Metric 15:	Statistical Analysis	N/A	No statistical modeling was conducted.

Additional Comments: Occupational study of aircraft plant workers exposed to dichloroethane via air. Study reports number of cases of overall morbidity and "other diseases" per 100 workers in the plant (no or lower exposure) and in the shop (likely exposed). No information is provided on the dichloroethane levels in the plant. Statistical analyses and comparisons are not provided for outcomes and only case numbers are reported, limiting the informativeness of the study. Study refers only to dichloroethane, thus, 1,1 and 1,2 dichloroethane cannot be separated in this review. Both chemicals have been included in evaluations.

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	visual-motor reaction (simple, complex), changes in the function of the motor apparatus in the upper extremities, neuritis and radiculitis, diseases of the muscles, tendons, and ganglia.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Occupational cohort study in Russian aircraft manufacturing plant. The study focuses on the soft tank shop. The participation of all workers in the aircraft plant shops (including the soft tank shop and controls from the mechanical shop) is implied, however numbers of eligible participants and the total number of included participants across analyses are not reported. 17 gluers represented the exposed and were compared to 10 mechanical shop machinists.
	Metric 2:	Attrition	Medium	Rates of attrition cannot be determined based on the limited information provided. The study solely reports those included in analyses of visual-motor function and changes in the functions of motor apparatus in upper extremities.
	Metric 3:	Comparison Group	Low	Mechanical shop machinists (n=10) served as the controls. Though the controls were also workers in the same plant as those exposed, the dichloroethane levels in air in the mechanical shop are not provided; thus, the similarity between cases and controls is not clear. Additionally, authors note that controls did not perform work that strained the hands, which is distinct from the gluers (exposed).
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Authors report quantitative measures of dichloroethane in air, but do not provide any information on the method used to quantify exposure levels.
	Metric 5:	Exposure Levels	Low	Neurological health outcomes are reported for two groups: gluers (exposed) and mechanical shop mechanists (controls). A range of exposure levels are provided based on activities conducted by gluers. "The highest concentrations of dichloroethane (0.08 - 0.158 mg/L) occurred when the rubber sheets were coated with glue. These concentrations were maintained for only 5-6 min; they subsequently decreased to 0.062 - 0.082 mg/L as the glue dried, and at the end of the drying period 15 min later, they had decreased to 0.03 - 0.04 mg/L. The concentration of dichloroethane remains at the level of 0.05 mg/L and lower during most of the shift."
	Metric 6:	Temporality	Medium	The study reports visual-motor reaction at the end of the working day after exposure, establishing temporality, though it is unclear if exposure fell during relevant exposure windows for neuritis and radiculitis.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Uninformative	No information on outcome measurement and diagnostic criteria is provided for visual-motor reaction, neuritis, radiculitis, or changes in motor function of upper extremities.
	Metric 8:	Reporting Bias	Medium	Results are reported for visual-motor reactions (occurrence of errors for exposed and unexposed), but results for other outcomes are reported qualitatively (changes in motor function of upper extremities), and only case numbers are reported for neuritis and radiculitis. These results would not be useful for detailed extraction.

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Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	visual-motor reaction (simple, complex), changes in the function of the motor apparatus in the upper extremities, neuritis and radiculitis, diseases of the muscles, tendons, and ganglia.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	There is no discussion of confounders or analysis of differing characteristics.
	Metric 10:	Covariate Characterization	N/A	No confounders were measured.
	Metric 11:	Co-exposure Counfounding	Low	There is no indication that co-exposures of concern were assessed, though the study was conducted in an occupational setting with higher potential for chemical co-exposures.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Exposure levels and common chronic disease over time are appropriately measured with a cohort design.
	Metric 13:	Statistical Power	Low	It is unclear how many study participants are included in the measures of cases throughout the plant. Additionally, n=17 workers are included in the exposed group and n=10 in the unexposed control group.
	Metric 14:	Reproducibility of Analyses	Medium	The analyses are reproducible, as the study only reports number of cases, and number of disabled days in the shop and plant. Further analyses of these case numbers were not conducted.
	Metric 15:	Statistical Analysis	N/A	No statistical modeling was conducted.

Additional Comments: Occupational study of aircraft plant workers exposed to dichloroethane via air. Study reports number of cases of a variety of neurological conditions and provides one crude comparison of prevalence of visual-motor reaction impairment with a control group. Otherwise, statistical analyses and comparisons are not provided for outcomes and only case numbers are reported, limiting the informativeness of the study. Study refers only to dichloroethane, thus, 1,1 and 1,2 dichloroethane cannot be separated in this review. Both chemicals have been included in evaluations.

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Musculoskeletal
Reported Health Effect(s):	changes in the function of the motor apparatus in the upper extremities, diseases of the muscles, tendons, and ganglia.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Occupational cohort study in Russian aircraft manufacturing plant. The study focuses on the soft tank shop. The participation of all workers in the aircraft plant shops (including the soft tank shop and controls from the mechanical shop) is implied, however numbers of eligible participants and the total number of included participants across analyses are not reported. 17 gluers represented the exposed and were compared to 10 mechanical shop machinists.
	Metric 2:	Attrition	Medium	Rates of attrition cannot be determined based on the limited information provided. The study solely reports those included in assessment of changes in the functions of motor apparatus in upper extremities.
	Metric 3:	Comparison Group	Low	Mechanical shop machinists (n=10) served as the controls. Though the controls were also workers in the same plant as those exposed, the dichloroethane levels in air in the mechanical shop are not provided; thus, the similarity between cases and controls is not clear. Additionally, authors note that controls did not perform work that strained the hands, which is distinct from the gluers (exposed).
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Authors report quantitative measures of dichloroethane in air, but do not provide any information on the method used to quantify exposure levels.
	Metric 5:	Exposure Levels	Low	Musculoskeletal health outcomes are reported for two groups: gluers (exposed) and mechanical shop mechanists (controls). A range of exposure levels are provided based on activities conducted by gluers. "The highest concentrations of dichloroethane (0.08 - 0.158 mg/L) occurred when the rubber sheets were coated with glue. These concentrations were maintained for only 5-6 min; they subsequently decreased to 0.062 - 0.082 mg/L as the glue dried, and at the end of the drying period 15 min later, they had decreased to 0.03 - 0.04 mg/L. The concentration of dichloroethane remains at the level of 0.05 mg/L and lower during most of the shift."
	Metric 6:	Temporality	Medium	The study reports musculoskeletal outcomes at the end of the working day after exposure, establishing temporality, though specific details about measurement of exposure and outcome timings are not provided.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Uninformative	No information on outcome measurement and diagnostic criteria is provided for changes in motor function of upper extremities or diseases of the muscles, tendons, and ganglia.
	Metric 8:	Reporting Bias	Medium	Results are reported qualitatively (changes in motor function of upper extremities), and only case numbers are reported for diseases of the muscles, tendons, and ganglia. These results would not be useful for detailed extraction.

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Study Citation: Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s): Musculoskeletal
Reported Health Effect(s): changes in the function of the motor apparatus in the upper extremities, diseases of the muscles, tendons, and ganglia.
Chemical: 1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s): No linked references.
HERO ID: 18135

Domain	Metric		Rating	Comments
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	There is no discussion of confounders or analysis of differing characteristics.
	Metric 10:	Covariate Characterization	N/A	No confounders were measured.
	Metric 11:	Co-exposure Counfounding	Low	There is no indication that co-exposures of concern were assessed, though the study was conducted in an occupational setting with higher potential for chemical co-exposures.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Exposure levels and common chronic disease over time are appropriately measured with a cohort design.
	Metric 13:	Statistical Power	Low	It is unclear how many study participants are included in the measures of cases throughout the plant. Additionally, n=17 workers are included in the exposed group and n=10 in the unexposed control group.
	Metric 14:	Reproducibility of Analyses	Medium	The analyses are reproducible, as the study only reports number of cases, and number of disabled days in the shop and plant. Further analyses of these case numbers were not conducted.
	Metric 15:	Statistical Analysis	N/A	No statistical modeling was conducted.

Additional Comments: Occupational study of aircraft plant workers exposed to dichloroethane via air. Study reports number of cases of muscle, tendon, and ganglia disease and provides qualitative information on decreased motor function of upper extremities. Statistical analyses and comparisons are not provided for outcomes and only case numbers are reported, limiting the informativeness of the study. Study refers only to dichloroethane, thus, 1,1 and 1,2 dichloroethane cannot be separated in this review. Both chemicals have been included in evaluations.

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	liver and gall bladder diseases.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Occupational cohort study in Russian aircraft manufacturing plant. The study focuses on the soft tank shop. The participation of all workers in the aircraft plant shops (including the soft tank shop and controls from the mechanical shop) is implied, however numbers of eligible participants and the total number of included participants across analyses are not reported. 17 gluers represented the exposed and were compared to 10 mechanical shop machinists.
	Metric 2:	Attrition	Medium	Rates of attrition cannot be determined based on the limited information provided. The study solely reports those included in assessment of changes in the functions of motor apparatus in upper extremities, but not of liver disease.
	Metric 3:	Comparison Group	Uninformative	Solely case numbers are reported for liver and gall bladder disease. Case numbers among those unexposed are not clear.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Authors report quantitative measures of dichloroethane in air, but do not provide any information on the method used to quantify exposure levels.
	Metric 5:	Exposure Levels	Uninformative	Liver and gall bladder disease are reported as case numbers only, with no indication of likely exposure.
	Metric 6:	Temporality	Low	Temporality is unclear, as limited information is provided about the measurement of exposure and outcome.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Uninformative	No information on outcome measurement and diagnostic criteria is provided for liver and gall bladder diseases.
	Metric 8:	Reporting Bias	Medium	Only case numbers are reported for liver and gall bladder disease with no information about their relationship to exposure. These results would not be useful for detailed extraction.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	There is no discussion of confounders or analysis of differing characteristics.
	Metric 10:	Covariate Characterization	N/A	No confounders were measured.
	Metric 11:	Co-exposure Counfounding	Low	There is no indication that co-exposures of concern were assessed, though the study was conducted in an occupational setting with higher potential for chemical co-exposures.
Domain 5: Analysis				

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Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	liver and gall bladder diseases.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Exposure levels and common chronic disease over time are appropriately measured with a cohort design.
	Metric 13:	Statistical Power	Low	It is unclear how many study participants are included in the measures of cases throughout the plant.
	Metric 14:	Reproducibility of Analyses	Medium	The analyses are reproducible, as the study only reports number of cases, and number of disabled days per 100 workers. Further analyses of these case numbers were not conducted.
	Metric 15:	Statistical Analysis	N/A	No statistical modeling was conducted.

Additional Comments: Occupational study of aircraft plant workers exposed to dichloroethane via air. Study reports number of cases of liver and gall bladder diseases. Statistical analyses and comparisons are not provided for outcomes and only case numbers are reported, limiting the informativeness of the study. Study refers only to dichloroethane, thus, 1,1 and 1,2 dichloroethane cannot be separated in this review. Both chemicals have been included in evaluations.

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Gastrointestinal
Reported Health Effect(s):	acute gastrointestinal diseases, acute gastritis, and chronic gastritis.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Occupational cohort study in Russian aircraft manufacturing plant. The study focuses on the soft tank shop. The participation of all workers in the aircraft plant shops (including the soft tank shop and controls from the mechanical shop) is implied, however numbers of eligible participants and the total number of included participants across analyses are not reported. 17 gluers represented the exposed and were compared to 10 mechanical shop machinists.
	Metric 2:	Attrition	Medium	Rates of attrition cannot be determined based on the limited information provided. The study solely reports those included in assessment of changes in the functions of motor apparatus in upper extremities, but not of gastrointestinal outcomes.
	Metric 3:	Comparison Group	Low	Case numbers per 100 workers are reported for those exposed (working in the shop) and those unexposed (working in the plant) for acute gastrointestinal diseases. Solely case numbers per 100 workers are reported for other gastrointestinal outcomes (acute and chronic gastritis, acute gastrointestinal diseases).
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Authors report quantitative measures of dichloroethane in air, but do not provide any information on the method used to quantify exposure levels.
	Metric 5:	Exposure Levels	Uninformative	No description is provided on the levels or range of exposure for those in the shop compared to the plant. The exposure difference between groups is unclear.
	Metric 6:	Temporality	Low	Temporality is unclear, as limited information is provided about the measurement of exposure and outcome.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Uninformative	No information on outcome measurement and diagnostic criteria is provided for gastrointestinal outcomes.
	Metric 8:	Reporting Bias	Medium	Case numbers are reported for gastrointestinal outcomes for the shop and the plant, but there is no clear information about their relationship to exposure levels. These results would not be useful for detailed extraction.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	There is no discussion of confounders or analysis of differing characteristics.
	Metric 10:	Covariate Characterization	N/A	No confounders measured.
	Metric 11:	Co-exposure Counfounding	Low	There is no indication that co-exposures of concern were assessed, though the study was conducted in an occupational setting with higher potential for chemical co-exposures.
Domain 5: Analysis				

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Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Gastrointestinal
Reported Health Effect(s):	acute gastrointestinal diseases, acute gastritis, and chronic gastritis.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Exposure levels and common chronic disease over time are appropriately measured with a cohort design.
	Metric 13:	Statistical Power	Low	It is unclear how many study participants are included in the measures of cases throughout the plant.
	Metric 14:	Reproducibility of Analyses	Medium	The analyses are reproducible, as the study only reports number of cases and number of disabled days per 100 workers. Further analyses of these case numbers were not conducted.
	Metric 15:	Statistical Analysis	N/A	No statistical modeling was conducted.

Additional Comments: Occupational study of aircraft plant workers exposed to dichloroethane via air. Study reports number of cases of gastrointestinal diseases per 100 workers in the plant and in the shop (likely exposed). No information is provided on the dichloroethane levels in the plant. Statistical analyses and comparisons are not provided for outcomes and only case numbers are reported, limiting the informativeness of the study. Study refers only to dichloroethane, thus, 1,1 and 1,2 dichloroethane cannot be separated in this review. Both chemicals have been included in evaluations.

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Morbidity
Reported Health Effect(s):	Overall morbidity, and other diseases.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Occupational cohort study in Russian aircraft manufacturing plant. The study focuses on the soft tank shop. The participation of all workers in the aircraft plant shops (including the soft tank shop and controls from the mechanical shop) is implied, however numbers of eligible participants and the total number of included participants across analyses are not reported. 17 gluers represented the exposed and were compared to 10 mechanical shop machinists.
	Metric 2:	Attrition	Medium	Rates of attrition cannot be determined based on the limited information provided. The study solely reports those included in assessment of changes in the functions of motor apparatus in upper extremities, but not of other diseases/overall morbidity.
	Metric 3:	Comparison Group	Low	Case numbers per 100 workers are reported for those exposed (working in the shop) and those unexposed (working in the plant) for overall morbidity and other diseases.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Authors report quantitative measures of dichloroethane in air, but do not provide any information on the method used to quantify exposure levels.
	Metric 5:	Exposure Levels	Uninformative	No description is provided on the levels or range of exposure for those in the shop compared to the plant. The exposure difference between groups is unclear.
	Metric 6:	Temporality	Low	Temporality is unclear, as limited information is provided about the measurement of exposure and outcome.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Uninformative	No information on outcome measurement and diagnostic criteria is provided for overall morbidity or other diseases.
	Metric 8:	Reporting Bias	Medium	Case numbers are reported for overall morbidity and other diseases for the shop and the plant, but there is no clear information about their relationship to exposure levels. These results would not be useful for detailed extraction.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	There is no discussion of confounders or analysis of differing characteristics.
	Metric 10:	Covariate Characterization	N/A	No confounders were measured.
	Metric 11:	Co-exposure Counfounding	Low	There is no indication that co-exposures of concern were assessed, though the study was conducted in an occupational setting with higher potential for chemical co-exposures.
Domain 5: Analysis				

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Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Morbidity
Reported Health Effect(s):	Overall morbidity, and other diseases.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Exposure levels and common chronic disease over time are appropriately measured with a cohort design.
	Metric 13:	Statistical Power	Low	It is unclear how many study participants are included in the measures of cases throughout the plant.
	Metric 14:	Reproducibility of Analyses	Medium	The analyses are reproducible, as the study only reports number of cases and number of disabled days per 100 workers. Further analyses of these case numbers were not conducted.
	Metric 15:	Statistical Analysis	N/A	No statistical modeling was conducted.

Additional Comments: Occupational study of aircraft plant workers exposed to dichloroethane via air. Study reports number of cases of overall morbidity and "other diseases" per 100 workers in the plant (no or lower exposure) and in the shop (likely exposed). No information is provided on the dichloroethane levels in the plant. Statistical analyses and comparisons are not provided for outcomes and only case numbers are reported, limiting the informativeness of the study. Study refers only to dichloroethane, thus, 1,1 and 1,2 dichloroethane cannot be separated in this review. Both chemicals have been included in evaluations.

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	visual-motor reaction (simple, complex), changes in the function of the motor apparatus in the upper extremities, neuritis and radiculitis, diseases of the muscles, tendons, and ganglia.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Occupational cohort study in Russian aircraft manufacturing plant. The study focuses on the soft tank shop. The participation of all workers in the aircraft plant shops (including the soft tank shop and controls from the mechanical shop) is implied, however numbers of eligible participants and the total number of included participants across analyses are not reported. 17 gluers represented the exposed and were compared to 10 mechanical shop machinists.
	Metric 2:	Attrition	Medium	Rates of attrition cannot be determined based on the limited information provided. The study solely reports those included in analyses of visual-motor function and changes in the functions of motor apparatus in upper extremities.
	Metric 3:	Comparison Group	Low	Mechanical shop machinists (n=10) served as the controls. Though the controls were also workers in the same plant as those exposed, the dichloroethane levels in air in the mechanical shop are not provided; thus, the similarity between cases and controls is not clear. Additionally, authors note that controls did not perform work that strained the hands, which is distinct from the gluers (exposed).
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Authors report quantitative measures of dichloroethane in air, but do not provide any information on the method used to quantify exposure levels.
	Metric 5:	Exposure Levels	Low	Neurological health outcomes are reported for two groups: gluers (exposed) and mechanical shop mechanists (controls). A range of exposure levels are provided based on activities conducted by gluers. "The highest concentrations of dichloroethane (0.08 - 0.158 mg/L) occurred when the rubber sheets were coated with glue. These concentrations were maintained for only 5-6 min; they subsequently decreased to 0.062 - 0.082 mg/L as the glue dried, and at the end of the drying period 15 min later, they had decreased to 0.03 - 0.04 mg/L. The concentration of dichloroethane remains at the level of 0.05 mg/L and lower during most of the shift."
	Metric 6:	Temporality	Medium	The study reports visual-motor reaction at the end of the working day after exposure, establishing temporality, though it is unclear if exposure fell during relevant exposure windows for neuritis and radiculitis.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Uninformative	No information on outcome measurement and diagnostic criteria is provided for visual-motor reaction, neuritis, radiculitis, or changes in motor function of upper extremities.

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Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	visual-motor reaction (simple, complex), changes in the function of the motor apparatus in the upper extremities, neuritis and radiculitis, diseases of the muscles, tendons, and ganglia.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
	Metric 8:	Reporting Bias	Medium	Results are reported for visual-motor reactions (occurrence of errors for exposed and unexposed), but results for other outcomes are reported qualitatively (changes in motor function of upper extremities), and only case numbers are reported for neuritis and radiculitis. These results would not be useful for detailed extraction.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	There is no discussion of confounders or analysis of differing characteristics.
	Metric 10:	Covariate Characterization	N/A	No confounders were measured.
	Metric 11:	Co-exposure Counfounding	Low	There is no indication that co-exposures of concern were assessed, though the study was conducted in an occupational setting with higher potential for chemical co-exposures.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Exposure levels and common chronic disease over time are appropriately measured with a cohort design.
	Metric 13:	Statistical Power	Low	It is unclear how many study participants are included in the measures of cases throughout the plant. Additionally, n=17 workers are included in the exposed group and n=10 in the unexposed control group.
	Metric 14:	Reproducibility of Analyses	Medium	The analyses are reproducible, as the study only reports number of cases, and number of disabled days in the shop and plant. Further analyses of these case numbers were not conducted.
	Metric 15:	Statistical Analysis	N/A	No statistical modeling was conducted.

Additional Comments: Occupational study of aircraft plant workers exposed to dichloroethane via air. Study reports number of cases of a variety of neurological conditions and provides one crude comparison of prevalence of visual-motor reaction impairment with a control group. Otherwise, statistical analyses and comparisons are not provided for outcomes and only case numbers are reported, limiting the informativeness of the study. Study refers only to dichloroethane, thus, 1,1 and 1,2 dichloroethane cannot be separated in this review. Both chemicals have been included in evaluations.

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Musculoskeletal
Reported Health Effect(s):	changes in the function of the motor apparatus in the upper extremities, diseases of the muscles, tendons, and ganglia.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Occupational cohort study in Russian aircraft manufacturing plant. The study focuses on the soft tank shop. The participation of all workers in the aircraft plant shops (including the soft tank shop and controls from the mechanical shop) is implied, however numbers of eligible participants and the total number of included participants across analyses are not reported. 17 gluers represented the exposed and were compared to 10 mechanical shop machinists.
	Metric 2:	Attrition	Medium	Rates of attrition cannot be determined based on the limited information provided. The study solely reports those included in assessment of changes in the functions of motor apparatus in upper extremities.
	Metric 3:	Comparison Group	Low	Mechanical shop machinists (n=10) served as the controls. Though the controls were also workers in the same plant as those exposed, the dichloroethane levels in air in the mechanical shop are not provided; thus, the similarity between cases and controls is not clear. Additionally, authors note that controls did not perform work that strained the hands, which is distinct from the gluers (exposed).
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Authors report quantitative measures of dichloroethane in air, but do not provide any information on the method used to quantify exposure levels.
	Metric 5:	Exposure Levels	Low	Musculoskeletal health outcomes are reported for two groups: gluers (exposed) and mechanical shop mechanists (controls). A range of exposure levels are provided based on activities conducted by gluers. "The highest concentrations of dichloroethane (0.08 - 0.158 mg/L) occurred when the rubber sheets were coated with glue. These concentrations were maintained for only 5-6 min; they subsequently decreased to 0.062 - 0.082 mg/L as the glue dried, and at the end of the drying period 15 min later, they had decreased to 0.03 - 0.04 mg/L. The concentration of dichloroethane remains at the level of 0.05 mg/L and lower during most of the shift."
	Metric 6:	Temporality	Medium	The study reports musculoskeletal outcomes at the end of the working day after exposure, establishing temporality, though specific details about measurement of exposure and outcome timings are not provided.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Uninformative	No information on outcome measurement and diagnostic criteria is provided for changes in motor function of upper extremities or diseases of the muscles, tendons, and ganglia.
	Metric 8:	Reporting Bias	Medium	Results are reported qualitatively (changes in motor function of upper extremities), and only case numbers are reported for diseases of the muscles, tendons, and ganglia. These results would not be useful for detailed extraction.

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Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Musculoskeletal
Reported Health Effect(s):	changes in the function of the motor apparatus in the upper extremities, diseases of the muscles, tendons, and ganglia.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	There is no discussion of confounders or analysis of differing characteristics.
	Metric 10:	Covariate Characterization	N/A	No confounders were measured.
	Metric 11:	Co-exposure Counfounding	Low	There is no indication that co-exposures of concern were assessed, though the study was conducted in an occupational setting with higher potential for chemical co-exposures.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Exposure levels and common chronic disease over time are appropriately measured with a cohort design.
	Metric 13:	Statistical Power	Low	It is unclear how many study participants are included in the measures of cases throughout the plant. Additionally, n=17 workers are included in the exposed group and n=10 in the unexposed control group.
	Metric 14:	Reproducibility of Analyses	Medium	The analyses are reproducible, as the study only reports number of cases, and number of disabled days in the shop and plant. Further analyses of these case numbers were not conducted.
	Metric 15:	Statistical Analysis	N/A	No statistical modeling was conducted.

Additional Comments: Occupational study of aircraft plant workers exposed to dichloroethane via air. Study reports number of cases of muscle, tendon, and ganglia disease and provides qualitative information on decreased motor function of upper extremities. Statistical analyses and comparisons are not provided for outcomes and only case numbers are reported, limiting the informativeness of the study. Study refers only to dichloroethane, thus, 1,1 and 1,2 dichloroethane cannot be separated in this review. Both chemicals have been included in evaluations.

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	liver and gall bladder diseases.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Occupational cohort study in Russian aircraft manufacturing plant. The study focuses on the soft tank shop. The participation of all workers in the aircraft plant shops (including the soft tank shop and controls from the mechanical shop) is implied, however numbers of eligible participants and the total number of included participants across analyses are not reported. 17 gluers represented the exposed and were compared to 10 mechanical shop machinists.
	Metric 2:	Attrition	Medium	Rates of attrition cannot be determined based on the limited information provided. The study solely reports those included in assessment of changes in the functions of motor apparatus in upper extremities, but not of liver disease.
	Metric 3:	Comparison Group	Uninformative	Solely case numbers are reported for liver and gall bladder disease. Case numbers among those unexposed are not clear.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Authors report quantitative measures of dichloroethane in air, but do not provide any information on the method used to quantify exposure levels.
	Metric 5:	Exposure Levels	Uninformative	Liver and gall bladder disease are reported as case numbers only, with no indication of likely exposure.
	Metric 6:	Temporality	Low	Temporality is unclear, as limited information is provided about the measurement of exposure and outcome.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Uninformative	No information on outcome measurement and diagnostic criteria is provided for liver and gall bladder diseases.
	Metric 8:	Reporting Bias	Medium	Only case numbers are reported for liver and gall bladder disease with no information about their relationship to exposure. These results would not be useful for detailed extraction.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	There is no discussion of confounders or analysis of differing characteristics.
	Metric 10:	Covariate Characterization	N/A	No confounders were measured.
	Metric 11:	Co-exposure Counfounding	Low	There is no indication that co-exposures of concern were assessed, though the study was conducted in an occupational setting with higher potential for chemical co-exposures.
Domain 5: Analysis				

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Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	liver and gall bladder diseases.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Exposure levels and common chronic disease over time are appropriately measured with a cohort design.
	Metric 13:	Statistical Power	Low	It is unclear how many study participants are included in the measures of cases throughout the plant.
	Metric 14:	Reproducibility of Analyses	Medium	The analyses are reproducible, as the study only reports number of cases, and number of disabled days per 100 workers. Further analyses of these case numbers were not conducted.
	Metric 15:	Statistical Analysis	N/A	No statistical modeling was conducted.

Additional Comments: Occupational study of aircraft plant workers exposed to dichloroethane via air. Study reports number of cases of liver and gall bladder diseases. Statistical analyses and comparisons are not provided for outcomes and only case numbers are reported, limiting the informativeness of the study. Study refers only to dichloroethane, thus, 1,1 and 1,2 dichloroethane cannot be separated in this review. Both chemicals have been included in evaluations.

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Gastrointestinal
Reported Health Effect(s):	acute gastrointestinal diseases, acute gastritis, and chronic gastritis.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Occupational cohort study in Russian aircraft manufacturing plant. The study focuses on the soft tank shop. The participation of all workers in the aircraft plant shops (including the soft tank shop and controls from the mechanical shop) is implied, however numbers of eligible participants and the total number of included participants across analyses are not reported. 17 gluers represented the exposed and were compared to 10 mechanical shop machinists.
	Metric 2:	Attrition	Medium	Rates of attrition cannot be determined based on the limited information provided. The study solely reports those included in assessment of changes in the functions of motor apparatus in upper extremities, but not of gastrointestinal outcomes.
	Metric 3:	Comparison Group	Low	Case numbers per 100 workers are reported for those exposed (working in the shop) and those unexposed (working in the plant) for acute gastrointestinal diseases. Solely case numbers per 100 workers are reported for other gastrointestinal outcomes (acute and chronic gastritis, acute gastrointestinal diseases).
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Authors report quantitative measures of dichloroethane in air, but do not provide any information on the method used to quantify exposure levels.
	Metric 5:	Exposure Levels	Uninformative	No description is provided on the levels or range of exposure for those in the shop compared to the plant. The exposure difference between groups is unclear.
	Metric 6:	Temporality	Low	Temporality is unclear, as limited information is provided about the measurement of exposure and outcome.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Uninformative	No information on outcome measurement and diagnostic criteria is provided for gastrointestinal outcomes.
	Metric 8:	Reporting Bias	Medium	Case numbers are reported for gastrointestinal outcomes for the shop and the plant, but there is no clear information about their relationship to exposure levels. These results would not be useful for detailed extraction.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	There is no discussion of confounders or analysis of differing characteristics.
	Metric 10:	Covariate Characterization	N/A	No confounders were measured.
	Metric 11:	Co-exposure Counfounding	Low	There is no indication that co-exposures of concern were assessed, though the study was conducted in an occupational setting with higher potential for chemical co-exposures.
Domain 5: Analysis				

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Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Gastrointestinal
Reported Health Effect(s):	acute gastrointestinal diseases, acute gastritis, and chronic gastritis.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Exposure levels and common chronic disease over time are appropriately measured with a cohort design.
	Metric 13:	Statistical Power	Low	It is unclear how many study participants are included in the measures of cases throughout the plant.
	Metric 14:	Reproducibility of Analyses	Medium	The analyses are reproducible, as the study only reports number of cases and number of disabled days per 100 workers. Further analyses of these case numbers were not conducted.
	Metric 15:	Statistical Analysis	N/A	No statistical modeling was conducted.

Additional Comments: Occupational study of aircraft plant workers exposed to dichloroethane via air. Study reports number of cases of gastrointestinal diseases per 100 workers in the plant and in the shop (likely exposed). No information is provided on the dichloroethane levels in the plant. Statistical analyses and comparisons are not provided for outcomes and only case numbers are reported, limiting the informativeness of the study. Study refers only to dichloroethane, thus, 1,1 and 1,2 dichloroethane cannot be separated in this review. Both chemicals have been included in evaluations.

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Morbidity
Reported Health Effect(s):	Overall morbidity, and other diseases.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Occupational cohort study in Russian aircraft manufacturing plant. The study focuses on the soft tank shop. The participation of all workers in the aircraft plant shops (including the soft tank shop and controls from the mechanical shop) is implied, however numbers of eligible participants and the total number of included participants across analyses are not reported. 17 gluers represented the exposed and were compared to 10 mechanical shop machinists.
	Metric 2:	Attrition	Medium	Rates of attrition cannot be determined based on the limited information provided. The study solely reports those included in assessment of changes in the functions of motor apparatus in upper extremities, but not of other diseases/overall morbidity.
	Metric 3:	Comparison Group	Low	Case numbers per 100 workers are reported for those exposed (working in the shop) and those unexposed (working in the plant) for overall morbidity and other diseases.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Authors report quantitative measures of dichloroethane in air, but do not provide any information on the method used to quantify exposure levels.
	Metric 5:	Exposure Levels	Uninformative	No description is provided on the levels or range of exposure for those in the shop compared to the plant. The exposure difference between groups is unclear.
	Metric 6:	Temporality	Low	Temporality is unclear, as limited information is provided about the measurement of exposure and outcome.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Uninformative	No information on outcome measurement and diagnostic criteria is provided for overall morbidity or other diseases.
	Metric 8:	Reporting Bias	Medium	Case numbers are reported for overall morbidity and other diseases for the shop and the plant, but there is no clear information about their relationship to exposure levels. These results would not be useful for detailed extraction.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	There is no discussion of confounders or analysis of differing characteristics.
	Metric 10:	Covariate Characterization	N/A	No confounders measured.
	Metric 11:	Co-exposure Counfounding	Low	There is no indication that co-exposures of concern were assessed, though the study was conducted in an occupational setting with higher potential for chemical co-exposures.
Domain 5: Analysis				

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Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Morbidity
Reported Health Effect(s):	Overall morbidity, and other diseases.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Exposure levels and common chronic disease over time are appropriately measured with a cohort design.
	Metric 13:	Statistical Power	Low	It is unclear how many study participants are included in the measures of cases throughout the plant.
	Metric 14:	Reproducibility of Analyses	Medium	The analyses are reproducible, as the study only reports number of cases and number of disabled days per 100 workers. Further analyses of these case numbers were not conducted.
	Metric 15:	Statistical Analysis	N/A	No statistical modeling was conducted.

Additional Comments: Occupational study of aircraft plant workers exposed to dichloroethane via air. Study reports number of cases of overall morbidity and "other diseases" per 100 workers in the plant (no or lower exposure) and in the shop (likely exposed). No information is provided on the dichloroethane levels in the plant. Statistical analyses and comparisons are not provided for outcomes and only case numbers are reported, limiting the informativeness of the study. Study refers only to dichloroethane, thus, 1,1 and 1,2 dichloroethane cannot be separated in this review. Both chemicals have been included in evaluations.

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	visual-motor reaction (simple, complex), changes in the function of the motor apparatus in the upper extremities, neuritis and radiculitis, diseases of the muscles, tendons, and ganglia.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Occupational cohort study in Russian aircraft manufacturing plant. The study focuses on the soft tank shop. The participation of all workers in the aircraft plant shops (including the soft tank shop and controls from the mechanical shop) is implied, however numbers of eligible participants and the total number of included participants across analyses are not reported. 17 gluers represented the exposed and were compared to 10 mechanical shop machinists.
	Metric 2:	Attrition	Medium	Rates of attrition cannot be determined based on the limited information provided. The study solely reports those included in analyses of visual-motor function and changes in the functions of motor apparatus in upper extremities.
	Metric 3:	Comparison Group	Low	Mechanical shop machinists (n=10) served as the controls. Though the controls were also workers in the same plant as those exposed, the dichloroethane levels in air in the mechanical shop are not provided; thus, the similarity between cases and controls is not clear. Additionally, authors note that controls did not perform work that strained the hands, which is distinct from the gluers (exposed).
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Authors report quantitative measures of dichloroethane in air, but do not provide any information on the method used to quantify exposure levels.
	Metric 5:	Exposure Levels	Low	Neurological health outcomes are reported for two groups: gluers (exposed) and mechanical shop mechanists (controls). A range of exposure levels are provided based on activities conducted by gluers. "The highest concentrations of dichloroethane (0.08 - 0.158 mg/L) occurred when the rubber sheets were coated with glue. These concentrations were maintained for only 5-6 min; they subsequently decreased to 0.062 - 0.082 mg/L as the glue dried, and at the end of the drying period 15 min later, they had decreased to 0.03 - 0.04 mg/L. The concentration of dichloroethane remains at the level of 0.05 mg/L and lower during most of the shift."
	Metric 6:	Temporality	Medium	The study reports visual-motor reaction at the end of the working day after exposure, establishing temporality, though it is unclear if exposure fell during relevant exposure windows for neuritis and radiculitis.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Uninformative	No information on outcome measurement and diagnostic criteria is provided for visual-motor reaction, neuritis, radiculitis, or changes in motor function of upper extremities.
	Metric 8:	Reporting Bias	Medium	Results are reported for visual-motor reactions (occurrence of errors for exposed and unexposed), but results for other outcomes are reported qualitatively (changes in motor function of upper extremities), and only case numbers are reported for neuritis and radiculitis. These results would not be useful for detailed extraction.

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Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	visual-motor reaction (simple, complex), changes in the function of the motor apparatus in the upper extremities, neuritis and radiculitis, diseases of the muscles, tendons, and ganglia.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	There is no discussion of confounders or analysis of differing characteristics.
	Metric 10:	Covariate Characterization	N/A	No confounders were measured.
	Metric 11:	Co-exposure Counfounding	Low	There is no indication that co-exposures of concern were assessed, though the study was conducted in an occupational setting with higher potential for chemical co-exposures.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Exposure levels and common chronic disease over time are appropriately measured with a cohort design.
	Metric 13:	Statistical Power	Low	It is unclear how many study participants are included in the measures of cases throughout the plant. Additionally, n=17 workers are included in the exposed group and n=10 in the unexposed control group.
	Metric 14:	Reproducibility of Analyses	Medium	The analyses are reproducible, as the study only reports number of cases, and number of disabled days in the shop and plant. Further analyses of these case numbers were not conducted.
	Metric 15:	Statistical Analysis	N/A	No statistical modeling was conducted.

Additional Comments: Occupational study of aircraft plant workers exposed to dichloroethane via air. Study reports number of cases of a variety of neurological conditions and provides one crude comparison of prevalence of visual-motor reaction impairment with a control group. Otherwise, statistical analyses and comparisons are not provided for outcomes and only case numbers are reported, limiting the informativeness of the study. Study refers only to dichloroethane, thus, 1,1 and 1,2 dichloroethane cannot be separated in this review. Both chemicals have been included in evaluations.

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Musculoskeletal
Reported Health Effect(s):	changes in the function of the motor apparatus in the upper extremities, diseases of the muscles, tendons, and ganglia.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Occupational cohort study in Russian aircraft manufacturing plant. The study focuses on the soft tank shop. The participation of all workers in the aircraft plant shops (including the soft tank shop and controls from the mechanical shop) is implied, however numbers of eligible participants and the total number of included participants across analyses are not reported. 17 gluers represented the exposed and were compared to 10 mechanical shop machinists.
	Metric 2:	Attrition	Medium	Rates of attrition cannot be determined based on the limited information provided. The study solely reports those included in assessment of changes in the functions of motor apparatus in upper extremities.
	Metric 3:	Comparison Group	Low	Mechanical shop machinists (n=10) served as the controls. Though the controls were also workers in the same plant as those exposed, the dichloroethane levels in air in the mechanical shop are not provided; thus, the similarity between cases and controls is not clear. Additionally, authors note that controls did not perform work that strained the hands, which is distinct from the gluers (exposed).
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Authors report quantitative measures of dichloroethane in air, but do not provide any information on the method used to quantify exposure levels.
	Metric 5:	Exposure Levels	Low	Musculoskeletal health outcomes are reported for two groups: gluers (exposed) and mechanical shop mechanists (controls). A range of exposure levels are provided based on activities conducted by gluers. "The highest concentrations of dichloroethane (0.08 - 0.158 mg/L) occurred when the rubber sheets were coated with glue. These concentrations were maintained for only 5-6 min; they subsequently decreased to 0.062 - 0.082 mg/L as the glue dried, and at the end of the drying period 15 min later, they had decreased to 0.03 - 0.04 mg/L. The concentration of dichloroethane remains at the level of 0.05 mg/L and lower during most of the shift."
	Metric 6:	Temporality	Medium	The study reports musculoskeletal outcomes at the end of the working day after exposure, establishing temporality, though specific details about measurement of exposure and outcome timings are not provided.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Uninformative	No information on outcome measurement and diagnostic criteria is provided for changes in motor function of upper extremities or diseases of the muscles, tendons, and ganglia.
	Metric 8:	Reporting Bias	Medium	Results are reported qualitatively (changes in motor function of upper extremities), and only case numbers are reported for diseases of the muscles, tendons, and ganglia. These results would not be useful for detailed extraction.

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Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Musculoskeletal
Reported Health Effect(s):	changes in the function of the motor apparatus in the upper extremities, diseases of the muscles, tendons, and ganglia.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	There is no discussion of confounders or analysis of differing characteristics.
	Metric 10:	Covariate Characterization	N/A	No confounders were measured.
	Metric 11:	Co-exposure Counfounding	Low	There is no indication that co-exposures of concern were assessed, though the study was conducted in an occupational setting with higher potential for chemical co-exposures.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Exposure levels and common chronic disease over time are appropriately measured with a cohort design.
	Metric 13:	Statistical Power	Low	It is unclear how many study participants are included in the measures of cases throughout the plant. Additionally, n=17 workers are included in the exposed group and n=10 in the unexposed control group.
	Metric 14:	Reproducibility of Analyses	Medium	The analyses are reproducible, as the study only reports number of cases, and number of disabled days in the shop and plant. Further analyses of these case numbers were not conducted.
	Metric 15:	Statistical Analysis	N/A	No statistical modeling was conducted.

Additional Comments: Occupational study of aircraft plant workers exposed to dichloroethane via air. Study reports number of cases of muscle, tendon, and ganglia disease and provides qualitative information on decreased motor function of upper extremities. Statistical analyses and comparisons are not provided for outcomes and only case numbers are reported, limiting the informativeness of the study. Study refers only to dichloroethane, thus, 1,1 and 1,2 dichloroethane cannot be separated in this review. Both chemicals have been included in evaluations.

Overall Quality Determination — Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	liver and gall bladder diseases.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Occupational cohort study in Russian aircraft manufacturing plant. The study focuses on the soft tank shop. The participation of all workers in the aircraft plant shops (including the soft tank shop and controls from the mechanical shop) is implied, however numbers of eligible participants and the total number of included participants across analyses are not reported. 17 gluers represented the exposed and were compared to 10 mechanical shop machinists.
	Metric 2:	Attrition	Medium	Rates of attrition cannot be determined based on the limited information provided. The study solely reports those included in assessment of changes in the functions of motor apparatus in upper extremities, but not of liver disease.
	Metric 3:	Comparison Group	Uninformative	Solely case numbers are reported for liver and gall bladder disease. Case numbers among those unexposed are not clear.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Authors report quantitative measures of dichloroethane in air, but do not provide any information on the method used to quantify exposure levels.
	Metric 5:	Exposure Levels	Uninformative	Liver and gall bladder disease are reported as case numbers only, with no indication of likely exposure.
	Metric 6:	Temporality	Low	Temporality is unclear, as limited information is provided about the measurement of exposure and outcome.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Uninformative	No information on outcome measurement and diagnostic criteria is provided for liver and gall bladder diseases.
	Metric 8:	Reporting Bias	Medium	Only case numbers are reported for liver and gall bladder disease with no information about their relationship to exposure. These results would not be useful for detailed extraction.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	There is no discussion of confounders or analysis of differing characteristics.
	Metric 10:	Covariate Characterization	N/A	No confounders were measured.
	Metric 11:	Co-exposure Counfounding	Low	There is no indication that co-exposures of concern were assessed, though the study was conducted in an occupational setting with higher potential for chemical co-exposures.
Domain 5: Analysis				

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Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	liver and gall bladder diseases.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Exposure levels and common chronic disease over time are appropriately measured with a cohort design.
	Metric 13:	Statistical Power	Low	It is unclear how many study participants are included in the measures of cases throughout the plant.
	Metric 14:	Reproducibility of Analyses	Medium	The analyses are reproducible, as the study only reports number of cases, and number of disabled days per 100 workers. Further analyses of these case numbers were not conducted.
	Metric 15:	Statistical Analysis	N/A	No statistical modeling was conducted.

Additional Comments: Occupational study of aircraft plant workers exposed to dichloroethane via air. Study reports number of cases of liver and gall bladder diseases. Statistical analyses and comparisons are not provided for outcomes and only case numbers are reported, limiting the informativeness of the study. Study refers only to dichloroethane, thus, 1,1 and 1,2 dichloroethane cannot be separated in this review. Both chemicals have been included in evaluations.

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Gastrointestinal
Reported Health Effect(s):	acute gastrointestinal diseases, acute gastritis, and chronic gastritis.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Occupational cohort study in Russian aircraft manufacturing plant. The study focuses on the soft tank shop. The participation of all workers in the aircraft plant shops (including the soft tank shop and controls from the mechanical shop) is implied, however numbers of eligible participants and the total number of included participants across analyses are not reported. 17 gluers represented the exposed and were compared to 10 mechanical shop machinists.
	Metric 2:	Attrition	Medium	Rates of attrition cannot be determined based on the limited information provided. The study solely reports those included in assessment of changes in the functions of motor apparatus in upper extremities, but not of gastrointestinal outcomes.
	Metric 3:	Comparison Group	Low	Case numbers per 100 workers are reported for those exposed (working in the shop) and those unexposed (working in the plant) for acute gastrointestinal diseases. Solely case numbers per 100 workers are reported for other gastrointestinal outcomes (acute and chronic gastritis, acute gastrointestinal diseases).
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Authors report quantitative measures of dichloroethane in air, but do not provide any information on the method used to quantify exposure levels.
	Metric 5:	Exposure Levels	Uninformative	No description is provided on the levels or range of exposure for those in the shop compared to the plant. The exposure difference between groups is unclear.
	Metric 6:	Temporality	Low	Temporality is unclear, as limited information is provided about the measurement of exposure and outcome.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Uninformative	No information on outcome measurement and diagnostic criteria is provided for gastrointestinal outcomes.
	Metric 8:	Reporting Bias	Medium	Case numbers are reported for gastrointestinal outcomes for the shop and the plant, but there is no clear information about their relationship to exposure levels. These results would not be useful for detailed extraction.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	There is no discussion of confounders or analysis of differing characteristics.
	Metric 10:	Covariate Characterization	N/A	No confounders measured.
	Metric 11:	Co-exposure Counfounding	Low	There is no indication that co-exposures of concern were assessed, though the study was conducted in an occupational setting with higher potential for chemical co-exposures.
Domain 5: Analysis				

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Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Gastrointestinal
Reported Health Effect(s):	acute gastrointestinal diseases, acute gastritis, and chronic gastritis.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Exposure levels and common chronic disease over time are appropriately measured with a cohort design.
	Metric 13:	Statistical Power	Low	It is unclear how many study participants are included in the measures of cases throughout the plant.
	Metric 14:	Reproducibility of Analyses	Medium	The analyses are reproducible, as the study only reports number of cases and number of disabled days per 100 workers. Further analyses of these case numbers were not conducted.
	Metric 15:	Statistical Analysis	N/A	No statistical modeling was conducted.

Additional Comments: Occupational study of aircraft plant workers exposed to dichloroethane via air. Study reports number of cases of gastrointestinal diseases per 100 workers in the plant and in the shop (likely exposed). No information is provided on the dichloroethane levels in the plant. Statistical analyses and comparisons are not provided for outcomes and only case numbers are reported, limiting the informativeness of the study. Study refers only to dichloroethane, thus, 1,1 and 1,2 dichloroethane cannot be separated in this review. Both chemicals have been included in evaluations.

Overall Quality Determination — Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Morbidity
Reported Health Effect(s):	Overall morbidity, and other diseases.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Occupational cohort study in Russian aircraft manufacturing plant. The study focuses on the soft tank shop. The participation of all workers in the aircraft plant shops (including the soft tank shop and controls from the mechanical shop) is implied, however numbers of eligible participants and the total number of included participants across analyses are not reported. 17 gluers represented the exposed and were compared to 10 mechanical shop machinists.
	Metric 2:	Attrition	Medium	Rates of attrition cannot be determined based on the limited information provided. The study solely reports those included in assessment of changes in the functions of motor apparatus in upper extremities, but not of other diseases/overall morbidity.
	Metric 3:	Comparison Group	Low	Case numbers per 100 workers are reported for those exposed (working in the shop) and those unexposed (working in the plant) for overall morbidity and other diseases.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Authors report quantitative measures of dichloroethane in air, but do not provide any information on the method used to quantify exposure levels.
	Metric 5:	Exposure Levels	Uninformative	No description is provided on the levels or range of exposure for those in the shop compared to the plant. The exposure difference between groups is unclear.
	Metric 6:	Temporality	Low	Temporality is unclear, as limited information is provided about the measurement of exposure and outcome.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Uninformative	No information on outcome measurement and diagnostic criteria is provided for overall morbidity or other diseases.
	Metric 8:	Reporting Bias	Medium	Case numbers are reported for overall morbidity and other diseases for the shop and the plant, but there is no clear information about their relationship to exposure levels. These results would not be useful for detailed extraction.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	There is no discussion of confounders or analysis of differing characteristics.
	Metric 10:	Covariate Characterization	N/A	No confounders were measured.
	Metric 11:	Co-exposure Counfounding	Low	There is no indication that co-exposures of concern were assessed, though the study was conducted in an occupational setting with higher potential for chemical co-exposures.
Domain 5: Analysis				

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Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Morbidity
Reported Health Effect(s):	Overall morbidity, and other diseases.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Exposure levels and common chronic disease over time are appropriately measured with a cohort design.
	Metric 13:	Statistical Power	Low	It is unclear how many study participants are included in the measures of cases throughout the plant.
	Metric 14:	Reproducibility of Analyses	Medium	The analyses are reproducible, as the study only reports number of cases and number of disabled days per 100 workers. Further analyses of these case numbers were not conducted.
	Metric 15:	Statistical Analysis	N/A	No statistical modeling was conducted.

Additional Comments: Occupational study of aircraft plant workers exposed to dichloroethane via air. Study reports number of cases of overall morbidity and "other diseases" per 100 workers in the plant (no or lower exposure) and in the shop (likely exposed). No information is provided on the dichloroethane levels in the plant. Statistical analyses and comparisons are not provided for outcomes and only case numbers are reported, limiting the informativeness of the study. Study refers only to dichloroethane, thus, 1,1 and 1,2 dichloroethane cannot be separated in this review. Both chemicals have been included in evaluations.

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	visual-motor reaction (simple, complex), changes in the function of the motor apparatus in the upper extremities, neuritis and radiculitis, diseases of the muscles, tendons, and ganglia.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Occupational cohort study in Russian aircraft manufacturing plant. The study focuses on the soft tank shop. The participation of all workers in the aircraft plant shops (including the soft tank shop and controls from the mechanical shop) is implied, however numbers of eligible participants and the total number of included participants across analyses are not reported. 17 gluers represented the exposed and were compared to 10 mechanical shop machinists.
	Metric 2:	Attrition	Medium	Rates of attrition cannot be determined based on the limited information provided. The study solely reports those included in analyses of visual-motor function and changes in the functions of motor apparatus in upper extremities.
	Metric 3:	Comparison Group	Low	Mechanical shop machinists (n=10) served as the controls. Though the controls were also workers in the same plant as those exposed, the dichloroethane levels in air in the mechanical shop are not provided; thus, the similarity between cases and controls is not clear. Additionally, authors note that controls did not perform work that strained the hands, which is distinct from the gluers (exposed).
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Authors report quantitative measures of dichloroethane in air, but do not provide any information on the method used to quantify exposure levels.
	Metric 5:	Exposure Levels	Low	Neurological health outcomes are reported for two groups: gluers (exposed) and mechanical shop mechanists (controls). A range of exposure levels are provided based on activities conducted by gluers. "The highest concentrations of dichloroethane (0.08 - 0.158 mg/L) occurred when the rubber sheets were coated with glue. These concentrations were maintained for only 5-6 min; they subsequently decreased to 0.062 - 0.082 mg/L as the glue dried, and at the end of the drying period 15 min later, they had decreased to 0.03 - 0.04 mg/L. The concentration of dichloroethane remains at the level of 0.05 mg/L and lower during most of the shift."
	Metric 6:	Temporality	Medium	The study reports visual-motor reaction at the end of the working day after exposure, establishing temporality, though it is unclear if exposure fell during relevant exposure windows for neuritis and radiculitis.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Uninformative	No information on outcome measurement and diagnostic criteria is provided for visual-motor reaction, neuritis, radiculitis, or changes in motor function of upper extremities.

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Study Citation: Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s): Neurological/Behavioral
Reported Health Effect(s): visual-motor reaction (simple, complex), changes in the function of the motor apparatus in the upper extremities, neuritis and radiculitis, diseases of the muscles, tendons, and ganglia.
Chemical: 1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s): No linked references.
HERO ID: 18135

Domain	Metric		Rating	Comments
	Metric 8:	Reporting Bias	Medium	Results are reported for visual-motor reactions (occurrence of errors for exposed and unexposed), but results for other outcomes are reported qualitatively (changes in motor function of upper extremities), and only case numbers are reported for neuritis and radiculitis. These results would not be useful for detailed extraction.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	There is no discussion of confounders or analysis of differing characteristics.
	Metric 10:	Covariate Characterization	N/A	No confounders were measured.
	Metric 11:	Co-exposure Counfounding	Low	There is no indication that co-exposures of concern were assessed, though the study was conducted in an occupational setting with higher potential for chemical co-exposures.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Exposure levels and common chronic disease over time are appropriately measured with a cohort design.
	Metric 13:	Statistical Power	Low	It is unclear how many study participants are included in the measures of cases throughout the plant. Additionally, n=17 workers are included in the exposed group and n=10 in the unexposed control group.
	Metric 14:	Reproducibility of Analyses	Medium	The analyses are reproducible, as the study only reports number of cases, and number of disabled days in the shop and plant. Further analyses of these case numbers were not conducted.
	Metric 15:	Statistical Analysis	N/A	No statistical modeling was conducted.

Additional Comments: Occupational study of aircraft plant workers exposed to dichloroethane via air. Study reports number of cases of a variety of neurological conditions and provides one crude comparison of prevalence of visual-motor reaction impairment with a control group. Otherwise, statistical analyses and comparisons are not provided for outcomes and only case numbers are reported, limiting the informativeness of the study. Study refers only to dichloroethane, thus, 1,1 and 1,2 dichloroethane cannot be separated in this review. Both chemicals have been included in evaluations.

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Musculoskeletal
Reported Health Effect(s):	changes in the function of the motor apparatus in the upper extremities, diseases of the muscles, tendons, and ganglia.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Occupational cohort study in Russian aircraft manufacturing plant. The study focuses on the soft tank shop. The participation of all workers in the aircraft plant shops (including the soft tank shop and controls from the mechanical shop) is implied, however numbers of eligible participants and the total number of included participants across analyses are not reported. 17 gluers represented the exposed and were compared to 10 mechanical shop machinists.
	Metric 2:	Attrition	Medium	Rates of attrition cannot be determined based on the limited information provided. The study solely reports those included in assessment of changes in the functions of motor apparatus in upper extremities.
	Metric 3:	Comparison Group	Low	Mechanical shop machinists (n=10) served as the controls. Though the controls were also workers in the same plant as those exposed, the dichloroethane levels in air in the mechanical shop are not provided; thus, the similarity between cases and controls is not clear. Additionally, authors note that controls did not perform work that strained the hands, which is distinct from the gluers (exposed).
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Authors report quantitative measures of dichloroethane in air, but do not provide any information on the method used to quantify exposure levels.
	Metric 5:	Exposure Levels	Low	Musculoskeletal health outcomes are reported for two groups: gluers (exposed) and mechanical shop mechanists (controls). A range of exposure levels are provided based on activities conducted by gluers. "The highest concentrations of dichloroethane (0.08 - 0.158 mg/L) occurred when the rubber sheets were coated with glue. These concentrations were maintained for only 5-6 min; they subsequently decreased to 0.062 - 0.082 mg/L as the glue dried, and at the end of the drying period 15 min later, they had decreased to 0.03 - 0.04 mg/L. The concentration of dichloroethane remains at the level of 0.05 mg/L and lower during most of the shift."
	Metric 6:	Temporality	Medium	The study reports musculoskeletal outcomes at the end of the working day after exposure, establishing temporality, though specific details about measurement of exposure and outcome timings are not provided.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Uninformative	No information on outcome measurement and diagnostic criteria is provided for changes in motor function of upper extremities or diseases of the muscles, tendons, and ganglia.
	Metric 8:	Reporting Bias	Medium	Results are reported qualitatively (changes in motor function of upper extremities), and only case numbers are reported for diseases of the muscles, tendons, and ganglia. These results would not be useful for detailed extraction.

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Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Musculoskeletal
Reported Health Effect(s):	changes in the function of the motor apparatus in the upper extremities, diseases of the muscles, tendons, and ganglia.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	There is no discussion of confounders or analysis of differing characteristics.
	Metric 10:	Covariate Characterization	N/A	No confounders were measured.
	Metric 11:	Co-exposure Counfounding	Low	There is no indication that co-exposures of concern were assessed, though the study was conducted in an occupational setting with higher potential for chemical co-exposures.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Exposure levels and common chronic disease over time are appropriately measured with a cohort design.
	Metric 13:	Statistical Power	Low	It is unclear how many study participants are included in the measures of cases throughout the plant. Additionally, n=17 workers are included in the exposed group and n=10 in the unexposed control group.
	Metric 14:	Reproducibility of Analyses	Medium	The analyses are reproducible, as the study only reports number of cases, and number of disabled days in the shop and plant. Further analyses of these case numbers were not conducted.
	Metric 15:	Statistical Analysis	N/A	No statistical modeling was conducted.

Additional Comments: Occupational study of aircraft plant workers exposed to dichloroethane via air. Study reports number of cases of muscle, tendon, and ganglia disease and provides qualitative information on decreased motor function of upper extremities. Statistical analyses and comparisons are not provided for outcomes and only case numbers are reported, limiting the informativeness of the study. Study refers only to dichloroethane, thus, 1,1 and 1,2 dichloroethane cannot be separated in this review. Both chemicals have been included in evaluations.

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	liver and gall bladder diseases.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Occupational cohort study in Russian aircraft manufacturing plant. The study focuses on the soft tank shop. The participation of all workers in the aircraft plant shops (including the soft tank shop and controls from the mechanical shop) is implied, however numbers of eligible participants and the total number of included participants across analyses are not reported. 17 gluers represented the exposed and were compared to 10 mechanical shop machinists.
	Metric 2:	Attrition	Medium	Rates of attrition cannot be determined based on the limited information provided. The study solely reports those included in assessment of changes in the functions of motor apparatus in upper extremities, but not of liver disease.
	Metric 3:	Comparison Group	Uninformative	Solely case numbers are reported for liver and gall bladder disease. Case numbers among those unexposed are not clear.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Authors report quantitative measures of dichloroethane in air, but do not provide any information on the method used to quantify exposure levels.
	Metric 5:	Exposure Levels	Uninformative	Liver and gall bladder disease are reported as case numbers only, with no indication of likely exposure.
	Metric 6:	Temporality	Low	Temporality is unclear, as limited information is provided about the measurement of exposure and outcome.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Uninformative	No information on outcome measurement and diagnostic criteria is provided for liver and gall bladder diseases.
	Metric 8:	Reporting Bias	Medium	Only case numbers are reported for liver and gall bladder disease with no information about their relationship to exposure. These results would not be useful for detailed extraction.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	There is no discussion of confounders or analysis of differing characteristics.
	Metric 10:	Covariate Characterization	N/A	No confounders were measured.
	Metric 11:	Co-exposure Counfounding	Low	There is no indication that co-exposures of concern were assessed, though the study was conducted in an occupational setting with higher potential for chemical co-exposures.
Domain 5: Analysis				

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Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	liver and gall bladder diseases.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Exposure levels and common chronic disease over time are appropriately measured with a cohort design.
	Metric 13:	Statistical Power	Low	It is unclear how many study participants are included in the measures of cases throughout the plant.
	Metric 14:	Reproducibility of Analyses	Medium	The analyses are reproducible, as the study only reports number of cases, and number of disabled days per 100 workers. Further analyses of these case numbers were not conducted.
	Metric 15:	Statistical Analysis	N/A	No statistical modeling was conducted.

Additional Comments: Occupational study of aircraft plant workers exposed to dichloroethane via air. Study reports number of cases of liver and gall bladder diseases. Statistical analyses and comparisons are not provided for outcomes and only case numbers are reported, limiting the informativeness of the study. Study refers only to dichloroethane, thus, 1,1 and 1,2 dichloroethane cannot be separated in this review. Both chemicals have been included in evaluations.

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Gastrointestinal
Reported Health Effect(s):	acute gastrointestinal diseases, acute gastritis, and chronic gastritis.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Occupational cohort study in Russian aircraft manufacturing plant. The study focuses on the soft tank shop. The participation of all workers in the aircraft plant shops (including the soft tank shop and controls from the mechanical shop) is implied, however numbers of eligible participants and the total number of included participants across analyses are not reported. 17 gluers represented the exposed and were compared to 10 mechanical shop machinists.
	Metric 2:	Attrition	Medium	Rates of attrition cannot be determined based on the limited information provided. The study solely reports those included in assessment of changes in the functions of motor apparatus in upper extremities, but not of gastrointestinal outcomes.
	Metric 3:	Comparison Group	Low	Case numbers per 100 workers are reported for those exposed (working in the shop) and those unexposed (working in the plant) for acute gastrointestinal diseases. Solely case numbers per 100 workers are reported for other gastrointestinal outcomes (acute and chronic gastritis, acute gastrointestinal diseases).
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Authors report quantitative measures of dichloroethane in air, but do not provide any information on the method used to quantify exposure levels.
	Metric 5:	Exposure Levels	Uninformative	No description is provided on the levels or range of exposure for those in the shop compared to the plant. The exposure difference between groups is unclear.
	Metric 6:	Temporality	Low	Temporality is unclear, as limited information is provided about the measurement of exposure and outcome.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Uninformative	No information on outcome measurement and diagnostic criteria is provided for gastrointestinal outcomes.
	Metric 8:	Reporting Bias	Medium	Case numbers are reported for gastrointestinal outcomes for the shop and the plant, but there is no clear information about their relationship to exposure levels. These results would not be useful for detailed extraction.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	There is no discussion of confounders or analysis of differing characteristics.
	Metric 10:	Covariate Characterization	N/A	No confounders were measured.
	Metric 11:	Co-exposure Counfounding	Low	There is no indication that co-exposures of concern were assessed, though the study was conducted in an occupational setting with higher potential for chemical co-exposures.
Domain 5: Analysis				

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Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Gastrointestinal
Reported Health Effect(s):	acute gastrointestinal diseases, acute gastritis, and chronic gastritis.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Exposure levels and common chronic disease over time are appropriately measured with a cohort design.
	Metric 13:	Statistical Power	Low	It is unclear how many study participants are included in the measures of cases throughout the plant.
	Metric 14:	Reproducibility of Analyses	Medium	The analyses are reproducible, as the study only reports number of cases and number of disabled days per 100 workers. Further analyses of these case numbers were not conducted.
	Metric 15:	Statistical Analysis	N/A	No statistical modeling was conducted.

Additional Comments: Occupational study of aircraft plant workers exposed to dichloroethane via air. Study reports number of cases of gastrointestinal diseases per 100 workers in the plant and in the shop (likely exposed). No information is provided on the dichloroethane levels in the plant. Statistical analyses and comparisons are not provided for outcomes and only case numbers are reported, limiting the informativeness of the study. Study refers only to dichloroethane, thus, 1,1 and 1,2 dichloroethane cannot be separated in this review. Both chemicals have been included in evaluations.

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Morbidity
Reported Health Effect(s):	Overall morbidity, and other diseases.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Occupational cohort study in Russian aircraft manufacturing plant. The study focuses on the soft tank shop. The participation of all workers in the aircraft plant shops (including the soft tank shop and controls from the mechanical shop) is implied, however numbers of eligible participants and the total number of included participants across analyses are not reported. 17 gluers represented the exposed and were compared to 10 mechanical shop machinists.
	Metric 2:	Attrition	Medium	Rates of attrition cannot be determined based on the limited information provided. The study solely reports those included in assessment of changes in the functions of motor apparatus in upper extremities, but not of other diseases/overall morbidity.
	Metric 3:	Comparison Group	Low	Case numbers per 100 workers are reported for those exposed (working in the shop) and those unexposed (working in the plant) for overall morbidity and other diseases.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Authors report quantitative measures of dichloroethane in air, but do not provide any information on the method used to quantify exposure levels.
	Metric 5:	Exposure Levels	Uninformative	No description is provided on the levels or range of exposure for those in the shop compared to the plant. The exposure difference between groups is unclear.
	Metric 6:	Temporality	Low	Temporality is unclear, as limited information is provided about the measurement of exposure and outcome.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Uninformative	No information on outcome measurement and diagnostic criteria is provided for overall morbidity or other diseases.
	Metric 8:	Reporting Bias	Medium	Case numbers are reported for overall morbidity and other diseases for the shop and the plant, but there is no clear information about their relationship to exposure levels. These results would not be useful for detailed extraction.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	There is no discussion of confounders or analysis of differing characteristics.
	Metric 10:	Covariate Characterization	N/A	No confounders measured.
	Metric 11:	Co-exposure Counfounding	Low	There is no indication that co-exposures of concern were assessed, though the study was conducted in an occupational setting with higher potential for chemical co-exposures.
Domain 5: Analysis				

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Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Morbidity
Reported Health Effect(s):	Overall morbidity, and other diseases.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Exposure levels and common chronic disease over time are appropriately measured with a cohort design.
	Metric 13:	Statistical Power	Low	It is unclear how many study participants are included in the measures of cases throughout the plant.
	Metric 14:	Reproducibility of Analyses	Medium	The analyses are reproducible, as the study only reports number of cases and number of disabled days per 100 workers. Further analyses of these case numbers were not conducted.
	Metric 15:	Statistical Analysis	N/A	No statistical modeling was conducted.

Additional Comments: Occupational study of aircraft plant workers exposed to dichloroethane via air. Study reports number of cases of overall morbidity and "other diseases" per 100 workers in the plant (no or lower exposure) and in the shop (likely exposed). No information is provided on the dichloroethane levels in the plant. Statistical analyses and comparisons are not provided for outcomes and only case numbers are reported, limiting the informativeness of the study. Study refers only to dichloroethane, thus, 1,1 and 1,2 dichloroethane cannot be separated in this review. Both chemicals have been included in evaluations.

Overall Quality Determination **Uninformative**

* No biomarkers were identified for this evaluation.

Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	visual-motor reaction (simple, complex), changes in the function of the motor apparatus in the upper extremities, neuritis and radiculitis, diseases of the muscles, tendons, and ganglia.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Occupational cohort study in Russian aircraft manufacturing plant. The study focuses on the soft tank shop. The participation of all workers in the aircraft plant shops (including the soft tank shop and controls from the mechanical shop) is implied, however numbers of eligible participants and the total number of included participants across analyses are not reported. 17 gluers represented the exposed and were compared to 10 mechanical shop machinists.
	Metric 2:	Attrition	Medium	Rates of attrition cannot be determined based on the limited information provided. The study solely reports those included in analyses of visual-motor function and changes in the functions of motor apparatus in upper extremities.
	Metric 3:	Comparison Group	Low	Mechanical shop machinists (n=10) served as the controls. Though the controls were also workers in the same plant as those exposed, the dichloroethane levels in air in the mechanical shop are not provided; thus, the similarity between cases and controls is not clear. Additionally, authors note that controls did not perform work that strained the hands, which is distinct from the gluers (exposed).
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Authors report quantitative measures of dichloroethane in air, but do not provide any information on the method used to quantify exposure levels.
	Metric 5:	Exposure Levels	Low	Neurological health outcomes are reported for two groups: gluers (exposed) and mechanical shop mechanists (controls). A range of exposure levels are provided based on activities conducted by gluers. "The highest concentrations of dichloroethane (0.08 - 0.158 mg/L) occurred when the rubber sheets were coated with glue. These concentrations were maintained for only 5-6 min; they subsequently decreased to 0.062 - 0.082 mg/L as the glue dried, and at the end of the drying period 15 min later, they had decreased to 0.03 - 0.04 mg/L. The concentration of dichloroethane remains at the level of 0.05 mg/L and lower during most of the shift."
	Metric 6:	Temporality	Medium	The study reports visual-motor reaction at the end of the working day after exposure, establishing temporality, though it is unclear if exposure fell during relevant exposure windows for neuritis and radiculitis.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Uninformative	No information on outcome measurement and diagnostic criteria is provided for visual-motor reaction, neuritis, radiculitis, or changes in motor function of upper extremities.
	Metric 8:	Reporting Bias	Medium	Results are reported for visual-motor reactions (occurrence of errors for exposed and unexposed), but results for other outcomes are reported qualitatively (changes in motor function of upper extremities), and only case numbers are reported for neuritis and radiculitis. These results would not be useful for detailed extraction.

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Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	visual-motor reaction (simple, complex), changes in the function of the motor apparatus in the upper extremities, neuritis and radiculitis, diseases of the muscles, tendons, and ganglia.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	There is no discussion of confounders or analysis of differing characteristics.
	Metric 10:	Covariate Characterization	N/A	No confounders were measured.
	Metric 11:	Co-exposure Counfounding	Low	There is no indication that co-exposures of concern were assessed, though the study was conducted in an occupational setting with higher potential for chemical co-exposures.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Exposure levels and common chronic disease over time are appropriately measured with a cohort design.
	Metric 13:	Statistical Power	Low	It is unclear how many study participants are included in the measures of cases throughout the plant. Additionally, n=17 workers are included in the exposed group and n=10 in the unexposed control group.
	Metric 14:	Reproducibility of Analyses	Medium	The analyses are reproducible, as the study only reports number of cases, and number of disabled days in the shop and plant. Further analyses of these case numbers were not conducted.
	Metric 15:	Statistical Analysis	N/A	No statistical modeling was conducted.

Additional Comments: Occupational study of aircraft plant workers exposed to dichloroethane via air. Study reports number of cases of a variety of neurological conditions and provides one crude comparison of prevalence of visual-motor reaction impairment with a control group. Otherwise, statistical analyses and comparisons are not provided for outcomes and only case numbers are reported, limiting the informativeness of the study. Study refers only to dichloroethane, thus, 1,1 and 1,2 dichloroethane cannot be separated in this review. Both chemicals have been included in evaluations.

Overall Quality Determination — Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Musculoskeletal
Reported Health Effect(s):	changes in the function of the motor apparatus in the upper extremities, diseases of the muscles, tendons, and ganglia.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Occupational cohort study in Russian aircraft manufacturing plant. The study focuses on the soft tank shop. The participation of all workers in the aircraft plant shops (including the soft tank shop and controls from the mechanical shop) is implied, however numbers of eligible participants and the total number of included participants across analyses are not reported. 17 gluers represented the exposed and were compared to 10 mechanical shop machinists.
	Metric 2:	Attrition	Medium	Rates of attrition cannot be determined based on the limited information provided. The study solely reports those included in assessment of changes in the functions of motor apparatus in upper extremities.
	Metric 3:	Comparison Group	Low	Mechanical shop machinists (n=10) served as the controls. Though the controls were also workers in the same plant as those exposed, the dichloroethane levels in air in the mechanical shop are not provided; thus, the similarity between cases and controls is not clear. Additionally, authors note that controls did not perform work that strained the hands, which is distinct from the gluers (exposed).
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Authors report quantitative measures of dichloroethane in air, but do not provide any information on the method used to quantify exposure levels.
	Metric 5:	Exposure Levels	Low	Musculoskeletal health outcomes are reported for two groups: gluers (exposed) and mechanical shop mechanists (controls). A range of exposure levels are provided based on activities conducted by gluers. "The highest concentrations of dichloroethane (0.08 - 0.158 mg/L) occurred when the rubber sheets were coated with glue. These concentrations were maintained for only 5-6 min; they subsequently decreased to 0.062 - 0.082 mg/L as the glue dried, and at the end of the drying period 15 min later, they had decreased to 0.03 - 0.04 mg/L. The concentration of dichloroethane remains at the level of 0.05 mg/L and lower during most of the shift."
	Metric 6:	Temporality	Medium	The study reports musculoskeletal outcomes at the end of the working day after exposure, establishing temporality, though specific details about measurement of exposure and outcome timings are not provided.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Uninformative	No information on outcome measurement and diagnostic criteria is provided for changes in motor function of upper extremities or diseases of the muscles, tendons, and ganglia.
	Metric 8:	Reporting Bias	Medium	Results are reported qualitatively (changes in motor function of upper extremities), and only case numbers are reported for diseases of the muscles, tendons, and ganglia. These results would not be useful for detailed extraction.

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Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Musculoskeletal
Reported Health Effect(s):	changes in the function of the motor apparatus in the upper extremities, diseases of the muscles, tendons, and ganglia.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	There is no discussion of confounders or analysis of differing characteristics.
	Metric 10:	Covariate Characterization	N/A	No confounders were measured.
	Metric 11:	Co-exposure Counfounding	Low	There is no indication that co-exposures of concern were assessed, though the study was conducted in an occupational setting with higher potential for chemical co-exposures.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Exposure levels and common chronic disease over time are appropriately measured with a cohort design.
	Metric 13:	Statistical Power	Low	It is unclear how many study participants are included in the measures of cases throughout the plant. Additionally, n=17 workers are included in the exposed group and n=10 in the unexposed control group.
	Metric 14:	Reproducibility of Analyses	Medium	The analyses are reproducible, as the study only reports number of cases, and number of disabled days in the shop and plant. Further analyses of these case numbers were not conducted.
	Metric 15:	Statistical Analysis	N/A	No statistical modeling was conducted.

Additional Comments: Occupational study of aircraft plant workers exposed to dichloroethane via air. Study reports number of cases of muscle, tendon, and ganglia disease and provides qualitative information on decreased motor function of upper extremities. Statistical analyses and comparisons are not provided for outcomes and only case numbers are reported, limiting the informativeness of the study. Study refers only to dichloroethane, thus, 1,1 and 1,2 dichloroethane cannot be separated in this review. Both chemicals have been included in evaluations.

Overall Quality Determination — Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	liver and gall bladder diseases.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Occupational cohort study in Russian aircraft manufacturing plant. The study focuses on the soft tank shop. The participation of all workers in the aircraft plant shops (including the soft tank shop and controls from the mechanical shop) is implied, however numbers of eligible participants and the total number of included participants across analyses are not reported. 17 gluers represented the exposed and were compared to 10 mechanical shop machinists.
	Metric 2:	Attrition	Medium	Rates of attrition cannot be determined based on the limited information provided. The study solely reports those included in assessment of changes in the functions of motor apparatus in upper extremities, but not of liver disease.
	Metric 3:	Comparison Group	Uninformative	Solely case numbers are reported for liver and gall bladder disease. Case numbers among those unexposed are not clear.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Authors report quantitative measures of dichloroethane in air, but do not provide any information on the method used to quantify exposure levels.
	Metric 5:	Exposure Levels	Uninformative	Liver and gall bladder disease are reported as case numbers only, with no indication of likely exposure.
	Metric 6:	Temporality	Low	Temporality is unclear, as limited information is provided about the measurement of exposure and outcome.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Uninformative	No information on outcome measurement and diagnostic criteria is provided for liver and gall bladder diseases.
	Metric 8:	Reporting Bias	Medium	Only case numbers are reported for liver and gall bladder disease with no information about their relationship to exposure. These results would not be useful for detailed extraction.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	There is no discussion of confounders or analysis of differing characteristics.
	Metric 10:	Covariate Characterization	N/A	No confounders were measured.
	Metric 11:	Co-exposure Counfounding	Low	There is no indication that co-exposures of concern were assessed, though the study was conducted in an occupational setting with higher potential for chemical co-exposures.
Domain 5: Analysis				

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Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	liver and gall bladder diseases.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Exposure levels and common chronic disease over time are appropriately measured with a cohort design.
	Metric 13:	Statistical Power	Low	It is unclear how many study participants are included in the measures of cases throughout the plant.
	Metric 14:	Reproducibility of Analyses	Medium	The analyses are reproducible, as the study only reports number of cases, and number of disabled days per 100 workers. Further analyses of these case numbers were not conducted.
	Metric 15:	Statistical Analysis	N/A	No statistical modeling was conducted.

Additional Comments: Occupational study of aircraft plant workers exposed to dichloroethane via air. Study reports number of cases of liver and gall bladder diseases. Statistical analyses and comparisons are not provided for outcomes and only case numbers are reported, limiting the informativeness of the study. Study refers only to dichloroethane, thus, 1,1 and 1,2 dichloroethane cannot be separated in this review. Both chemicals have been included in evaluations.

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Gastrointestinal
Reported Health Effect(s):	acute gastrointestinal diseases, acute gastritis, and chronic gastritis.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Occupational cohort study in Russian aircraft manufacturing plant. The study focuses on the soft tank shop. The participation of all workers in the aircraft plant shops (including the soft tank shop and controls from the mechanical shop) is implied, however numbers of eligible participants and the total number of included participants across analyses are not reported. 17 gluers represented the exposed and were compared to 10 mechanical shop machinists.
	Metric 2:	Attrition	Medium	Rates of attrition cannot be determined based on the limited information provided. The study solely reports those included in assessment of changes in the functions of motor apparatus in upper extremities, but not of gastrointestinal outcomes.
	Metric 3:	Comparison Group	Low	Case numbers per 100 workers are reported for those exposed (working in the shop) and those unexposed (working in the plant) for acute gastrointestinal diseases. Solely case numbers per 100 workers are reported for other gastrointestinal outcomes (acute and chronic gastritis, acute gastrointestinal diseases).
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Authors report quantitative measures of dichloroethane in air, but do not provide any information on the method used to quantify exposure levels.
	Metric 5:	Exposure Levels	Uninformative	No description is provided on the levels or range of exposure for those in the shop compared to the plant. The exposure difference between groups is unclear.
	Metric 6:	Temporality	Low	Temporality is unclear, as limited information is provided about the measurement of exposure and outcome.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Uninformative	No information on outcome measurement and diagnostic criteria is provided for gastrointestinal outcomes.
	Metric 8:	Reporting Bias	Medium	Case numbers are reported for gastrointestinal outcomes for the shop and the plant, but there is no clear information about their relationship to exposure levels. These results would not be useful for detailed extraction.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	There is no discussion of confounders or analysis of differing characteristics.
	Metric 10:	Covariate Characterization	N/A	No confounders measured.
	Metric 11:	Co-exposure Counfounding	Low	There is no indication that co-exposures of concern were assessed, though the study was conducted in an occupational setting with higher potential for chemical co-exposures.
Domain 5: Analysis				

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Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Gastrointestinal
Reported Health Effect(s):	acute gastrointestinal diseases, acute gastritis, and chronic gastritis.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Exposure levels and common chronic disease over time are appropriately measured with a cohort design.
	Metric 13:	Statistical Power	Low	It is unclear how many study participants are included in the measures of cases throughout the plant.
	Metric 14:	Reproducibility of Analyses	Medium	The analyses are reproducible, as the study only reports number of cases and number of disabled days per 100 workers. Further analyses of these case numbers were not conducted.
	Metric 15:	Statistical Analysis	N/A	No statistical modeling was conducted.

Additional Comments: Occupational study of aircraft plant workers exposed to dichloroethane via air. Study reports number of cases of gastrointestinal diseases per 100 workers in the plant and in the shop (likely exposed). No information is provided on the dichloroethane levels in the plant. Statistical analyses and comparisons are not provided for outcomes and only case numbers are reported, limiting the informativeness of the study. Study refers only to dichloroethane, thus, 1,1 and 1,2 dichloroethane cannot be separated in this review. Both chemicals have been included in evaluations.

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Morbidity
Reported Health Effect(s):	Overall morbidity, and other diseases.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Occupational cohort study in Russian aircraft manufacturing plant. The study focuses on the soft tank shop. The participation of all workers in the aircraft plant shops (including the soft tank shop and controls from the mechanical shop) is implied, however numbers of eligible participants and the total number of included participants across analyses are not reported. 17 gluers represented the exposed and were compared to 10 mechanical shop machinists.
	Metric 2:	Attrition	Medium	Rates of attrition cannot be determined based on the limited information provided. The study solely reports those included in assessment of changes in the functions of motor apparatus in upper extremities, but not of other diseases/overall morbidity.
	Metric 3:	Comparison Group	Low	Case numbers per 100 workers are reported for those exposed (working in the shop) and those unexposed (working in the plant) for overall morbidity and other diseases.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Authors report quantitative measures of dichloroethane in air, but do not provide any information on the method used to quantify exposure levels.
	Metric 5:	Exposure Levels	Uninformative	No description is provided on the levels or range of exposure for those in the shop compared to the plant. The exposure difference between groups is unclear.
	Metric 6:	Temporality	Low	Temporality is unclear, as limited information is provided about the measurement of exposure and outcome.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Uninformative	No information on outcome measurement and diagnostic criteria is provided for overall morbidity or other diseases.
	Metric 8:	Reporting Bias	Medium	Case numbers are reported for overall morbidity and other diseases for the shop and the plant, but there is no clear information about their relationship to exposure levels. These results would not be useful for detailed extraction.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	There is no discussion of confounders or analysis of differing characteristics.
	Metric 10:	Covariate Characterization	N/A	No confounders were measured.
	Metric 11:	Co-exposure Counfounding	Low	There is no indication that co-exposures of concern were assessed, though the study was conducted in an occupational setting with higher potential for chemical co-exposures.
Domain 5: Analysis				

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Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Morbidity
Reported Health Effect(s):	Overall morbidity, and other diseases.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Exposure levels and common chronic disease over time are appropriately measured with a cohort design.
	Metric 13:	Statistical Power	Low	It is unclear how many study participants are included in the measures of cases throughout the plant.
	Metric 14:	Reproducibility of Analyses	Medium	The analyses are reproducible, as the study only reports number of cases and number of disabled days per 100 workers. Further analyses of these case numbers were not conducted.
	Metric 15:	Statistical Analysis	N/A	No statistical modeling was conducted.

Additional Comments: Occupational study of aircraft plant workers exposed to dichloroethane via air. Study reports number of cases of overall morbidity and "other diseases" per 100 workers in the plant (no or lower exposure) and in the shop (likely exposed). No information is provided on the dichloroethane levels in the plant. Statistical analyses and comparisons are not provided for outcomes and only case numbers are reported, limiting the informativeness of the study. Study refers only to dichloroethane, thus, 1,1 and 1,2 dichloroethane cannot be separated in this review. Both chemicals have been included in evaluations.

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	visual-motor reaction (simple, complex), changes in the function of the motor apparatus in the upper extremities, neuritis and radiculitis, diseases of the muscles, tendons, and ganglia.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Occupational cohort study in Russian aircraft manufacturing plant. The study focuses on the soft tank shop. The participation of all workers in the aircraft plant shops (including the soft tank shop and controls from the mechanical shop) is implied, however numbers of eligible participants and the total number of included participants across analyses are not reported. 17 gluers represented the exposed and were compared to 10 mechanical shop machinists.
	Metric 2:	Attrition	Medium	Rates of attrition cannot be determined based on the limited information provided. The study solely reports those included in analyses of visual-motor function and changes in the functions of motor apparatus in upper extremities.
	Metric 3:	Comparison Group	Low	Mechanical shop machinists (n=10) served as the controls. Though the controls were also workers in the same plant as those exposed, the dichloroethane levels in air in the mechanical shop are not provided; thus, the similarity between cases and controls is not clear. Additionally, authors note that controls did not perform work that strained the hands, which is distinct from the gluers (exposed).
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Authors report quantitative measures of dichloroethane in air, but do not provide any information on the method used to quantify exposure levels.
	Metric 5:	Exposure Levels	Low	Neurological health outcomes are reported for two groups: gluers (exposed) and mechanical shop mechanists (controls). A range of exposure levels are provided based on activities conducted by gluers. "The highest concentrations of dichloroethane (0.08 - 0.158 mg/L) occurred when the rubber sheets were coated with glue. These concentrations were maintained for only 5-6 min; they subsequently decreased to 0.062 - 0.082 mg/L as the glue dried, and at the end of the drying period 15 min later, they had decreased to 0.03 - 0.04 mg/L. The concentration of dichloroethane remains at the level of 0.05 mg/L and lower during most of the shift."
	Metric 6:	Temporality	Medium	The study reports visual-motor reaction at the end of the working day after exposure, establishing temporality, though it is unclear if exposure fell during relevant exposure windows for neuritis and radiculitis.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Uninformative	No information on outcome measurement and diagnostic criteria is provided for visual-motor reaction, neuritis, radiculitis, or changes in motor function of upper extremities.

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Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	visual-motor reaction (simple, complex), changes in the function of the motor apparatus in the upper extremities, neuritis and radiculitis, diseases of the muscles, tendons, and ganglia.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
	Metric 8:	Reporting Bias	Medium	Results are reported for visual-motor reactions (occurrence of errors for exposed and unexposed), but results for other outcomes are reported qualitatively (changes in motor function of upper extremities), and only case numbers are reported for neuritis and radiculitis. These results would not be useful for detailed extraction.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	There is no discussion of confounders or analysis of differing characteristics.
	Metric 10:	Covariate Characterization	N/A	No confounders were measured.
	Metric 11:	Co-exposure Counfounding	Low	There is no indication that co-exposures of concern were assessed, though the study was conducted in an occupational setting with higher potential for chemical co-exposures.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Exposure levels and common chronic disease over time are appropriately measured with a cohort design.
	Metric 13:	Statistical Power	Low	It is unclear how many study participants are included in the measures of cases throughout the plant. Additionally, n=17 workers are included in the exposed group and n=10 in the unexposed control group.
	Metric 14:	Reproducibility of Analyses	Medium	The analyses are reproducible, as the study only reports number of cases, and number of disabled days in the shop and plant. Further analyses of these case numbers were not conducted.
	Metric 15:	Statistical Analysis	N/A	No statistical modeling was conducted.

Additional Comments: Occupational study of aircraft plant workers exposed to dichloroethane via air. Study reports number of cases of a variety of neurological conditions and provides one crude comparison of prevalence of visual-motor reaction impairment with a control group. Otherwise, statistical analyses and comparisons are not provided for outcomes and only case numbers are reported, limiting the informativeness of the study. Study refers only to dichloroethane, thus, 1,1 and 1,2 dichloroethane cannot be separated in this review. Both chemicals have been included in evaluations.

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Musculoskeletal
Reported Health Effect(s):	changes in the function of the motor apparatus in the upper extremities, diseases of the muscles, tendons, and ganglia.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Occupational cohort study in Russian aircraft manufacturing plant. The study focuses on the soft tank shop. The participation of all workers in the aircraft plant shops (including the soft tank shop and controls from the mechanical shop) is implied, however numbers of eligible participants and the total number of included participants across analyses are not reported. 17 gluers represented the exposed and were compared to 10 mechanical shop machinists.
	Metric 2:	Attrition	Medium	Rates of attrition cannot be determined based on the limited information provided. The study solely reports those included in assessment of changes in the functions of motor apparatus in upper extremities.
	Metric 3:	Comparison Group	Low	Mechanical shop machinists (n=10) served as the controls. Though the controls were also workers in the same plant as those exposed, the dichloroethane levels in air in the mechanical shop are not provided; thus, the similarity between cases and controls is not clear. Additionally, authors note that controls did not perform work that strained the hands, which is distinct from the gluers (exposed).
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Authors report quantitative measures of dichloroethane in air, but do not provide any information on the method used to quantify exposure levels.
	Metric 5:	Exposure Levels	Low	Musculoskeletal health outcomes are reported for two groups: gluers (exposed) and mechanical shop mechanists (controls). A range of exposure levels are provided based on activities conducted by gluers. "The highest concentrations of dichloroethane (0.08 - 0.158 mg/L) occurred when the rubber sheets were coated with glue. These concentrations were maintained for only 5-6 min; they subsequently decreased to 0.062 - 0.082 mg/L as the glue dried, and at the end of the drying period 15 min later, they had decreased to 0.03 - 0.04 mg/L. The concentration of dichloroethane remains at the level of 0.05 mg/L and lower during most of the shift."
	Metric 6:	Temporality	Medium	The study reports musculoskeletal outcomes at the end of the working day after exposure, establishing temporality, though specific details about measurement of exposure and outcome timings are not provided.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Uninformative	No information on outcome measurement and diagnostic criteria is provided for changes in motor function of upper extremities or diseases of the muscles, tendons, and ganglia.
	Metric 8:	Reporting Bias	Medium	Results are reported qualitatively (changes in motor function of upper extremities), and only case numbers are reported for diseases of the muscles, tendons, and ganglia. These results would not be useful for detailed extraction.

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Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Musculoskeletal
Reported Health Effect(s):	changes in the function of the motor apparatus in the upper extremities, diseases of the muscles, tendons, and ganglia.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	There is no discussion of confounders or analysis of differing characteristics.
	Metric 10:	Covariate Characterization	N/A	No confounders were measured.
	Metric 11:	Co-exposure Counfounding	Low	There is no indication that co-exposures of concern were assessed, though the study was conducted in an occupational setting with higher potential for chemical co-exposures.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Exposure levels and common chronic disease over time are appropriately measured with a cohort design.
	Metric 13:	Statistical Power	Low	It is unclear how many study participants are included in the measures of cases throughout the plant. Additionally, n=17 workers are included in the exposed group and n=10 in the unexposed control group.
	Metric 14:	Reproducibility of Analyses	Medium	The analyses are reproducible, as the study only reports number of cases, and number of disabled days in the shop and plant. Further analyses of these case numbers were not conducted.
	Metric 15:	Statistical Analysis	N/A	No statistical modeling was conducted.

Additional Comments: Occupational study of aircraft plant workers exposed to dichloroethane via air. Study reports number of cases of muscle, tendon, and ganglia disease and provides qualitative information on decreased motor function of upper extremities. Statistical analyses and comparisons are not provided for outcomes and only case numbers are reported, limiting the informativeness of the study. Study refers only to dichloroethane, thus, 1,1 and 1,2 dichloroethane cannot be separated in this review. Both chemicals have been included in evaluations.

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	liver and gall bladder diseases.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Occupational cohort study in Russian aircraft manufacturing plant. The study focuses on the soft tank shop. The participation of all workers in the aircraft plant shops (including the soft tank shop and controls from the mechanical shop) is implied, however numbers of eligible participants and the total number of included participants across analyses are not reported. 17 gluers represented the exposed and were compared to 10 mechanical shop machinists.
	Metric 2:	Attrition	Medium	Rates of attrition cannot be determined based on the limited information provided. The study solely reports those included in assessment of changes in the functions of motor apparatus in upper extremities, but not of liver disease.
	Metric 3:	Comparison Group	Uninformative	Solely case numbers are reported for liver and gall bladder disease. Case numbers among those unexposed are not clear.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Authors report quantitative measures of dichloroethane in air, but do not provide any information on the method used to quantify exposure levels.
	Metric 5:	Exposure Levels	Uninformative	Liver and gall bladder disease are reported as case numbers only, with no indication of likely exposure.
	Metric 6:	Temporality	Low	Temporality is unclear, as limited information is provided about the measurement of exposure and outcome.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Uninformative	No information on outcome measurement and diagnostic criteria is provided for liver and gall bladder diseases.
	Metric 8:	Reporting Bias	Medium	Only case numbers are reported for liver and gall bladder disease with no information about their relationship to exposure. These results would not be useful for detailed extraction.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	There is no discussion of confounders or analysis of differing characteristics.
	Metric 10:	Covariate Characterization	N/A	No confounders were measured.
	Metric 11:	Co-exposure Counfounding	Low	There is no indication that co-exposures of concern were assessed, though the study was conducted in an occupational setting with higher potential for chemical co-exposures.
Domain 5: Analysis				

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Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	liver and gall bladder diseases.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Exposure levels and common chronic disease over time are appropriately measured with a cohort design.
	Metric 13:	Statistical Power	Low	It is unclear how many study participants are included in the measures of cases throughout the plant.
	Metric 14:	Reproducibility of Analyses	Medium	The analyses are reproducible, as the study only reports number of cases, and number of disabled days per 100 workers. Further analyses of these case numbers were not conducted.
	Metric 15:	Statistical Analysis	N/A	No statistical modeling was conducted.

Additional Comments: Occupational study of aircraft plant workers exposed to dichloroethane via air. Study reports number of cases of liver and gall bladder diseases. Statistical analyses and comparisons are not provided for outcomes and only case numbers are reported, limiting the informativeness of the study. Study refers only to dichloroethane, thus, 1,1 and 1,2 dichloroethane cannot be separated in this review. Both chemicals have been included in evaluations.

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Gastrointestinal
Reported Health Effect(s):	acute gastrointestinal diseases, acute gastritis, and chronic gastritis.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Occupational cohort study in Russian aircraft manufacturing plant. The study focuses on the soft tank shop. The participation of all workers in the aircraft plant shops (including the soft tank shop and controls from the mechanical shop) is implied, however numbers of eligible participants and the total number of included participants across analyses are not reported. 17 gluers represented the exposed and were compared to 10 mechanical shop machinists.
	Metric 2:	Attrition	Medium	Rates of attrition cannot be determined based on the limited information provided. The study solely reports those included in assessment of changes in the functions of motor apparatus in upper extremities, but not of gastrointestinal outcomes.
	Metric 3:	Comparison Group	Low	Case numbers per 100 workers are reported for those exposed (working in the shop) and those unexposed (working in the plant) for acute gastrointestinal diseases. Solely case numbers per 100 workers are reported for other gastrointestinal outcomes (acute and chronic gastritis, acute gastrointestinal diseases).
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Authors report quantitative measures of dichloroethane in air, but do not provide any information on the method used to quantify exposure levels.
	Metric 5:	Exposure Levels	Uninformative	No description is provided on the levels or range of exposure for those in the shop compared to the plant. The exposure difference between groups is unclear.
	Metric 6:	Temporality	Low	Temporality is unclear, as limited information is provided about the measurement of exposure and outcome.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Uninformative	No information on outcome measurement and diagnostic criteria is provided for gastrointestinal outcomes.
	Metric 8:	Reporting Bias	Medium	Case numbers are reported for gastrointestinal outcomes for the shop and the plant, but there is no clear information about their relationship to exposure levels. These results would not be useful for detailed extraction.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	There is no discussion of confounders or analysis of differing characteristics.
	Metric 10:	Covariate Characterization	N/A	No confounders were measured.
	Metric 11:	Co-exposure Counfounding	Low	There is no indication that co-exposures of concern were assessed, though the study was conducted in an occupational setting with higher potential for chemical co-exposures.
Domain 5: Analysis				

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Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Gastrointestinal
Reported Health Effect(s):	acute gastrointestinal diseases, acute gastritis, and chronic gastritis.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Exposure levels and common chronic disease over time are appropriately measured with a cohort design.
	Metric 13:	Statistical Power	Low	It is unclear how many study participants are included in the measures of cases throughout the plant.
	Metric 14:	Reproducibility of Analyses	Medium	The analyses are reproducible, as the study only reports number of cases and number of disabled days per 100 workers. Further analyses of these case numbers were not conducted.
	Metric 15:	Statistical Analysis	N/A	No statistical modeling was conducted.

Additional Comments: Occupational study of aircraft plant workers exposed to dichloroethane via air. Study reports number of cases of gastrointestinal diseases per 100 workers in the plant and in the shop (likely exposed). No information is provided on the dichloroethane levels in the plant. Statistical analyses and comparisons are not provided for outcomes and only case numbers are reported, limiting the informativeness of the study. Study refers only to dichloroethane, thus, 1,1 and 1,2 dichloroethane cannot be separated in this review. Both chemicals have been included in evaluations.

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Morbidity
Reported Health Effect(s):	Overall morbidity, and other diseases.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Occupational cohort study in Russian aircraft manufacturing plant. The study focuses on the soft tank shop. The participation of all workers in the aircraft plant shops (including the soft tank shop and controls from the mechanical shop) is implied, however numbers of eligible participants and the total number of included participants across analyses are not reported. 17 gluers represented the exposed and were compared to 10 mechanical shop machinists.
	Metric 2:	Attrition	Medium	Rates of attrition cannot be determined based on the limited information provided. The study solely reports those included in assessment of changes in the functions of motor apparatus in upper extremities, but not of other diseases/overall morbidity.
	Metric 3:	Comparison Group	Low	Case numbers per 100 workers are reported for those exposed (working in the shop) and those unexposed (working in the plant) for overall morbidity and other diseases.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Authors report quantitative measures of dichloroethane in air, but do not provide any information on the method used to quantify exposure levels.
	Metric 5:	Exposure Levels	Uninformative	No description is provided on the levels or range of exposure for those in the shop compared to the plant. The exposure difference between groups is unclear.
	Metric 6:	Temporality	Low	Temporality is unclear, as limited information is provided about the measurement of exposure and outcome.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Uninformative	No information on outcome measurement and diagnostic criteria is provided for overall morbidity or other diseases.
	Metric 8:	Reporting Bias	Medium	Case numbers are reported for overall morbidity and other diseases for the shop and the plant, but there is no clear information about their relationship to exposure levels. These results would not be useful for detailed extraction.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	There is no discussion of confounders or analysis of differing characteristics.
	Metric 10:	Covariate Characterization	N/A	No confounders measured.
	Metric 11:	Co-exposure Counfounding	Low	There is no indication that co-exposures of concern were assessed, though the study was conducted in an occupational setting with higher potential for chemical co-exposures.
Domain 5: Analysis				

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Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Morbidity
Reported Health Effect(s):	Overall morbidity, and other diseases.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Exposure levels and common chronic disease over time are appropriately measured with a cohort design.
	Metric 13:	Statistical Power	Low	It is unclear how many study participants are included in the measures of cases throughout the plant.
	Metric 14:	Reproducibility of Analyses	Medium	The analyses are reproducible, as the study only reports number of cases and number of disabled days per 100 workers. Further analyses of these case numbers were not conducted.
	Metric 15:	Statistical Analysis	N/A	No statistical modeling was conducted.

Additional Comments: Occupational study of aircraft plant workers exposed to dichloroethane via air. Study reports number of cases of overall morbidity and "other diseases" per 100 workers in the plant (no or lower exposure) and in the shop (likely exposed). No information is provided on the dichloroethane levels in the plant. Statistical analyses and comparisons are not provided for outcomes and only case numbers are reported, limiting the informativeness of the study. Study refers only to dichloroethane, thus, 1,1 and 1,2 dichloroethane cannot be separated in this review. Both chemicals have been included in evaluations.

Overall Quality Determination **Uninformative**

* No biomarkers were identified for this evaluation.

Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	visual-motor reaction (simple, complex), changes in the function of the motor apparatus in the upper extremities, neuritis and radiculitis, diseases of the muscles, tendons, and ganglia.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Occupational cohort study in Russian aircraft manufacturing plant. The study focuses on the soft tank shop. The participation of all workers in the aircraft plant shops (including the soft tank shop and controls from the mechanical shop) is implied, however numbers of eligible participants and the total number of included participants across analyses are not reported. 17 gluers represented the exposed and were compared to 10 mechanical shop machinists.
	Metric 2:	Attrition	Medium	Rates of attrition cannot be determined based on the limited information provided. The study solely reports those included in analyses of visual-motor function and changes in the functions of motor apparatus in upper extremities.
	Metric 3:	Comparison Group	Low	Mechanical shop machinists (n=10) served as the controls. Though the controls were also workers in the same plant as those exposed, the dichloroethane levels in air in the mechanical shop are not provided; thus, the similarity between cases and controls is not clear. Additionally, authors note that controls did not perform work that strained the hands, which is distinct from the gluers (exposed).
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Authors report quantitative measures of dichloroethane in air, but do not provide any information on the method used to quantify exposure levels.
	Metric 5:	Exposure Levels	Low	Neurological health outcomes are reported for two groups: gluers (exposed) and mechanical shop mechanists (controls). A range of exposure levels are provided based on activities conducted by gluers. "The highest concentrations of dichloroethane (0.08 - 0.158 mg/L) occurred when the rubber sheets were coated with glue. These concentrations were maintained for only 5-6 min; they subsequently decreased to 0.062 - 0.082 mg/L as the glue dried, and at the end of the drying period 15 min later, they had decreased to 0.03 - 0.04 mg/L. The concentration of dichloroethane remains at the level of 0.05 mg/L and lower during most of the shift."
	Metric 6:	Temporality	Medium	The study reports visual-motor reaction at the end of the working day after exposure, establishing temporality, though it is unclear if exposure fell during relevant exposure windows for neuritis and radiculitis.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Uninformative	No information on outcome measurement and diagnostic criteria is provided for visual-motor reaction, neuritis, radiculitis, or changes in motor function of upper extremities.
	Metric 8:	Reporting Bias	Medium	Results are reported for visual-motor reactions (occurrence of errors for exposed and unexposed), but results for other outcomes are reported qualitatively (changes in motor function of upper extremities), and only case numbers are reported for neuritis and radiculitis. These results would not be useful for detailed extraction.

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Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	visual-motor reaction (simple, complex), changes in the function of the motor apparatus in the upper extremities, neuritis and radiculitis, diseases of the muscles, tendons, and ganglia.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	There is no discussion of confounders or analysis of differing characteristics.
	Metric 10:	Covariate Characterization	N/A	No confounders were measured.
	Metric 11:	Co-exposure Counfounding	Low	There is no indication that co-exposures of concern were assessed, though the study was conducted in an occupational setting with higher potential for chemical co-exposures.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Exposure levels and common chronic disease over time are appropriately measured with a cohort design.
	Metric 13:	Statistical Power	Low	It is unclear how many study participants are included in the measures of cases throughout the plant. Additionally, n=17 workers are included in the exposed group and n=10 in the unexposed control group.
	Metric 14:	Reproducibility of Analyses	Medium	The analyses are reproducible, as the study only reports number of cases, and number of disabled days in the shop and plant. Further analyses of these case numbers were not conducted.
	Metric 15:	Statistical Analysis	N/A	No statistical modeling was conducted.

Additional Comments: Occupational study of aircraft plant workers exposed to dichloroethane via air. Study reports number of cases of a variety of neurological conditions and provides one crude comparison of prevalence of visual-motor reaction impairment with a control group. Otherwise, statistical analyses and comparisons are not provided for outcomes and only case numbers are reported, limiting the informativeness of the study. Study refers only to dichloroethane, thus, 1,1 and 1,2 dichloroethane cannot be separated in this review. Both chemicals have been included in evaluations.

Overall Quality Determination — Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Musculoskeletal
Reported Health Effect(s):	changes in the function of the motor apparatus in the upper extremities, diseases of the muscles, tendons, and ganglia.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Occupational cohort study in Russian aircraft manufacturing plant. The study focuses on the soft tank shop. The participation of all workers in the aircraft plant shops (including the soft tank shop and controls from the mechanical shop) is implied, however numbers of eligible participants and the total number of included participants across analyses are not reported. 17 gluers represented the exposed and were compared to 10 mechanical shop machinists.
	Metric 2:	Attrition	Medium	Rates of attrition cannot be determined based on the limited information provided. The study solely reports those included in assessment of changes in the functions of motor apparatus in upper extremities.
	Metric 3:	Comparison Group	Low	Mechanical shop machinists (n=10) served as the controls. Though the controls were also workers in the same plant as those exposed, the dichloroethane levels in air in the mechanical shop are not provided; thus, the similarity between cases and controls is not clear. Additionally, authors note that controls did not perform work that strained the hands, which is distinct from the gluers (exposed).
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Authors report quantitative measures of dichloroethane in air, but do not provide any information on the method used to quantify exposure levels.
	Metric 5:	Exposure Levels	Low	Musculoskeletal health outcomes are reported for two groups: gluers (exposed) and mechanical shop mechanists (controls). A range of exposure levels are provided based on activities conducted by gluers. "The highest concentrations of dichloroethane (0.08 - 0.158 mg/L) occurred when the rubber sheets were coated with glue. These concentrations were maintained for only 5-6 min; they subsequently decreased to 0.062 - 0.082 mg/L as the glue dried, and at the end of the drying period 15 min later, they had decreased to 0.03 - 0.04 mg/L. The concentration of dichloroethane remains at the level of 0.05 mg/L and lower during most of the shift."
	Metric 6:	Temporality	Medium	The study reports musculoskeletal outcomes at the end of the working day after exposure, establishing temporality, though specific details about measurement of exposure and outcome timings are not provided.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Uninformative	No information on outcome measurement and diagnostic criteria is provided for changes in motor function of upper extremities or diseases of the muscles, tendons, and ganglia.
	Metric 8:	Reporting Bias	Medium	Results are reported qualitatively (changes in motor function of upper extremities), and only case numbers are reported for diseases of the muscles, tendons, and ganglia. These results would not be useful for detailed extraction.

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Study Citation: Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s): Musculoskeletal
Reported Health Effect(s): changes in the function of the motor apparatus in the upper extremities, diseases of the muscles, tendons, and ganglia.
Chemical: 1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s): No linked references.
HERO ID: 18135

Domain	Metric		Rating	Comments
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	There is no discussion of confounders or analysis of differing characteristics.
	Metric 10:	Covariate Characterization	N/A	No confounders were measured.
	Metric 11:	Co-exposure Counfounding	Low	There is no indication that co-exposures of concern were assessed, though the study was conducted in an occupational setting with higher potential for chemical co-exposures.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Exposure levels and common chronic disease over time are appropriately measured with a cohort design.
	Metric 13:	Statistical Power	Low	It is unclear how many study participants are included in the measures of cases throughout the plant. Additionally, n=17 workers are included in the exposed group and n=10 in the unexposed control group.
	Metric 14:	Reproducibility of Analyses	Medium	The analyses are reproducible, as the study only reports number of cases, and number of disabled days in the shop and plant. Further analyses of these case numbers were not conducted.
	Metric 15:	Statistical Analysis	N/A	No statistical modeling was conducted.

Additional Comments: Occupational study of aircraft plant workers exposed to dichloroethane via air. Study reports number of cases of muscle, tendon, and ganglia disease and provides qualitative information on decreased motor function of upper extremities. Statistical analyses and comparisons are not provided for outcomes and only case numbers are reported, limiting the informativeness of the study. Study refers only to dichloroethane, thus, 1,1 and 1,2 dichloroethane cannot be separated in this review. Both chemicals have been included in evaluations.

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	liver and gall bladder diseases.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Occupational cohort study in Russian aircraft manufacturing plant. The study focuses on the soft tank shop. The participation of all workers in the aircraft plant shops (including the soft tank shop and controls from the mechanical shop) is implied, however numbers of eligible participants and the total number of included participants across analyses are not reported. 17 gluers represented the exposed and were compared to 10 mechanical shop machinists.
	Metric 2:	Attrition	Medium	Rates of attrition cannot be determined based on the limited information provided. The study solely reports those included in assessment of changes in the functions of motor apparatus in upper extremities, but not of liver disease.
	Metric 3:	Comparison Group	Uninformative	Solely case numbers are reported for liver and gall bladder disease. Case numbers among those unexposed are not clear.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Authors report quantitative measures of dichloroethane in air, but do not provide any information on the method used to quantify exposure levels.
	Metric 5:	Exposure Levels	Uninformative	Liver and gall bladder disease are reported as case numbers only, with no indication of likely exposure.
	Metric 6:	Temporality	Low	Temporality is unclear, as limited information is provided about the measurement of exposure and outcome.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Uninformative	No information on outcome measurement and diagnostic criteria is provided for liver and gall bladder diseases.
	Metric 8:	Reporting Bias	Medium	Only case numbers are reported for liver and gall bladder disease with no information about their relationship to exposure. These results would not be useful for detailed extraction.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	There is no discussion of confounders or analysis of differing characteristics.
	Metric 10:	Covariate Characterization	N/A	No confounders were measured.
	Metric 11:	Co-exposure Counfounding	Low	There is no indication that co-exposures of concern were assessed, though the study was conducted in an occupational setting with higher potential for chemical co-exposures.
Domain 5: Analysis				

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Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	liver and gall bladder diseases.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Exposure levels and common chronic disease over time are appropriately measured with a cohort design.
	Metric 13:	Statistical Power	Low	It is unclear how many study participants are included in the measures of cases throughout the plant.
	Metric 14:	Reproducibility of Analyses	Medium	The analyses are reproducible, as the study only reports number of cases, and number of disabled days per 100 workers. Further analyses of these case numbers were not conducted.
	Metric 15:	Statistical Analysis	N/A	No statistical modeling was conducted.

Additional Comments: Occupational study of aircraft plant workers exposed to dichloroethane via air. Study reports number of cases of liver and gall bladder diseases. Statistical analyses and comparisons are not provided for outcomes and only case numbers are reported, limiting the informativeness of the study. Study refers only to dichloroethane, thus, 1,1 and 1,2 dichloroethane cannot be separated in this review. Both chemicals have been included in evaluations.

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Gastrointestinal
Reported Health Effect(s):	acute gastrointestinal diseases, acute gastritis, and chronic gastritis.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Occupational cohort study in Russian aircraft manufacturing plant. The study focuses on the soft tank shop. The participation of all workers in the aircraft plant shops (including the soft tank shop and controls from the mechanical shop) is implied, however numbers of eligible participants and the total number of included participants across analyses are not reported. 17 gluers represented the exposed and were compared to 10 mechanical shop machinists.
	Metric 2:	Attrition	Medium	Rates of attrition cannot be determined based on the limited information provided. The study solely reports those included in assessment of changes in the functions of motor apparatus in upper extremities, but not of gastrointestinal outcomes.
	Metric 3:	Comparison Group	Low	Case numbers per 100 workers are reported for those exposed (working in the shop) and those unexposed (working in the plant) for acute gastrointestinal diseases. Solely case numbers per 100 workers are reported for other gastrointestinal outcomes (acute and chronic gastritis, acute gastrointestinal diseases).
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Authors report quantitative measures of dichloroethane in air, but do not provide any information on the method used to quantify exposure levels.
	Metric 5:	Exposure Levels	Uninformative	No description is provided on the levels or range of exposure for those in the shop compared to the plant. The exposure difference between groups is unclear.
	Metric 6:	Temporality	Low	Temporality is unclear, as limited information is provided about the measurement of exposure and outcome.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Uninformative	No information on outcome measurement and diagnostic criteria is provided for gastrointestinal outcomes.
	Metric 8:	Reporting Bias	Medium	Case numbers are reported for gastrointestinal outcomes for the shop and the plant, but there is no clear information about their relationship to exposure levels. These results would not be useful for detailed extraction.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	There is no discussion of confounders or analysis of differing characteristics.
	Metric 10:	Covariate Characterization	N/A	No confounders measured.
	Metric 11:	Co-exposure Counfounding	Low	There is no indication that co-exposures of concern were assessed, though the study was conducted in an occupational setting with higher potential for chemical co-exposures.
Domain 5: Analysis				

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Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Gastrointestinal
Reported Health Effect(s):	acute gastrointestinal diseases, acute gastritis, and chronic gastritis.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Exposure levels and common chronic disease over time are appropriately measured with a cohort design.
	Metric 13:	Statistical Power	Low	It is unclear how many study participants are included in the measures of cases throughout the plant.
	Metric 14:	Reproducibility of Analyses	Medium	The analyses are reproducible, as the study only reports number of cases and number of disabled days per 100 workers. Further analyses of these case numbers were not conducted.
	Metric 15:	Statistical Analysis	N/A	No statistical modeling was conducted.

Additional Comments: Occupational study of aircraft plant workers exposed to dichloroethane via air. Study reports number of cases of gastrointestinal diseases per 100 workers in the plant and in the shop (likely exposed). No information is provided on the dichloroethane levels in the plant. Statistical analyses and comparisons are not provided for outcomes and only case numbers are reported, limiting the informativeness of the study. Study refers only to dichloroethane, thus, 1,1 and 1,2 dichloroethane cannot be separated in this review. Both chemicals have been included in evaluations.

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Morbidity
Reported Health Effect(s):	Overall morbidity, and other diseases.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Occupational cohort study in Russian aircraft manufacturing plant. The study focuses on the soft tank shop. The participation of all workers in the aircraft plant shops (including the soft tank shop and controls from the mechanical shop) is implied, however numbers of eligible participants and the total number of included participants across analyses are not reported. 17 gluers represented the exposed and were compared to 10 mechanical shop machinists.
	Metric 2:	Attrition	Medium	Rates of attrition cannot be determined based on the limited information provided. The study solely reports those included in assessment of changes in the functions of motor apparatus in upper extremities, but not of other diseases/overall morbidity.
	Metric 3:	Comparison Group	Low	Case numbers per 100 workers are reported for those exposed (working in the shop) and those unexposed (working in the plant) for overall morbidity and other diseases.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Authors report quantitative measures of dichloroethane in air, but do not provide any information on the method used to quantify exposure levels.
	Metric 5:	Exposure Levels	Uninformative	No description is provided on the levels or range of exposure for those in the shop compared to the plant. The exposure difference between groups is unclear.
	Metric 6:	Temporality	Low	Temporality is unclear, as limited information is provided about the measurement of exposure and outcome.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Uninformative	No information on outcome measurement and diagnostic criteria is provided for overall morbidity or other diseases.
	Metric 8:	Reporting Bias	Medium	Case numbers are reported for overall morbidity and other diseases for the shop and the plant, but there is no clear information about their relationship to exposure levels. These results would not be useful for detailed extraction.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	There is no discussion of confounders or analysis of differing characteristics.
	Metric 10:	Covariate Characterization	N/A	No confounders were measured.
	Metric 11:	Co-exposure Counfounding	Low	There is no indication that co-exposures of concern were assessed, though the study was conducted in an occupational setting with higher potential for chemical co-exposures.
Domain 5: Analysis				

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Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Morbidity
Reported Health Effect(s):	Overall morbidity, and other diseases.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Exposure levels and common chronic disease over time are appropriately measured with a cohort design.
	Metric 13:	Statistical Power	Low	It is unclear how many study participants are included in the measures of cases throughout the plant.
	Metric 14:	Reproducibility of Analyses	Medium	The analyses are reproducible, as the study only reports number of cases and number of disabled days per 100 workers. Further analyses of these case numbers were not conducted.
	Metric 15:	Statistical Analysis	N/A	No statistical modeling was conducted.

Additional Comments: Occupational study of aircraft plant workers exposed to dichloroethane via air. Study reports number of cases of overall morbidity and "other diseases" per 100 workers in the plant (no or lower exposure) and in the shop (likely exposed). No information is provided on the dichloroethane levels in the plant. Statistical analyses and comparisons are not provided for outcomes and only case numbers are reported, limiting the informativeness of the study. Study refers only to dichloroethane, thus, 1,1 and 1,2 dichloroethane cannot be separated in this review. Both chemicals have been included in evaluations.

Overall Quality Determination **Uninformative**

* No biomarkers were identified for this evaluation.

Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	visual-motor reaction (simple, complex), changes in the function of the motor apparatus in the upper extremities, neuritis and radiculitis, diseases of the muscles, tendons, and ganglia.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Occupational cohort study in Russian aircraft manufacturing plant. The study focuses on the soft tank shop. The participation of all workers in the aircraft plant shops (including the soft tank shop and controls from the mechanical shop) is implied, however numbers of eligible participants and the total number of included participants across analyses are not reported. 17 gluers represented the exposed and were compared to 10 mechanical shop machinists.
	Metric 2:	Attrition	Medium	Rates of attrition cannot be determined based on the limited information provided. The study solely reports those included in analyses of visual-motor function and changes in the functions of motor apparatus in upper extremities.
	Metric 3:	Comparison Group	Low	Mechanical shop machinists (n=10) served as the controls. Though the controls were also workers in the same plant as those exposed, the dichloroethane levels in air in the mechanical shop are not provided; thus, the similarity between cases and controls is not clear. Additionally, authors note that controls did not perform work that strained the hands, which is distinct from the gluers (exposed).
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Authors report quantitative measures of dichloroethane in air, but do not provide any information on the method used to quantify exposure levels.
	Metric 5:	Exposure Levels	Low	Neurological health outcomes are reported for two groups: gluers (exposed) and mechanical shop mechanists (controls). A range of exposure levels are provided based on activities conducted by gluers. "The highest concentrations of dichloroethane (0.08 - 0.158 mg/L) occurred when the rubber sheets were coated with glue. These concentrations were maintained for only 5-6 min; they subsequently decreased to 0.062 - 0.082 mg/L as the glue dried, and at the end of the drying period 15 min later, they had decreased to 0.03 - 0.04 mg/L. The concentration of dichloroethane remains at the level of 0.05 mg/L and lower during most of the shift."
	Metric 6:	Temporality	Medium	The study reports visual-motor reaction at the end of the working day after exposure, establishing temporality, though it is unclear if exposure fell during relevant exposure windows for neuritis and radiculitis.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Uninformative	No information on outcome measurement and diagnostic criteria is provided for visual-motor reaction, neuritis, radiculitis, or changes in motor function of upper extremities.

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Study Citation: Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s): Neurological/Behavioral
Reported Health Effect(s): visual-motor reaction (simple, complex), changes in the function of the motor apparatus in the upper extremities, neuritis and radiculitis, diseases of the muscles, tendons, and ganglia.
Chemical: 1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s): No linked references.
HERO ID: 18135

Domain	Metric		Rating	Comments
	Metric 8:	Reporting Bias	Medium	Results are reported for visual-motor reactions (occurrence of errors for exposed and unexposed), but results for other outcomes are reported qualitatively (changes in motor function of upper extremities), and only case numbers are reported for neuritis and radiculitis. These results would not be useful for detailed extraction.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	There is no discussion of confounders or analysis of differing characteristics.
	Metric 10:	Covariate Characterization	N/A	No confounders were measured.
	Metric 11:	Co-exposure Counfounding	Low	There is no indication that co-exposures of concern were assessed, though the study was conducted in an occupational setting with higher potential for chemical co-exposures.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Exposure levels and common chronic disease over time are appropriately measured with a cohort design.
	Metric 13:	Statistical Power	Low	It is unclear how many study participants are included in the measures of cases throughout the plant. Additionally, n=17 workers are included in the exposed group and n=10 in the unexposed control group.
	Metric 14:	Reproducibility of Analyses	Medium	The analyses are reproducible, as the study only reports number of cases, and number of disabled days in the shop and plant. Further analyses of these case numbers were not conducted.
	Metric 15:	Statistical Analysis	N/A	No statistical modeling was conducted.

Additional Comments: Occupational study of aircraft plant workers exposed to dichloroethane via air. Study reports number of cases of a variety of neurological conditions and provides one crude comparison of prevalence of visual-motor reaction impairment with a control group. Otherwise, statistical analyses and comparisons are not provided for outcomes and only case numbers are reported, limiting the informativeness of the study. Study refers only to dichloroethane, thus, 1,1 and 1,2 dichloroethane cannot be separated in this review. Both chemicals have been included in evaluations.

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Musculoskeletal
Reported Health Effect(s):	changes in the function of the motor apparatus in the upper extremities, diseases of the muscles, tendons, and ganglia.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Occupational cohort study in Russian aircraft manufacturing plant. The study focuses on the soft tank shop. The participation of all workers in the aircraft plant shops (including the soft tank shop and controls from the mechanical shop) is implied, however numbers of eligible participants and the total number of included participants across analyses are not reported. 17 gluers represented the exposed and were compared to 10 mechanical shop machinists.
	Metric 2:	Attrition	Medium	Rates of attrition cannot be determined based on the limited information provided. The study solely reports those included in assessment of changes in the functions of motor apparatus in upper extremities.
	Metric 3:	Comparison Group	Low	Mechanical shop machinists (n=10) served as the controls. Though the controls were also workers in the same plant as those exposed, the dichloroethane levels in air in the mechanical shop are not provided; thus, the similarity between cases and controls is not clear. Additionally, authors note that controls did not perform work that strained the hands, which is distinct from the gluers (exposed).
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Authors report quantitative measures of dichloroethane in air, but do not provide any information on the method used to quantify exposure levels.
	Metric 5:	Exposure Levels	Low	Musculoskeletal health outcomes are reported for two groups: gluers (exposed) and mechanical shop mechanists (controls). A range of exposure levels are provided based on activities conducted by gluers. "The highest concentrations of dichloroethane (0.08 - 0.158 mg/L) occurred when the rubber sheets were coated with glue. These concentrations were maintained for only 5-6 min; they subsequently decreased to 0.062 - 0.082 mg/L as the glue dried, and at the end of the drying period 15 min later, they had decreased to 0.03 - 0.04 mg/L. The concentration of dichloroethane remains at the level of 0.05 mg/L and lower during most of the shift."
	Metric 6:	Temporality	Medium	The study reports musculoskeletal outcomes at the end of the working day after exposure, establishing temporality, though specific details about measurement of exposure and outcome timings are not provided.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Uninformative	No information on outcome measurement and diagnostic criteria is provided for changes in motor function of upper extremities or diseases of the muscles, tendons, and ganglia.
	Metric 8:	Reporting Bias	Medium	Results are reported qualitatively (changes in motor function of upper extremities), and only case numbers are reported for diseases of the muscles, tendons, and ganglia. These results would not be useful for detailed extraction.

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Study Citation: Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s): Musculoskeletal
Reported Health Effect(s): changes in the function of the motor apparatus in the upper extremities, diseases of the muscles, tendons, and ganglia.
Chemical: 1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s): No linked references.
HERO ID: 18135

Domain	Metric		Rating	Comments
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	There is no discussion of confounders or analysis of differing characteristics.
	Metric 10:	Covariate Characterization	N/A	No confounders were measured.
	Metric 11:	Co-exposure Counfounding	Low	There is no indication that co-exposures of concern were assessed, though the study was conducted in an occupational setting with higher potential for chemical co-exposures.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Exposure levels and common chronic disease over time are appropriately measured with a cohort design.
	Metric 13:	Statistical Power	Low	It is unclear how many study participants are included in the measures of cases throughout the plant. Additionally, n=17 workers are included in the exposed group and n=10 in the unexposed control group.
	Metric 14:	Reproducibility of Analyses	Medium	The analyses are reproducible, as the study only reports number of cases, and number of disabled days in the shop and plant. Further analyses of these case numbers were not conducted.
	Metric 15:	Statistical Analysis	N/A	No statistical modeling was conducted.

Additional Comments: Occupational study of aircraft plant workers exposed to dichloroethane via air. Study reports number of cases of muscle, tendon, and ganglia disease and provides qualitative information on decreased motor function of upper extremities. Statistical analyses and comparisons are not provided for outcomes and only case numbers are reported, limiting the informativeness of the study. Study refers only to dichloroethane, thus, 1,1 and 1,2 dichloroethane cannot be separated in this review. Both chemicals have been included in evaluations.

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	liver and gall bladder diseases.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Occupational cohort study in Russian aircraft manufacturing plant. The study focuses on the soft tank shop. The participation of all workers in the aircraft plant shops (including the soft tank shop and controls from the mechanical shop) is implied, however numbers of eligible participants and the total number of included participants across analyses are not reported. 17 gluers represented the exposed and were compared to 10 mechanical shop machinists.
	Metric 2:	Attrition	Medium	Rates of attrition cannot be determined based on the limited information provided. The study solely reports those included in assessment of changes in the functions of motor apparatus in upper extremities, but not of liver disease.
	Metric 3:	Comparison Group	Uninformative	Solely case numbers are reported for liver and gall bladder disease. Case numbers among those unexposed are not clear.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Authors report quantitative measures of dichloroethane in air, but do not provide any information on the method used to quantify exposure levels.
	Metric 5:	Exposure Levels	Uninformative	Liver and gall bladder disease are reported as case numbers only, with no indication of likely exposure.
	Metric 6:	Temporality	Low	Temporality is unclear, as limited information is provided about the measurement of exposure and outcome.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Uninformative	No information on outcome measurement and diagnostic criteria is provided for liver and gall bladder diseases.
	Metric 8:	Reporting Bias	Medium	Only case numbers are reported for liver and gall bladder disease with no information about their relationship to exposure. These results would not be useful for detailed extraction.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	There is no discussion of confounders or analysis of differing characteristics.
	Metric 10:	Covariate Characterization	N/A	No confounders were measured.
	Metric 11:	Co-exposure Counfounding	Low	There is no indication that co-exposures of concern were assessed, though the study was conducted in an occupational setting with higher potential for chemical co-exposures.
Domain 5: Analysis				

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Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	liver and gall bladder diseases.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Exposure levels and common chronic disease over time are appropriately measured with a cohort design.
	Metric 13:	Statistical Power	Low	It is unclear how many study participants are included in the measures of cases throughout the plant.
	Metric 14:	Reproducibility of Analyses	Medium	The analyses are reproducible, as the study only reports number of cases, and number of disabled days per 100 workers. Further analyses of these case numbers were not conducted.
	Metric 15:	Statistical Analysis	N/A	No statistical modeling was conducted.

Additional Comments: Occupational study of aircraft plant workers exposed to dichloroethane via air. Study reports number of cases of liver and gall bladder diseases. Statistical analyses and comparisons are not provided for outcomes and only case numbers are reported, limiting the informativeness of the study. Study refers only to dichloroethane, thus, 1,1 and 1,2 dichloroethane cannot be separated in this review. Both chemicals have been included in evaluations.

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Gastrointestinal
Reported Health Effect(s):	acute gastrointestinal diseases, acute gastritis, and chronic gastritis.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Occupational cohort study in Russian aircraft manufacturing plant. The study focuses on the soft tank shop. The participation of all workers in the aircraft plant shops (including the soft tank shop and controls from the mechanical shop) is implied, however numbers of eligible participants and the total number of included participants across analyses are not reported. 17 gluers represented the exposed and were compared to 10 mechanical shop machinists.
	Metric 2:	Attrition	Medium	Rates of attrition cannot be determined based on the limited information provided. The study solely reports those included in assessment of changes in the functions of motor apparatus in upper extremities, but not of gastrointestinal outcomes.
	Metric 3:	Comparison Group	Low	Case numbers per 100 workers are reported for those exposed (working in the shop) and those unexposed (working in the plant) for acute gastrointestinal diseases. Solely case numbers per 100 workers are reported for other gastrointestinal outcomes (acute and chronic gastritis, acute gastrointestinal diseases).
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Authors report quantitative measures of dichloroethane in air, but do not provide any information on the method used to quantify exposure levels.
	Metric 5:	Exposure Levels	Uninformative	No description is provided on the levels or range of exposure for those in the shop compared to the plant. The exposure difference between groups is unclear.
	Metric 6:	Temporality	Low	Temporality is unclear, as limited information is provided about the measurement of exposure and outcome.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Uninformative	No information on outcome measurement and diagnostic criteria is provided for gastrointestinal outcomes.
	Metric 8:	Reporting Bias	Medium	Case numbers are reported for gastrointestinal outcomes for the shop and the plant, but there is no clear information about their relationship to exposure levels. These results would not be useful for detailed extraction.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	There is no discussion of confounders or analysis of differing characteristics.
	Metric 10:	Covariate Characterization	N/A	No confounders were measured.
	Metric 11:	Co-exposure Counfounding	Low	There is no indication that co-exposures of concern were assessed, though the study was conducted in an occupational setting with higher potential for chemical co-exposures.
Domain 5: Analysis				

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Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Gastrointestinal
Reported Health Effect(s):	acute gastrointestinal diseases, acute gastritis, and chronic gastritis.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Exposure levels and common chronic disease over time are appropriately measured with a cohort design.
	Metric 13:	Statistical Power	Low	It is unclear how many study participants are included in the measures of cases throughout the plant.
	Metric 14:	Reproducibility of Analyses	Medium	The analyses are reproducible, as the study only reports number of cases and number of disabled days per 100 workers. Further analyses of these case numbers were not conducted.
	Metric 15:	Statistical Analysis	N/A	No statistical modeling was conducted.

Additional Comments: Occupational study of aircraft plant workers exposed to dichloroethane via air. Study reports number of cases of gastrointestinal diseases per 100 workers in the plant and in the shop (likely exposed). No information is provided on the dichloroethane levels in the plant. Statistical analyses and comparisons are not provided for outcomes and only case numbers are reported, limiting the informativeness of the study. Study refers only to dichloroethane, thus, 1,1 and 1,2 dichloroethane cannot be separated in this review. Both chemicals have been included in evaluations.

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Morbidity
Reported Health Effect(s):	Overall morbidity, and other diseases.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Occupational cohort study in Russian aircraft manufacturing plant. The study focuses on the soft tank shop. The participation of all workers in the aircraft plant shops (including the soft tank shop and controls from the mechanical shop) is implied, however numbers of eligible participants and the total number of included participants across analyses are not reported. 17 gluers represented the exposed and were compared to 10 mechanical shop machinists.
	Metric 2:	Attrition	Medium	Rates of attrition cannot be determined based on the limited information provided. The study solely reports those included in assessment of changes in the functions of motor apparatus in upper extremities, but not of other diseases/overall morbidity.
	Metric 3:	Comparison Group	Low	Case numbers per 100 workers are reported for those exposed (working in the shop) and those unexposed (working in the plant) for overall morbidity and other diseases.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Authors report quantitative measures of dichloroethane in air, but do not provide any information on the method used to quantify exposure levels.
	Metric 5:	Exposure Levels	Uninformative	No description is provided on the levels or range of exposure for those in the shop compared to the plant. The exposure difference between groups is unclear.
	Metric 6:	Temporality	Low	Temporality is unclear, as limited information is provided about the measurement of exposure and outcome.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Uninformative	No information on outcome measurement and diagnostic criteria is provided for overall morbidity or other diseases.
	Metric 8:	Reporting Bias	Medium	Case numbers are reported for overall morbidity and other diseases for the shop and the plant, but there is no clear information about their relationship to exposure levels. These results would not be useful for detailed extraction.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	There is no discussion of confounders or analysis of differing characteristics.
	Metric 10:	Covariate Characterization	N/A	No confounders measured.
	Metric 11:	Co-exposure Counfounding	Low	There is no indication that co-exposures of concern were assessed, though the study was conducted in an occupational setting with higher potential for chemical co-exposures.
Domain 5: Analysis				

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Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Morbidity
Reported Health Effect(s):	Overall morbidity, and other diseases.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Exposure levels and common chronic disease over time are appropriately measured with a cohort design.
	Metric 13:	Statistical Power	Low	It is unclear how many study participants are included in the measures of cases throughout the plant.
	Metric 14:	Reproducibility of Analyses	Medium	The analyses are reproducible, as the study only reports number of cases and number of disabled days per 100 workers. Further analyses of these case numbers were not conducted.
	Metric 15:	Statistical Analysis	N/A	No statistical modeling was conducted.

Additional Comments: Occupational study of aircraft plant workers exposed to dichloroethane via air. Study reports number of cases of overall morbidity and "other diseases" per 100 workers in the plant (no or lower exposure) and in the shop (likely exposed). No information is provided on the dichloroethane levels in the plant. Statistical analyses and comparisons are not provided for outcomes and only case numbers are reported, limiting the informativeness of the study. Study refers only to dichloroethane, thus, 1,1 and 1,2 dichloroethane cannot be separated in this review. Both chemicals have been included in evaluations.

Overall Quality Determination **Uninformative**

* No biomarkers were identified for this evaluation.

Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	visual-motor reaction (simple, complex), changes in the function of the motor apparatus in the upper extremities, neuritis and radiculitis, diseases of the muscles, tendons, and ganglia.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Occupational cohort study in Russian aircraft manufacturing plant. The study focuses on the soft tank shop. The participation of all workers in the aircraft plant shops (including the soft tank shop and controls from the mechanical shop) is implied, however numbers of eligible participants and the total number of included participants across analyses are not reported. 17 gluers represented the exposed and were compared to 10 mechanical shop machinists.
	Metric 2:	Attrition	Medium	Rates of attrition cannot be determined based on the limited information provided. The study solely reports those included in analyses of visual-motor function and changes in the functions of motor apparatus in upper extremities.
	Metric 3:	Comparison Group	Low	Mechanical shop machinists (n=10) served as the controls. Though the controls were also workers in the same plant as those exposed, the dichloroethane levels in air in the mechanical shop are not provided; thus, the similarity between cases and controls is not clear. Additionally, authors note that controls did not perform work that strained the hands, which is distinct from the gluers (exposed).
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Authors report quantitative measures of dichloroethane in air, but do not provide any information on the method used to quantify exposure levels.
	Metric 5:	Exposure Levels	Low	Neurological health outcomes are reported for two groups: gluers (exposed) and mechanical shop mechanists (controls). A range of exposure levels are provided based on activities conducted by gluers. "The highest concentrations of dichloroethane (0.08 - 0.158 mg/L) occurred when the rubber sheets were coated with glue. These concentrations were maintained for only 5-6 min; they subsequently decreased to 0.062 - 0.082 mg/L as the glue dried, and at the end of the drying period 15 min later, they had decreased to 0.03 - 0.04 mg/L. The concentration of dichloroethane remains at the level of 0.05 mg/L and lower during most of the shift."
	Metric 6:	Temporality	Medium	The study reports visual-motor reaction at the end of the working day after exposure, establishing temporality, though it is unclear if exposure fell during relevant exposure windows for neuritis and radiculitis.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Uninformative	No information on outcome measurement and diagnostic criteria is provided for visual-motor reaction, neuritis, radiculitis, or changes in motor function of upper extremities.
	Metric 8:	Reporting Bias	Medium	Results are reported for visual-motor reactions (occurrence of errors for exposed and unexposed), but results for other outcomes are reported qualitatively (changes in motor function of upper extremities), and only case numbers are reported for neuritis and radiculitis. These results would not be useful for detailed extraction.

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Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	visual-motor reaction (simple, complex), changes in the function of the motor apparatus in the upper extremities, neuritis and radiculitis, diseases of the muscles, tendons, and ganglia.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	There is no discussion of confounders or analysis of differing characteristics.
	Metric 10:	Covariate Characterization	N/A	No confounders were measured.
	Metric 11:	Co-exposure Counfounding	Low	There is no indication that co-exposures of concern were assessed, though the study was conducted in an occupational setting with higher potential for chemical co-exposures.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Exposure levels and common chronic disease over time are appropriately measured with a cohort design.
	Metric 13:	Statistical Power	Low	It is unclear how many study participants are included in the measures of cases throughout the plant. Additionally, n=17 workers are included in the exposed group and n=10 in the unexposed control group.
	Metric 14:	Reproducibility of Analyses	Medium	The analyses are reproducible, as the study only reports number of cases, and number of disabled days in the shop and plant. Further analyses of these case numbers were not conducted.
	Metric 15:	Statistical Analysis	N/A	No statistical modeling was conducted.

Additional Comments: Occupational study of aircraft plant workers exposed to dichloroethane via air. Study reports number of cases of a variety of neurological conditions and provides one crude comparison of prevalence of visual-motor reaction impairment with a control group. Otherwise, statistical analyses and comparisons are not provided for outcomes and only case numbers are reported, limiting the informativeness of the study. Study refers only to dichloroethane, thus, 1,1 and 1,2 dichloroethane cannot be separated in this review. Both chemicals have been included in evaluations.

Overall Quality Determination — Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Musculoskeletal
Reported Health Effect(s):	changes in the function of the motor apparatus in the upper extremities, diseases of the muscles, tendons, and ganglia.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Occupational cohort study in Russian aircraft manufacturing plant. The study focuses on the soft tank shop. The participation of all workers in the aircraft plant shops (including the soft tank shop and controls from the mechanical shop) is implied, however numbers of eligible participants and the total number of included participants across analyses are not reported. 17 gluers represented the exposed and were compared to 10 mechanical shop machinists.
	Metric 2:	Attrition	Medium	Rates of attrition cannot be determined based on the limited information provided. The study solely reports those included in assessment of changes in the functions of motor apparatus in upper extremities.
	Metric 3:	Comparison Group	Low	Mechanical shop machinists (n=10) served as the controls. Though the controls were also workers in the same plant as those exposed, the dichloroethane levels in air in the mechanical shop are not provided; thus, the similarity between cases and controls is not clear. Additionally, authors note that controls did not perform work that strained the hands, which is distinct from the gluers (exposed).
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Authors report quantitative measures of dichloroethane in air, but do not provide any information on the method used to quantify exposure levels.
	Metric 5:	Exposure Levels	Low	Musculoskeletal health outcomes are reported for two groups: gluers (exposed) and mechanical shop mechanists (controls). A range of exposure levels are provided based on activities conducted by gluers. "The highest concentrations of dichloroethane (0.08 - 0.158 mg/L) occurred when the rubber sheets were coated with glue. These concentrations were maintained for only 5-6 min; they subsequently decreased to 0.062 - 0.082 mg/L as the glue dried, and at the end of the drying period 15 min later, they had decreased to 0.03 - 0.04 mg/L. The concentration of dichloroethane remains at the level of 0.05 mg/L and lower during most of the shift."
	Metric 6:	Temporality	Medium	The study reports musculoskeletal outcomes at the end of the working day after exposure, establishing temporality, though specific details about measurement of exposure and outcome timings are not provided.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Uninformative	No information on outcome measurement and diagnostic criteria is provided for changes in motor function of upper extremities or diseases of the muscles, tendons, and ganglia.
	Metric 8:	Reporting Bias	Medium	Results are reported qualitatively (changes in motor function of upper extremities), and only case numbers are reported for diseases of the muscles, tendons, and ganglia. These results would not be useful for detailed extraction.

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Study Citation: Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s): Musculoskeletal
Reported Health Effect(s): changes in the function of the motor apparatus in the upper extremities, diseases of the muscles, tendons, and ganglia.
Chemical: 1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s): No linked references.
HERO ID: 18135

Domain	Metric		Rating	Comments
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	There is no discussion of confounders or analysis of differing characteristics.
	Metric 10:	Covariate Characterization	N/A	No confounders were measured.
	Metric 11:	Co-exposure Counfounding	Low	There is no indication that co-exposures of concern were assessed, though the study was conducted in an occupational setting with higher potential for chemical co-exposures.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Exposure levels and common chronic disease over time are appropriately measured with a cohort design.
	Metric 13:	Statistical Power	Low	It is unclear how many study participants are included in the measures of cases throughout the plant. Additionally, n=17 workers are included in the exposed group and n=10 in the unexposed control group.
	Metric 14:	Reproducibility of Analyses	Medium	The analyses are reproducible, as the study only reports number of cases, and number of disabled days in the shop and plant. Further analyses of these case numbers were not conducted.
	Metric 15:	Statistical Analysis	N/A	No statistical modeling was conducted.

Additional Comments: Occupational study of aircraft plant workers exposed to dichloroethane via air. Study reports number of cases of muscle, tendon, and ganglia disease and provides qualitative information on decreased motor function of upper extremities. Statistical analyses and comparisons are not provided for outcomes and only case numbers are reported, limiting the informativeness of the study. Study refers only to dichloroethane, thus, 1,1 and 1,2 dichloroethane cannot be separated in this review. Both chemicals have been included in evaluations.

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	liver and gall bladder diseases.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Occupational cohort study in Russian aircraft manufacturing plant. The study focuses on the soft tank shop. The participation of all workers in the aircraft plant shops (including the soft tank shop and controls from the mechanical shop) is implied, however numbers of eligible participants and the total number of included participants across analyses are not reported. 17 gluers represented the exposed and were compared to 10 mechanical shop machinists.
	Metric 2:	Attrition	Medium	Rates of attrition cannot be determined based on the limited information provided. The study solely reports those included in assessment of changes in the functions of motor apparatus in upper extremities, but not of liver disease.
	Metric 3:	Comparison Group	Uninformative	Solely case numbers are reported for liver and gall bladder disease. Case numbers among those unexposed are not clear.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Authors report quantitative measures of dichloroethane in air, but do not provide any information on the method used to quantify exposure levels.
	Metric 5:	Exposure Levels	Uninformative	Liver and gall bladder disease are reported as case numbers only, with no indication of likely exposure.
	Metric 6:	Temporality	Low	Temporality is unclear, as limited information is provided about the measurement of exposure and outcome.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Uninformative	No information on outcome measurement and diagnostic criteria is provided for liver and gall bladder diseases.
	Metric 8:	Reporting Bias	Medium	Only case numbers are reported for liver and gall bladder disease with no information about their relationship to exposure. These results would not be useful for detailed extraction.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	There is no discussion of confounders or analysis of differing characteristics.
	Metric 10:	Covariate Characterization	N/A	No confounders were measured.
	Metric 11:	Co-exposure Counfounding	Low	There is no indication that co-exposures of concern were assessed, though the study was conducted in an occupational setting with higher potential for chemical co-exposures.
Domain 5: Analysis				

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Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	liver and gall bladder diseases.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Exposure levels and common chronic disease over time are appropriately measured with a cohort design.
	Metric 13:	Statistical Power	Low	It is unclear how many study participants are included in the measures of cases throughout the plant.
	Metric 14:	Reproducibility of Analyses	Medium	The analyses are reproducible, as the study only reports number of cases, and number of disabled days per 100 workers. Further analyses of these case numbers were not conducted.
	Metric 15:	Statistical Analysis	N/A	No statistical modeling was conducted.

Additional Comments: Occupational study of aircraft plant workers exposed to dichloroethane via air. Study reports number of cases of liver and gall bladder diseases. Statistical analyses and comparisons are not provided for outcomes and only case numbers are reported, limiting the informativeness of the study. Study refers only to dichloroethane, thus, 1,1 and 1,2 dichloroethane cannot be separated in this review. Both chemicals have been included in evaluations.

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Gastrointestinal
Reported Health Effect(s):	acute gastrointestinal diseases, acute gastritis, and chronic gastritis.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Occupational cohort study in Russian aircraft manufacturing plant. The study focuses on the soft tank shop. The participation of all workers in the aircraft plant shops (including the soft tank shop and controls from the mechanical shop) is implied, however numbers of eligible participants and the total number of included participants across analyses are not reported. 17 gluers represented the exposed and were compared to 10 mechanical shop machinists.
	Metric 2:	Attrition	Medium	Rates of attrition cannot be determined based on the limited information provided. The study solely reports those included in assessment of changes in the functions of motor apparatus in upper extremities, but not of gastrointestinal outcomes.
	Metric 3:	Comparison Group	Low	Case numbers per 100 workers are reported for those exposed (working in the shop) and those unexposed (working in the plant) for acute gastrointestinal diseases. Solely case numbers per 100 workers are reported for other gastrointestinal outcomes (acute and chronic gastritis, acute gastrointestinal diseases).
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Authors report quantitative measures of dichloroethane in air, but do not provide any information on the method used to quantify exposure levels.
	Metric 5:	Exposure Levels	Uninformative	No description is provided on the levels or range of exposure for those in the shop compared to the plant. The exposure difference between groups is unclear.
	Metric 6:	Temporality	Low	Temporality is unclear, as limited information is provided about the measurement of exposure and outcome.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Uninformative	No information on outcome measurement and diagnostic criteria is provided for gastrointestinal outcomes.
	Metric 8:	Reporting Bias	Medium	Case numbers are reported for gastrointestinal outcomes for the shop and the plant, but there is no clear information about their relationship to exposure levels. These results would not be useful for detailed extraction.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	There is no discussion of confounders or analysis of differing characteristics.
	Metric 10:	Covariate Characterization	N/A	No confounders measured.
	Metric 11:	Co-exposure Counfounding	Low	There is no indication that co-exposures of concern were assessed, though the study was conducted in an occupational setting with higher potential for chemical co-exposures.
Domain 5: Analysis				

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Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Gastrointestinal
Reported Health Effect(s):	acute gastrointestinal diseases, acute gastritis, and chronic gastritis.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Exposure levels and common chronic disease over time are appropriately measured with a cohort design.
	Metric 13:	Statistical Power	Low	It is unclear how many study participants are included in the measures of cases throughout the plant.
	Metric 14:	Reproducibility of Analyses	Medium	The analyses are reproducible, as the study only reports number of cases and number of disabled days per 100 workers. Further analyses of these case numbers were not conducted.
	Metric 15:	Statistical Analysis	N/A	No statistical modeling was conducted.

Additional Comments: Occupational study of aircraft plant workers exposed to dichloroethane via air. Study reports number of cases of gastrointestinal diseases per 100 workers in the plant and in the shop (likely exposed). No information is provided on the dichloroethane levels in the plant. Statistical analyses and comparisons are not provided for outcomes and only case numbers are reported, limiting the informativeness of the study. Study refers only to dichloroethane, thus, 1,1 and 1,2 dichloroethane cannot be separated in this review. Both chemicals have been included in evaluations.

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Morbidity
Reported Health Effect(s):	Overall morbidity, and other diseases.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Occupational cohort study in Russian aircraft manufacturing plant. The study focuses on the soft tank shop. The participation of all workers in the aircraft plant shops (including the soft tank shop and controls from the mechanical shop) is implied, however numbers of eligible participants and the total number of included participants across analyses are not reported. 17 gluers represented the exposed and were compared to 10 mechanical shop machinists.
	Metric 2:	Attrition	Medium	Rates of attrition cannot be determined based on the limited information provided. The study solely reports those included in assessment of changes in the functions of motor apparatus in upper extremities, but not of other diseases/overall morbidity.
	Metric 3:	Comparison Group	Low	Case numbers per 100 workers are reported for those exposed (working in the shop) and those unexposed (working in the plant) for overall morbidity and other diseases.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Authors report quantitative measures of dichloroethane in air, but do not provide any information on the method used to quantify exposure levels.
	Metric 5:	Exposure Levels	Uninformative	No description is provided on the levels or range of exposure for those in the shop compared to the plant. The exposure difference between groups is unclear.
	Metric 6:	Temporality	Low	Temporality is unclear, as limited information is provided about the measurement of exposure and outcome.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Uninformative	No information on outcome measurement and diagnostic criteria is provided for overall morbidity or other diseases.
	Metric 8:	Reporting Bias	Medium	Case numbers are reported for overall morbidity and other diseases for the shop and the plant, but there is no clear information about their relationship to exposure levels. These results would not be useful for detailed extraction.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	There is no discussion of confounders or analysis of differing characteristics.
	Metric 10:	Covariate Characterization	N/A	No confounders were measured.
	Metric 11:	Co-exposure Counfounding	Low	There is no indication that co-exposures of concern were assessed, though the study was conducted in an occupational setting with higher potential for chemical co-exposures.
Domain 5: Analysis				

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Study Citation:	Kozik, I. V. (1957). [Problems of occupational hygiene in the use of dichloroethane in the aviation industry]. Gigiena Truda i Professional'nye Zabolevaniya 1:31-38.
Health Outcome(s):	Morbidity
Reported Health Effect(s):	Overall morbidity, and other diseases.
Chemical:	1,1-Dichloroethane- Isomer: Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	18135

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Exposure levels and common chronic disease over time are appropriately measured with a cohort design.
	Metric 13:	Statistical Power	Low	It is unclear how many study participants are included in the measures of cases throughout the plant.
	Metric 14:	Reproducibility of Analyses	Medium	The analyses are reproducible, as the study only reports number of cases and number of disabled days per 100 workers. Further analyses of these case numbers were not conducted.
	Metric 15:	Statistical Analysis	N/A	No statistical modeling was conducted.

Additional Comments: Occupational study of aircraft plant workers exposed to dichloroethane via air. Study reports number of cases of overall morbidity and "other diseases" per 100 workers in the plant (no or lower exposure) and in the shop (likely exposed). No information is provided on the dichloroethane levels in the plant. Statistical analyses and comparisons are not provided for outcomes and only case numbers are reported, limiting the informativeness of the study. Study refers only to dichloroethane, thus, 1,1 and 1,2 dichloroethane cannot be separated in this review. Both chemicals have been included in evaluations.

Overall Quality Determination — Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Cases in this case-control study were former Union Carbide Corporation (UCC) chemical plant employees in Texas City, Texas. Cases were identified through death certificate searches and tumor registries, and may have included individuals formerly employed at UCC whose cause of death was unknown to the company. Additionally, control deaths were stated to be pulled from corporate employee benefits department and through locally published obituary notices routinely screened by the medical department - it is possible to assume that cases were identified in a similar manner. The study identified cases of brain tumors by searching death certificates primarily, although tumor registries throughout the state of Texas were also searched. The study clarifies that it is possible that some cases were not found if they survived or died due to another cause - while this is likely to have impacted selection, there is no evidence that this would be differential by exposure status. Overall, there is limited information on the source population of workers from which cases were identified.
	Metric 2:	Attrition	Medium	Attrition is not discussed in the study, and outcome data appear to be complete. There was a large proportion of missing exposure data (roughly 50%) due to workers being employed in roles such as maintenance, where exposure to any chemical is possible but unknown. Analyses were run separately where these ”unknown” individuals were a) treated as exposed, b) treated as unexposed, or c) treated as unknown and thus excluded. The study only presents results for when these individuals were excluded but specifies that the first scenario resulted in increased exposure estimates for controls relative to cases.

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Study Citation:	Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
	Metric 3:	Comparison Group	Medium	The study identifies two series of control groups, selected from all former Union Carbide Corporation (UCC) employees. However, the total number of employees is not stated. Only those who were deceased were used as controls since they had known causes of death and could thus be verified as non-brain tumors. One group of controls excluded employees whose cause of death was due to any malignant neoplasm to allow for the possibility that a general chemical carcinogen may have been associated with cancers of other sites. The other group of controls included deaths from all causes; this included malignant neoplasms other than brain tumors. Both control groups had 80 male employees randomly selected from 450 deceased employees known to the company in June 1979. Control deaths were stated to be pulled from corporate employee benefits department and through locally published obituary notices routinely screened by the medical department - it is possible to assume that cases were identified in a similar manner. The study reports that cases were slightly more likely to have been employed for less than 10 years than controls - the study attributes this in part to the fact that employees whose deaths were known to the company were more likely to have worked for longer - regardless the mean number of years employed was similar between cases and controls. However, cases were more likely to have been terminated from their job for reasons other than death, disability, or retirement (quitting, being fired, etc.), were generally younger at hire, and were less likely to survive to their 70th birthday. None of these factors are controlled for in statistical analyses - however, since controls and cases were pulled from the same population, there is indirect evidence that the groups were similar.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was determined based on official employment records. Records included job title and department assignment codes for each employment from date of hire to date of termination. For each unique department code, UCC and NIOSH industrial hygienists identified principal chemicals used or produced at any time in the history of the plant and correlated those with individual departments. This assessment was not performed on a year-by-year basis due to concerns for recall bias for longer-term employees where less detailed records were kept. An employee was categorized as ”exposed” to 1,2-dichloroethane if they ever worked in a department associated with that chemical. An ”unknown” exposure group was also created to account for employees who had only worked in departments for which no specific chemical could be identified.
	Metric 5:	Exposure Levels	Low	The study does not report any quantitative information and only splits exposure into ”exposed”, ”unexposed”, and ”unknown”.
	Metric 6:	Temporality	High	In this study exposure is confirmed to occur before the outcome is measured. The study reports latency periods, with subjects dichotomized into less than 15 years of latency or more than 15 years of latency. The majority of cases and controls had a latency of greater than 15 years, which is sufficiently long for brain tumors.

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Study Citation:	Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Cases were identified through death certificate searches and partially through tumor registries in the state of Texas. Case validation was performed by NIOSH, and 5 different levels of confirmation were reported: 1) tissue specimen interpreted by the Armed Forces Institute of Pathology; 2) autopsy report; 3) histopathology report; 4) clinical diagnosis from hospital record; 5) dearth certificate diagnosis. Codes 1-3 were considered to be ”confirmed” cases of brain tumors, while 4-5 were considered unconfirmed. 5/21 cases were only evaluated using ”unconfirmed methods”, meaning there is likely a high amount of accuracy in roughly 75% of cases. While no case validation is reported for controls, the study specifies that only controls who had died and thus could be confirmed to be non-brain tumors were included.
	Metric 8:	Reporting Bias	Medium	All primary and secondary outcomes that are outlined in the methods are reported in the results. However, the only statistical outcome of their analysis were unadjusted p-values that were not reported and were just described qualitatively.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	The only statistical analysis performed were Mantel-Haenszel chi-squared tests, which did not allow for confounder adjustment. The study does not present a distribution of potential confounders by exposure status but by case/control status. Several variables, such as reason for termination, age at hire, and age at death were significantly different between cases and controls and were not accounted for in statistical modeling. The study explains that these differences are not likely to have any epidemiologic significance and appear to be relatively small differences.
	Metric 10:	Covariate Characterization	Medium	While the study does not explain where they obtained covariate information, it is reasonable to assume that they gathered the information from company records.
	Metric 11:	Co-exposure Counfounding	Low	The study assesses a wide range of other potential occupational co-exposures. While these co-exposures are not adjusted for in any statistical models, effect estimates are presented separately for benzene, diethyl sulfate, ethylene oxide, and vinyl chloride. The distribution of co-exposures across cases and controls is demonstrated to be mostly balanced by comparing proportions of exposed/unexposed between cases and controls. The only notable instance of imbalance is for benzene, where 11.1% of cases were exposed whereas 37.9% of all controls and 19.2% of non-neoplasm related controls were exposed.
Domain 5: Analysis				

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Study Citation:	Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	The study chose a case-control design, which was appropriate to study the rare disease of brain tumors and its association with occupational exposures. The only statistical analysis conducted is a Mantzel-Haenszel chi-squared test, but there is no reason to suggest that this would be inappropriate.
	Metric 13:	Statistical Power	Medium	The study does not calculate statistical power, but the number of cases (n=21) and controls (n=80 in each analysis) is likely sufficient to detect an effect.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to understand what was done and could be reproduced given access to the analytic data.
	Metric 15:	Statistical Analysis	High	The only statistical analysis conducted is a Mantel-Haenszel chi-squared test, and all assumptions were met. The statistical process is transparent.

Additional Comments: This case-control study pulled deceased former employees of the Union Carbide Corporation in Texas City, Texas. The study examined dichotomous exposure to a wide range of occupational exposures, including 1,2-dichloroethane, in relation to brain tumor cases. There is no quantitative estimate of exposure. The only statistical analysis in the study is a Mantel-Haenszel chi-squared test statistic and no statistically significant differences in exposure between cases and controls were observed. The fact that there are no effect estimates, no adjustment for confounders, and no quantitative exposure estimates limits the usefulness of this paper.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Cases in this case-control study were former Union Carbide Corporation (UCC) chemical plant employees in Texas City, Texas. Cases were identified through death certificate searches and tumor registries, and may have included individuals formerly employed at UCC whose cause of death was unknown to the company. Additionally, control deaths were stated to be pulled from corporate employee benefits department and through locally published obituary notices routinely screened by the medical department - it is possible to assume that cases were identified in a similar manner. The study identified cases of brain tumors by searching death certificates primarily, although tumor registries throughout the state of Texas were also searched. The study clarifies that it is possible that some cases were not found if they survived or died due to another cause - while this is likely to have impacted selection, there is no evidence that this would be differential by exposure status. Overall, there is limited information on the source population of workers from which cases were identified.
	Metric 2:	Attrition	Medium	Attrition is not discussed in the study, and outcome data appear to be complete. There was a large proportion of missing exposure data (roughly 50%) due to workers being employed in roles such as maintenance, where exposure to any chemical is possible but unknown. Analyses were run separately where these ”unknown” individuals were a) treated as exposed, b) treated as unexposed, or c) treated as unknown and thus excluded. The study only presents results for when these individuals were excluded but specifies that the first scenario resulted in increased exposure estimates for controls relative to cases.

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Study Citation:	Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
	Metric 3:	Comparison Group	Medium	The study identifies two series of control groups, selected from all former Union Carbide Corporation (UCC) employees. However, the total number of employees is not stated. Only those who were deceased were used as controls since they had known causes of death and could thus be verified as non-brain tumors. One group of controls excluded employees whose cause of death was due to any malignant neoplasm to allow for the possibility that a general chemical carcinogen may have been associated with cancers of other sites. The other group of controls included deaths from all causes; this included malignant neoplasms other than brain tumors. Both control groups had 80 male employees randomly selected from 450 deceased employees known to the company in June 1979. Control deaths were stated to be pulled from corporate employee benefits department and through locally published obituary notices routinely screened by the medical department - it is possible to assume that cases were identified in a similar manner. The study reports that cases were slightly more likely to have been employed for less than 10 years than controls - the study attributes this in part to the fact that employees whose deaths were known to the company were more likely to have worked for longer - regardless the mean number of years employed was similar between cases and controls. However, cases were more likely to have been terminated from their job for reasons other than death, disability, or retirement (quitting, being fired, etc.), were generally younger at hire, and were less likely to survive to their 70th birthday. None of these factors are controlled for in statistical analyses - however, since controls and cases were pulled from the same population, there is indirect evidence that the groups were similar.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was determined based on official employment records. Records included job title and department assignment codes for each employment from date of hire to date of termination. For each unique department code, UCC and NIOSH industrial hygienists identified principal chemicals used or produced at any time in the history of the plant and correlated those with individual departments. This assessment was not performed on a year-by-year basis due to concerns for recall bias for longer-term employees where less detailed records were kept. An employee was categorized as ”exposed” to 1,2-dichloroethane if they ever worked in a department associated with that chemical. An ”unknown” exposure group was also created to account for employees who had only worked in departments for which no specific chemical could be identified.
	Metric 5:	Exposure Levels	Low	The study does not report any quantitative information and only splits exposure into ”exposed”, ”unexposed”, and ”unknown”.
	Metric 6:	Temporality	High	In this study exposure is confirmed to occur before the outcome is measured. The study reports latency periods, with subjects dichotomized into less than 15 years of latency or more than 15 years of latency. The majority of cases and controls had a latency of greater than 15 years, which is sufficiently long for brain tumors.

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Study Citation:	Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Cases were identified through death certificate searches and partially through tumor registries in the state of Texas. Case validation was performed by NIOSH, and 5 different levels of confirmation were reported: 1) tissue specimen interpreted by the Armed Forces Institute of Pathology; 2) autopsy report; 3) histopathology report; 4) clinical diagnosis from hospital record; 5) dearth certificate diagnosis. Codes 1-3 were considered to be ”confirmed” cases of brain tumors, while 4-5 were considered unconfirmed. 5/21 cases were only evaluated using ”unconfirmed methods”, meaning there is likely a high amount of accuracy in roughly 75% of cases. While no case validation is reported for controls, the study specifies that only controls who had died and thus could be confirmed to be non-brain tumors were included.
	Metric 8:	Reporting Bias	Medium	All primary and secondary outcomes that are outlined in the methods are reported in the results. However, the only statistical outcome of their analysis were unadjusted p-values that were not reported and were just described qualitatively.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	The only statistical analysis performed were Mantel-Haenszel chi-squared tests, which did not allow for confounder adjustment. The study does not present a distribution of potential confounders by exposure status but by case/control status. Several variables, such as reason for termination, age at hire, and age at death were significantly different between cases and controls and were not accounted for in statistical modeling. The study explains that these differences are not likely to have any epidemiologic significance and appear to be relatively small differences.
	Metric 10:	Covariate Characterization	Medium	While the study does not explain where they obtained covariate information, it is reasonable to assume that they gathered the information from company records.
	Metric 11:	Co-exposure Counfounding	Low	The study assesses a wide range of other potential occupational co-exposures. While these co-exposures are not adjusted for in any statistical models, effect estimates are presented separately for benzene, diethyl sulfate, ethylene oxide, and vinyl chloride. The distribution of co-exposures across cases and controls is demonstrated to be mostly balanced by comparing proportions of exposed/unexposed between cases and controls. The only notable instance of imbalance is for benzene, where 11.1% of cases were exposed whereas 37.9% of all controls and 19.2% of non-neoplasm related controls were exposed.
Domain 5: Analysis				

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Study Citation:	Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	The study chose a case-control design, which was appropriate to study the rare disease of brain tumors and its association with occupational exposures. The only statistical analysis conducted is a Mantzel-Haenszel chi-squared test, but there is no reason to suggest that this would be inappropriate.
	Metric 13:	Statistical Power	Medium	The study does not calculate statistical power, but the number of cases (n=21) and controls (n=80 in each analysis) is likely sufficient to detect an effect.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to understand what was done and could be reproduced given access to the analytic data.
	Metric 15:	Statistical Analysis	High	The only statistical analysis conducted is a Mantel-Haenszel chi-squared test, and all assumptions were met. The statistical process is transparent.

Additional Comments: This case-control study pulled deceased former employees of the Union Carbide Corporation in Texas City, Texas. The study examined dichotomous exposure to a wide range of occupational exposures, including 1,2-dichloroethane, in relation to brain tumor cases. There is no quantitative estimate of exposure. The only statistical analysis in the study is a Mantel-Haenszel chi-squared test statistic and no statistically significant differences in exposure between cases and controls were observed. The fact that there are no effect estimates, no adjustment for confounders, and no quantitative exposure estimates limits the usefulness of this paper.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	Urinary system cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	Urinary system cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	Urinary system cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Immune/Hematological
Reported Health Effect(s):	Lymphatic and hematopoietic tissue cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Immune/Hematological
Reported Health Effect(s):	Lymphatic and hematopoietic tissue cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Immune/Hematological
Reported Health Effect(s):	Lymphatic and hematopoietic tissue cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Other cancers (not specified)
Reported Health Effect(s):	Other cancers (not specified)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Other cancers (not specified)
Reported Health Effect(s):	Other cancers (not specified)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Other cancers (not specified)
Reported Health Effect(s):	Other cancers (not specified)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Mortality
Reported Health Effect(s):	All-cause mortality
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Vital status was tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Medium	Death rates among unit employees were compared to death rates in the U.S. population adjusted for age and gender. Demographics of the exposed workers are not provided; therefore, it is not clear whether additional adjustment for race may have been appropriate. No justification is provided for the choice of the entire U.S. population as the comparison group. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis. Additional analyses are conducted limiting workers to those with the greatest likelihood of exposure (i.e., those working in jobs with high likelihood of contact with chemicals for more than a year, those working for the full year of 1979 during which chemical exposures were most frequently reported); these smaller groups are also compared to the unexposed general population.
	Metric 6:	Temporality	High	Temporality was established due to the longitudinal design and the use of mortality as the outcome. Exposures occurred between 1979 and 1987 and follow-up for vital status was conducted through 2003.
Domain 3: Outcome Assessment				

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Mortality
Reported Health Effect(s):	All-cause mortality
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Medium	The study did not provide information on how mortality was assessed either in the exposed population or in the comparison population; use of death certificates is implied but not stated.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected deaths are reported, but SIRs and 95% confidence intervals are not provided.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Comparisons of observed versus expected deaths were adjusted for age and gender. Demographics of the exposed workers are not provided; therefore, it is not clear whether additional adjustment for race may have been appropriate.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records or death records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed deaths among a population of exposed workers compared to expected deaths among the U.S. population, adjusted for age and gender.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected deaths; no SIR was provided. Expected death rates were adjusted for age and gender.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Mortality
Reported Health Effect(s):	All-cause mortality
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	All cancer (excluding non-melanoma skin cancer), digestive system cancer, colorectal cancer, respiratory cancer, prostate cancer, urinary system cancer, lymphatic and hematopoietic tissue cancer, other cancers (not specified)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	All cancer (excluding non-melanoma skin cancer), digestive system cancer, colorectal cancer, respiratory cancer, prostate cancer, urinary system cancer, lymphatic and hematopoietic tissue cancer, other cancers (not specified)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	All cancer (excluding non-melanoma skin cancer), digestive system cancer, colorectal cancer, respiratory cancer, prostate cancer, urinary system cancer, lymphatic and hematopoietic tissue cancer, other cancers (not specified)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Gastrointestinal
Reported Health Effect(s):	Digestive system cancer, colorectal cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Gastrointestinal
Reported Health Effect(s):	Digestive system cancer, colorectal cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Gastrointestinal
Reported Health Effect(s):	Digestive system cancer, colorectal cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Lung/Respiratory
Reported Health Effect(s):	Respiratory cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Health Outcome(s):	Lung/Respiratory
Reported Health Effect(s):	Respiratory cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Health Outcome(s):	Lung/Respiratory
Reported Health Effect(s):	Respiratory cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Prostate cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Prostate cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Prostate cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Male workers who had ever been assigned to the chlorohydrin unit between 1 January 1940 and 31 December 1967 at Union Carbide's South Charleston plant were enrolled and matched to the US National Death Index. Status on 5 workers could not be identified. Information on how workers were matched to death index was not specified.
	Metric 2:	Attrition	Medium	Rate of inclusion/participation was very high, as records were able to be matched for 98% of participants. Medium rating given because information on how participants whose vital status was not known was not specified.
	Metric 3:	Comparison Group	Uninformative	Unacceptable rating given because SMRs were calculated based on expected deaths from a reference population matched on sex, but not age.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Exposure was assessed based on duration of work in the plant. No information is provided on exposure levels, and a JEM was not used.
	Metric 5:	Exposure Levels	Uninformative	No information provided on levels of exposure.
	Metric 6:	Temporality	High	Temporality is well established; person-years stopped accumulating in 1967 and outcome was assessed beginning at that time.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar period, and interval since assignments, but distribution of these covariates was not reported.
	Metric 10:	Covariate Characterization	Medium	Information on covariate characterization not provided, but the selected covariates (age, calendar period, and interval since assignments) were likely extracted from employee records and unlikely to be largely problematic
	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.

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Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Study design was appropriate for the research method. Statistical methods were also appropriate.
	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.
	Metric 14:	Reproducibility of Analyses	Medium	Methods are well-enough described that study could be adequately reproduced.
	Metric 15:	Statistical Analysis	High	SMRs calculated based on US general population mortality for white males through 1988. RRs were ”evaluated over levels of duration of assignment to the chlorohydrin unit, stratified by age, calendar year, and interval since first assignment to the chlorohydrin unit”.

Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Male workers who had ever been assigned to the chlorohydrin unit between 1 January 1940 and 31 December 1967 at Union Carbide's South Charleston plant were enrolled and matched to the US National Death Index. Status on 5 workers could not be identified. Information on how workers were matched to death index was not specified.
	Metric 2:	Attrition	Medium	Rate of inclusion/participation was very high, as records were able to be matched for 98% of participants. Medium rating given because information on how participants whose vital status was not known was not specified.
	Metric 3:	Comparison Group	Uninformative	Unacceptable rating given because SMRs were calculated based on expected deaths from a reference population matched on sex, but not age.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Exposure was assessed based on duration of work in the plant. No information is provided on exposure levels, and a JEM was not used.
	Metric 5:	Exposure Levels	Uninformative	No information provided on levels of exposure.
	Metric 6:	Temporality	High	Temporality is well established; person-years stopped accumulating in 1967 and outcome was assessed beginning at that time.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar period, and interval since assignments, but distribution of these covariates was not reported.
	Metric 10:	Covariate Characterization	Medium	Information on covariate characterization not provided, but the selected covariates (age, calendar period, and interval since assignments) were likely extracted from employee records and unlikely to be largely problematic
	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.
Domain 5: Analysis				

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Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
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Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Study design was appropriate for the research method. Statistical methods were also appropriate.
	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.
	Metric 14:	Reproducibility of Analyses	Medium	Methods are well-enough described that study could be adequately reproduced.
	Metric 15:	Statistical Analysis	High	SMRs calculated based on US general population mortality for white males through 1988. RRs were ”evaluated over levels of duration of assignment to the chlorohydrin unit, stratified by age, calendar year, and interval since first assignment to the chlorohydrin unit”.

Additional Comments: None

Overall Quality Determination Uninformative

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Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar period, and interval since assignments, but distribution of these covariates was not reported.
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	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.
Domain 5: Analysis				

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Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
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	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.
	Metric 14:	Reproducibility of Analyses	Medium	Methods are well-enough described that study could be adequately reproduced.
	Metric 15:	Statistical Analysis	High	SMRs calculated based on US general population mortality for white males through 1988. RRs were ”evaluated over levels of duration of assignment to the chlorohydrin unit, stratified by age, calendar year, and interval since first assignment to the chlorohydrin unit”.

Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

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	Metric 3:	Comparison Group	Uninformative	Unacceptable rating given because SMRs were calculated based on expected deaths from a reference population matched on sex, but not age.
Domain 2: Exposure Characterization				
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Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar period, and interval since assignments, but distribution of these covariates was not reported.
	Metric 10:	Covariate Characterization	Medium	Information on covariate characterization not provided, but the selected covariates (age, calendar period, and interval since assignments) were likely extracted from employee records and unlikely to be largely problematic
	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.
Domain 5: Analysis				

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HERO ID:	200224

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Additional Comments: None

Overall Quality Determination Uninformative

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Domain 5: Analysis				

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Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
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Domain 5: Analysis				

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Additional Comments: None

Overall Quality Determination Uninformative

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Domain 5: Analysis				

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Additional Comments: None

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Domain 5: Analysis				

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Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Bove, F. J. (1996). Public drinking water contamination and birthweight, prematurity, fetal deaths, and birth defects. Toxicology and Industrial Health 12(2):255-266.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	200239

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	This cross-sectional study (n=80,938) included all registered singleton live births and fetal deaths (>20 weeks' gestation) in 1985-88 in 75 New Jersey towns located in 4 counties with "some" water supplies contaminated with substances of interest and where: (i) residents were "mostly" served by public water systems; and (ii) births occurred "mostly" in state. Estimated proportions of residents served by public water systems, and of pregnancies/births captured, were not described. However, the inclusion of all eligible registered births, fetal deaths, and birth defects, as well as the selection of towns without knowledge of birth outcome prevalence, limited the likelihood of selection bias.
	Metric 2:	Attrition	Medium	All registered births and fetal deaths were included. Attrition due to missing values for multiple variables was not quantified and is therefore uncertain. However, attrition was likely modest as the proportion of missing values for individual variables was relatively low: (i) ~6% of subjects were excluded from analyses of outcomes such as preterm birth due to invalid or missing gestational ages; and (ii) other covariates evaluated as confounders had up to 4.9% missing values.
	Metric 3:	Comparison Group	High	After excluding plural pregnancies and chromosomal abnormalities, all registered live births during the study period in the areas included without the outcomes of interest were included in the comparison group. This comprehensive approach limited the potential for bias. Chromosomal abnormalities were not included as outcomes as they were not hypothesized to be associated with the exposures under study but were appropriately excluded given their uncertain etiology.
Domain 2: Exposure Characterization				

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Study Citation:	Bove, F. J. (1996). Public drinking water contamination and birthweight, prematurity, fetal deaths, and birth defects. Toxicology and Industrial Health 12(2):255-266.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	200239

Domain	Metric		Rating	Comments
	Metric 4:	Measurement of Exposure	Medium	Along with several other contaminants, residential drinking water exposure to 1,2-dichloroethane (as well as 1,1,1-trichloroethane and 'total dichloroethylenes') – was assigned based on maternal town of residence at birth. Exposure estimates were calculated using the average of water company sampling reports during the first trimester (for birth defects and fetal death) or the duration of pregnancy (for other outcomes). Detection limits and data availability were not specified in detail but were described as below 1 ppb, with reporting compliance >85%. A minimum of 1 sample per 6-month interval was required; variability in the number of measures available across water systems and towns was not described. Additional sources of measurement error included: changes in residence during pregnancy; water from alternate sources (ex. private wells, bottles, workplaces); variability in residential contaminant levels vs measured samples; unknown levels of tap water intake; and errors in estimated dermal and inhalation exposure while bathing or showering. While the extent of exposure misclassification is uncertain, there is no evidence to suggest it was differential rather than random.
	Metric 5:	Exposure Levels	Medium	Due to the high proportion of measures below detection limits, analyses relating exposure to health outcomes used only 2 categories for each of the chlorinated solvents of interest: cutoffs close to detection limits were used to define elevated exposure. Proportions defined as having elevated exposure was low (1.8% had 1,1-dichloroethylene ≥1 ppb). An important concern is that relatively low levels of exposure to these contaminants from sources other than residential drinking water, for which data were not available, could potentially have resulted in considerable misclassification.
	Metric 6:	Temporality	High	Exposure levels were assigned based on contaminant exposures estimated during: (i) the first trimester for analyses of birth defects and fetal deaths; and (ii) the duration of pregnancy for other pregnancy outcomes.

Domain 3: Outcome Assessment

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Study Citation:	Bove, F. J. (1996). Public drinking water contamination and birthweight, prematurity, fetal deaths, and birth defects. Toxicology and Industrial Health 12(2):255-266.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	200239

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcomes included measures of birthweight (continuous among term births, low term birthweight, very low birthweight), prematurity, fetal death, and congenital anomalies in live births or fetal deaths. The anomalies analyzed included defects of the central nervous system, neural tube, oral cleft, total cardiac, major cardiac, ventricular septum, and any surveillance defect excluding chromosomal defects. All outcomes were identified using birth certificates, fetal death certificates (>20 weeks' gestation), and the NJ congenital birth defect registry (ICD codes provided). These registry data are likely to be sufficiently valid for late pregnancy outcomes. However, their limited ability to capture early pregnancy losses is a weakness. The sample included only 594 fetal deaths (less than 1% of the >80,0000 sample). Typical estimates are that 10-20%, of recognized pregnancies ending in losses. Moreover, developmental defects contributing to early pregnancy losses were also not captured. A further limitation is that that potentially etiologically heterogeneous preterm birth types were analyzed together, as these data did not distinguish premature rupture of membranes vs idiopathic prematurity.
	Metric 8:	Reporting Bias	Medium	Models were constructed only for contaminants with associations > 1.0, and tables included only associations with odds ratios ≥1.5. No clear rationale was provided. Several positive odds ratios below the 1.5 cutoff were described in the results text (without confidence intervals), but no null/negative odds ratios were presented or described.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Potential confounding by maternal race, education, parity, and prior pregnancy loss, along with infant sex (for birth outcomes) and adequacy of prenatal care, was examined. Gestational age was addressed by analyzing birthweight among full term births, term low birth weight, and small size for gestational age. Only fully adjusted models were presented. In a companion case-control study (with low participation rates), adjustment for other variables not available on birth certificates (ex. maternal smoking, occupational exposures, medical history, and gestational weight gain) did not influence associations with other studied contaminants. This separate study reduces concerns for important confounding bias, but confounding cannot be ruled out.
	Metric 10:	Covariate Characterization	Medium	Data on covariates came from registry data: birth certificates, fetal death certificates, and the NJ congenital birth defects registry.
	Metric 11:	Co-exposure Counfounding	Medium	Co-exposure confounding by drinking water trihalomethane concentrations was evaluated. There was no evidence to suggest substantial confounding by this or other co-exposures.
Domain 5: Analysis				

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Study Citation:	Bove, F. J. (1996). Public drinking water contamination and birthweight, prematurity, fetal deaths, and birth defects. Toxicology and Industrial Health 12(2):255-266.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	200239

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Methods were appropriate. The study used logistic regression models to estimate odds ratios and confidence intervals for dichotomous outcomes, and linear regression for analysis of continuous birth weight.
	Metric 13:	Statistical Power	Medium	Statistical power was likely to have been limited as a consequence of the small proportion of the sample defined as having "elevated" residential water concentrations of the chemicals of interest. The range of exposure examined was limited, as cutoffs for elevated levels were close to the detection limits of 1 ppb. In addition, for most birth defect outcomes, fewer than 10 cases had elevated exposure.
	Metric 14:	Reproducibility of Analyses	Medium	The authors clearly described steps used to estimate exposure-outcome associations, including exposure category cutoffs and criteria for confounding. However, many results were not shown as tables included odds ratios ≥1.5.
	Metric 15:	Statistical Analysis	High	The authors estimated coefficients, odds ratios and 95% confidence intervals using adequate methods. Confounding was based on 15% change-in-estimate comparing nested models. Effect modification (ex by infant sex) was not evaluated as there was no a priori evidence to suggest such analyses at that time.

Additional Comments: This study analyzed the association between estimated residential drinking water concentrations of several chlorinated solvents including 1,2-dichloroethane (as well as 1,1,1-trichloroethane; ∑[trans-1,2-dichloroethylene and 1,1-dichloroethylene]) and pregnancy outcomes (size at birth, prematurity, fetal deaths, and congenital birth defects). The sample included more than 80,000 births during 1985-88 for residents of 75 towns in NJ using public water system records to estimate exposure during gestation, and registry data (birth certificate, fetal death certificates for pregnancies >20 weeks, state birth defect registry) to characterize outcomes. Strengths included the large sample size and inclusion of all eligible registered births and fetal deaths in the study period. A critical concern is the inability to capture early fetal deaths and any related malformations (1% of the sample had fetal deaths vs typical estimates of >10%). An important limitation was the low percentage of the sample with detectable (> 1ppb) concentrations of these contaminants (<1% to 6.2%). Small numbers for birth defect outcomes also limited power. Exposure misclassification (ex. drinking water from wells/ work/ bottles, changes in residence, exposure from other sources) is also a concern. However, such misclassification was likely non-differential, and thus more likely to under- vs. to over-estimate associations.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Bove, F. J., Fulcomer, M. C., Klotz, J. B., Esmart, J., Dufficy, E. M., Savrin, J. E. (1995). Public drinking water contamination and birth outcomes. American Journal of Epidemiology 141(9):850-862.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	194932

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	This semi-ecological study (n=80,938) included all registered singleton live births and fetal deaths (>20 weeks) in 1985-88 in 75 New Jersey towns located in 4 counties with "some" water supplies contaminated with substances of interest and where: (i) residents were "mostly" served by public water systems; and (ii) births occurred "mostly" in state. Estimated proportions of residents served by public water systems, and of pregnancies/births captured, were not described. However, the inclusion of all eligible registered births, fetal deaths, and birth defects, as well as the selection of towns without knowledge of birth outcome prevalence, limited the likelihood of selection bias.
	Metric 2:	Attrition	Medium	All registered births and fetal deaths were included. Attrition due to missing values for multiple variables was not quantified and is therefore uncertain. However, attrition was likely modest as the proportion of missing values for individual variables was relatively low: (i) ~6% of subjects were excluded from analyses of outcomes such as preterm birth due to invalid or missing gestational ages; and (ii) other covariates evaluated as confounders had up to 4.9% missing values.
	Metric 3:	Comparison Group	High	After excluding plural pregnancies and chromosomal abnormalities, all registered live births during the study period in the areas included without the outcomes of interest were included in the comparison group. This comprehensive approach limited the potential for bias. Chromosomal abnormalities were not included as outcomes as they were not hypothesized to be associated with the exposures under study but were appropriately excluded given their uncertain etiology.
Domain 2: Exposure Characterization				

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Study Citation:	Bove, F. J., Fulcomer, M. C., Klotz, J. B., Esmart, J., Dufficy, E. M., Savrin, J. E. (1995). Public drinking water contamination and birth outcomes. American Journal of Epidemiology 141(9):850-862.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	194932

Domain	Metric		Rating	Comments
	Metric 4:	Measurement of Exposure	Medium	Along with several other contaminants, residential drinking water exposure to 1,2-dichloroethane (as well as 1,1,1-trichloroethane and 'total dichloroethylenes') was assigned based on maternal town of residence at birth. Exposure estimates were calculated using the average of water company sampling reports during the first trimester (for birth defects and fetal death) or the duration of pregnancy (for other outcomes). Detection limits and data availability were not specified in detail but were described as below 1 ppb, with reporting compliance >85%. A minimum of 1 sample per 6-month interval was required; variability in the number of measures available across water systems and towns was not described. Additional sources of measurement error included: changes in residence during pregnancy; water from alternate sources (ex. private wells, bottles, workplaces); variability in residential contaminant levels vs measured samples; unknown levels of tap water intake; and errors in estimated dermal and inhalation exposure while bathing or showering. While the extent of exposure misclassification is uncertain, there is no evidence to suggest it was differential rather than random.
	Metric 5:	Exposure Levels	Low	Due to the high proportion of measures below detection limits, analyses relating exposure to health outcomes used only 2 categories for each of the three chemicals of interest: cutoffs close to detection limits were used to define elevated exposure. Proportions defined as having elevated exposure were low (1.8% had 1,1-dichloroethylene ≥1 ppb). An important concern is that relatively low levels of exposure to this contaminant from sources other than residential drinking water, for which data were not available, could potentially have resulted in considerable misclassification.
	Metric 6:	Temporality	High	Exposure levels were assigned based on contaminant exposures estimated during: (i) the first trimester for analyses of birth defects and fetal deaths; and (ii) the duration of pregnancy for other pregnancy outcomes.

Domain 3: Outcome Assessment

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Study Citation:	Bove, F. J., Fulcomer, M. C., Klotz, J. B., Esmart, J., Dufficy, E. M., Savrin, J. E. (1995). Public drinking water contamination and birth outcomes. American Journal of Epidemiology 141(9):850-862.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	194932

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcomes included measures of birthweight (continuous among term births, low term birthweight, very low birthweight), prematurity, fetal death, and congenital anomalies in live births or fetal deaths. The anomalies analyzed included defects of the central nervous system, neural tube, oral cleft, total cardiac, major cardiac, ventricular septum, and any surveillance defect excluding chromosomal defects. All outcomes were identified using birth certificates, fetal death certificates (>20 weeks' gestation), and the NJ congenital birth defect registry (ICD codes provided). These registry data are likely to be sufficiently valid for late pregnancy outcomes. However, their limited ability to capture early pregnancy losses is a weakness. The sample included only 594 fetal deaths (less than 1% of the >80,0000 sample). Typical estimates are that 10-20%, of recognized pregnancies ending in losses. Moreover, developmental defects contributing to early pregnancy losses were also not captured. A further limitation is that that potentially etiologically heterogeneous preterm birth types were analyzed together, as these data did not distinguish premature rupture of membranes vs idiopathic prematurity.
	Metric 8:	Reporting Bias	Low	Models were constructed only for contaminants with associations > 1.0, and tables included only associations with odds ratios ≥1.5. No clear rationale was provided. Several positive odds ratios below the 1.5 cutoff were described in the results text (without confidence intervals), but no null/negative odds ratios were presented or described.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Potential confounding by maternal race, education, parity, and prior pregnancy loss, along with infant sex (for birth outcomes) and adequacy of prenatal care, was examined. Gestational age was addressed by analyzing birthweight among full term births, term low birth weight, and small size for gestational age. Only fully adjusted models were presented. In a companion case-control study (with low participation rates), adjustment for other variables not available on birth certificates (ex. maternal smoking, occupational exposures, medical history, and gestational weight gain) did not influence associations with other studied contaminants. This separate study reduces concerns for important confounding bias, but confounding cannot be ruled out.
	Metric 10:	Covariate Characterization	Medium	Data on covariates came from registry data: birth certificates, fetal death certificates, and the NJ congenital birth defects registry.
	Metric 11:	Co-exposure Counfounding	Medium	Co-exposure confounding by drinking water trihalomethane concentrations was evaluated. There was no evidence to suggest substantial confounding by this or other co-exposures.
Domain 5: Analysis				

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Study Citation:	Bove, F. J., Fulcomer, M. C., Klotz, J. B., Esmart, J., Dufficy, E. M., Savrin, J. E. (1995). Public drinking water contamination and birth outcomes. American Journal of Epidemiology 141(9):850-862.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	194932

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Methods were appropriate. The study used logistic regression models to estimate odds ratios and confidence intervals for dichotomous outcomes, and linear regression for analysis of continuous birth weight.
	Metric 13:	Statistical Power	Low	Statistical power was likely to have been limited as a consequence of the small proportion of the sample defined as having "elevated" residential water concentrations of the chemicals of interest. The range of exposure examined was limited, as cutoffs for elevated levels were close to the detection limits of 1 ppb. In addition, for most birth defect outcomes, fewer than 10 cases had elevated exposure. However, the authors emphasized the magnitude of associations rather than statistical significance and presented multiple confidence intervals to aid interpretation of the precision of estimates (50%, 90% and 99%).
	Metric 14:	Reproducibility of Analyses	Medium	The authors clearly described steps used to estimate exposure-outcome associations, including exposure category cutoffs and criteria for confounding. However, many results were not shown as tables included odds ratios ≥1.5.
	Metric 15:	Statistical Analysis	High	The authors estimated coefficients, odds ratios and confidence intervals using adequate methods. Confounding was based on 15% change-in-estimate comparing nested models. Effect modification (ex by infant sex) was not evaluated as there was no a priori evidence to suggest such analyses at that time.

Additional Comments: This study analyzed the association between estimated residential drinking water concentrations of several chlorinated solvents including 1,2-dichloroethane (as well as 1,1,1-trichloroethane and the ∑[trans-1,2-dichloroethylene & 1,1-dichloroethylene]) and pregnancy outcomes (size at birth, prematurity, fetal deaths, and congenital birth defects). The sample included more than 80,000 births during 1985-88 for residents of 75 towns in NJ using public water system records to estimate exposure during gestation, and registry data (birth certificate, fetal death certificates for pregnancies >20 weeks' gestation, state birth defect registry) to characterize outcomes. Strengths included the large sample size and inclusion of all eligible registered births and fetal deaths in the study period. A critical concern is the inability to capture early fetal deaths and any related malformations (1% of the sample had fetal deaths vs typical estimates of >10%). An important limitation was the low percentage of the sample with detectable (> 1ppb) concentrations of this solvent (<2%), which likely limited power. Small numbers for birth defect outcomes also limited power. Exposure misclassification (ex. drinking water from wells/ work/ bottles, changes in residence, exposure from other sources) is also a concern. However, such misclassification was likely non-differential, and thus more likely to under- vs. to over-estimate associations.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Bowler, R.M., Gysens, S., Hartney, C. (2003). Neuropsychological effects of ethylene dichloride exposure. NeuroToxicology 24(4-5):553-562.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Wechsler Adult Intelligence Scale III (WAIS-III), Wechsler Memory Scale III (WMS-III), Boston Naming Test (BNT), Trail Making Test (TMT), Stroop Color-Word Test, Grooved Pegboard, Dynamometer, Wide Range Achievement Test (WRAT), Finger tapping, Beck Anxiety Index, Beck Depression Index, Symptom Checklist-90 (SCL-90).
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	200241

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Uninformative	221 workers that had been exposed to 1,2-DCE in the Southern United States were initially included. Exclusion criteria were provided, including the number of individuals excluded for each reason. The study authors note that those initially included in the analysis sample were referred by physicians after neurological complaints were documented. Detailed criteria for referral were not provided. Referral-based recruitment of neurological cases will likely result in an analysis sample with an exposure-outcome distribution that is not representative of the eligible population (i.e., contamination site clean-up workers).
	Metric 2:	Attrition	Medium	There was moderate subject loss. Reasons for exclusion from the analysis sample are provided, and only those with complete information were included in the analysis.
	Metric 3:	Comparison Group	Low	Impairment scores were compared to normative data from manuals and/or a "demographically similar control group" cited to Bowler et al. (2001). The controls from this study appeared similar (albeit somewhat older) than 1,2-DCE-exposed workers and reported no prior chemical exposure.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	A job-exposure matrix was not considered plausible; variables considered as surrogates of exposure were obtained from interviews. This method is expected to have poor validity because it relies on workers' recall of subjective events and their frequency (e.g., contact with water); workers (who are taking part in a lawsuit) may overestimate their exposure.
	Metric 5:	Exposure Levels	Low	Two levels of exposure (exposed and not exposed) were used to evaluate neurophysiological effects.
	Metric 6:	Temporality	Medium	Exposures primarily occurred between 1993 and 1995 and neurophysiological effects were evaluated in 2000. Temporality is established, but it is unclear whether exposures fall within relevant exposure windows for the outcome of interest.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Neurophysiological effects were evaluated using a number of standardized tests, including (but not limited to) the Wechsler Adult Intelligence Scale (WAIS-III), the Wechsler Memory Scale (WMS-III), and the Symptom Checklist 90-Revised (SCL90-R). There was no information whether tests were performed using the same methods for exposed and referent groups (e.g., timing and order of tests).

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Study Citation:	Bowler, R.M., Gysens, S., Hartney, C. (2003). Neuropsychological effects of ethylene dichloride exposure. NeuroToxicology 24(4-5):553-562.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Wechsler Adult Intelligence Scale III (WAIS-III), Wechsler Memory Scale III (WMS-III), Boston Naming Test (BNT), Trail Making Test (TMT), Stroop Color-Word Test, Grooved Pegboard, Dynamometer, Wide Range Achievement Test (WRAT), Finger tapping, Beck Anxiety Index, Beck Depression Index, Symptom Checklist-90 (SCL-90).
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	200241

Domain	Metric		Rating	Comments
	Metric 8:	Reporting Bias	Low	Neurobehavioral outcomes mentioned in the methods were reported for 1,2-DCE-exposed workers (as mean score, standard deviation, and percentage impaired); results for controls/normative data were not shown and/or p-values from t-tests were not provided. Control data were used to define impairment (based on z-score) but these values were not reported. Data pertaining to specific exposure variables were reported in the text only; no data were shown in a table.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Normative data permitted adjustments based on age, education, and gender. The control group was ”socio-demographically” similar but specific parameters used to define similarity were not indicated. Separate ANCOVA analyses on workers only were stratified by race (citation provided), and adjusted for ethnicity, age, and education. The methods for identifying and including potential confounders in the analytic approach was not described.
	Metric 10:	Covariate Characterization	Low	No description of the covariate collection method was provided. It was not clear whether the method used was valid or not.
	Metric 11:	Co-exposure Counfounding	Low	A number of workers (18%) reported current exposure to chemicals in their work environment. These potential co-exposures were not were not appropriately adjusted for in the analytical approach used.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Low	The study design was appropriate to evaluate the neurophysiological status of 1,2-DCE-exposed workers; however, statistical methods were not comprehensive.
	Metric 13:	Statistical Power	Medium	The report indicates ”significant impairments” were observed on various neurophysiological tests using t-tests, and significant exposure relationships were reported based on test scores and specific exposure variables (used as surrogates of exposure). Therefore, the number of participants was sufficient to detect an effect.
	Metric 14:	Reproducibility of Analyses	Low	Tests were scored according to relevant manuals; the calculation of z-scores, used in all impairment comparisons and analyses of exposure relationships, was not explained in adequate detail. The methods used to determine relationships between specific exposure variables and test scores (i.e., ANCOVA analyses) were not fully described.
	Metric 15:	Statistical Analysis	Low	Description of the ANCOVA analysis was largely not present. It is not clear whether model assumptions were met.

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Study Citation:	Bowler, R.M., Gysens, S., Hartney, C. (2003). Neuropsychological effects of ethylene dichloride exposure. NeuroToxicology 24(4-5):553-562.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Wechsler Adult Intelligence Scale III (WAIS-III), Wechsler Memory Scale III (WMS-III), Boston Naming Test (BNT), Trail Making Test (TMT), Stroop Color-Word Test, Grooved Pegboard, Dynamometer, Wide Range Achievement Test (WRAT), Finger tapping, Beck Anxiety Index, Beck Depression Index, Symptom Checklist-90 (SCL-90).
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	200241

Domain	Metric	Rating	Comments
Additional Comments:	The study evaluated the neurobehavioral status of a group of workers with known exposure to 1,2-DCE at a clean-up site. Impairments related to processing speed, attention, cognitive flexibility, motor coordination and speed, verbal memory/fluency, vision and visual-spatial abilities, and mood were reported in exposed workers. Serious and consequential flaws are associated with the study including methods of participant selection and retention, and exposure characterization among others.		

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Brender, J.D., Shinde, M.U., Zhan, F.B., Gong, X., Langlois, P.H. (2014). Maternal residential proximity to chlorinated solvent emissions and birth defects in offspring: A case-control study. Environmental Health: A Global Access Science Source 13(1):96.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	birth defects (neural tube defects, limbs deficiencies, oral cleft defects, heart defects, spina bifida, anencephaly)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	2799700

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Participants were drawn from the Texas Birth Defects Registry (TBDR) for years 1996-2008. Controls were frequency matched from the same registry. Study authors state that neural tube cases were more likely to not be successfully geocoded which may introduce selection bias, however, the authors note that both cases and controls with addresses that could not be geocoded were similar. In spite of that, the inclusion criteria, methods of participant selection, and frequency match were reported.
	Metric 2:	Attrition	Medium	13.3% case mother addresses and 12.8% control mother addresses were unable to be geocoded, however this most likely only lowered the precision of the study and most likely does not vary based on exposure level.
	Metric 3:	Comparison Group	Medium	Controls were matched to cases and pulled from the same eligible population by year of delivery and public health service region. Other demographic factors, e.g., race was not matched in population selection. However, statistical analyses were adjusted for year of delivery, maternal age, race/ethnicity, education, and public health region of residence.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Used Emission Weighted Proximity Model to estimate exposure at a given address based on proximity to emission sources and the specific amount or type of pollutant emitted. There may be some exposure misclassification due to mothers moving away from geocoded addresses. Previous studies indicate ~67% of mothers do not move between conception and delivery.
	Metric 5:	Exposure Levels	Medium	Reports exposure as "exposure risk value" and groups the risk values into quartiles, with exposure risk values < 0 being the referent group
	Metric 6:	Temporality	Medium	The study authors estimated exposure based on residence during pregnancy and evaluated birth outcomes. Temporality is established. Previous studies indicate ~67% mothers don't move between trimester and delivery. For mothers who moved during the pregnancy, the temporality is unknown.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Outcomes determined by Texas Birth Defect Registry, checking for birth defect diagnosis. Birth certificates came from Center for Health Statistics at Texas Department of State Health Services
	Metric 8:	Reporting Bias	High	Outcome data measured and reported clearly, stratified by specific type of birth defect
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Brender, J.D., Shinde, M.U., Zhan, F.B., Gong, X., Langlois, P.H. (2014). Maternal residential proximity to chlorinated solvent emissions and birth defects in offspring: A case-control study. Environmental Health: A Global Access Science Source 13(1):96.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	birth defects (neural tube defects, limbs deficiencies, oral cleft defects, heart defects, spina bifida, anencephaly)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	2799700

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	High	Cases were frequency matched by year of delivery and public health service region. Final models were adjusted for year of delivery, public health region, maternal age (<20, 20-24, 25-29, 30-34, 35-39, >39 years), education (<12 years, 12 years, >12 years), and race/ethnicity (Whit non-Hispanic, Black non-Hispanic, Hispanic, other non-Hispanic).
	Metric 10:	Covariate Characterization	High	Used birth and death certificates for demographic information
	Metric 11:	Co-exposure Counfounding	Medium	other co-exposures were not described
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	study used logistic regression to measure association between exposure and birth defects
	Metric 13:	Statistical Power	Medium	Overall adequate number of cases and controls - some effects have low cell counts, but at least one health effect has sufficient statistical power.
	Metric 14:	Reproducibility of Analyses	Medium	Methods sufficiently detailed for reproducibility
	Metric 15:	Statistical Analysis	High	No logistic regression model assumption violations were identified.

Additional Comments: This study examined the association between proximity to several point sources of chlorinated solvents and birth defects. Exposure was assessed using EPA's Toxic Release Inventory, and birth defects were assessed using Texas birth registries. The geocoded address of mothers on day of delivery and the amount of solvent was plugged into the Emission Weighted Probability model to assign each mother an exposure risk value. Limitations include limited evidence of temporality. Additionally, elective terminations lacked a vital record, which meant only 69% of mothers with neural tube defects were geocoded. Mothers highly exposed to 1,2-dichloroethane were 1.85 times more likely to have the spina bifida birth defect than mothers who were not significantly exposed.

Overall Quality Determination High

* No biomarkers were identified for this evaluation.

Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Nested case-control design; cases selected from deaths in cohort study was described by Rinsky et al (1988; HERO 597923) (29,139 workers in Union Carbide facilities in West Virginia followed from 1940 to 1978). Vital status complete for 95% of cohort members.
	Metric 2:	Attrition	High	There was minimal exclusion of subjects/missing data, because vital status follow-up was complete for 96% of the 29,139 men in the cohort study.
	Metric 3:	Comparison Group	Medium	Controls were randomly selected in a 5:1 ratio to cases from the total employee cohort such that they were first employed in the same decade and survived to the same five-year survival period as cases. Controls survived at least to the beginning of the five-year interval in which cases died. Controls were independently selected for each of the individual disease subcategories. However, the demographic information between cases and controls were not compared in the paper.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was partially described: (1) Potential employee contact with a specific substance was determined by tracing each employee's work assignments and linking these assignment records to a separate computer file that contained a history of departmental usage for each substance; (2) Potential exposure to each chemical group was assumed on the basis of assignment o a production unit with a history of usage of any member of that chemical group. However, exposure level either based on work assignment in departments such as job exposure matrix or on the chemical levels were not presented.
	Metric 5:	Exposure Levels	Low	The range of exposure is limited. For example, exposure was presented by the duration of work in two categories: <5 years and 5+ years.
	Metric 6:	Temporality	Medium	Temporality is established, but it is unclear whether the exposures fall within the relevant exposure window. Authors used a lag time of 5 years; since controls were selected for 5 yr intervals, the effective lag time ranged from 5-9 years with an average of 7.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Case definition was based on death certificate diagnosis; but no method validation was conducted against this well-established methods.
	Metric 8:	Reporting Bias	Medium	All outcomes reported, but ORs for many analyses presented without CIs (some CIs reported in text).
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Low	There is indirect evidence that considerations were not made for potential confounders (ORs not adjusted, controls not age- or race-matched). Even though authors note that "Age-adjusted stratified analyses, which were also conducted, did not materially modify the odds ratio estimates". Also stratified examination of odds ratios were conducted to assess duration of exposure effects. However, other key confounders e.g., smoking status and race were not accounted for.
	Metric 10:	Covariate Characterization	Medium	The only potential confounder considered was age; this was presumably evaluated based on employment records (no discussion presented). Age-adjusted stratified analyses were conducted.
	Metric 11:	Co-exposure Counfounding	Low	Co-exposures were present and were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Nested case-control study design is appropriate for research question. Initial data analysis included crude odds ratio and then stratified examination of odds ratios was conducted to ass duration of exposure effect. Also, age-adjusted stratified analysis was conducted.
	Metric 13:	Statistical Power	Low	Statistical power calculations were not reported. Case numbers for each disease were low. The number of subjects was not sufficient to detect an effect of 1,2-dichloroethylene exposure.
	Metric 14:	Reproducibility of Analyses	Medium	Description was sufficient to be conceptually reproducible.
	Metric 15:	Statistical Analysis	Low	Statistical model to calculate odds ratio was not described.

Additional Comments: This nested case-control study within a cohort study is a good study design to answer the research question regarding the association between multiple chemical exposures and four cancer sites. Cases and controls are selected appropriate. However, there are several limitations in this study: (1) confounders were not all considered and adjusted for, except that age-adjusted odds ratios were conducted; (2) it is not described if co-exposures were adjusted for; (3) numbers of cancer cases for each cancer type were small, so the statistical power is limited; (4) statistical models for calculating odds ratios were not described.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Nested case-control design; cases selected from deaths in cohort study was described by Rinsky et al (1988; HERO 597923) (29,139 workers in Union Carbide facilities in West Virginia followed from 1940 to 1978). Vital status complete for 95% of cohort members.
	Metric 2:	Attrition	High	There was minimal exclusion of subjects/missing data, because vital status follow-up was complete for 96% of the 29,139 men in the cohort study.
	Metric 3:	Comparison Group	Medium	Controls were randomly selected in a 5:1 ratio to cases from the total employee cohort such that they were first employed in the same decade and survived to the same five-year survival period as cases. Controls survived at least to the beginning of the five-year interval in which cases died. Controls were independently selected for each of the individual disease subcategories. However, the demographic information between cases and controls were not compared in the paper.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was partially described: (1) Potential employee contact with a specific substance was determined by tracing each employee's work assignments and linking these assignment records to a separate computer file that contained a history of departmental usage for each substance; (2) Potential exposure to each chemical group was assumed on the basis of assignment o a production unit with a history of usage of any member of that chemical group. However, exposure level either based on work assignment in departments such as job exposure matrix or on the chemical levels were not presented.
	Metric 5:	Exposure Levels	Low	The range of exposure is limited. For example, exposure was presented by the duration of work in two categories: <5 years and 5+ years.
	Metric 6:	Temporality	Medium	Temporality is established, but it is unclear whether the exposures fall within the relevant exposure window. Authors used a lag time of 5 years; since controls were selected for 5 yr intervals, the effective lag time ranged from 5-9 years with an average of 7.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Case definition was based on death certificate diagnosis; but no method validation was conducted against this well-established methods.
	Metric 8:	Reporting Bias	Medium	All outcomes reported, but ORs for many analyses presented without CIs (some CIs reported in text).
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Low	There is indirect evidence that considerations were not made for potential confounders (ORs not adjusted, controls not age- or race-matched). Even though authors note that "Age-adjusted stratified analyses, which were also conducted, did not materially modify the odds ratio estimates". Also stratified examination of odds ratios were conducted to assess duration of exposure effects. However, other key confounders e.g., smoking status and race were not accounted for.
	Metric 10:	Covariate Characterization	Medium	The only potential confounder considered was age; this was presumably evaluated based on employment records (no discussion presented). Age-adjusted stratified analyses were conducted.
	Metric 11:	Co-exposure Counfounding	Low	Co-exposures were present and were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Nested case-control study design is appropriate for research question. Initial data analysis included crude odds ratio and then stratified examination of odds ratios was conducted to ass duration of exposure effect. Also, age-adjusted stratified analysis was conducted.
	Metric 13:	Statistical Power	Low	Statistical power calculations were not reported. Case numbers for each disease were low. The number of subjects was not sufficient to detect an effect of 1,2-dichloroethylene exposure.
	Metric 14:	Reproducibility of Analyses	Medium	Description was sufficient to be conceptually reproducible.
	Metric 15:	Statistical Analysis	Low	Statistical model to calculate odds ratio was not described.

Additional Comments: This nested case-control study within a cohort study is a good study design to answer the research question regarding the association between multiple chemical exposures and four cancer sites. Cases and controls are selected appropriate. However, there are several limitations in this study: (1) confounders were not all considered and adjusted for, except that age-adjusted odds ratios were conducted; (2) it is not described if co-exposures were adjusted for; (3) numbers of cancer cases for each cancer type were small, so the statistical power is limited; (4) statistical models for calculating odds ratios were not described.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Nested case-control design; cases selected from deaths in cohort study was described by Rinsky et al (1988; HERO 597923) (29,139 workers in Union Carbide facilities in West Virginia followed from 1940 to 1978). Vital status complete for 95% of cohort members.
	Metric 2:	Attrition	High	There was minimal exclusion of subjects/missing data, because vital status follow-up was complete for 96% of the 29,139 men in the cohort study.
	Metric 3:	Comparison Group	Medium	Controls were randomly selected in a 5:1 ratio to cases from the total employee cohort such that they were first employed in the same decade and survived to the same five-year survival period as cases. Controls survived at least to the beginning of the five-year interval in which cases died. Controls were independently selected for each of the individual disease subcategories. However, the demographic information between cases and controls were not compared in the paper.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was partially described: (1) Potential employee contact with a specific substance was determined by tracing each employee's work assignments and linking these assignment records to a separate computer file that contained a history of departmental usage for each substance; (2) Potential exposure to each chemical group was assumed on the basis of assignment o a production unit with a history of usage of any member of that chemical group. However, exposure level either based on work assignment in departments such as job exposure matrix or on the chemical levels were not presented.
	Metric 5:	Exposure Levels	Low	The range of exposure is limited. For example, exposure was presented by the duration of work in two categories: <5 years and 5+ years.
	Metric 6:	Temporality	Medium	Temporality is established, but it is unclear whether the exposures fall within the relevant exposure window. Authors used a lag time of 5 years; since controls were selected for 5 yr intervals, the effective lag time ranged from 5-9 years with an average of 7.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Case definition was based on death certificate diagnosis; but no method validation was conducted against this well-established methods.
	Metric 8:	Reporting Bias	Medium	All outcomes reported, but ORs for many analyses presented without CIs (some CIs reported in text).
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Low	There is indirect evidence that considerations were not made for potential confounders (ORs not adjusted, controls not age- or race-matched). Even though authors note that "Age-adjusted stratified analyses, which were also conducted, did not materially modify the odds ratio estimates". Also stratified examination of odds ratios were conducted to assess duration of exposure effects. However, other key confounders e.g., smoking status and race were not accounted for.
	Metric 10:	Covariate Characterization	Medium	The only potential confounder considered was age; this was presumably evaluated based on employment records (no discussion presented). Age-adjusted stratified analyses were conducted.
	Metric 11:	Co-exposure Counfounding	Low	Co-exposures were present and were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Nested case-control study design is appropriate for research question. Initial data analysis included crude odds ratio and then stratified examination of odds ratios was conducted to ass duration of exposure effect. Also, age-adjusted stratified analysis was conducted.
	Metric 13:	Statistical Power	Low	Statistical power calculations were not reported. Case numbers for each disease were low. The number of subjects was not sufficient to detect an effect of 1,2-dichloroethylene exposure.
	Metric 14:	Reproducibility of Analyses	Medium	Description was sufficient to be conceptually reproducible.
	Metric 15:	Statistical Analysis	Low	Statistical model to calculate odds ratio was not described.

Additional Comments: This nested case-control study within a cohort study is a good study design to answer the research question regarding the association between multiple chemical exposures and four cancer sites. Cases and controls are selected appropriate. However, there are several limitations in this study: (1) confounders were not all considered and adjusted for, except that age-adjusted odds ratios were conducted; (2) it is not described if co-exposures were adjusted for; (3) numbers of cancer cases for each cancer type were small, so the statistical power is limited; (4) statistical models for calculating odds ratios were not described.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Nested case-control design; cases selected from deaths in cohort study was described by Rinsky et al (1988; HERO 597923) (29,139 workers in Union Carbide facilities in West Virginia followed from 1940 to 1978). Vital status complete for 95% of cohort members.
	Metric 2:	Attrition	High	There was minimal exclusion of subjects/missing data, because vital status follow-up was complete for 96% of the 29,139 men in the cohort study.
	Metric 3:	Comparison Group	Medium	Controls were randomly selected in a 5:1 ratio to cases from the total employee cohort such that they were first employed in the same decade and survived to the same five-year survival period as cases. Controls survived at least to the beginning of the five-year interval in which cases died. Controls were independently selected for each of the individual disease subcategories. However, the demographic information between cases and controls were not compared in the paper.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was partially described: (1) Potential employee contact with a specific substance was determined by tracing each employee's work assignments and linking these assignment records to a separate computer file that contained a history of departmental usage for each substance; (2) Potential exposure to each chemical group was assumed on the basis of assignment o a production unit with a history of usage of any member of that chemical group. However, exposure level either based on work assignment in departments such as job exposure matrix or on the chemical levels were not presented.
	Metric 5:	Exposure Levels	Low	The range of exposure is limited. For example, exposure was presented by the duration of work in two categories: <5 years and 5+ years.
	Metric 6:	Temporality	Medium	Temporality is established, but it is unclear whether the exposures fall within the relevant exposure window. Authors used a lag time of 5 years; since controls were selected for 5 yr intervals, the effective lag time ranged from 5-9 years with an average of 7.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Case definition was based on death certificate diagnosis; but no method validation was conducted against this well-established methods.
	Metric 8:	Reporting Bias	Medium	All outcomes reported, but ORs for many analyses presented without CIs (some CIs reported in text).
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Low	There is indirect evidence that considerations were not made for potential confounders (ORs not adjusted, controls not age- or race-matched). Even though authors note that "Age-adjusted stratified analyses, which were also conducted, did not materially modify the odds ratio estimates". Also stratified examination of odds ratios were conducted to assess duration of exposure effects. However, other key confounders e.g., smoking status and race were not accounted for.
	Metric 10:	Covariate Characterization	Medium	The only potential confounder considered was age; this was presumably evaluated based on employment records (no discussion presented). Age-adjusted stratified analyses were conducted.
	Metric 11:	Co-exposure Counfounding	Low	Co-exposures were present and were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Nested case-control study design is appropriate for research question. Initial data analysis included crude odds ratio and then stratified examination of odds ratios was conducted to ass duration of exposure effect. Also, age-adjusted stratified analysis was conducted.
	Metric 13:	Statistical Power	Low	Statistical power calculations were not reported. Case numbers for each disease were low. The number of subjects was not sufficient to detect an effect of 1,2-dichloroethylene exposure.
	Metric 14:	Reproducibility of Analyses	Medium	Description was sufficient to be conceptually reproducible.
	Metric 15:	Statistical Analysis	Low	Statistical model to calculate odds ratio was not described.

Additional Comments: This nested case-control study within a cohort study is a good study design to answer the research question regarding the association between multiple chemical exposures and four cancer sites. Cases and controls are selected appropriate. However, there are several limitations in this study: (1) confounders were not all considered and adjusted for, except that age-adjusted odds ratios were conducted; (2) it is not described if co-exposures were adjusted for; (3) numbers of cancer cases for each cancer type were small, so the statistical power is limited; (4) statistical models for calculating odds ratios were not described.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Cheng, T.J., Huang, M.L., You, N.C., Du, C.L., Chau, T.T. (1999). Abnormal liver function in workers exposed to low levels of ethylene dichloride and vinyl chloride monomer. Journal of Occupational and Environmental Medicine 41(12):1128-1133.
Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	AST, ALT, GGT, Hepatitis B virus surface antigen (HBsAg), and anti-hepatitis C virus antibody (anti-HCV).
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	200266

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	A total of 251 male workers were included from 4 vinyl chloride monomer manufacturing plants. Other details on recruitment strategy, eligibility criteria, year of enrollment, and participation rates were not provided.
	Metric 2:	Attrition	Low	There was no indication of attrition and details on the number of eligible participants throughout the study was limited. Attrition could not be adequately assessed due to a lack of information regarding recruitment and selection.
	Metric 3:	Comparison Group	Medium	The low-EDC-low-VCM group (187 participants) was used as the comparison group, and there is indirect evidence groups are similar. Limited details were provided for setting, inclusion and exclusion criteria, and methods of participant selection.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	NIOSH recommended methods 1003 and 1007 were used for personal and area sampling, respectively. Air samples were collected, stored at 4 deg. C, and analyzed within 2 weeks of the sampling event. However, historical job changes, changes in exposure levels over time, and timing (year or days during work week) or duration of area or personal sampling were not reported.
	Metric 5:	Exposure Levels	Medium	EDC and VCM levels were reported for the different categories of jobs, which were classified into low-EDC-low-VCM, mod-EDC-low-VCM, and low-EDC-mod-VCM groups.
	Metric 6:	Temporality	High	The age of participants (mean age 33.7-40.1 years) and employment duration (mean 7.5-14.3 years) were reported, and the temporality between the exposure and outcome appears to be appropriate.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	AST, ALT, and GGT "were analyzed with a Hitachi 7050 autoanalyzer". A basis for the cutoff values used in Table 4 to determine "abnormal" AST, ALT, and GGT levels was not provided.
	Metric 8:	Reporting Bias	High	Odds ratios for abnormal liver function were provided with 95% confidence intervals, the number per exposure level, and significance when applicable.
Domain 4: Potential Confounding / Variability Control				

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Study Citation: Cheng, T.J., Huang, M.L., You, N.C., Du, C.L., Chau, T.T. (1999). Abnormal liver function in workers exposed to low levels of ethylene dichloride and vinyl chloride monomer. Journal of Occupational and Environmental Medicine 41(12):1128-1133.
Health Outcome(s): Hepatic/Liver
Reported Health Effect(s): AST, ALT, GGT, Hepatitis B virus surface antigen (HBsAg), and anti-hepatitis C virus antibody (anti-HCV).
Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s): No linked references.
HERO ID: 200266

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Medium	The study reports information on potential confounders (age, hepatitis, BMI, alcohol use, and employment duration), and controls for hepatitis, BMI and alcohol consumption in the multiple logistic regression analyses. There is indirect evidence that appropriate adjustments were made.
	Metric 10:	Covariate Characterization	Medium	An interviewer administered the questionnaires to collect information about potential confounders and occupational history.
	Metric 11:	Co-exposure Counfounding	Low	Exposure to ethylene dichloride was evaluated in a vinyl chloride monomer (VCM) manufacturing facility, and VCM was also subsequently analyzed using personal and area sampling. Results for VCM exposure concentrations were provided. VCM is also suspected to cause liver damage.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design (cohort) was appropriate to assess the outcome of interest (”markers of liver damage”). Chi-squared (X2) test and multiple logistic regression were used for statistical analyses.
	Metric 13:	Statistical Power	Medium	The number of participants was adequate to detect an effect in the exposed populations, although power calculations were not provided. There were >20 participants in each group.
	Metric 14:	Reproducibility of Analyses	Low	A description of the logistic regression analysis was provided, however, study authors do not provide information on categorization of abnormal liver function.
	Metric 15:	Statistical Analysis	High	There were no identifiable logistic regression model assumption violations.
Domain 6: Other (if applicable) Considerations for Biomarker Selection and Measurement (Lakind et al. 2014)				
	Metric 16:	Use of Biomarker of Exposure	N/A	Biomarker of exposures were not assessed.
	Metric 17:	Effect Biomarker	High	This study uses aspartate aminotransferase, alanine aminotransferase, and y-glutamyltransferase as biomarkers of effect. While these no works cited to explain their connection to liver function, all three are well-known marker of liver function. Similarly, Hepatitis B virus surface antigen and antihepatitis C virus anitbody are also well-known measures of liver function and health.
	Metric 18:	Method Sensitivity	Low	No limit of detection information is provided for any of the effect biomarkers.
	Metric 19:	Biomarker Stability	Medium	While the study does not provide a lot of information regarding biomarker storage or stability, the authors do mention that venous blood used to detect biomarkers was stored at 4 degrees C.
	Metric 20:	Sample Contamination	Medium	No specific information regarding potential sample contamination was provided.
	Metric 21:	Method Requirements	Medium	Aspartate aminotransferase, alanine aminotransferase, and y-glutamyltransferase were analyzed using a Hitachi 7050 autoanalyzer. Hepatitis B virus surface antibody and antihepatitis C virus antibody were assessed with radioimmunoassay and enzyme-linked immunosorbent assay.

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Study Citation:	Cheng, T.J., Huang, M.L., You, N.C., Du, C.L., Chau, T.T. (1999). Abnormal liver function in workers exposed to low levels of ethylene dichloride and vinyl chloride monomer. Journal of Occupational and Environmental Medicine 41(12):1128-1133.
Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	AST, ALT, GGT, Hepatitis B virus surface antigen (HBsAg), and anti-hepatitis C virus antibody (anti-HCV).
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	200266

Domain	Metric	Rating	Comments
	Metric 22: Matrix Adjustment	N/A	No information on matrix adjustment was provided/available.

Additional Comments: A group of 251 male workers from 4 vinyl chloride monomer (VCM) manufacturing plants were included in this assessment to examine if occupational exposure to VCM and ethylene dichloride (EDC) "resulted in increased risk of liver damage" by examining AST, ALT, and GGT levels in the blood. Increased ORs for abnormal AST (>37 IU/L) and ALT (>41 IU/L) in the mod-EDC-low-VCM group (0.17-333.7 ppm EDC, 0.18-0.34 ppm VCM), compared with the low-EDC-low-VCM group, was reported. Exposure levels were measured using area and personal sampling, but the timing and duration of the sampling events were not reported.

Overall Quality Determination Medium

Study Citation:	Dosemeci, M., Cocco, P., Chow, W.H. (1999). Gender differences in risk of renal cell carcinoma and occupational exposures to chlorinated aliphatic hydrocarbons. American Journal of Industrial Medicine 36(1):54-59.
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	renal cell carcinoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	4697224

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	The details of the study design were reported elsewhere (Chow et al. 1994, HERO ID 701514). Brief details about the setting, date, number of eligible participants, and control matching were reported. Reasons for exclusions/non-participation were described with details by Chow et al. (1994).
	Metric 2:	Attrition	High	For the details of the study design and attrition of study subjects, the study authors referred to another publication by Chow et al., 1994. Chow et al. (1994) mentioned that at the end of the personal interview, the respondents were given a self-administered food-frequency questionnaire. Of the subjects interviewed for the study, 632 patients (79% of 796 eligible patients) and 653 control subjects (79% of 707 eligible control subjects) returned the diet questionnaire. A number of subjects, whose responses were considered unreliable, were excluded from the analysis, including 48 patients and three control subjects who had seven or more skipped food items or had questionable data and 50 patients whose next-of-kin respondent was not a spouse. Also excluded were two patients with unknown smoking status, since smoking is a risk factor.
	Metric 3:	Comparison Group	Medium	The cases were pulled from the Minnesota Cancer Surveillance System. Controls were selected from the general population of Minnesota; controls age 20-64 years were selected through random digital dialing and controls age 65-85 years were collected from files through the Health Care Financing Administration. Controls were age- and gender-stratified and were of the same race. Characteristics of cases and controls were not provided in the text or a table.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	High	Occupational histories including the most recent and usual occupation and industry, job activities, started-year and ended-year, and part-time/full-time status were collected. Occupations and industries were coded according to the standard occupational classification (SOC) and standard industrial classification (SIC) schemes. The National Cancer Institute developed job exposure matrices (JEM) for nine individual chlorinated aliphatic hydrocarbons (CAHCs), all CAHCs-combined, and all organic solvents-combined. These JEMs were merged with assigned SOC and SIC to determine the exposure status to these chemicals for each study subject. Application of the JEM was described elsewhere (Dosemeci et al. 1994, HERO ID 632334; Gomez et al. 1994, HERO ID 702154).
	Metric 5:	Exposure Levels	Medium	Details of the application of the JEM were described elsewhere (Dosemeci et al. 1994, HERO ID 632334; Gomez et al. 1994, HERO ID 702154). Dosemeci et al. (1994) described more details about that this study assigned three levels of probability (low, medium, high) to industries and occupations for chemical exposure levels.

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Study Citation:	Dosemeci, M., Cocco, P., Chow, W.H. (1999). Gender differences in risk of renal cell carcinoma and occupational exposures to chlorinated aliphatic hydrocarbons. American Journal of Industrial Medicine 36(1):54-59.
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	renal cell carcinoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	4697224

Domain	Metric		Rating	Comments
	Metric 6:	Temporality	Medium	Occupational questionnaires identified prior exposures based on reported recent and usual occupations as well as duration of employment. Outcome status was determined from registry data. The authors note that some occupational history was incomplete which may result in some uncertainty in regard to temporality.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Cases were identified as newly diagnosed and histologically confirmed renal cell carcinoma through the Minnesota Cancer Surveillance System and information about each participant was collected using a questionnaire. Validation was not specified.
	Metric 8:	Reporting Bias	Medium	A description of measured outcomes is reported and ORs were stratified by sex. Effect estimates are reported with a confidence interval. One table showed the total numbers of men and women respectively for each chemical, but numbers of cases/controls were not reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Appropriate adjustments were made in the final analysis, including age, gender, smoking, hypertension and the use of diuretics and/or anti-hypertension drugs, and BMI. Results were stratified by sex.
	Metric 10:	Covariate Characterization	Medium	Information about participants was collected using a questionnaire, and it includes potential confounders, e.g., smoking habits. Validation was not specified.
	Metric 11:	Co-exposure Counfounding	Medium	Co-exposures were identified through the job exposure matrices. Chemicals were evaluated individually and as a group.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen (case-control) was appropriate for the research question (renal cell carcinoma risk from occupational organic solvent exposure). Logistic regression models were used to estimate the relative risk and 95% CI.
	Metric 13:	Statistical Power	Low	Statistical power calculations were not provided. No significant effects were observed with 1,2-dichloroethane. The number of participated women to calculate odds ratio was inadequate to detect an effect in the participants for other chemicals or the combined risk, because it was very low.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis was brief, but is sufficient to understand precisely what has been done and to be conceptually reproducible with access to the analytic data.
	Metric 15:	Statistical Analysis	High	Model assumptions for logistic regression were met. The odds ratios were adjusted for age, smoking, hypertension status and/or use of diuretic and/or anti-hypertension drugs, and body mass index for men and women separately.

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Study Citation:	Dosemeci, M., Cocco, P., Chow, W.H. (1999). Gender differences in risk of renal cell carcinoma and occupational exposures to chlorinated aliphatic hydrocarbons. American Journal of Industrial Medicine 36(1):54-59.
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	renal cell carcinoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	4697224

Domain	Metric	Rating	Comments
Additional Comments:	A group of 438 cases (273 men and 165 women) were selected from the Minnesota Cancer Surveillance System that had been newly diagnosed with renal cell carcinoma. Controls included 687 participants (462 men and 225 women) age- and gender- stratified that were selected from either the general population of Minnesota (age 20-64 years) or from the Health Care Financing Administration files (age 65-85). No significant increase in the risk of renal cell carcinoma was observed with exposure to 1,2-dichloroethane among men or women separately, or for all participants exposed.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Dosemeci, M., Cocco, P., Chow, W.H. (1999). Gender differences in risk of renal cell carcinoma and occupational exposures to chlorinated aliphatic hydrocarbons. American Journal of Industrial Medicine 36(1):54-59.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	renal cell carcinoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	4697224

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	The details of the study design were reported elsewhere (Chow et al. 1994, HERO ID 701514). Brief details about the setting, date, number of eligible participants, and control matching were reported. Reasons for exclusions/non-participation were described with details by Chow et al. (1994).
	Metric 2:	Attrition	Medium	For the details of the study design and attrition of study subjects, the study authors referred to another publication by Chow et al., 1994. Chow et al. (1994) mentioned that at the end of the personal interview, the respondents were given a self-administered food-frequency questionnaire. Of the subjects interviewed for the study, 632 patients (79% of 796 eligible patients) and 653 control subjects (79% of 707 eligible control subjects) returned the diet questionnaire. A number of subjects, whose responses were considered unreliable, were excluded from the analysis, including 48 patients and three control subjects who had seven or more skipped food items or had questionable data and 50 patients whose next-of-kin respondent was not a spouse. Also excluded were two patients with unknown smoking status, since smoking is a risk factor.
	Metric 3:	Comparison Group	Medium	The cases were pulled from the Minnesota Cancer Surveillance System. Controls were selected from the general population of Minnesota; controls age 20-64 years were selected through random digital dialing and controls age 65-85 years were collected from files through the Health Care Financing Administration. Controls were age- and gender-stratified and were of the same race. Characteristics of cases and controls were not provided in the text or a table.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	High	Occupational histories including the most recent and usual occupation and industry, job activities, started-year and ended-year, and part-time/full-time status were collected. Occupations and industries were coded according to the standard occupational classification (SOC) and standard industrial classification (SIC) schemes. The National Cancer Institute developed job exposure matrices (JEM) for nine individual chlorinated aliphatic hydrocarbons (CAHCs), all CAHCs-combined, and all organic solvents-combined. These JEMs were merged with assigned SOC and SIC to determine the exposure status to these chemicals for each study subject. Application of the JEM was described elsewhere (Dosemeci et al. 1994, HERO ID 632334; Gomez et al. 1994, HERO ID 702154).
	Metric 5:	Exposure Levels	Medium	Details of the application of the JEM were described elsewhere (Dosemeci et al. 1994, HERO ID 632334; Gomez et al. 1994, HERO ID 702154). Dosemeci et al. (1994) described more details about that this study assigned three levels of probability (low, medium, high) to industries and occupations for chemical exposure levels.

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Study Citation:	Dosemeci, M., Cocco, P., Chow, W.H. (1999). Gender differences in risk of renal cell carcinoma and occupational exposures to chlorinated aliphatic hydrocarbons. American Journal of Industrial Medicine 36(1):54-59.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	renal cell carcinoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	4697224

Domain	Metric		Rating	Comments
	Metric 6:	Temporality	Medium	Occupational questionnaires identified prior exposures based on reported recent and usual occupations as well as duration of employment. Outcome status was determined from registry data. The authors note that some occupational history was incomplete which may result in some uncertainty in regard to temporality.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Cases were identified as newly diagnosed and histologically confirmed renal cell carcinoma through the Minnesota Cancer Surveillance System and information about each participant was collected using a questionnaire. Validation was not specified.
	Metric 8:	Reporting Bias	Medium	A description of measured outcomes is reported and ORs were stratified by sex. Effect estimates are reported with a confidence interval. One table showed the total numbers of men and women respectively for each chemical, but numbers of cases/controls were not reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Appropriate adjustments were made in the final analysis, including age, gender, smoking, hypertension and the use of diuretics and/or anti-hypertension drugs, and BMI. Results were stratified by sex.
	Metric 10:	Covariate Characterization	Medium	Information about participants was collected using a questionnaire, and it includes potential confounders, e.g., smoking habits. Validation was not specified.
	Metric 11:	Co-exposure Counfounding	Medium	Co-exposures were identified through the job exposure matrices. Chemicals were evaluated individually and as a group.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen (case-control) was appropriate for the research question (renal cell carcinoma risk from occupational organic solvent exposure). Logistic regression models were used to estimate the relative risk and 95% CI.
	Metric 13:	Statistical Power	Low	Statistical power calculations were not provided. No significant effects were observed with 1,2-dichloroethane. The number of participated women to calculate odds ratio was inadequate to detect an effect in the participants for other chemicals or the combined risk, because it was very low.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis was brief, but is sufficient to understand precisely what has been done and to be conceptually reproducible with access to the analytic data.
	Metric 15:	Statistical Analysis	High	Model assumptions for logistic regression were met. The odds ratios were adjusted for age, smoking, hypertension status and/or use of diuretic and/or anti-hypertension drugs, and body mass index for men and women separately.

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Study Citation:	Dosemeci, M., Cocco, P., Chow, W.H. (1999). Gender differences in risk of renal cell carcinoma and occupational exposures to chlorinated aliphatic hydrocarbons. American Journal of Industrial Medicine 36(1):54-59.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	renal cell carcinoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	4697224

Domain	Metric	Rating	Comments
Additional Comments:	A group of 438 cases (273 men and 165 women) were selected from the Minnesota Cancer Surveillance System that had been newly diagnosed with renal cell carcinoma. Controls included 687 participants (462 men and 225 women) age- and gender- stratified that were selected from either the general population of Minnesota (age 20-64 years) or from the Health Care Financing Administration files (age 65-85). No significant increase in the risk of renal cell carcinoma was observed with exposure to 1,2-dichloroethane among men or women separately, or for all participants exposed.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Garcia, E., Hurley, S., Nelson, D.O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health: A Global Access Science Source 14(1):14.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	breast cancer in females
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	3014082

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	A total of 112,378 women were included in this study out of 133,479 eligible female participants from the California Teacher Study cohort. A full description of the cohort is provided in Bernstein et al. 2002 (HERO ID 808446). Reasons for exclusion were provided. The reported information indicates that participant selection in or out of the study and participation was not likely to be biased.
	Metric 2:	Attrition	High	112,378/133,479 participants were included in the study. Exclusions were for the purpose of the study and analysis. Exclusion criteria were documented. Included participants had completed questionnaires. The California Cancer Registry is estimated to be 99% complete.
	Metric 3:	Comparison Group	Medium	There is only indirect evidence that groups are similar. Participants were recruited from the same eligible population with the same method of ascertainment. Comparisons were provided for participants with and without breast cancer. Characteristics between these two groups were generally similar. 5 Quintiles of exposure were used, and Q2-5 were compared with Q1.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	High	The Assessment System for Population Exposure Nationwide and the Human Exposure Model are used as part of the National-Scale Air Toxics Assessment produced by the EPA and was used to estimate ambient HAP concentrations for geographic locations. Methods are described online through the US EPA Assessment Methods.
	Metric 5:	Exposure Levels	Medium	The distribution of the NATA annual ambient concentration for each compound was plotted in Figure 1 using a box plot, and 5 Quintiles were used in the analyses.
	Metric 6:	Temporality	Medium	The follow-up period was from 1995-2011, and the NATA estimates were made in 2002 because it was approximately half way between the start and end of the follow-up period. However, it is unclear whether exposures fall within relevant exposure windows for the outcome of interest.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Annual linkage between the CTS cohort and the California Cancer Registry (CCR) was used to identify cases of invasive breast cancer. The CCR is estimated to be 99% complete. The case of invasive breast cancer was defined by ICD codes.

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Study Citation:	Garcia, E., Hurley, S., Nelson, D.O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health: A Global Access Science Source 14(1):14.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	breast cancer in females
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	3014082

Domain	Metric		Rating	Comments
	Metric 8:	Reporting Bias	Medium	A description of measured outcome is reported for adjustments by age and race, and effect estimates are reported with a 95% confidence interval. The measured outcomes using multiple comparisons were generally described in the text, but non-significant results were excluded from Table 3.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	The models were stratified by age and race. Additionally, adjustments were made for multiple comparisons among subsets of the participants (significant results reported in Table 3). Socioeconomic status (SES) of each participant was not evaluated, however, cohort SES characteristics were thought to be similar by study authors.
	Metric 10:	Covariate Characterization	Medium	Information about baseline characteristics for each participant was collected through a questionnaire. It is unknown if the questionnaire was validated.
	Metric 11:	Co-exposure Counfounding	Medium	A total of 37 compounds were identified as mammary gland carcinogens, but 13 were not included in this analysis. Thirteen compounds were excluded from the analysis due to insufficient variability (nine because they had the same value for all census tracts in the state of California; and four because they had less than 25% non-zero values). Ethylene dichloride (1,2-dichloroethane) was among the 24 compounds evaluated in this assessment, and evaluations for breast cancer were conducted for each of these 24 individual compounds.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen (prospective cohort) was appropriate for the research question (incidence of breast cancer). Cox proportional hazard models and SAS 9.3 were used in this assessment. Data analysis was described.
	Metric 13:	Statistical Power	Medium	Statistical power calculations were not provided. No significant effects were observed with ethylene dichloride (1,2-dichloroethane), however, this study utilized a large cohort, approximately 112,000 individuals. Distributions of chemicals of interest suggest there were sufficient numbers of participants in exposure subgroups.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to understand precisely what has been done and to be conceptually reproducible with access to the analytic data.
	Metric 15:	Statistical Analysis	High	The statistical models that were used were identified and described. ”No apparent violation of the underlying assumption of proportional hazards was detected”.

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Study Citation:	Garcia, E., Hurley, S., Nelson, D.O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health: A Global Access Science Source 14(1):14.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	breast cancer in females
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	3014082

Domain	Metric	Rating	Comments
Additional Comments:	A group of 112,378 female participants from the California Teacher Study cohort were assessed for their estimated exposure to ambient air pollutants, including ethylene dichloride (1,2-dichloroethane), and the incidence of invasive breast cancer. Air contaminant concentrations were estimated using the US EPA NATA and the ASPEN and HEM models. The approximate median concentration of 1,2-dichloroethane is between 1E-4 and 1E-2 (estimated from Figure 1). Exposures were categorized into 5 Quintiles, and compared against Quintile 1. No significant increase in the estimated hazard rate ratio for invasive breast cancer was observed with Quintile 2-5 exposure estimates for 1,2-dichloroethane, adjusted for age and race, when compared against Quintile 1, or when further adjusted using multiple comparisons.		

Overall Quality Determination High

* No biomarkers were identified for this evaluation.

Study Citation:	Garcia, E., Hurley, S., Nelson, D.O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health: A Global Access Science Source 14(1):14.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	breast cancer in females
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	3014082

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	A total of 112,378 women were included in this study out of 133,479 eligible female participants from the California Teacher Study cohort. A full description of the cohort is provided in Bernstein et al. 2002 (HERO ID 808446). Reasons for exclusion were provided. The reported information indicates that participant selection in or out of the study and participation was not likely to be biased.
	Metric 2:	Attrition	High	112,378/133,479 participants were included in the study. Exclusions were for the purpose of the study and analysis. Exclusion criteria were documented. Included participants had completed questionnaires. The California Cancer Registry is estimated to be 99% complete.
	Metric 3:	Comparison Group	Medium	There is only indirect evidence that groups are similar. Participants were recruited from the same eligible population with the same method of ascertainment. Comparisons were provided for participants with and without breast cancer. Characteristics between these two groups were generally similar. 5 Quintiles of exposure were used, and Q2-5 were compared with Q1.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	High	The Assessment System for Population Exposure Nationwide and the Human Exposure Model are used as part of the National-Scale Air Toxics Assessment produced by the EPA and was used to estimate ambient HAP concentrations for geographic locations. Methods are described online through the US EPA Assessment Methods.
	Metric 5:	Exposure Levels	Medium	The distribution of the NATA annual ambient concentration for each compound was plotted in Figure 1 using a box plot, and 5 Quintiles were used in the analyses.
	Metric 6:	Temporality	Medium	The follow-up period was from 1995-2011, and the NATA estimates were made in 2002 because it was approximately half way between the start and end of the follow-up period. However, it is unclear whether exposures fall within relevant exposure windows for the outcome of interest.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Annual linkage between the CTS cohort and the California Cancer Registry (CCR) was used to identify cases of invasive breast cancer. The CCR is estimated to be 99% complete. The case of invasive breast cancer was defined by ICD codes.
	Metric 8:	Reporting Bias	Medium	A description of measured outcome is reported for adjustments by age and race, and effect estimates are reported with a 95% confidence interval. The measured outcomes using multiple comparisons were generally described in the text, but non-significant results were excluded from Table 3.

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Study Citation:	Garcia, E., Hurley, S., Nelson, D.O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health: A Global Access Science Source 14(1):14.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	breast cancer in females
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	3014082

Domain	Metric		Rating	Comments
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	The models were stratified by age and race. Additionally, adjustments were made for multiple comparisons among subsets of the participants (significant results reported in Table 3). Socioeconomic status (SES) of each participant was not evaluated, however, cohort SES characteristics were thought to be similar by study authors.
	Metric 10:	Covariate Characterization	Medium	Information about baseline characteristics for each participant was collected through a questionnaire. It is unknown if the questionnaire was validated.
	Metric 11:	Co-exposure Counfounding	Medium	A total of 37 compounds were identified as mammary gland carcinogens, but 13 were not included in this analysis. Thirteen compounds were excluded from the analysis due to insufficient variability (nine because they had the same value for all census tracts in the state of California; and four because they had less than 25% non-zero values). Ethylene dichloride (1,2-dichloroethane) was among the 24 compounds evaluated in this assessment, and evaluations for breast cancer were conducted for each of these 24 individual compounds.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen (prospective cohort) was appropriate for the research question (incidence of breast cancer). Cox proportional hazard models and SAS 9.3 were used in this assessment. Data analysis was described.
	Metric 13:	Statistical Power	Medium	Statistical power calculations were not provided. No significant effects were observed with ethylene dichloride (1,2-dichloroethane), however, this study utilized a large cohort, approximately 112,000 individuals. Distributions of chemicals of interest suggest there were sufficient numbers of participants in exposure subgroups.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to understand precisely what has been done and to be conceptually reproducible with access to the analytic data.
	Metric 15:	Statistical Analysis	High	The statistical models that were used were identified and described. ”No apparent violation of the underlying assumption of proportional hazards was detected”.

Additional Comments: A group of 112,378 female participants from the California Teacher Study cohort were assessed for their estimated exposure to ambient air pollutants, including ethylene dichloride (1,2-dichloroethane), and the incidence of invasive breast cancer. Air contaminant concentrations were estimated using the US EPA NATA and the ASPEN and HEM models. The approximate median concentration of 1,2-dichloroethane is between 1E-4 and 1E-2 (estimated from Figure 1). Exposures were categorized into 5 Quintiles, and compared against Quintile 1. No significant increase in the estimated hazard rate ratio for invasive breast cancer was observed with Quintile 2-5 exposure estimates for 1,2-dichloroethane, adjusted for age and race, when compared against Quintile 1, or when further adjusted using multiple comparisons.

Overall Quality Determination High

* No biomarkers were identified for this evaluation.

Study Citation:	Guo, P., Yokoyama, K., Piao, F., Sakai, K., Khalequzzaman, M., Kamijima, M., Nakajima, T., Kitamura, F. (2013). Sick building syndrome by indoor air pollution in Dalian, China. International Journal of Environmental Research and Public Health 10(4):1489-1504.
Health Outcome(s):	sick building syndrome
Reported Health Effect(s):	The statistical analysis considers all subjective self-reported symptoms together (not segregated by health outcome) as a group health outcome –sick building syndrome. The study compared two conditions for each studied chemical: combined self-reported symptoms to no symptoms. Therefore, only one form 3 was completed.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1938385

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Residents of a housing estate of 3000 homes were invited to a community meeting to explain the purpose of the study and volunteers were invited to participate. It was not reported whether these volunteers were different from the overall eligible population.
	Metric 2:	Attrition	Low	Of the 70 families that agreed to participate, questionnaires were provided by 59. Reasons of uncompleted questionnaires were not fully provided, and there was no comparison between those who participated and those who did not.
	Metric 3:	Comparison Group	Low	The overall description of the analysis sample indicated a wide range of ages and lengths of stay at the current residence. Thus it is hard to know that subjects in all exposure groups were similar. In addition, the methods of selecting participants in all exposure groups were not fully reported. The numbers of male and female smokers were reported, respectively, but the smoking status and age were not controlled in the statistical analysis.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure concentrations for each home were obtained by diffusion sampling over 24 hrs in the bedroom, kitchen, and outdoors; temperature, the vertical height of samplers, and ventilation (hours windows left open) were reported. Samples were analyzed by GC/MS. The number of samples per home is unclear. The frequency of measurements for each house was not reported.
	Metric 5:	Exposure Levels	Low	The frequency of detection was not reported, so it is difficult to ascertain the actual exposure range. In addition, the reported exposure levels were median, geometric mean, and 95% CI, so they are inadequate to develop an exposure-response estimate.
	Metric 6:	Temporality	Uninformative	For 1,2-dichloroethane, the study evaluated self-reported symptoms in the past (”since they moved into their flats”) and their association with sampling conducted during the study; thus, exposure was measured after the outcome.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Low	Participants provided self-reported symptoms using a questionnaire. Study authors cited a previous study, Kamijima et al., 2005 (in Japanese, HERO ID 1598645) for further details on the questionnaire. It was not clear whether the questionnaire was validated.

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Study Citation:	Guo, P., Yokoyama, K., Piao, F., Sakai, K., Khalequzzaman, M., Kamijima, M., Nakajima, T., Kitamura, F. (2013). Sick building syndrome by indoor air pollution in Dalian, China. International Journal of Environmental Research and Public Health 10(4):1489-1504.
Health Outcome(s):	sick building syndrome
Reported Health Effect(s):	The statistical analysis considers all subjective self-reported symptoms together (not segregated by health outcome) as a group health outcome –sick building syndrome. The study compared two conditions for each studied chemical: combined self-reported symptoms to no symptoms. Therefore, only one form 3 was completed.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1938385

Domain	Metric		Rating	Comments
	Metric 8:	Reporting Bias	Low	The study only mentioned subjective symptoms in the abstract or methods. The abstract and method sections did not report the specific symptoms included in the questionnaire or whether the questionnaire was open-ended for symptoms. The questionnaire was cited to Kamijima et al. 2005 (in Japanese).
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	Comparisons were made separately by sex. The distribution of age and time spent living in residence differed greatly between those reporting symptoms and those not reporting symptoms. Smoking was indicated but not controlled for in the analysis. In short, the statistical analysis did not consider these three potential confounders, age, time spent living in residence, and smoking.
	Metric 10:	Covariate Characterization	Low	Covariates were presumably evaluated via a questionnaire that was cited to Kamijima et al. 2005 (in Japanese).
	Metric 11:	Co-exposure Counfounding	Low	The analysis did not account for other exposures. A number of other VOCs, HCHO, and NO2 were measured in the homes. The concentrations of several other VOCs and HCHO were much higher (5-30x) than 1,2-dichloroethane and may also be associated with these symptoms.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Low	The study design is best characterized as cross-sectional. Only one analysis to compare exposure concentrations between those with and without symptoms was adjusted for a confounder, sex, via stratification. Other potential confounders were not adjusted for. Study authors combine responses for symptoms reported before and during the sampling period in one statistical analysis, which may not reflect the relationship between symptoms and contaminants' exposure at each period.
	Metric 13:	Statistical Power	Medium	Statistical power was not reported. The number of participants was sufficient to detect a difference in median concentration between those with and without symptoms.
	Metric 14:	Reproducibility of Analyses	Medium	Study presents sufficient description of analysis (statistical methods) to be conceptually reproducible with access to the raw data.
	Metric 15:	Statistical Analysis	Low	Study uses a Wilcoxon's rank sum test to compare exposure concentrations in persons with and without symptoms; test for equal variance is not reported.

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Study Citation:	Guo, P., Yokoyama, K., Piao, F., Sakai, K., Khalequzzaman, M., Kamijima, M., Nakajima, T., Kitamura, F. (2013). Sick building syndrome by indoor air pollution in Dalian, China. International Journal of Environmental Research and Public Health 10(4):1489-1504.
Health Outcome(s):	sick building syndrome
Reported Health Effect(s):	The statistical analysis considers all subjective self-reported symptoms together (not segregated by health outcome) as a group health outcome –sick building syndrome. The study compared two conditions for each studied chemical: combined self-reported symptoms to no symptoms. Therefore, only one form 3 was completed.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1938385

Domain	Metric	Rating	Comments
Additional Comments:	Concentrations of VOCs (including 1,2-dichloroethane), HCHO, and NO2 were measured in the 59 homes of families that agreed to participate after being informed of the nature of the study. Participants completed questionnaires asking about symptoms since they moved into the homes and the concentrations of selected compounds were compared among men and women reporting any symptoms vs no symptoms. Concentrations of 1,2-dichloroethane in homes of people with symptoms were higher than in homes without. p-Dichlorobenzene was measured in the homes as well, but median concentration was <DL and no further analysis was made. Unacceptable due to selection bias, lack of confounding control, inadequate outcome characterization, and lack of temporality.		

Overall Quality Determination — Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Kernan, G.J., Ji, B.T., Dosemeci, M., Silverman, D.T., Balbus, J., Zahm, S.H. (1999). Occupational risk factors for pancreatic cancer: A case-control study based on death certificates from 24 U.S. states. American Journal of Industrial Medicine 36(2):260-270.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Death from pancreatic cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	194820

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	The National Cancer Institute, National Institute of Occupational Safety and Health, and the National Center for Health Statistics reviewed death certificates from 24 states to select cases from those that had died from pancreatic cancer and matched controls. Controls with cause of death related to the outcome of interest (i.e. pancreatic diseases) were excluded from the study. All key elements of the study design were reported.
	Metric 2:	Attrition	Medium	There was no direct evidence of subject loss or exclusion of subgroups from analyses. The authors provide the total number of cases and controls in the analysis. Case and control data were taken from a registry. It can be assumed that the data are complete for each subject.
	Metric 3:	Comparison Group	High	Controls were selected from the same pool of death certificates from 24 states that cases were selected from. Controls with cause of death related to the outcome of interest were eliminated. Differences in baseline characteristics were controlled for via matching, stratification, and adjustment.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure was assessed via occupation and industry data on death certificates. A job matrix was further applied to assess the likely levels of exposure. Probability and intensity of exposure were estimated across four levels for each occupation. Only employment captured on the death certificate could be considered. The exposure assessment needs exposure information before the job listed on the death certificates.
	Metric 5:	Exposure Levels	Medium	The study offers 4 levels of estimated probability and intensity of exposure (referent, low, medium, high).
	Metric 6:	Temporality	Medium	Exposure was determined by occupational and industry codes on death certificates and indicate that exposure would precede disease, however, the timing and latency period is less clear.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Causes of mortality were determined from death certificates for both cases and controls. Death certificates were drawn from death registries of participating states (n=24). Causes of death were coded using ICD-9 codes, and pancreatic cancer was identified as ICD 157.
	Metric 8:	Reporting Bias	Medium	Measured outcomes, effect estimates and confidence intervals are reported. Number of exposed cases is reported for each analysis, however the number of controls (exposed and unexposed) are not reported for analyses.

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Study Citation:	Kernan, G.J., Ji, B.T., Dosemeci, M., Silverman, D.T., Balbus, J., Zahm, S.H. (1999). Occupational risk factors for pancreatic cancer: A case-control study based on death certificates from 24 U.S. states. American Journal of Industrial Medicine 36(2):260-270.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Death from pancreatic cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	194820

Domain	Metric		Rating	Comments
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Potential confounders were accounted for in the following ways: matching (five year age group, state, race, and gender); adjustment in models (age, marital status, metropolitan, and residential status); and stratification (race and gender). Smoking was not included as a confounder.
	Metric 10:	Covariate Characterization	Medium	Data used to assess potential confounders was derived from death certificates, an adequate measure. However, no information about cigarette smoking and other lifestyle factors were available for adjustment in the analysis.
	Metric 11:	Co-exposure Counfounding	Medium	The variety of industries considered in the analysis diminishes concerns about co-exposures.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The case-control study design and statistical analysis methods were appropriate to assess the exposures/outcome of interest.
	Metric 13:	Statistical Power	Medium	This study had an adequate sample size to detect an effect (n for cases = 63,097; n for controls = 252,386).
	Metric 14:	Reproducibility of Analyses	Medium	The description of analysis was sufficient and would be reproducible.
	Metric 15:	Statistical Analysis	High	The model to calculate risk estimates was transparent.

Additional Comments: This case-control study examined the risk of death from pancreatic cancer in different occupational settings. Exposure was solely assessed using occupation/industry at time of death (reported on death certificate) and the application of a job matrix assessing likely levels of exposure for different positions. This means of estimating exposure may not fully represent a participant's exposure history. Additionally, the number of impacted participants (exposed cases) was inadequate to perform quality analyses for some exposure levels.

Overall Quality Determination High

* No biomarkers were identified for this evaluation.

Study Citation:	Kernan, G.J., Ji, B.T., Dosemeci, M., Silverman, D.T., Balbus, J., Zahm, S.H. (1999). Occupational risk factors for pancreatic cancer: A case-control study based on death certificates from 24 U.S. states. American Journal of Industrial Medicine 36(2):260-270.
Health Outcome(s):	Endocrine
Reported Health Effect(s):	Death from pancreatic cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	194820

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	The National Cancer Institute, National Institute of Occupational Safety and Health, and the National Center for Health Statistics reviewed death certificates from 24 states to select cases from those that had died from pancreatic cancer and matched controls. Controls with cause of death related to the outcome of interest (i.e. pancreatic diseases) were excluded from the study. All key elements of the study design were reported.
	Metric 2:	Attrition	Medium	There was no direct evidence of subject loss or exclusion of subgroups from analyses. The authors provide the total number of cases and controls in the analysis. Case and control data were taken from a registry. It can be assumed that the data are complete for each subject.
	Metric 3:	Comparison Group	High	Controls were selected from the same pool of death certificates from 24 states that cases were selected from. Controls with cause of death related to the outcome of interest were eliminated. Differences in baseline characteristics were controlled for via matching, stratification, and adjustment.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure was assessed via occupation and industry data on death certificates. A job matrix was further applied to assess the likely levels of exposure. Probability and intensity of exposure were estimated across four levels for each occupation. Only employment captured on the death certificate could be considered. The exposure assessment needs exposure information before the job listed on the death certificates.
	Metric 5:	Exposure Levels	Medium	The study offers 4 levels of estimated probability and intensity of exposure (referent, low, medium, high).
	Metric 6:	Temporality	Medium	Exposure was determined by occupational and industry codes on death certificates and indicate that exposure would precede disease, however, the timing and latency period is less clear.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Causes of mortality were determined from death certificates for both cases and controls. Death certificates were drawn from death registries of participating states (n=24). Causes of death were coded using ICD-9 codes, and pancreatic cancer was identified as ICD 157.
	Metric 8:	Reporting Bias	Medium	Measured outcomes, effect estimates and confidence intervals are reported. Number of exposed cases is reported for each analysis, however the number of controls (exposed and unexposed) are not reported for analyses.
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Kernan, G.J., Ji, B.T., Dosemeci, M., Silverman, D.T., Balbus, J., Zahm, S.H. (1999). Occupational risk factors for pancreatic cancer: A case-control study based on death certificates from 24 U.S. states. American Journal of Industrial Medicine 36(2):260-270.
Health Outcome(s):	Endocrine
Reported Health Effect(s):	Death from pancreatic cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	194820

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Medium	Potential confounders were accounted for in the following ways: matching (five year age group, state, race, and gender); adjustment in models (age, marital status, metropolitan, and residential status); and stratification (race and gender). Smoking was not included as a confounder.
	Metric 10:	Covariate Characterization	Medium	Data used to assess potential confounders was derived from death certificates, an adequate measure. However, no information about cigarette smoking and other lifestyle factors were available for adjustment in the analysis.
	Metric 11:	Co-exposure Counfounding	Medium	The variety of industries considered in the analysis diminishes concerns about co-exposures.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The case-control study design and statistical analysis methods were appropriate to assess the exposures/outcome of interest.
	Metric 13:	Statistical Power	Medium	This study had an adequate sample size to detect an effect (n for cases = 63,097; n for controls = 252,386).
	Metric 14:	Reproducibility of Analyses	Medium	The description of analysis was sufficient and would be reproducible.
	Metric 15:	Statistical Analysis	High	The model to calculate risk estimates was transparent.

Additional Comments: This case-control study examined the risk of death from pancreatic cancer in different occupational settings. Exposure was solely assessed using occupation/industry at time of death (reported on death certificate) and the application of a job matrix assessing likely levels of exposure for different positions. This means of estimating exposure may not fully represent a participant's exposure history. Additionally, the number of impacted participants (exposed cases) was inadequate to perform quality analyses for some exposure levels.

Overall Quality Determination High

* No biomarkers were identified for this evaluation.

Study Citation:	Niehoff, N.M., Gammon, M.D., Keil, A.P., Nichols, H.B., Engel, L.S., Sandler, D.P., White, A.J. (2019). Airborne mammary carcinogens and breast cancer risk in the Sister Study. Environment International 130:104897.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Breast cancer diagnosis (overall), tumor characteristics, and estrogen receptor positive (ER+) invasive breast cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5440630

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	Data from the Sister Study were used. The Sister Study is "a prospective cohort of 50,884 women from across the US who were ages 35–74 at enrollment (Sandler et al., 2017). Participants were recruited from 2003 to 2009 using a national advertising campaign in English and Spanish. Women were eligible for the Sister Study if they had a sister who had been diagnosed with breast cancer, but no prior breast cancer themselves."Exclusions from the study occurred for the following reasons:-breast cancer diagnosed before enrollment was complete, or did not have follow-up information (n = 163)-Residential address couldn't be geocoded (n = 1003, < 2%) - This is a small perecentage, but all of those who were excluded for this reason were from Puerto Rico, West Virginia, Missouri, or Oklahoma.Key elements of the study design are reported. There is some potential for selection bias, but based on the small percentage of those eligible who were excluded, participation was not likely to be substantially biased.
	Metric 2:	Attrition	High	Response rates in the overall Sister study remained over 91% over follow-up. Reasons for non-response were not reported, and characteristics of those lost to follow up were not reported or compared with those included, but 9% loss to follow-up is minimal.
	Metric 3:	Comparison Group	High	Differences in baseline characteristics of groups were considered as potential confounding variables.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	The EPA NATA database of census-tract level modeled air toxics data was used. The study authors note the potential for exposure misclassification: "Concentrations at the census tract level do not fully account for variation in an individual's daily activities that could lead to higher or lower exposure, and all women within a census tract are assigned the same concentration."
	Metric 5:	Exposure Levels	Medium	There were five quintiles of exposure, so there was a sufficient range and distribution of exposure.
	Metric 6:	Temporality	Medium	This is a prospective cohort study.Exposure data from 2005 were chosen because they represented the middle of the enrollment period (2003-2009).The study reported that "94% of women enrolled in 2005 or later, and thus the exposure assessment primarily predated enrollment for the majority of Sister Study participants."The six percent of women who had the potential to have the outcome before exposure was measured in 2005 are a concern. But sensitivity analyses were used to assess whether the associations changed when restricted to those who enrolled in 2005 or later.The authors note that the study is making assumptions about the relevant exposure windows - therefore the exposure window is not certain.

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Study Citation:	Niehoff, N.M., Gammon, M.D., Keil, A.P., Nichols, H.B., Engel, L.S., Sandler, D.P., White, A.J. (2019). Airborne mammary carcinogens and breast cancer risk in the Sister Study. Environment International 130:104897.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Breast cancer diagnosis (overall), tumor characteristics, and estrogen receptor positive (ER+) invasive breast cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5440630

Domain	Metric		Rating	Comments
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Women who reported a breast cancer diagnosis on the annual health updates or follow-up questionnaires were asked to provide additional diagnosis information, and to grant permission for the study to obtain medical records and pathology reports. Medical records were obtained for 81% of breast cancer diagnoses. Agreement between self-reported breast cancers and medical records was high (positive predictive value > 99%) (Sandler et al., 2017), so self-report was used when medical records were not available. Tumor characteristics (stage; histology; and estrogen receptor (ER) status) were abstracted from medical records, or self-reported.
	Metric 8:	Reporting Bias	High	A description of measured outcomes is reported. Effect estimates are reported with confidence intervals.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Covariates considered included age, race, BMI, residence type, education, and smoking status. Potential confounders were identified using DAGs and literature review. Appropriate considerations were made for potential confounders.
	Metric 10:	Covariate Characterization	Medium	”Most covariates were assessed by self-report at the baseline interview.””At baseline, women completed a computer-assisted telephone interview and written questionnaires.”Previous publications might describe whether the questionnaires were validated, but validation was not specified in this publication.
	Metric 11:	Co-exposure Counfounding	Medium	Co-exposures to other air pollutants were assessed, but at the census tract level.Multipollutant classification trees were used, which might provide useful qualitative information.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design (large prospective cohort) and analysis method (Cox proportional hazard single and multi-pollutant models accounting for potential confounders) were appropriate to assess the association between exposure and disease.
	Metric 13:	Statistical Power	Medium	The study had an adequate sample size (1975 cancer cases) and follow-up time (mean=8.4 years).
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to be conceptually reproducible.

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Study Citation:	Niehoff, N.M., Gammon, M.D., Keil, A.P., Nichols, H.B., Engel, L.S., Sandler, D.P., White, A.J. (2019). Airborne mammary carcinogens and breast cancer risk in the Sister Study. Environment International 130:104897.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Breast cancer diagnosis (overall), tumor characteristics, and estrogen receptor positive (ER+) invasive breast cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5440630

Domain	Metric	Rating	Comments
	Metric 15: Statistical Analysis	High	Hazard ratios and 95% confidence intervals (CIs) are reported "comparing index categories of exposure to exposures below the first quintile using Cox proportional hazards regression, with age as the time scale." The method of calculating the hazard ratios is transparent. The authors reported that "the proportional hazards assumption was evaluated by conducting a Wald test for an interaction between the continuous form of the air toxic measure and time." Censoring times and times at-risk are described.

Additional Comments: This was a well-conducted study of a large prospective cohort, but the measurement of exposure at the census-tract rather than the individual level is a limitation.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Sobel, W., Bond, G.G., Skowronski, B.J., Brownson, P.J., Cook, R.R. (1987). A soft tissue sarcoma case control study in a large multi-chemical manufacturing facility. Chemosphere 16(8-9):2095-2099.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	soft-tissue sarcoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1357737

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	From a pool of > 37,000 subjects who worked at least 1 year at chemical company between January 1940-December 1979, the study identified 14 people who died due to soft-cell sarcoma (via death certificate, medical records, or histopathology report). Referents were matched 9:1 with cases (126 matched controls).
	Metric 2:	Attrition	High	There was minimal subject exclusion from the analysis sample; one case could not be matched to controls and was excluded from analysis.
	Metric 3:	Comparison Group	High	Cases and controls were recruited from the same eligible population within the same time frame and matched on sex, race, year of birth and year of hire. Both cases and controls had to have worked ≥1 yr at the plant during the study period.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Work histories for cases and referents were coded to determine an individual's potential exposure to chemical of interest and reviewed by an industrial hygienist blinded to case status.
	Metric 5:	Exposure Levels	Low	Exposure was considered dichotomous, ever exposed or never exposed. There is no quantitative information on exposure levels or range of exposures.
	Metric 6:	Temporality	Low	Temporality of exposure and outcome is established. It is unclear if the interval between exposure and outcome is sufficient for soft tissue sarcoma outcomes.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	The soft-tissue sarcoma outcome was assessed by information provided by death certificates, medical records, and histopathology reports, but study authors did not report the proportions determined by each method.
	Metric 8:	Reporting Bias	High	All outcomes outlined were reported. Authors reported the number of cases and controls in the table. Maximum likelihood estimate ORs with respective 95 % confidence intervals were reported.
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Sobel, W., Bond, G.G., Skowronski, B.J., Brownson, P.J., Cook, R.R. (1987). A soft tissue sarcoma case control study in a large multi-chemical manufacturing facility. Chemosphere 16(8-9):2095-2099.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	soft-tissue sarcoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1357737

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Low	Controls were matched with cases on age, sex, year of hire and survival information. There is indirect evidence that the considerations were made to identify potential confounders through evaluation of medical records of cases and controls (various heritable syndromes, family history of cancer, history of lymphedema, steroids, throrotrast, foreign body implants, chronic extensive scarring, radiation therapy, and immunological defects). Identified confounders between cases and controls were not reported and it is unclear if adjustments for these confounders were included in the final analyses.
	Metric 10:	Covariate Characterization	High	Potential covariates were assessed through evaluation of work histories and medical records.
	Metric 11:	Co-exposure Counfounding	Low	The study documented 13 chemicals, known to be associated with soft-tissue sarcoma (according to NTP, 1983) that were used at the manufacturing facility at some point since 1940. The authors note that some individuals were exposed to multiple chemicals during their employment history and were counted multiple times in the analysis for different chemical exposures. Co-exposures to chemicals to not appear to be adjusted for in analysis.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Low	The study design was adequate to assess the association between exposure and the outcome of interest (soft-tissue sarcoma). The study authors noted they used programs developed by Rothman and Boice to calculate odds ratios with CI intervals; the statistical methods are not further described. The page containing the Rothman and Boice reference appears to be missing from the PDF (or the citation is missing).
	Metric 13:	Statistical Power	Low	Statistical power was not calculated. For 1,2-dichloroethane, there was one case and 6 controls included in the analysis, which was not adequate to detect and effect.
	Metric 14:	Reproducibility of Analyses	Low	The study calculated odd ratios, and 95% CIs were calculated using point estimates and chi from hypothesis testing. The study authors noted they used programs developed by Rothman and Boice to calculate odds ratios with 95% CIs; the statistical methods are not further described and there was no reference for the programs cited.
	Metric 15:	Statistical Analysis	Low	A description of analyses/assumptions was not reported.

Additional Comments: A case-control study of workers at a chemical production facility who worked at least 1 year between January 1940-December 1979 (n=37,000) investigated the incidence of deaths due to soft-tissue sarcoma. The study identified 14 people who died due to soft-tissue sarcoma (through death certificate, medical records, or histopathology reports). Cases were matched to controls based on sex, race, year of birth and year of hire. 13 chemicals, including 1,2-dichloroethane, associated with soft-tissue sarcoma were used at the facility; it does not appear that co-exposures were adjusted for in the analysis. Odds ratios and corresponding CIs were calculated. No significant association was found between exposure to 1,2-DCE and soft-tissue sarcoma.

Overall Quality Determination Medium

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Study Citation:	Sobel, W., Bond, G.G., Skowronski, B.J., Brownson, P.J., Cook, R.R. (1987). A soft tissue sarcoma case control study in a large multi-chemical manufacturing facility. Chemosphere 16(8-9):2095-2099.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	soft-tissue sarcoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1357737

Domain	Metric	Rating	Comments

* No biomarkers were identified for this evaluation.

Study Citation:	Sobel, W., Bond, G.G., Skowronski, B.J., Brownson, P.J., Cook, R.R. (1987). A soft tissue sarcoma case control study in a large multi-chemical manufacturing facility. Chemosphere 16(8-9):2095-2099.
Health Outcome(s):	Skin and Connective Tissue
Reported Health Effect(s):	soft-tissue sarcoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1357737

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	From a pool of > 37,000 subjects who worked at least 1 year at chemical company between January 1940-December 1979, the study identified 14 people who died due to soft-cell sarcoma (via death certificate, medical records, or histopathology report). Referents were matched 9:1 with cases (126 matched controls).
	Metric 2:	Attrition	High	There was minimal subject exclusion from the analysis sample; one case could not be matched to controls and was excluded from analysis.
	Metric 3:	Comparison Group	High	Cases and controls were recruited from the same eligible population within the same time frame and matched on sex, race, year of birth and year of hire. Both cases and controls had to have worked ≥1 yr at the plant during the study period.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Work histories for cases and referents were coded to determine an individual's potential exposure to chemical of interest and reviewed by an industrial hygienist blinded to case status.
	Metric 5:	Exposure Levels	Low	Exposure was considered dichotomous, ever exposed or never exposed. There is no quantitative information on exposure levels or range of exposures.
	Metric 6:	Temporality	Low	Temporality of exposure and outcome is established. It is unclear if the interval between exposure and outcome is sufficient for soft tissue sarcoma outcomes.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	The soft-tissue sarcoma outcome was assessed by information provided by death certificates, medical records, and histopathology reports, but study authors did not report the proportions determined by each method.
	Metric 8:	Reporting Bias	High	All outcomes outlined were reported. Authors reported the number of cases and controls in the table. Maximum likelihood estimate ORs with respective confidence intervals were reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	Controls were matched with cases on age, sex, year of hire and survival information. There is indirect evidence that that considerations were made to identify potential confounders through evaluation of medical records of cases and controls (various heritable syndromes, family history of cancer, history of lymphedema, steroids, throrotrast, foreign body implants, chronic extensive scarring, radiation therapy, and immunological defects). Identified confounders between cases and controls were not reported and it is unclear if adjustments for these confounders were included in the final analyses.

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Study Citation:	Sobel, W., Bond, G.G., Skowronski, B.J., Brownson, P.J., Cook, R.R. (1987). A soft tissue sarcoma case control study in a large multi-chemical manufacturing facility. Chemosphere 16(8-9):2095-2099.
Health Outcome(s):	Skin and Connective Tissue
Reported Health Effect(s):	soft-tissue sarcoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1357737

Domain	Metric		Rating	Comments
	Metric 10:	Covariate Characterization	High	Potential covariates were assessed through evaluation of work histories and medical records.
	Metric 11:	Co-exposure Counfounding	Low	The study documented 13 chemicals, known to be associated with soft-tissue sarcoma (according to NTP, 1983) that were used at the manufacturing facility at some point since 1940. The authors note that some individuals were exposed to multiple chemicals during their employment history and were counted multiple times in the analysis for different chemical exposures. Co-exposures to chemicals to not appear to be adjusted for in analysis.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Low	The study design was adequate to assess the association between exposure and the outcome of interest (soft-tissue sarcoma). The study authors noted they used programs developed by Rothman and Boice to calculate odds ratios with (95% CIs; the statistical methods are not further described. The page containing the Rothman and Boice reference appears to be missing from the PDF (or the citation is missing).
	Metric 13:	Statistical Power	Low	Statistical power was not calculated. For 1,2-dichloroethane, there was one case and 6 controls included in the analysis, which was not adequate to detect and effect.
	Metric 14:	Reproducibility of Analyses	Low	The study calculated odd ratios, and 95% CIs were calculated using point estimates and chi from hypothesis testing. The study authors noted they used programs developed by Rothman and Boice to calculate odds ratios with CI intervals; the statistical methods are not further described and there was no reference for the programs cited.
	Metric 15:	Statistical Analysis	Low	A description of analyses/assumptions was not reported.

Additional Comments: A case-control study of workers at a chemical production facility who worked at least 1 year between January 1940-December 1979 (n=37,000) investigated the incidence of deaths due to soft-tissue sarcoma. The study identified 14 people who died due to soft-tissue sarcoma (through death certificate, medical records, or histopathology reports). Cases were matched to controls based on sex, race, year of birth and year of hire. 13 chemicals, including 1,2-dichloroethane, associated with soft-tissue sarcoma were used at the facility; it does not appear that co-exposures were adjusted for in the analysis. Odds ratios and corresponding CIs were calculated. No significant association was found between exposure to 1,2-DCE and soft-tissue sarcoma.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Teta, M. J., Ott, M. G., Schnatter, A. R. (1991). An update of mortality due to brain neoplasms and other causes among employees of a petrochemical facility. Journal of Occupational Medicine 33(1):45-51.
Health Outcome(s):	Mortality
Reported Health Effect(s):	all cause mortality, gastrointestinal cancer mortality, respiratory system cancer mortality, kidney and other urinary organ cancer mortality, skin cancer mortality, brain cancer mortality, lymphatic and hematopoietic tissue cancer mortality, benign neoplasm mortality, heart disease mortality, and liver cirrhosis mortality.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200633, 1629047
HERO ID:	200633

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	The facility was described in some detail. All male employees working for one day or more between 1941 and 1983 were included. There may be some healthy worker effect in this population.
	Metric 2:	Attrition	High	Study authors reported that vital status was complete for 99% of the population, and death certificates were obtained for 99% of decedents.
	Metric 3:	Comparison Group	High	SMRs were calculated using age-, race-, and calendar year-specific mortality rates of males in the United States. All included employees were male.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	All employees were treated as exposed. Table 4 indicates that relatively few employees were employed in areas designated as 1,2-DCA work areas. There is potential for substantial exposure misclassification.
	Metric 5:	Exposure Levels	Low	All employed individuals were categorized as exposed, and the reference population was described as unexposed. This represents two levels of exposure. The distribution of exposure within the employed population is unclear.
	Metric 6:	Temporality	Medium	Employees were followed from 1950 (or date of first hire) through 1983. The relevant timing of exposure is not entirely clear; however, this represents a sufficiently long period of follow-up.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Mortality was tracked using company records, Social Security Administration records, and the National Death Index. Specific ICD codes and use of a nosologist were not described, but there was no evidence to suggest the method had poor validity.
	Metric 8:	Reporting Bias	High	SMRs were provided with confidence intervals in addition to observed and expected cases. The authors state they did not carry out regional specific SMRs due to the higher prevalence of neoplasms in the surrounding area.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	SMRs were restricted to males. Rates were age-, race-, and calendar period-specific. No consideration was made for smoking.
	Metric 10:	Covariate Characterization	Medium	Demographic information was obtained from employment records. This was not a validated method, but there was no evidence to suggest it was an invalid method.

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Study Citation:	Teta, M. J., Ott, M. G., Schnatter, A. R. (1991). An update of mortality due to brain neoplasms and other causes among employees of a petrochemical facility. Journal of Occupational Medicine 33(1):45-51.
Health Outcome(s):	Mortality
Reported Health Effect(s):	all cause mortality, gastrointestinal cancer mortality, respiratory system cancer mortality, kidney and other urinary organ cancer mortality, skin cancer mortality, brain cancer mortality, lymphatic and hematopoietic tissue cancer mortality, benign neoplasm mortality, heart disease mortality, and liver cirrhosis mortality.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200633, 1629047
HERO ID:	200633

Domain	Metric		Rating	Comments
	Metric 11:	Co-exposure Counfounding	Low	Several other occupational exposures linked to cancer mortality were present, including vinyl chloride, butanol, and other petrochemicals.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	This study design was appropriate for the research question. Authors utilized retrospective occupational cohort data to determine standardized mortality rates for cancer-specific mortalities.
	Metric 13:	Statistical Power	Medium	While power was not calculated, there were over 1350 deaths from 7849 employees which was adequate to detect robust effect estimates.
	Metric 14:	Reproducibility of Analyses	Low	Most details were provided; however, ICD codes used to determine and group cancer mortality diagnoses were not provided.
	Metric 15:	Statistical Analysis	High	No issues identified.

Additional Comments: This study utilized an occupational cohort to retrospectively evaluate elevated rates of cancer mortality among petrochemical plant workers. There were numerous potentially hazardous chemicals mentioned in the plant description which may lead to co-exposure. Additionally, it appears that only a moderate portion of workers may have been exposed to 1,2-DCA or worked in 1,2-DCA areas which may lead to some exposure misclassification and limit the study's ability to inform hazard on 1,2-DCA.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Cases in this case-control study were former Union Carbide Corporation (UCC) chemical plant employees in Texas City, Texas. Cases were identified through death certificate searches and tumor registries, and may have included individuals formerly employed at UCC whose cause of death was unknown to the company. Additionally, control deaths were stated to be pulled from corporate employee benefits department and through locally published obituary notices routinely screened by the medical department - it is possible to assume that cases were identified in a similar manner. The study identified cases of brain tumors by searching death certificates primarily, although tumor registries throughout the state of Texas were also searched. The study clarifies that it is possible that some cases were not found if they survived or died due to another cause - while this is likely to have impacted selection, there is no evidence that this would be differential by exposure status. Overall, there is limited information on the source population of workers from which cases were identified.
	Metric 2:	Attrition	Medium	Attrition is not discussed in the study, and outcome data appear to be complete. There was a large proportion of missing exposure data (roughly 50%) due to workers being employed in roles such as maintenance, where exposure to any chemical is possible but unknown. Analyses were run separately where these ”unknown” individuals were a) treated as exposed, b) treated as unexposed, or c) treated as unknown and thus excluded. The study only presents results for when these individuals were excluded but specifies that the first scenario resulted in increased exposure estimates for controls relative to cases.

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Study Citation:	Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
	Metric 3:	Comparison Group	Medium	The study identifies two series of control groups, selected from all former Union Carbide Corporation (UCC) employees. However, the total number of employees is not stated. Only those who were deceased were used as controls since they had known causes of death and could thus be verified as non-brain tumors. One group of controls excluded employees whose cause of death was due to any malignant neoplasm to allow for the possibility that a general chemical carcinogen may have been associated with cancers of other sites. The other group of controls included deaths from all causes; this included malignant neoplasms other than brain tumors. Both control groups had 80 male employees randomly selected from 450 deceased employees known to the company in June 1979. Control deaths were stated to be pulled from corporate employee benefits department and through locally published obituary notices routinely screened by the medical department - it is possible to assume that cases were identified in a similar manner. The study reports that cases were slightly more likely to have been employed for less than 10 years than controls - the study attributes this in part to the fact that employees whose deaths were known to the company were more likely to have worked for longer - regardless the mean number of years employed was similar between cases and controls. However, cases were more likely to have been terminated from their job for reasons other than death, disability, or retirement (quitting, being fired, etc.), were generally younger at hire, and were less likely to survive to their 70th birthday. None of these factors are controlled for in statistical analyses - however, since controls and cases were pulled from the same population, there is indirect evidence that the groups were similar.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was determined based on official employment records. Records included job title and department assignment codes for each employment from date of hire to date of termination. For each unique department code, UCC and NIOSH industrial hygienists identified principal chemicals used or produced at any time in the history of the plant and correlated those with individual departments. This assessment was not performed on a year-by-year basis due to concerns for recall bias for longer-term employees where less detailed records were kept. An employee was categorized as ”exposed” to 1,2-dichloroethane if they ever worked in a department associated with that chemical. An ”unknown” exposure group was also created to account for employees who had only worked in departments for which no specific chemical could be identified.
	Metric 5:	Exposure Levels	Low	The study does not report any quantitative information and only splits exposure into ”exposed”, ”unexposed”, and ”unknown”.
	Metric 6:	Temporality	High	In this study exposure is confirmed to occur before the outcome is measured. The study reports latency periods, with subjects dichotomized into less than 15 years of latency or more than 15 years of latency. The majority of cases and controls had a latency of greater than 15 years, which is sufficiently long for brain tumors.

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Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Cases were identified through death certificate searches and partially through tumor registries in the state of Texas. Case validation was performed by NIOSH, and 5 different levels of confirmation were reported: 1) tissue specimen interpreted by the Armed Forces Institute of Pathology; 2) autopsy report; 3) histopathology report; 4) clinical diagnosis from hospital record; 5) dearth certificate diagnosis. Codes 1-3 were considered to be ”confirmed” cases of brain tumors, while 4-5 were considered unconfirmed. 5/21 cases were only evaluated using ”unconfirmed methods”, meaning there is likely a high amount of accuracy in roughly 75% of cases. While no case validation is reported for controls, the study specifies that only controls who had died and thus could be confirmed to be non-brain tumors were included.
	Metric 8:	Reporting Bias	Medium	All primary and secondary outcomes that are outlined in the methods are reported in the results. However, the only statistical outcome of their analysis were unadjusted p-values that were not reported and were just described qualitatively.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	The only statistical analysis performed were Mantel-Haenszel chi-squared tests, which did not allow for confounder adjustment. The study does not present a distribution of potential confounders by exposure status but by case/control status. Several variables, such as reason for termination, age at hire, and age at death were significantly different between cases and controls and were not accounted for in statistical modeling. The study explains that these differences are not likely to have any epidemiologic significance and appear to be relatively small differences.
	Metric 10:	Covariate Characterization	Medium	While the study does not explain where they obtained covariate information, it is reasonable to assume that they gathered the information from company records.
	Metric 11:	Co-exposure Counfounding	Low	The study assesses a wide range of other potential occupational co-exposures. While these co-exposures are not adjusted for in any statistical models, effect estimates are presented separately for benzene, diethyl sulfate, ethylene oxide, and vinyl chloride. The distribution of co-exposures across cases and controls is demonstrated to be mostly balanced by comparing proportions of exposed/unexposed between cases and controls. The only notable instance of imbalance is for benzene, where 11.1% of cases were exposed whereas 37.9% of all controls and 19.2% of non-neoplasm related controls were exposed.
Domain 5: Analysis				

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Study Citation:	Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	The study chose a case-control design, which was appropriate to study the rare disease of brain tumors and its association with occupational exposures. The only statistical analysis conducted is a Mantzel-Haenszel chi-squared test, but there is no reason to suggest that this would be inappropriate.
	Metric 13:	Statistical Power	Medium	The study does not calculate statistical power, but the number of cases (n=21) and controls (n=80 in each analysis) is likely sufficient to detect an effect.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to understand what was done and could be reproduced given access to the analytic data.
	Metric 15:	Statistical Analysis	High	The only statistical analysis conducted is a Mantel-Haenszel chi-squared test, and all assumptions were met. The statistical process is transparent.

Additional Comments: This case-control study pulled deceased former employees of the Union Carbide Corporation in Texas City, Texas. The study examined dichotomous exposure to a wide range of occupational exposures, including 1,2-dichloroethane, in relation to brain tumor cases. There is no quantitative estimate of exposure. The only statistical analysis in the study is a Mantel-Haenszel chi-squared test statistic and no statistically significant differences in exposure between cases and controls were observed. The fact that there are no effect estimates, no adjustment for confounders, and no quantitative exposure estimates limits the usefulness of this paper.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Cases in this case-control study were former Union Carbide Corporation (UCC) chemical plant employees in Texas City, Texas. Cases were identified through death certificate searches and tumor registries, and may have included individuals formerly employed at UCC whose cause of death was unknown to the company. Additionally, control deaths were stated to be pulled from corporate employee benefits department and through locally published obituary notices routinely screened by the medical department - it is possible to assume that cases were identified in a similar manner. The study identified cases of brain tumors by searching death certificates primarily, although tumor registries throughout the state of Texas were also searched. The study clarifies that it is possible that some cases were not found if they survived or died due to another cause - while this is likely to have impacted selection, there is no evidence that this would be differential by exposure status. Overall, there is limited information on the source population of workers from which cases were identified.
	Metric 2:	Attrition	Medium	Attrition is not discussed in the study, and outcome data appear to be complete. There was a large proportion of missing exposure data (roughly 50%) due to workers being employed in roles such as maintenance, where exposure to any chemical is possible but unknown. Analyses were run separately where these ”unknown” individuals were a) treated as exposed, b) treated as unexposed, or c) treated as unknown and thus excluded. The study only presents results for when these individuals were excluded but specifies that the first scenario resulted in increased exposure estimates for controls relative to cases.

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Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
	Metric 3:	Comparison Group	Medium	The study identifies two series of control groups, selected from all former Union Carbide Corporation (UCC) employees. However, the total number of employees is not stated. Only those who were deceased were used as controls since they had known causes of death and could thus be verified as non-brain tumors. One group of controls excluded employees whose cause of death was due to any malignant neoplasm to allow for the possibility that a general chemical carcinogen may have been associated with cancers of other sites. The other group of controls included deaths from all causes; this included malignant neoplasms other than brain tumors. Both control groups had 80 male employees randomly selected from 450 deceased employees known to the company in June 1979. Control deaths were stated to be pulled from corporate employee benefits department and through locally published obituary notices routinely screened by the medical department - it is possible to assume that cases were identified in a similar manner. The study reports that cases were slightly more likely to have been employed for less than 10 years than controls - the study attributes this in part to the fact that employees whose deaths were known to the company were more likely to have worked for longer - regardless the mean number of years employed was similar between cases and controls. However, cases were more likely to have been terminated from their job for reasons other than death, disability, or retirement (quitting, being fired, etc.), were generally younger at hire, and were less likely to survive to their 70th birthday. None of these factors are controlled for in statistical analyses - however, since controls and cases were pulled from the same population, there is indirect evidence that the groups were similar.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was determined based on official employment records. Records included job title and department assignment codes for each employment from date of hire to date of termination. For each unique department code, UCC and NIOSH industrial hygienists identified principal chemicals used or produced at any time in the history of the plant and correlated those with individual departments. This assessment was not performed on a year-by-year basis due to concerns for recall bias for longer-term employees where less detailed records were kept. An employee was categorized as ”exposed” to 1,2-dichloroethane if they ever worked in a department associated with that chemical. An ”unknown” exposure group was also created to account for employees who had only worked in departments for which no specific chemical could be identified.
	Metric 5:	Exposure Levels	Low	The study does not report any quantitative information and only splits exposure into ”exposed”, ”unexposed”, and ”unknown”.
	Metric 6:	Temporality	High	In this study exposure is confirmed to occur before the outcome is measured. The study reports latency periods, with subjects dichotomized into less than 15 years of latency or more than 15 years of latency. The majority of cases and controls had a latency of greater than 15 years, which is sufficiently long for brain tumors.

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Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Cases were identified through death certificate searches and partially through tumor registries in the state of Texas. Case validation was performed by NIOSH, and 5 different levels of confirmation were reported: 1) tissue specimen interpreted by the Armed Forces Institute of Pathology; 2) autopsy report; 3) histopathology report; 4) clinical diagnosis from hospital record; 5) dearth certificate diagnosis. Codes 1-3 were considered to be ”confirmed” cases of brain tumors, while 4-5 were considered unconfirmed. 5/21 cases were only evaluated using ”unconfirmed methods”, meaning there is likely a high amount of accuracy in roughly 75% of cases. While no case validation is reported for controls, the study specifies that only controls who had died and thus could be confirmed to be non-brain tumors were included.
	Metric 8:	Reporting Bias	Medium	All primary and secondary outcomes that are outlined in the methods are reported in the results. However, the only statistical outcome of their analysis were unadjusted p-values that were not reported and were just described qualitatively.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	The only statistical analysis performed were Mantel-Haenszel chi-squared tests, which did not allow for confounder adjustment. The study does not present a distribution of potential confounders by exposure status but by case/control status. Several variables, such as reason for termination, age at hire, and age at death were significantly different between cases and controls and were not accounted for in statistical modeling. The study explains that these differences are not likely to have any epidemiologic significance and appear to be relatively small differences.
	Metric 10:	Covariate Characterization	Medium	While the study does not explain where they obtained covariate information, it is reasonable to assume that they gathered the information from company records.
	Metric 11:	Co-exposure Counfounding	Low	The study assesses a wide range of other potential occupational co-exposures. While these co-exposures are not adjusted for in any statistical models, effect estimates are presented separately for benzene, diethyl sulfate, ethylene oxide, and vinyl chloride. The distribution of co-exposures across cases and controls is demonstrated to be mostly balanced by comparing proportions of exposed/unexposed between cases and controls. The only notable instance of imbalance is for benzene, where 11.1% of cases were exposed whereas 37.9% of all controls and 19.2% of non-neoplasm related controls were exposed.
Domain 5: Analysis				

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Study Citation:	Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	The study chose a case-control design, which was appropriate to study the rare disease of brain tumors and its association with occupational exposures. The only statistical analysis conducted is a Mantzel-Haenszel chi-squared test, but there is no reason to suggest that this would be inappropriate.
	Metric 13:	Statistical Power	Medium	The study does not calculate statistical power, but the number of cases (n=21) and controls (n=80 in each analysis) is likely sufficient to detect an effect.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to understand what was done and could be reproduced given access to the analytic data.
	Metric 15:	Statistical Analysis	High	The only statistical analysis conducted is a Mantel-Haenszel chi-squared test, and all assumptions were met. The statistical process is transparent.

Additional Comments: This case-control study pulled deceased former employees of the Union Carbide Corporation in Texas City, Texas. The study examined dichotomous exposure to a wide range of occupational exposures, including 1,2-dichloroethane, in relation to brain tumor cases. There is no quantitative estimate of exposure. The only statistical analysis in the study is a Mantel-Haenszel chi-squared test statistic and no statistically significant differences in exposure between cases and controls were observed. The fact that there are no effect estimates, no adjustment for confounders, and no quantitative exposure estimates limits the usefulness of this paper.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	Urinary system cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	Urinary system cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	Urinary system cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Immune/Hematological
Reported Health Effect(s):	Lymphatic and hematopoietic tissue cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Immune/Hematological
Reported Health Effect(s):	Lymphatic and hematopoietic tissue cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Immune/Hematological
Reported Health Effect(s):	Lymphatic and hematopoietic tissue cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Other cancers (not specified)
Reported Health Effect(s):	Other cancers (not specified)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Other cancers (not specified)
Reported Health Effect(s):	Other cancers (not specified)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Other cancers (not specified)
Reported Health Effect(s):	Other cancers (not specified)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Mortality
Reported Health Effect(s):	All-cause mortality
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Vital status was tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Medium	Death rates among unit employees were compared to death rates in the U.S. population adjusted for age and gender. Demographics of the exposed workers are not provided; therefore, it is not clear whether additional adjustment for race may have been appropriate. No justification is provided for the choice of the entire U.S. population as the comparison group. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis. Additional analyses are conducted limiting workers to those with the greatest likelihood of exposure (i.e., those working in jobs with high likelihood of contact with chemicals for more than a year, those working for the full year of 1979 during which chemical exposures were most frequently reported); these smaller groups are also compared to the unexposed general population.
	Metric 6:	Temporality	High	Temporality was established due to the longitudinal design and the use of mortality as the outcome. Exposures occurred between 1979 and 1987 and follow-up for vital status was conducted through 2003.
Domain 3: Outcome Assessment				

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Mortality
Reported Health Effect(s):	All-cause mortality
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Medium	The study did not provide information on how mortality was assessed either in the exposed population or in the comparison population; use of death certificates is implied but not stated.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected deaths are reported, but SIRs and 95% confidence intervals are not provided.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Comparisons of observed versus expected deaths were adjusted for age and gender. Demographics of the exposed workers are not provided; therefore, it is not clear whether additional adjustment for race may have been appropriate.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records or death records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed deaths among a population of exposed workers compared to expected deaths among the U.S. population, adjusted for age and gender.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected deaths; no SIR was provided. Expected death rates were adjusted for age and gender.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Mortality
Reported Health Effect(s):	All-cause mortality
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	All cancer (excluding non-melanoma skin cancer), digestive system cancer, colorectal cancer, respiratory cancer, prostate cancer, urinary system cancer, lymphatic and hematopoietic tissue cancer, other cancers (not specified)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	All cancer (excluding non-melanoma skin cancer), digestive system cancer, colorectal cancer, respiratory cancer, prostate cancer, urinary system cancer, lymphatic and hematopoietic tissue cancer, other cancers (not specified)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	All cancer (excluding non-melanoma skin cancer), digestive system cancer, colorectal cancer, respiratory cancer, prostate cancer, urinary system cancer, lymphatic and hematopoietic tissue cancer, other cancers (not specified)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Gastrointestinal
Reported Health Effect(s):	Digestive system cancer, colorectal cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Gastrointestinal
Reported Health Effect(s):	Digestive system cancer, colorectal cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Gastrointestinal
Reported Health Effect(s):	Digestive system cancer, colorectal cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Lung/Respiratory
Reported Health Effect(s):	Respiratory cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Lung/Respiratory
Reported Health Effect(s):	Respiratory cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Lung/Respiratory
Reported Health Effect(s):	Respiratory cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Prostate cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Prostate cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Prostate cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Male workers who had ever been assigned to the chlorohydrin unit between 1 January 1940 and 31 December 1967 at Union Carbide's South Charleston plant were enrolled and matched to the US National Death Index. Status on 5 workers could not be identified. Information on how workers were matched to death index was not specified.
	Metric 2:	Attrition	Medium	Rate of inclusion/participation was very high, as records were able to be matched for 98% of participants. Medium rating given because information on how participants whose vital status was not known was not specified.
	Metric 3:	Comparison Group	Uninformative	Unacceptable rating given because SMRs were calculated based on expected deaths from a reference population matched on sex, but not age.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Exposure was assessed based on duration of work in the plant. No information is provided on exposure levels, and a JEM was not used.
	Metric 5:	Exposure Levels	Uninformative	No information provided on levels of exposure.
	Metric 6:	Temporality	High	Temporality is well established; person-years stopped accumulating in 1967 and outcome was assessed beginning at that time.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar period, and interval since assignments, but distribution of these covariates was not reported.
	Metric 10:	Covariate Characterization	Medium	Information on covariate characterization not provided, but the selected covariates (age, calendar period, and interval since assignments) were likely extracted from employee records and unlikely to be largely problematic
	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.

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Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Study design was appropriate for the research method. Statistical methods were also appropriate.
	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.
	Metric 14:	Reproducibility of Analyses	Medium	Methods are well-enough described that study could be adequately reproduced.
	Metric 15:	Statistical Analysis	High	SMRs calculated based on US general population mortality for white males through 1988. RRs were ”evaluated over levels of duration of assignment to the chlorohydrin unit, stratified by age, calendar year, and interval since first assignment to the chlorohydrin unit”.

Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Male workers who had ever been assigned to the chlorohydrin unit between 1 January 1940 and 31 December 1967 at Union Carbide's South Charleston plant were enrolled and matched to the US National Death Index. Status on 5 workers could not be identified. Information on how workers were matched to death index was not specified.
	Metric 2:	Attrition	Medium	Rate of inclusion/participation was very high, as records were able to be matched for 98% of participants. Medium rating given because information on how participants whose vital status was not known was not specified.
	Metric 3:	Comparison Group	Uninformative	Unacceptable rating given because SMRs were calculated based on expected deaths from a reference population matched on sex, but not age.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Exposure was assessed based on duration of work in the plant. No information is provided on exposure levels, and a JEM was not used.
	Metric 5:	Exposure Levels	Uninformative	No information provided on levels of exposure.
	Metric 6:	Temporality	High	Temporality is well established; person-years stopped accumulating in 1967 and outcome was assessed beginning at that time.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar period, and interval since assignments, but distribution of these covariates was not reported.
	Metric 10:	Covariate Characterization	Medium	Information on covariate characterization not provided, but the selected covariates (age, calendar period, and interval since assignments) were likely extracted from employee records and unlikely to be largely problematic
	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.
Domain 5: Analysis				

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Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Study design was appropriate for the research method. Statistical methods were also appropriate.
	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.
	Metric 14:	Reproducibility of Analyses	Medium	Methods are well-enough described that study could be adequately reproduced.
	Metric 15:	Statistical Analysis	High	SMRs calculated based on US general population mortality for white males through 1988. RRs were ”evaluated over levels of duration of assignment to the chlorohydrin unit, stratified by age, calendar year, and interval since first assignment to the chlorohydrin unit”.

Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Male workers who had ever been assigned to the chlorohydrin unit between 1 January 1940 and 31 December 1967 at Union Carbide's South Charleston plant were enrolled and matched to the US National Death Index. Status on 5 workers could not be identified. Information on how workers were matched to death index was not specified.
	Metric 2:	Attrition	Medium	Rate of inclusion/participation was very high, as records were able to be matched for 98% of participants. Medium rating given because information on how participants whose vital status was not known was not specified.
	Metric 3:	Comparison Group	Uninformative	Unacceptable rating given because SMRs were calculated based on expected deaths from a reference population matched on sex, but not age.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Exposure was assessed based on duration of work in the plant. No information is provided on exposure levels, and a JEM was not used.
	Metric 5:	Exposure Levels	Uninformative	No information provided on levels of exposure.
	Metric 6:	Temporality	High	Temporality is well established; person-years stopped accumulating in 1967 and outcome was assessed beginning at that time.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar period, and interval since assignments, but distribution of these covariates was not reported.
	Metric 10:	Covariate Characterization	Medium	Information on covariate characterization not provided, but the selected covariates (age, calendar period, and interval since assignments) were likely extracted from employee records and unlikely to be largely problematic
	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.
Domain 5: Analysis				

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Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Study design was appropriate for the research method. Statistical methods were also appropriate.
	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.
	Metric 14:	Reproducibility of Analyses	Medium	Methods are well-enough described that study could be adequately reproduced.
	Metric 15:	Statistical Analysis	High	SMRs calculated based on US general population mortality for white males through 1988. RRs were ”evaluated over levels of duration of assignment to the chlorohydrin unit, stratified by age, calendar year, and interval since first assignment to the chlorohydrin unit”.

Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Male workers who had ever been assigned to the chlorohydrin unit between 1 January 1940 and 31 December 1967 at Union Carbide's South Charleston plant were enrolled and matched to the US National Death Index. Status on 5 workers could not be identified. Information on how workers were matched to death index was not specified.
	Metric 2:	Attrition	Medium	Rate of inclusion/participation was very high, as records were able to be matched for 98% of participants. Medium rating given because information on how participants whose vital status was not known was not specified.
	Metric 3:	Comparison Group	Uninformative	Unacceptable rating given because SMRs were calculated based on expected deaths from a reference population matched on sex, but not age.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Exposure was assessed based on duration of work in the plant. No information is provided on exposure levels, and a JEM was not used.
	Metric 5:	Exposure Levels	Uninformative	No information provided on levels of exposure.
	Metric 6:	Temporality	High	Temporality is well established; person-years stopped accumulating in 1967 and outcome was assessed beginning at that time.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar period, and interval since assignments, but distribution of these covariates was not reported.
	Metric 10:	Covariate Characterization	Medium	Information on covariate characterization not provided, but the selected covariates (age, calendar period, and interval since assignments) were likely extracted from employee records and unlikely to be largely problematic
	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.
Domain 5: Analysis				

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Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Study design was appropriate for the research method. Statistical methods were also appropriate.
	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.
	Metric 14:	Reproducibility of Analyses	Medium	Methods are well-enough described that study could be adequately reproduced.
	Metric 15:	Statistical Analysis	High	SMRs calculated based on US general population mortality for white males through 1988. RRs were ”evaluated over levels of duration of assignment to the chlorohydrin unit, stratified by age, calendar year, and interval since first assignment to the chlorohydrin unit”.

Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

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Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Male workers who had ever been assigned to the chlorohydrin unit between 1 January 1940 and 31 December 1967 at Union Carbide's South Charleston plant were enrolled and matched to the US National Death Index. Status on 5 workers could not be identified. Information on how workers were matched to death index was not specified.
	Metric 2:	Attrition	Medium	Rate of inclusion/participation was very high, as records were able to be matched for 98% of participants. Medium rating given because information on how participants whose vital status was not known was not specified.
	Metric 3:	Comparison Group	Uninformative	Unacceptable rating given because SMRs were calculated based on expected deaths from a reference population matched on sex, but not age.
Domain 2: Exposure Characterization				
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Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar period, and interval since assignments, but distribution of these covariates was not reported.
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Domain 5: Analysis				

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Linked HERO ID(s):	200224, 5447107
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Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Study design was appropriate for the research method. Statistical methods were also appropriate.
	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.
	Metric 14:	Reproducibility of Analyses	Medium	Methods are well-enough described that study could be adequately reproduced.
	Metric 15:	Statistical Analysis	High	SMRs calculated based on US general population mortality for white males through 1988. RRs were ”evaluated over levels of duration of assignment to the chlorohydrin unit, stratified by age, calendar year, and interval since first assignment to the chlorohydrin unit”.

Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

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Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Male workers who had ever been assigned to the chlorohydrin unit between 1 January 1940 and 31 December 1967 at Union Carbide's South Charleston plant were enrolled and matched to the US National Death Index. Status on 5 workers could not be identified. Information on how workers were matched to death index was not specified.
	Metric 2:	Attrition	Medium	Rate of inclusion/participation was very high, as records were able to be matched for 98% of participants. Medium rating given because information on how participants whose vital status was not known was not specified.
	Metric 3:	Comparison Group	Uninformative	Unacceptable rating given because SMRs were calculated based on expected deaths from a reference population matched on sex, but not age.
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Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar period, and interval since assignments, but distribution of these covariates was not reported.
	Metric 10:	Covariate Characterization	Medium	Information on covariate characterization not provided, but the selected covariates (age, calendar period, and interval since assignments) were likely extracted from employee records and unlikely to be largely problematic
	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.
Domain 5: Analysis				

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Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

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	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.
	Metric 14:	Reproducibility of Analyses	Medium	Methods are well-enough described that study could be adequately reproduced.
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Additional Comments: None

Overall Quality Determination Uninformative

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Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
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Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Male workers who had ever been assigned to the chlorohydrin unit between 1 January 1940 and 31 December 1967 at Union Carbide's South Charleston plant were enrolled and matched to the US National Death Index. Status on 5 workers could not be identified. Information on how workers were matched to death index was not specified.
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	Metric 3:	Comparison Group	Uninformative	Unacceptable rating given because SMRs were calculated based on expected deaths from a reference population matched on sex, but not age.
Domain 2: Exposure Characterization				
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	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar period, and interval since assignments, but distribution of these covariates was not reported.
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	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.
Domain 5: Analysis				

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Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Study design was appropriate for the research method. Statistical methods were also appropriate.
	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.
	Metric 14:	Reproducibility of Analyses	Medium	Methods are well-enough described that study could be adequately reproduced.
	Metric 15:	Statistical Analysis	High	SMRs calculated based on US general population mortality for white males through 1988. RRs were ”evaluated over levels of duration of assignment to the chlorohydrin unit, stratified by age, calendar year, and interval since first assignment to the chlorohydrin unit”.

Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
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Linked HERO ID(s):	200224, 5447107
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Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Male workers who had ever been assigned to the chlorohydrin unit between 1 January 1940 and 31 December 1967 at Union Carbide's South Charleston plant were enrolled and matched to the US National Death Index. Status on 5 workers could not be identified. Information on how workers were matched to death index was not specified.
	Metric 2:	Attrition	Medium	Rate of inclusion/participation was very high, as records were able to be matched for 98% of participants. Medium rating given because information on how participants whose vital status was not known was not specified.
	Metric 3:	Comparison Group	Uninformative	Unacceptable rating given because SMRs were calculated based on expected deaths from a reference population matched on sex, but not age.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Exposure was assessed based on duration of work in the plant. No information is provided on exposure levels, and a JEM was not used.
	Metric 5:	Exposure Levels	Uninformative	No information provided on levels of exposure.
	Metric 6:	Temporality	High	Temporality is well established; person-years stopped accumulating in 1967 and outcome was assessed beginning at that time.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar period, and interval since assignments, but distribution of these covariates was not reported.
	Metric 10:	Covariate Characterization	Medium	Information on covariate characterization not provided, but the selected covariates (age, calendar period, and interval since assignments) were likely extracted from employee records and unlikely to be largely problematic
	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.
Domain 5: Analysis				

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Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Study design was appropriate for the research method. Statistical methods were also appropriate.
	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.
	Metric 14:	Reproducibility of Analyses	Medium	Methods are well-enough described that study could be adequately reproduced.
	Metric 15:	Statistical Analysis	High	SMRs calculated based on US general population mortality for white males through 1988. RRs were ”evaluated over levels of duration of assignment to the chlorohydrin unit, stratified by age, calendar year, and interval since first assignment to the chlorohydrin unit”.

Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Bove, F. J. (1996). Public drinking water contamination and birthweight, prematurity, fetal deaths, and birth defects. Toxicology and Industrial Health 12(2):255-266.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	200239

Domain	Metric	Rating	Comments
Domain 1: Study Participation			
Metric 1:	Participant Selection	Medium	This cross-sectional study (n=80,938) included all registered singleton live births and fetal deaths (>20 weeks' gestation) in 1985-88 in 75 New Jersey towns located in 4 counties with "some" water supplies contaminated with substances of interest and where: (i) residents were "mostly" served by public water systems; and (ii) births occurred "mostly" in state. Estimated proportions of residents served by public water systems, and of pregnancies/births captured, were not described. However, the inclusion of all eligible registered births, fetal deaths, and birth defects, as well as the selection of towns without knowledge of birth outcome prevalence, limited the likelihood of selection bias.
Metric 2:	Attrition	Medium	All registered births and fetal deaths were included. Attrition due to missing values for multiple variables was not quantified and is therefore uncertain. However, attrition was likely modest as the proportion of missing values for individual variables was relatively low: (i) ~6% of subjects were excluded from analyses of outcomes such as preterm birth due to invalid or missing gestational ages; and (ii) other covariates evaluated as confounders had up to 4.9% missing values.
Metric 3:	Comparison Group	High	After excluding plural pregnancies and chromosomal abnormalities, all registered live births during the study period in the areas included without the outcomes of interest were included in the comparison group. This comprehensive approach limited the potential for bias. Chromosomal abnormalities were not included as outcomes as they were not hypothesized to be associated with the exposures under study but were appropriately excluded given their uncertain etiology.
Domain 2: Exposure Characterization			

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Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	200239

Domain	Metric		Rating	Comments
	Metric 4:	Measurement of Exposure	Medium	Along with several other contaminants, residential drinking water exposure to 1,2-dichloroethane (as well as 1,1,1-trichloroethane and 'total dichloroethylenes') – was assigned based on maternal town of residence at birth. Exposure estimates were calculated using the average of water company sampling reports during the first trimester (for birth defects and fetal death) or the duration of pregnancy (for other outcomes). Detection limits and data availability were not specified in detail but were described as below 1 ppb, with reporting compliance >85%. A minimum of 1 sample per 6-month interval was required; variability in the number of measures available across water systems and towns was not described. Additional sources of measurement error included: changes in residence during pregnancy; water from alternate sources (ex. private wells, bottles, workplaces); variability in residential contaminant levels vs measured samples; unknown levels of tap water intake; and errors in estimated dermal and inhalation exposure while bathing or showering. While the extent of exposure misclassification is uncertain, there is no evidence to suggest it was differential rather than random.
	Metric 5:	Exposure Levels	Medium	Due to the high proportion of measures below detection limits, analyses relating exposure to health outcomes used only 2 categories for each of the chlorinated solvents of interest: cutoffs close to detection limits were used to define elevated exposure. Proportions defined as having elevated exposure was low (1.8% had 1,1-dichloroethylene ≥1 ppb). An important concern is that relatively low levels of exposure to these contaminants from sources other than residential drinking water, for which data were not available, could potentially have resulted in considerable misclassification.
	Metric 6:	Temporality	High	Exposure levels were assigned based on contaminant exposures estimated during: (i) the first trimester for analyses of birth defects and fetal deaths; and (ii) the duration of pregnancy for other pregnancy outcomes.

Domain 3: Outcome Assessment

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Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	200239

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcomes included measures of birthweight (continuous among term births, low term birthweight, very low birthweight), prematurity, fetal death, and congenital anomalies in live births or fetal deaths. The anomalies analyzed included defects of the central nervous system, neural tube, oral cleft, total cardiac, major cardiac, ventricular septum, and any surveillance defect excluding chromosomal defects. All outcomes were identified using birth certificates, fetal death certificates (>20 weeks' gestation), and the NJ congenital birth defect registry (ICD codes provided). These registry data are likely to be sufficiently valid for late pregnancy outcomes. However, their limited ability to capture early pregnancy losses is a weakness. The sample included only 594 fetal deaths (less than 1% of the >80,0000 sample). Typical estimates are that 10-20%, of recognized pregnancies ending in losses. Moreover, developmental defects contributing to early pregnancy losses were also not captured. A further limitation is that that potentially etiologically heterogeneous preterm birth types were analyzed together, as these data did not distinguish premature rupture of membranes vs idiopathic prematurity.
	Metric 8:	Reporting Bias	Medium	Models were constructed only for contaminants with associations > 1.0, and tables included only associations with odds ratios ≥1.5. No clear rationale was provided. Several positive odds ratios below the 1.5 cutoff were described in the results text (without confidence intervals), but no null/negative odds ratios were presented or described.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Potential confounding by maternal race, education, parity, and prior pregnancy loss, along with infant sex (for birth outcomes) and adequacy of prenatal care, was examined. Gestational age was addressed by analyzing birthweight among full term births, term low birth weight, and small size for gestational age. Only fully adjusted models were presented. In a companion case-control study (with low participation rates), adjustment for other variables not available on birth certificates (ex. maternal smoking, occupational exposures, medical history, and gestational weight gain) did not influence associations with other studied contaminants. This separate study reduces concerns for important confounding bias, but confounding cannot be ruled out.
	Metric 10:	Covariate Characterization	Medium	Data on covariates came from registry data: birth certificates, fetal death certificates, and the NJ congenital birth defects registry.
	Metric 11:	Co-exposure Counfounding	Medium	Co-exposure confounding by drinking water trihalomethane concentrations was evaluated. There was no evidence to suggest substantial confounding by this or other co-exposures.
Domain 5: Analysis				

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Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	200239

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Methods were appropriate. The study used logistic regression models to estimate odds ratios and confidence intervals for dichotomous outcomes, and linear regression for analysis of continuous birth weight.
	Metric 13:	Statistical Power	Medium	Statistical power was likely to have been limited as a consequence of the small proportion of the sample defined as having "elevated" residential water concentrations of the chemicals of interest. The range of exposure examined was limited, as cutoffs for elevated levels were close to the detection limits of 1 ppb. In addition, for most birth defect outcomes, fewer than 10 cases had elevated exposure.
	Metric 14:	Reproducibility of Analyses	Medium	The authors clearly described steps used to estimate exposure-outcome associations, including exposure category cutoffs and criteria for confounding. However, many results were not shown as tables included odds ratios ≥1.5.
	Metric 15:	Statistical Analysis	High	The authors estimated coefficients, odds ratios and 95% confidence intervals using adequate methods. Confounding was based on 15% change-in-estimate comparing nested models. Effect modification (ex by infant sex) was not evaluated as there was no a priori evidence to suggest such analyses at that time.

Additional Comments: This study analyzed the association between estimated residential drinking water concentrations of several chlorinated solvents including 1,2-dichloroethane (as well as 1,1,1-trichloroethane; ∑[trans-1,2-dichloroethylene and 1,1-dichloroethylene]) and pregnancy outcomes (size at birth, prematurity, fetal deaths, and congenital birth defects). The sample included more than 80,000 births during 1985-88 for residents of 75 towns in NJ using public water system records to estimate exposure during gestation, and registry data (birth certificate, fetal death certificates for pregnancies >20 weeks, state birth defect registry) to characterize outcomes. Strengths included the large sample size and inclusion of all eligible registered births and fetal deaths in the study period. A critical concern is the inability to capture early fetal deaths and any related malformations (1% of the sample had fetal deaths vs typical estimates of >10%). An important limitation was the low percentage of the sample with detectable (> 1ppb) concentrations of these contaminants (<1% to 6.2%). Small numbers for birth defect outcomes also limited power. Exposure misclassification (ex. drinking water from wells/ work/ bottles, changes in residence, exposure from other sources) is also a concern. However, such misclassification was likely non-differential, and thus more likely to under- vs. to over-estimate associations.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Bove, F. J., Fulcomer, M. C., Klotz, J. B., Esmart, J., Dufficy, E. M., Savrin, J. E. (1995). Public drinking water contamination and birth outcomes. American Journal of Epidemiology 141(9):850-862.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	194932

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	This semi-ecological study (n=80,938) included all registered singleton live births and fetal deaths (>20 weeks) in 1985-88 in 75 New Jersey towns located in 4 counties with "some" water supplies contaminated with substances of interest and where: (i) residents were "mostly" served by public water systems; and (ii) births occurred "mostly" in state. Estimated proportions of residents served by public water systems, and of pregnancies/births captured, were not described. However, the inclusion of all eligible registered births, fetal deaths, and birth defects, as well as the selection of towns without knowledge of birth outcome prevalence, limited the likelihood of selection bias.
	Metric 2:	Attrition	Medium	All registered births and fetal deaths were included. Attrition due to missing values for multiple variables was not quantified and is therefore uncertain. However, attrition was likely modest as the proportion of missing values for individual variables was relatively low: (i) ~6% of subjects were excluded from analyses of outcomes such as preterm birth due to invalid or missing gestational ages; and (ii) other covariates evaluated as confounders had up to 4.9% missing values.
	Metric 3:	Comparison Group	High	After excluding plural pregnancies and chromosomal abnormalities, all registered live births during the study period in the areas included without the outcomes of interest were included in the comparison group. This comprehensive approach limited the potential for bias. Chromosomal abnormalities were not included as outcomes as they were not hypothesized to be associated with the exposures under study but were appropriately excluded given their uncertain etiology.
Domain 2: Exposure Characterization				

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Study Citation:	Bove, F. J., Fulcomer, M. C., Klotz, J. B., Esmart, J., Dufficy, E. M., Savrin, J. E. (1995). Public drinking water contamination and birth outcomes. American Journal of Epidemiology 141(9):850-862.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	194932

Domain	Metric		Rating	Comments
	Metric 4:	Measurement of Exposure	Medium	Along with several other contaminants, residential drinking water exposure to 1,2-dichloroethane (as well as 1,1,1-trichloroethane and 'total dichloroethylenes') was assigned based on maternal town of residence at birth. Exposure estimates were calculated using the average of water company sampling reports during the first trimester (for birth defects and fetal death) or the duration of pregnancy (for other outcomes). Detection limits and data availability were not specified in detail but were described as below 1 ppb, with reporting compliance >85%. A minimum of 1 sample per 6-month interval was required; variability in the number of measures available across water systems and towns was not described. Additional sources of measurement error included: changes in residence during pregnancy; water from alternate sources (ex. private wells, bottles, workplaces); variability in residential contaminant levels vs measured samples; unknown levels of tap water intake; and errors in estimated dermal and inhalation exposure while bathing or showering. While the extent of exposure misclassification is uncertain, there is no evidence to suggest it was differential rather than random.
	Metric 5:	Exposure Levels	Low	Due to the high proportion of measures below detection limits, analyses relating exposure to health outcomes used only 2 categories for each of the three chemicals of interest: cutoffs close to detection limits were used to define elevated exposure. Proportions defined as having elevated exposure were low (1.8% had 1,1-dichloroethylene ≥1 ppb). An important concern is that relatively low levels of exposure to this contaminant from sources other than residential drinking water, for which data were not available, could potentially have resulted in considerable misclassification.
	Metric 6:	Temporality	High	Exposure levels were assigned based on contaminant exposures estimated during: (i) the first trimester for analyses of birth defects and fetal deaths; and (ii) the duration of pregnancy for other pregnancy outcomes.

Domain 3: Outcome Assessment

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Study Citation:	Bove, F. J., Fulcomer, M. C., Klotz, J. B., Esmart, J., Dufficy, E. M., Savrin, J. E. (1995). Public drinking water contamination and birth outcomes. American Journal of Epidemiology 141(9):850-862.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	194932

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcomes included measures of birthweight (continuous among term births, low term birthweight, very low birthweight), prematurity, fetal death, and congenital anomalies in live births or fetal deaths. The anomalies analyzed included defects of the central nervous system, neural tube, oral cleft, total cardiac, major cardiac, ventricular septum, and any surveillance defect excluding chromosomal defects. All outcomes were identified using birth certificates, fetal death certificates (>20 weeks' gestation), and the NJ congenital birth defect registry (ICD codes provided). These registry data are likely to be sufficiently valid for late pregnancy outcomes. However, their limited ability to capture early pregnancy losses is a weakness. The sample included only 594 fetal deaths (less than 1% of the >80,0000 sample). Typical estimates are that 10-20%, of recognized pregnancies ending in losses. Moreover, developmental defects contributing to early pregnancy losses were also not captured. A further limitation is that that potentially etiologically heterogeneous preterm birth types were analyzed together, as these data did not distinguish premature rupture of membranes vs idiopathic prematurity.
	Metric 8:	Reporting Bias	Low	Models were constructed only for contaminants with associations > 1.0, and tables included only associations with odds ratios ≥1.5. No clear rationale was provided. Several positive odds ratios below the 1.5 cutoff were described in the results text (without confidence intervals), but no null/negative odds ratios were presented or described.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Potential confounding by maternal race, education, parity, and prior pregnancy loss, along with infant sex (for birth outcomes) and adequacy of prenatal care, was examined. Gestational age was addressed by analyzing birthweight among full term births, term low birth weight, and small size for gestational age. Only fully adjusted models were presented. In a companion case-control study (with low participation rates), adjustment for other variables not available on birth certificates (ex. maternal smoking, occupational exposures, medical history, and gestational weight gain) did not influence associations with other studied contaminants. This separate study reduces concerns for important confounding bias, but confounding cannot be ruled out.
	Metric 10:	Covariate Characterization	Medium	Data on covariates came from registry data: birth certificates, fetal death certificates, and the NJ congenital birth defects registry.
	Metric 11:	Co-exposure Counfounding	Medium	Co-exposure confounding by drinking water trihalomethane concentrations was evaluated. There was no evidence to suggest substantial confounding by this or other co-exposures.
Domain 5: Analysis				

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Study Citation:	Bove, F. J., Fulcomer, M. C., Klotz, J. B., Esmart, J., Dufficy, E. M., Savrin, J. E. (1995). Public drinking water contamination and birth outcomes. American Journal of Epidemiology 141(9):850-862.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	194932

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Methods were appropriate. The study used logistic regression models to estimate odds ratios and confidence intervals for dichotomous outcomes, and linear regression for analysis of continuous birth weight.
	Metric 13:	Statistical Power	Low	Statistical power was likely to have been limited as a consequence of the small proportion of the sample defined as having "elevated" residential water concentrations of the chemicals of interest. The range of exposure examined was limited, as cutoffs for elevated levels were close to the detection limits of 1 ppb. In addition, for most birth defect outcomes, fewer than 10 cases had elevated exposure. However, the authors emphasized the magnitude of associations rather than statistical significance and presented multiple confidence intervals to aid interpretation of the precision of estimates (50%, 90% and 99%).
	Metric 14:	Reproducibility of Analyses	Medium	The authors clearly described steps used to estimate exposure-outcome associations, including exposure category cutoffs and criteria for confounding. However, many results were not shown as tables included odds ratios ≥1.5.
	Metric 15:	Statistical Analysis	High	The authors estimated coefficients, odds ratios and confidence intervals using adequate methods. Confounding was based on 15% change-in-estimate comparing nested models. Effect modification (ex by infant sex) was not evaluated as there was no a priori evidence to suggest such analyses at that time.

Additional Comments: This study analyzed the association between estimated residential drinking water concentrations of several chlorinated solvents including 1,2-dichloroethane (as well as 1,1,1-trichloroethane and the ∑[trans-1,2-dichloroethylene & 1,1-dichloroethylene]) and pregnancy outcomes (size at birth, prematurity, fetal deaths, and congenital birth defects). The sample included more than 80,000 births during 1985-88 for residents of 75 towns in NJ using public water system records to estimate exposure during gestation, and registry data (birth certificate, fetal death certificates for pregnancies >20 weeks' gestation, state birth defect registry) to characterize outcomes. Strengths included the large sample size and inclusion of all eligible registered births and fetal deaths in the study period. A critical concern is the inability to capture early fetal deaths and any related malformations (1% of the sample had fetal deaths vs typical estimates of >10%). An important limitation was the low percentage of the sample with detectable (> 1ppb) concentrations of this solvent (<2%), which likely limited power. Small numbers for birth defect outcomes also limited power. Exposure misclassification (ex. drinking water from wells/ work/ bottles, changes in residence, exposure from other sources) is also a concern. However, such misclassification was likely non-differential, and thus more likely to under- vs. to over-estimate associations.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Bowler, R.M., Gysens, S., Hartney, C. (2003). Neuropsychological effects of ethylene dichloride exposure. NeuroToxicology 24(4-5):553-562.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Wechsler Adult Intelligence Scale III (WAIS-III), Wechsler Memory Scale III (WMS-III), Boston Naming Test (BNT), Trail Making Test (TMT), Stroop Color-Word Test, Grooved Pegboard, Dynamometer, Wide Range Achievement Test (WRAT), Finger tapping, Beck Anxiety Index, Beck Depression Index, Symptom Checklist-90 (SCL-90).
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	200241

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Uninformative	221 workers that had been exposed to 1,2-DCE in the Southern United States were initially included. Exclusion criteria were provided, including the number of individuals excluded for each reason. The study authors note that those initially included in the analysis sample were referred by physicians after neurological complaints were documented. Detailed criteria for referral were not provided. Referral-based recruitment of neurological cases will likely result in an analysis sample with an exposure-outcome distribution that is not representative of the eligible population (i.e., contamination site clean-up workers).
	Metric 2:	Attrition	Medium	There was moderate subject loss. Reasons for exclusion from the analysis sample are provided, and only those with complete information were included in the analysis.
	Metric 3:	Comparison Group	Low	Impairment scores were compared to normative data from manuals and/or a "demographically similar control group" cited to Bowler et al. (2001). The controls from this study appeared similar (albeit somewhat older) than 1,2-DCE-exposed workers and reported no prior chemical exposure.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	A job-exposure matrix was not considered plausible; variables considered as surrogates of exposure were obtained from interviews. This method is expected to have poor validity because it relies on workers' recall of subjective events and their frequency (e.g., contact with water); workers (who are taking part in a lawsuit) may overestimate their exposure.
	Metric 5:	Exposure Levels	Low	Two levels of exposure (exposed and not exposed) were used to evaluate neurophysiological effects.
	Metric 6:	Temporality	Medium	Exposures primarily occurred between 1993 and 1995 and neurophysiological effects were evaluated in 2000. Temporality is established, but it is unclear whether exposures fall within relevant exposure windows for the outcome of interest.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Neurophysiological effects were evaluated using a number of standardized tests, including (but not limited to) the Wechsler Adult Intelligence Scale (WAIS-III), the Wechsler Memory Scale (WMS-III), and the Symptom Checklist 90-Revised (SCL90-R). There was no information whether tests were performed using the same methods for exposed and referent groups (e.g., timing and order of tests).

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Study Citation:	Bowler, R.M., Gysens, S., Hartney, C. (2003). Neuropsychological effects of ethylene dichloride exposure. NeuroToxicology 24(4-5):553-562.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Wechsler Adult Intelligence Scale III (WAIS-III), Wechsler Memory Scale III (WMS-III), Boston Naming Test (BNT), Trail Making Test (TMT), Stroop Color-Word Test, Grooved Pegboard, Dynamometer, Wide Range Achievement Test (WRAT), Finger tapping, Beck Anxiety Index, Beck Depression Index, Symptom Checklist-90 (SCL-90).
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	200241

Domain	Metric		Rating	Comments
	Metric 8:	Reporting Bias	Low	Neurobehavioral outcomes mentioned in the methods were reported for 1,2-DCE-exposed workers (as mean score, standard deviation, and percentage impaired); results for controls/normative data were not shown and/or p-values from t-tests were not provided. Control data were used to define impairment (based on z-score) but these values were not reported. Data pertaining to specific exposure variables were reported in the text only; no data were shown in a table.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Normative data permitted adjustments based on age, education, and gender. The control group was "socio-demographically" similar but specific parameters used to define similarity were not indicated. Separate ANCOVA analyses on workers only were stratified by race (citation provided), and adjusted for ethnicity, age, and education. The methods for identifying and including potential confounders in the analytic approach was not described.
	Metric 10:	Covariate Characterization	Low	No description of the covariate collection method was provided. It was not clear whether the method used was valid or not.
	Metric 11:	Co-exposure Counfounding	Low	A number of workers (18%) reported current exposure to chemicals in their work environment. These potential co-exposures were not were not appropriately adjusted for in the analytical approach used.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Low	The study design was appropriate to evaluate the neurophysiological status of 1,2-DCE-exposed workers; however, statistical methods were not comprehensive.
	Metric 13:	Statistical Power	Medium	The report indicates "significant impairments" were observed on various neurophysiological tests using t-tests, and significant exposure relationships were reported based on test scores and specific exposure variables (used as surrogates of exposure). Therefore, the number of participants was sufficient to detect an effect.
	Metric 14:	Reproducibility of Analyses	Low	Tests were scored according to relevant manuals; the calculation of z-scores, used in all impairment comparisons and analyses of exposure relationships, was not explained in adequate detail. The methods used to determine relationships between specific exposure variables and test scores (i.e., ANCOVA analyses) were not fully described.
	Metric 15:	Statistical Analysis	Low	Description of the ANCOVA analysis was largely not present. It is not clear whether model assumptions were met.

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Study Citation:	Bowler, R.M., Gysens, S., Hartney, C. (2003). Neuropsychological effects of ethylene dichloride exposure. NeuroToxicology 24(4-5):553-562.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Wechsler Adult Intelligence Scale III (WAIS-III), Wechsler Memory Scale III (WMS-III), Boston Naming Test (BNT), Trail Making Test (TMT), Stroop Color-Word Test, Grooved Pegboard, Dynamometer, Wide Range Achievement Test (WRAT), Finger tapping, Beck Anxiety Index, Beck Depression Index, Symptom Checklist-90 (SCL-90).
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	200241

Domain	Metric	Rating	Comments
Additional Comments:	The study evaluated the neurobehavioral status of a group of workers with known exposure to 1,2-DCE at a clean-up site. Impairments related to processing speed, attention, cognitive flexibility, motor coordination and speed, verbal memory/fluency, vision and visual-spatial abilities, and mood were reported in exposed workers. Serious and consequential flaws are associated with the study including methods of participant selection and retention, and exposure characterization among others.		

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Brender, J.D., Shinde, M.U., Zhan, F.B., Gong, X., Langlois, P.H. (2014). Maternal residential proximity to chlorinated solvent emissions and birth defects in offspring: A case-control study. Environmental Health: A Global Access Science Source 13(1):96.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	birth defects (neural tube defects, limbs deficiencies, oral cleft defects, heart defects, spina bifida, anencephaly)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	2799700

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Participants were drawn from the Texas Birth Defects Registry (TBDR) for years 1996-2008. Controls were frequency matched from the same registry. Study authors state that neural tube cases were more likely to not be successfully geocoded which may introduce selection bias, however, the authors note that both cases and controls with addresses that could not be geocoded were similar. In spite of that, the inclusion criteria, methods of participant selection, and frequency match were reported.
	Metric 2:	Attrition	Medium	13.3% case mother addresses and 12.8% control mother addresses were unable to be geocoded, however this most likely only lowered the precision of the study and most likely does not vary based on exposure level.
	Metric 3:	Comparison Group	Medium	Controls were matched to cases and pulled from the same eligible population by year of delivery and public health service region. Other demographic factors, e.g., race was not matched in population selection. However, statistical analyses were adjusted for year of delivery, maternal age, race/ethnicity, education, and public health region of residence.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Used Emission Weighted Proximity Model to estimate exposure at a given address based on proximity to emission sources and the specific amount or type of pollutant emitted. There may be some exposure misclassification due to mothers moving away from geocoded addresses. Previous studies indicate ~67% of mothers do not move between conception and delivery.
	Metric 5:	Exposure Levels	Medium	Reports exposure as "exposure risk value" and groups the risk values into quartiles, with exposure risk values < 0 being the referent group
	Metric 6:	Temporality	Medium	The study authors estimated exposure based on residence during pregnancy and evaluated birth outcomes. Temporality is established. Previous studies indicate ~67% mothers don't move between trimester and delivery. For mothers who moved during the pregnancy, the temporality is unknown.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Outcomes determined by Texas Birth Defect Registry, checking for birth defect diagnosis. Birth certificates came from Center for Health Statistics at Texas Department of State Health Services
	Metric 8:	Reporting Bias	High	Outcome data measured and reported clearly, stratified by specific type of birth defect
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Brender, J.D., Shinde, M.U., Zhan, F.B., Gong, X., Langlois, P.H. (2014). Maternal residential proximity to chlorinated solvent emissions and birth defects in offspring: A case-control study. Environmental Health: A Global Access Science Source 13(1):96.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	birth defects (neural tube defects, limbs deficiencies, oral cleft defects, heart defects, spina bifida, anencephaly)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	2799700

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	High	Cases were frequency matched by year of delivery and public health service region. Final models were adjusted for year of delivery, public health region, maternal age (<20, 20-24, 25-29, 30-34, 35-39, >39 years), education (<12 years, 12 years, >12 years), and race/ethnicity (Whit non-Hispanic, Black non-Hispanic, Hispanic, other non-Hispanic).
	Metric 10:	Covariate Characterization	High	Used birth and death certificates for demographic information
	Metric 11:	Co-exposure Counfounding	Medium	other co-exposures were not described
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	study used logistic regression to measure association between exposure and birth defects
	Metric 13:	Statistical Power	Medium	Overall adequate number of cases and controls - some effects have low cell counts, but at least one health effect has sufficient statistical power.
	Metric 14:	Reproducibility of Analyses	Medium	Methods sufficiently detailed for reproducibility
	Metric 15:	Statistical Analysis	High	No logistic regression model assumption violations were identified.

Additional Comments: This study examined the association between proximity to several point sources of chlorinated solvents and birth defects. Exposure was assessed using EPA's Toxic Release Inventory, and birth defects were assessed using Texas birth registries. The geocoded address of mothers on day of delivery and the amount of solvent was plugged into the Emission Weighted Probability model to assign each mother an exposure risk value. Limitations include limited evidence of temporality. Additionally, elective terminations lacked a vital record, which meant only 69% of mothers with neural tube defects were geocoded. Mothers highly exposed to 1,2-dichloroethane were 1.85 times more likely to have the spina bifida birth defect than mothers who were not significantly exposed.

Overall Quality Determination High

* No biomarkers were identified for this evaluation.

Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Nested case-control design; cases selected from deaths in cohort study was described by Rinsky et al (1988; HERO 597923) (29,139 workers in Union Carbide facilities in West Virginia followed from 1940 to 1978). Vital status complete for 95% of cohort members.
	Metric 2:	Attrition	High	There was minimal exclusion of subjects/missing data, because vital status follow-up was complete for 96% of the 29,139 men in the cohort study.
	Metric 3:	Comparison Group	Medium	Controls were randomly selected in a 5:1 ratio to cases from the total employee cohort such that they were first employed in the same decade and survived to the same five-year survival period as cases. Controls survived at least to the beginning of the five-year interval in which cases died. Controls were independently selected for each of the individual disease subcategories. However, the demographic information between cases and controls were not compared in the paper.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was partially described: (1) Potential employee contact with a specific substance was determined by tracing each employee's work assignments and linking these assignment records to a separate computer file that contained a history of departmental usage for each substance; (2) Potential exposure to each chemical group was assumed on the basis of assignment o a production unit with a history of usage of any member of that chemical group. However, exposure level either based on work assignment in departments such as job exposure matrix or on the chemical levels were not presented.
	Metric 5:	Exposure Levels	Low	The range of exposure is limited. For example, exposure was presented by the duration of work in two categories: <5 years and 5+ years.
	Metric 6:	Temporality	Medium	Temporality is established, but it is unclear whether the exposures fall within the relevant exposure window. Authors used a lag time of 5 years; since controls were selected for 5 yr intervals, the effective lag time ranged from 5-9 years with an average of 7.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Case definition was based on death certificate diagnosis; but no method validation was conducted against this well-established methods.
	Metric 8:	Reporting Bias	Medium	All outcomes reported, but ORs for many analyses presented without CIs (some CIs reported in text).
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Low	There is indirect evidence that considerations were not made for potential confounders (ORs not adjusted, controls not age- or race-matched). Even though authors note that "Age-adjusted stratified analyses, which were also conducted, did not materially modify the odds ratio estimates". Also stratified examination of odds ratios were conducted to assess duration of exposure effects. However, other key confounders e.g., smoking status and race were not accounted for.
	Metric 10:	Covariate Characterization	Medium	The only potential confounder considered was age; this was presumably evaluated based on employment records (no discussion presented). Age-adjusted stratified analyses were conducted.
	Metric 11:	Co-exposure Counfounding	Low	Co-exposures were present and were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Nested case-control study design is appropriate for research question. Initial data analysis included crude odds ratio and then stratified examination of odds ratios was conducted to ass duration of exposure effect. Also, age-adjusted stratified analysis was conducted.
	Metric 13:	Statistical Power	Low	Statistical power calculations were not reported. Case numbers for each disease were low. The number of subjects was not sufficient to detect an effect of 1,2-dichloroethylene exposure.
	Metric 14:	Reproducibility of Analyses	Medium	Description was sufficient to be conceptually reproducible.
	Metric 15:	Statistical Analysis	Low	Statistical model to calculate odds ratio was not described.

Additional Comments: This nested case-control study within a cohort study is a good study design to answer the research question regarding the association between multiple chemical exposures and four cancer sites. Cases and controls are selected appropriate. However, there are several limitations in this study: (1) confounders were not all considered and adjusted for, except that age-adjusted odds ratios were conducted; (2) it is not described if co-exposures were adjusted for; (3) numbers of cancer cases for each cancer type were small, so the statistical power is limited; (4) statistical models for calculating odds ratios were not described.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Nested case-control design; cases selected from deaths in cohort study was described by Rinsky et al (1988; HERO 597923) (29,139 workers in Union Carbide facilities in West Virginia followed from 1940 to 1978). Vital status complete for 95% of cohort members.
	Metric 2:	Attrition	High	There was minimal exclusion of subjects/missing data, because vital status follow-up was complete for 96% of the 29,139 men in the cohort study.
	Metric 3:	Comparison Group	Medium	Controls were randomly selected in a 5:1 ratio to cases from the total employee cohort such that they were first employed in the same decade and survived to the same five-year survival period as cases. Controls survived at least to the beginning of the five-year interval in which cases died. Controls were independently selected for each of the individual disease subcategories. However, the demographic information between cases and controls were not compared in the paper.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was partially described: (1) Potential employee contact with a specific substance was determined by tracing each employee's work assignments and linking these assignment records to a separate computer file that contained a history of departmental usage for each substance; (2) Potential exposure to each chemical group was assumed on the basis of assignment o a production unit with a history of usage of any member of that chemical group. However, exposure level either based on work assignment in departments such as job exposure matrix or on the chemical levels were not presented.
	Metric 5:	Exposure Levels	Low	The range of exposure is limited. For example, exposure was presented by the duration of work in two categories: <5 years and 5+ years.
	Metric 6:	Temporality	Medium	Temporality is established, but it is unclear whether the exposures fall within the relevant exposure window. Authors used a lag time of 5 years; since controls were selected for 5 yr intervals, the effective lag time ranged from 5-9 years with an average of 7.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Case definition was based on death certificate diagnosis; but no method validation was conducted against this well-established methods.
	Metric 8:	Reporting Bias	Medium	All outcomes reported, but ORs for many analyses presented without CIs (some CIs reported in text).
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Low	There is indirect evidence that considerations were not made for potential confounders (ORs not adjusted, controls not age- or race-matched). Even though authors note that "Age-adjusted stratified analyses, which were also conducted, did not materially modify the odds ratio estimates". Also stratified examination of odds ratios were conducted to assess duration of exposure effects. However, other key confounders e.g., smoking status and race were not accounted for.
	Metric 10:	Covariate Characterization	Medium	The only potential confounder considered was age; this was presumably evaluated based on employment records (no discussion presented). Age-adjusted stratified analyses were conducted.
	Metric 11:	Co-exposure Counfounding	Low	Co-exposures were present and were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Nested case-control study design is appropriate for research question. Initial data analysis included crude odds ratio and then stratified examination of odds ratios was conducted to ass duration of exposure effect. Also, age-adjusted stratified analysis was conducted.
	Metric 13:	Statistical Power	Low	Statistical power calculations were not reported. Case numbers for each disease were low. The number of subjects was not sufficient to detect an effect of 1,2-dichloroethylene exposure.
	Metric 14:	Reproducibility of Analyses	Medium	Description was sufficient to be conceptually reproducible.
	Metric 15:	Statistical Analysis	Low	Statistical model to calculate odds ratio was not described.

Additional Comments: This nested case-control study within a cohort study is a good study design to answer the research question regarding the association between multiple chemical exposures and four cancer sites. Cases and controls are selected appropriate. However, there are several limitations in this study: (1) confounders were not all considered and adjusted for, except that age-adjusted odds ratios were conducted; (2) it is not described if co-exposures were adjusted for; (3) numbers of cancer cases for each cancer type were small, so the statistical power is limited; (4) statistical models for calculating odds ratios were not described.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Nested case-control design; cases selected from deaths in cohort study was described by Rinsky et al (1988; HERO 597923) (29,139 workers in Union Carbide facilities in West Virginia followed from 1940 to 1978). Vital status complete for 95% of cohort members.
	Metric 2:	Attrition	High	There was minimal exclusion of subjects/missing data, because vital status follow-up was complete for 96% of the 29,139 men in the cohort study.
	Metric 3:	Comparison Group	Medium	Controls were randomly selected in a 5:1 ratio to cases from the total employee cohort such that they were first employed in the same decade and survived to the same five-year survival period as cases. Controls survived at least to the beginning of the five-year interval in which cases died. Controls were independently selected for each of the individual disease subcategories. However, the demographic information between cases and controls were not compared in the paper.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was partially described: (1) Potential employee contact with a specific substance was determined by tracing each employee's work assignments and linking these assignment records to a separate computer file that contained a history of departmental usage for each substance; (2) Potential exposure to each chemical group was assumed on the basis of assignment o a production unit with a history of usage of any member of that chemical group. However, exposure level either based on work assignment in departments such as job exposure matrix or on the chemical levels were not presented.
	Metric 5:	Exposure Levels	Low	The range of exposure is limited. For example, exposure was presented by the duration of work in two categories: <5 years and 5+ years.
	Metric 6:	Temporality	Medium	Temporality is established, but it is unclear whether the exposures fall within the relevant exposure window. Authors used a lag time of 5 years; since controls were selected for 5 yr intervals, the effective lag time ranged from 5-9 years with an average of 7.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Case definition was based on death certificate diagnosis; but no method validation was conducted against this well-established methods.
	Metric 8:	Reporting Bias	Medium	All outcomes reported, but ORs for many analyses presented without CIs (some CIs reported in text).
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Low	There is indirect evidence that considerations were not made for potential confounders (ORs not adjusted, controls not age- or race-matched). Even though authors note that "Age-adjusted stratified analyses, which were also conducted, did not materially modify the odds ratio estimates". Also stratified examination of odds ratios were conducted to assess duration of exposure effects. However, other key confounders e.g., smoking status and race were not accounted for.
	Metric 10:	Covariate Characterization	Medium	The only potential confounder considered was age; this was presumably evaluated based on employment records (no discussion presented). Age-adjusted stratified analyses were conducted.
	Metric 11:	Co-exposure Counfounding	Low	Co-exposures were present and were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Nested case-control study design is appropriate for research question. Initial data analysis included crude odds ratio and then stratified examination of odds ratios was conducted to ass duration of exposure effect. Also, age-adjusted stratified analysis was conducted.
	Metric 13:	Statistical Power	Low	Statistical power calculations were not reported. Case numbers for each disease were low. The number of subjects was not sufficient to detect an effect of 1,2-dichloroethylene exposure.
	Metric 14:	Reproducibility of Analyses	Medium	Description was sufficient to be conceptually reproducible.
	Metric 15:	Statistical Analysis	Low	Statistical model to calculate odds ratio was not described.

Additional Comments: This nested case-control study within a cohort study is a good study design to answer the research question regarding the association between multiple chemical exposures and four cancer sites. Cases and controls are selected appropriate. However, there are several limitations in this study: (1) confounders were not all considered and adjusted for, except that age-adjusted odds ratios were conducted; (2) it is not described if co-exposures were adjusted for; (3) numbers of cancer cases for each cancer type were small, so the statistical power is limited; (4) statistical models for calculating odds ratios were not described.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Nested case-control design; cases selected from deaths in cohort study was described by Rinsky et al (1988; HERO 597923) (29,139 workers in Union Carbide facilities in West Virginia followed from 1940 to 1978). Vital status complete for 95% of cohort members.
	Metric 2:	Attrition	High	There was minimal exclusion of subjects/missing data, because vital status follow-up was complete for 96% of the 29,139 men in the cohort study.
	Metric 3:	Comparison Group	Medium	Controls were randomly selected in a 5:1 ratio to cases from the total employee cohort such that they were first employed in the same decade and survived to the same five-year survival period as cases. Controls survived at least to the beginning of the five-year interval in which cases died. Controls were independently selected for each of the individual disease subcategories. However, the demographic information between cases and controls were not compared in the paper.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was partially described: (1) Potential employee contact with a specific substance was determined by tracing each employee's work assignments and linking these assignment records to a separate computer file that contained a history of departmental usage for each substance; (2) Potential exposure to each chemical group was assumed on the basis of assignment o a production unit with a history of usage of any member of that chemical group. However, exposure level either based on work assignment in departments such as job exposure matrix or on the chemical levels were not presented.
	Metric 5:	Exposure Levels	Low	The range of exposure is limited. For example, exposure was presented by the duration of work in two categories: <5 years and 5+ years.
	Metric 6:	Temporality	Medium	Temporality is established, but it is unclear whether the exposures fall within the relevant exposure window. Authors used a lag time of 5 years; since controls were selected for 5 yr intervals, the effective lag time ranged from 5-9 years with an average of 7.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Case definition was based on death certificate diagnosis; but no method validation was conducted against this well-established methods.
	Metric 8:	Reporting Bias	Medium	All outcomes reported, but ORs for many analyses presented without CIs (some CIs reported in text).
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Low	There is indirect evidence that considerations were not made for potential confounders (ORs not adjusted, controls not age- or race-matched). Even though authors note that "Age-adjusted stratified analyses, which were also conducted, did not materially modify the odds ratio estimates". Also stratified examination of odds ratios were conducted to assess duration of exposure effects. However, other key confounders e.g., smoking status and race were not accounted for.
	Metric 10:	Covariate Characterization	Medium	The only potential confounder considered was age; this was presumably evaluated based on employment records (no discussion presented). Age-adjusted stratified analyses were conducted.
	Metric 11:	Co-exposure Counfounding	Low	Co-exposures were present and were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Nested case-control study design is appropriate for research question. Initial data analysis included crude odds ratio and then stratified examination of odds ratios was conducted to ass duration of exposure effect. Also, age-adjusted stratified analysis was conducted.
	Metric 13:	Statistical Power	Low	Statistical power calculations were not reported. Case numbers for each disease were low. The number of subjects was not sufficient to detect an effect of 1,2-dichloroethylene exposure.
	Metric 14:	Reproducibility of Analyses	Medium	Description was sufficient to be conceptually reproducible.
	Metric 15:	Statistical Analysis	Low	Statistical model to calculate odds ratio was not described.

Additional Comments: This nested case-control study within a cohort study is a good study design to answer the research question regarding the association between multiple chemical exposures and four cancer sites. Cases and controls are selected appropriate. However, there are several limitations in this study: (1) confounders were not all considered and adjusted for, except that age-adjusted odds ratios were conducted; (2) it is not described if co-exposures were adjusted for; (3) numbers of cancer cases for each cancer type were small, so the statistical power is limited; (4) statistical models for calculating odds ratios were not described.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Cheng, T.J., Huang, M.L., You, N.C., Du, C.L., Chau, T.T. (1999). Abnormal liver function in workers exposed to low levels of ethylene dichloride and vinyl chloride monomer. Journal of Occupational and Environmental Medicine 41(12):1128-1133.
Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	AST, ALT, GGT, Hepatitis B virus surface antigen (HBsAg), and anti-hepatitis C virus antibody (anti-HCV).
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	200266

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	A total of 251 male workers were included from 4 vinyl chloride monomer manufacturing plants. Other details on recruitment strategy, eligibility criteria, year of enrollment, and participation rates were not provided.
	Metric 2:	Attrition	Low	There was no indication of attrition and details on the number of eligible participants throughout the study was limited. Attrition could not be adequately assessed due to a lack of information regarding recruitment and selection.
	Metric 3:	Comparison Group	Medium	The low-EDC-low-VCM group (187 participants) was used as the comparison group, and there is indirect evidence groups are similar. Limited details were provided for setting, inclusion and exclusion criteria, and methods of participant selection.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	NIOSH recommended methods 1003 and 1007 were used for personal and area sampling, respectively. Air samples were collected, stored at 4 deg. C, and analyzed within 2 weeks of the sampling event. However, historical job changes, changes in exposure levels over time, and timing (year or days during work week) or duration of area or personal sampling were not reported.
	Metric 5:	Exposure Levels	Medium	EDC and VCM levels were reported for the different categories of jobs, which were classified into low-EDC-low-VCM, mod-EDC-low-VCM, and low-EDC-mod-VCM groups.
	Metric 6:	Temporality	High	The age of participants (mean age 33.7-40.1 years) and employment duration (mean 7.5-14.3 years) were reported, and the temporality between the exposure and outcome appears to be appropriate.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	AST, ALT, and GGT "were analyzed with a Hitachi 7050 autoanalyzer". A basis for the cutoff values used in Table 4 to determine "abnormal" AST, ALT, and GGT levels was not provided.
	Metric 8:	Reporting Bias	High	Odds ratios for abnormal liver function were provided with 95% confidence intervals, the number per exposure level, and significance when applicable.
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Cheng, T.J., Huang, M.L., You, N.C., Du, C.L., Chau, T.T. (1999). Abnormal liver function in workers exposed to low levels of ethylene dichloride and vinyl chloride monomer. Journal of Occupational and Environmental Medicine 41(12):1128-1133.
Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	AST, ALT, GGT, Hepatitis B virus surface antigen (HBsAg), and anti-hepatitis C virus antibody (anti-HCV).
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	200266

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Medium	The study reports information on potential confounders (age, hepatitis, BMI, alcohol use, and employment duration), and controls for hepatitis, BMI and alcohol consumption in the multiple logistic regression analyses. There is indirect evidence that appropriate adjustments were made.
	Metric 10:	Covariate Characterization	Medium	An interviewer administered the questionnaires to collect information about potential confounders and occupational history.
	Metric 11:	Co-exposure Counfounding	Low	Exposure to ethylene dichloride was evaluated in a vinyl chloride monomer (VCM) manufacturing facility, and VCM was also subsequently analyzed using personal and area sampling. Results for VCM exposure concentrations were provided. VCM is also suspected to cause liver damage.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design (cohort) was appropriate to assess the outcome of interest (”markers of liver damage”). Chi-squared (X2) test and multiple logistic regression were used for statistical analyses.
	Metric 13:	Statistical Power	Medium	The number of participants was adequate to detect an effect in the exposed populations, although power calculations were not provided. There were >20 participants in each group.
	Metric 14:	Reproducibility of Analyses	Low	A description of the logistic regression analysis was provided, however, study authors do not provide information on categorization of abnormal liver function.
	Metric 15:	Statistical Analysis	High	There were no identifiable logistic regression model assumption violations.
Domain 6: Other (if applicable) Considerations for Biomarker Selection and Measurement (Lakind et al. 2014)				
	Metric 16:	Use of Biomarker of Exposure	N/A	Biomarker of exposures were not assessed.
	Metric 17:	Effect Biomarker	High	This study uses aspartate aminotransferase, alanine aminotransferase, and y-glutamyltransferase as biomarkers of effect. While these no works cited to explain their connection to liver function, all three are well-known marker of liver function. Similarly, Hepatitis B virus surface antigen and antihepatitis C virus anitbody are also well-known measures of liver function and health.
	Metric 18:	Method Sensitivity	Low	No limit of detection information is provided for any of the effect biomarkers.
	Metric 19:	Biomarker Stability	Medium	While the study does not provide a lot of information regarding biomarker storage or stability, the authors do mention that venous blood used to detect biomarkers was stored at 4 degrees C.
	Metric 20:	Sample Contamination	Medium	No specific information regarding potential sample contamination was provided.
	Metric 21:	Method Requirements	Medium	Aspartate aminotransferase, alanine aminotransferase, and y-glutamyltransferase were analyzed using a Hitachi 7050 autoanalyzer. Hepatitis B virus surface antibody and antihepatitis C virus antibody were assessed with radioimmunoassay and enzyme-linked immunosorbent assay.

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Study Citation:	Cheng, T.J., Huang, M.L., You, N.C., Du, C.L., Chau, T.T. (1999). Abnormal liver function in workers exposed to low levels of ethylene dichloride and vinyl chloride monomer. Journal of Occupational and Environmental Medicine 41(12):1128-1133.
Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	AST, ALT, GGT, Hepatitis B virus surface antigen (HBsAg), and anti-hepatitis C virus antibody (anti-HCV).
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	200266

Domain	Metric	Rating	Comments
	Metric 22: Matrix Adjustment	N/A	No information on matrix adjustment was provided/available.

Additional Comments: A group of 251 male workers from 4 vinyl chloride monomer (VCM) manufacturing plants were included in this assessment to examine if occupational exposure to VCM and ethylene dichloride (EDC) "resulted in increased risk of liver damage" by examining AST, ALT, and GGT levels in the blood. Increased ORs for abnormal AST (>37 IU/L) and ALT (>41 IU/L) in the mod-EDC-low-VCM group (0.17-333.7 ppm EDC, 0.18-0.34 ppm VCM), compared with the low-EDC-low-VCM group, was reported. Exposure levels were measured using area and personal sampling, but the timing and duration of the sampling events were not reported.

Overall Quality Determination Medium

Study Citation:	Dosemeci, M., Cocco, P., Chow, W.H. (1999). Gender differences in risk of renal cell carcinoma and occupational exposures to chlorinated aliphatic hydrocarbons. American Journal of Industrial Medicine 36(1):54-59.
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	renal cell carcinoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	4697224

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	The details of the study design were reported elsewhere (Chow et al. 1994, HERO ID 701514). Brief details about the setting, date, number of eligible participants, and control matching were reported. Reasons for exclusions/non-participation were described with details by Chow et al. (1994).
	Metric 2:	Attrition	High	For the details of the study design and attrition of study subjects, the study authors referred to another publication by Chow et al., 1994. Chow et al. (1994) mentioned that at the end of the personal interview, the respondents were given a self-administered food-frequency questionnaire. Of the subjects interviewed for the study, 632 patients (79% of 796 eligible patients) and 653 control subjects (79% of 707 eligible control subjects) returned the diet questionnaire. A number of subjects, whose responses were considered unreliable, were excluded from the analysis, including 48 patients and three control subjects who had seven or more skipped food items or had questionable data and 50 patients whose next-of-kin respondent was not a spouse. Also excluded were two patients with unknown smoking status, since smoking is a risk factor.
	Metric 3:	Comparison Group	Medium	The cases were pulled from the Minnesota Cancer Surveillance System. Controls were selected from the general population of Minnesota; controls age 20-64 years were selected through random digital dialing and controls age 65-85 years were collected from files through the Health Care Financing Administration. Controls were age- and gender-stratified and were of the same race. Characteristics of cases and controls were not provided in the text or a table.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	High	Occupational histories including the most recent and usual occupation and industry, job activities, started-year and ended-year, and part-time/full-time status were collected. Occupations and industries were coded according to the standard occupational classification (SOC) and standard industrial classification (SIC) schemes. The National Cancer Institute developed job exposure matrices (JEM) for nine individual chlorinated aliphatic hydrocarbons (CAHCs), all CAHCs-combined, and all organic solvents-combined. These JEMs were merged with assigned SOC and SIC to determine the exposure status to these chemicals for each study subject. Application of the JEM was described elsewhere (Dosemeci et al. 1994, HERO ID 632334; Gomez et al. 1994, HERO ID 702154).
	Metric 5:	Exposure Levels	Medium	Details of the application of the JEM were described elsewhere (Dosemeci et al. 1994, HERO ID 632334; Gomez et al. 1994, HERO ID 702154). Dosemeci et al. (1994) described more details about that this study assigned three levels of probability (low, medium, high) to industries and occupations for chemical exposure levels.

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Study Citation:	Dosemeci, M., Cocco, P., Chow, W.H. (1999). Gender differences in risk of renal cell carcinoma and occupational exposures to chlorinated aliphatic hydrocarbons. American Journal of Industrial Medicine 36(1):54-59.
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	renal cell carcinoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	4697224

Domain	Metric		Rating	Comments
	Metric 6:	Temporality	Medium	Occupational questionnaires identified prior exposures based on reported recent and usual occupations as well as duration of employment. Outcome status was determined from registry data. The authors note that some occupational history was incomplete which may result in some uncertainty in regard to temporality.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Cases were identified as newly diagnosed and histologically confirmed renal cell carcinoma through the Minnesota Cancer Surveillance System and information about each participant was collected using a questionnaire. Validation was not specified.
	Metric 8:	Reporting Bias	Medium	A description of measured outcomes is reported and ORs were stratified by sex. Effect estimates are reported with a confidence interval. One table showed the total numbers of men and women respectively for each chemical, but numbers of cases/controls were not reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Appropriate adjustments were made in the final analysis, including age, gender, smoking, hypertension and the use of diuretics and/or anti-hypertension drugs, and BMI. Results were stratified by sex.
	Metric 10:	Covariate Characterization	Medium	Information about participants was collected using a questionnaire, and it includes potential confounders, e.g., smoking habits. Validation was not specified.
	Metric 11:	Co-exposure Counfounding	Medium	Co-exposures were identified through the job exposure matrices. Chemicals were evaluated individually and as a group.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen (case-control) was appropriate for the research question (renal cell carcinoma risk from occupational organic solvent exposure). Logistic regression models were used to estimate the relative risk and 95% CI.
	Metric 13:	Statistical Power	Low	Statistical power calculations were not provided. No significant effects were observed with 1,2-dichloroethane. The number of participated women to calculate odds ratio was inadequate to detect an effect in the participants for other chemicals or the combined risk, because it was very low.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis was brief, but is sufficient to understand precisely what has been done and to be conceptually reproducible with access to the analytic data.
	Metric 15:	Statistical Analysis	High	Model assumptions for logistic regression were met. The odds ratios were adjusted for age, smoking, hypertension status and/or use of diuretic and/or anti-hypertension drugs, and body mass index for men and women separately.

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Study Citation:	Dosemeci, M., Cocco, P., Chow, W.H. (1999). Gender differences in risk of renal cell carcinoma and occupational exposures to chlorinated aliphatic hydrocarbons. American Journal of Industrial Medicine 36(1):54-59.
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	renal cell carcinoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	4697224

Domain	Metric	Rating	Comments
Additional Comments:	A group of 438 cases (273 men and 165 women) were selected from the Minnesota Cancer Surveillance System that had been newly diagnosed with renal cell carcinoma. Controls included 687 participants (462 men and 225 women) age- and gender- stratified that were selected from either the general population of Minnesota (age 20-64 years) or from the Health Care Financing Administration files (age 65-85). No significant increase in the risk of renal cell carcinoma was observed with exposure to 1,2-dichloroethane among men or women separately, or for all participants exposed.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Dosemeci, M., Cocco, P., Chow, W.H. (1999). Gender differences in risk of renal cell carcinoma and occupational exposures to chlorinated aliphatic hydrocarbons. American Journal of Industrial Medicine 36(1):54-59.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	renal cell carcinoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	4697224

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	The details of the study design were reported elsewhere (Chow et al. 1994, HERO ID 701514). Brief details about the setting, date, number of eligible participants, and control matching were reported. Reasons for exclusions/non-participation were described with details by Chow et al. (1994).
	Metric 2:	Attrition	Medium	For the details of the study design and attrition of study subjects, the study authors referred to another publication by Chow et al., 1994. Chow et al. (1994) mentioned that at the end of the personal interview, the respondents were given a self-administered food-frequency questionnaire. Of the subjects interviewed for the study, 632 patients (79% of 796 eligible patients) and 653 control subjects (79% of 707 eligible control subjects) returned the diet questionnaire. A number of subjects, whose responses were considered unreliable, were excluded from the analysis, including 48 patients and three control subjects who had seven or more skipped food items or had questionable data and 50 patients whose next-of-kin respondent was not a spouse. Also excluded were two patients with unknown smoking status, since smoking is a risk factor.
	Metric 3:	Comparison Group	Medium	The cases were pulled from the Minnesota Cancer Surveillance System. Controls were selected from the general population of Minnesota; controls age 20-64 years were selected through random digital dialing and controls age 65-85 years were collected from files through the Health Care Financing Administration. Controls were age- and gender-stratified and were of the same race. Characteristics of cases and controls were not provided in the text or a table.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	High	Occupational histories including the most recent and usual occupation and industry, job activities, started-year and ended-year, and part-time/full-time status were collected. Occupations and industries were coded according to the standard occupational classification (SOC) and standard industrial classification (SIC) schemes. The National Cancer Institute developed job exposure matrices (JEM) for nine individual chlorinated aliphatic hydrocarbons (CAHCs), all CAHCs-combined, and all organic solvents-combined. These JEMs were merged with assigned SOC and SIC to determine the exposure status to these chemicals for each study subject. Application of the JEM was described elsewhere (Dosemeci et al. 1994, HERO ID 632334; Gomez et al. 1994, HERO ID 702154).
	Metric 5:	Exposure Levels	Medium	Details of the application of the JEM were described elsewhere (Dosemeci et al. 1994, HERO ID 632334; Gomez et al. 1994, HERO ID 702154). Dosemeci et al. (1994) described more details about that this study assigned three levels of probability (low, medium, high) to industries and occupations for chemical exposure levels.

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Study Citation:	Dosemeci, M., Cocco, P., Chow, W.H. (1999). Gender differences in risk of renal cell carcinoma and occupational exposures to chlorinated aliphatic hydrocarbons. American Journal of Industrial Medicine 36(1):54-59.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	renal cell carcinoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	4697224

Domain	Metric		Rating	Comments
	Metric 6:	Temporality	Medium	Occupational questionnaires identified prior exposures based on reported recent and usual occupations as well as duration of employment. Outcome status was determined from registry data. The authors note that some occupational history was incomplete which may result in some uncertainty in regard to temporality.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Cases were identified as newly diagnosed and histologically confirmed renal cell carcinoma through the Minnesota Cancer Surveillance System and information about each participant was collected using a questionnaire. Validation was not specified.
	Metric 8:	Reporting Bias	Medium	A description of measured outcomes is reported and ORs were stratified by sex. Effect estimates are reported with a confidence interval. One table showed the total numbers of men and women respectively for each chemical, but numbers of cases/controls were not reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Appropriate adjustments were made in the final analysis, including age, gender, smoking, hypertension and the use of diuretics and/or anti-hypertension drugs, and BMI. Results were stratified by sex.
	Metric 10:	Covariate Characterization	Medium	Information about participants was collected using a questionnaire, and it includes potential confounders, e.g., smoking habits. Validation was not specified.
	Metric 11:	Co-exposure Counfounding	Medium	Co-exposures were identified through the job exposure matrices. Chemicals were evaluated individually and as a group.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen (case-control) was appropriate for the research question (renal cell carcinoma risk from occupational organic solvent exposure). Logistic regression models were used to estimate the relative risk and 95% CI.
	Metric 13:	Statistical Power	Low	Statistical power calculations were not provided. No significant effects were observed with 1,2-dichloroethane. The number of participated women to calculate odds ratio was inadequate to detect an effect in the participants for other chemicals or the combined risk, because it was very low.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis was brief, but is sufficient to understand precisely what has been done and to be conceptually reproducible with access to the analytic data.
	Metric 15:	Statistical Analysis	High	Model assumptions for logistic regression were met. The odds ratios were adjusted for age, smoking, hypertension status and/or use of diuretic and/or anti-hypertension drugs, and body mass index for men and women separately.

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Study Citation:	Dosemeci, M., Cocco, P., Chow, W.H. (1999). Gender differences in risk of renal cell carcinoma and occupational exposures to chlorinated aliphatic hydrocarbons. American Journal of Industrial Medicine 36(1):54-59.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	renal cell carcinoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	4697224

Domain	Metric	Rating	Comments
Additional Comments:	A group of 438 cases (273 men and 165 women) were selected from the Minnesota Cancer Surveillance System that had been newly diagnosed with renal cell carcinoma. Controls included 687 participants (462 men and 225 women) age- and gender- stratified that were selected from either the general population of Minnesota (age 20-64 years) or from the Health Care Financing Administration files (age 65-85). No significant increase in the risk of renal cell carcinoma was observed with exposure to 1,2-dichloroethane among men or women separately, or for all participants exposed.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Garcia, E., Hurley, S., Nelson, D.O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health: A Global Access Science Source 14(1):14.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	breast cancer in females
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	3014082

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	A total of 112,378 women were included in this study out of 133,479 eligible female participants from the California Teacher Study cohort. A full description of the cohort is provided in Bernstein et al. 2002 (HERO ID 808446). Reasons for exclusion were provided. The reported information indicates that participant selection in or out of the study and participation was not likely to be biased.
	Metric 2:	Attrition	High	112,378/133,479 participants were included in the study. Exclusions were for the purpose of the study and analysis. Exclusion criteria were documented. Included participants had completed questionnaires. The California Cancer Registry is estimated to be 99% complete.
	Metric 3:	Comparison Group	Medium	There is only indirect evidence that groups are similar. Participants were recruited from the same eligible population with the same method of ascertainment. Comparisons were provided for participants with and without breast cancer. Characteristics between these two groups were generally similar. 5 Quintiles of exposure were used, and Q2-5 were compared with Q1.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	High	The Assessment System for Population Exposure Nationwide and the Human Exposure Model are used as part of the National-Scale Air Toxics Assessment produced by the EPA and was used to estimate ambient HAP concentrations for geographic locations. Methods are described online through the US EPA Assessment Methods.
	Metric 5:	Exposure Levels	Medium	The distribution of the NATA annual ambient concentration for each compound was plotted in Figure 1 using a box plot, and 5 Quintiles were used in the analyses.
	Metric 6:	Temporality	Medium	The follow-up period was from 1995-2011, and the NATA estimates were made in 2002 because it was approximately half way between the start and end of the follow-up period. However, it is unclear whether exposures fall within relevant exposure windows for the outcome of interest.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Annual linkage between the CTS cohort and the California Cancer Registry (CCR) was used to identify cases of invasive breast cancer. The CCR is estimated to be 99% complete. The case of invasive breast cancer was defined by ICD codes.

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Study Citation:	Garcia, E., Hurley, S., Nelson, D.O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health: A Global Access Science Source 14(1):14.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	breast cancer in females
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	3014082

Domain	Metric		Rating	Comments
	Metric 8:	Reporting Bias	Medium	A description of measured outcome is reported for adjustments by age and race, and effect estimates are reported with a 95% confidence interval. The measured outcomes using multiple comparisons were generally described in the text, but non-significant results were excluded from Table 3.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	The models were stratified by age and race. Additionally, adjustments were made for multiple comparisons among subsets of the participants (significant results reported in Table 3). Socioeconomic status (SES) of each participant was not evaluated, however, cohort SES characteristics were thought to be similar by study authors.
	Metric 10:	Covariate Characterization	Medium	Information about baseline characteristics for each participant was collected through a questionnaire. It is unknown if the questionnaire was validated.
	Metric 11:	Co-exposure Counfounding	Medium	A total of 37 compounds were identified as mammary gland carcinogens, but 13 were not included in this analysis. Thirteen compounds were excluded from the analysis due to insufficient variability (nine because they had the same value for all census tracts in the state of California; and four because they had less than 25% non-zero values). Ethylene dichloride (1,2-dichloroethane) was among the 24 compounds evaluated in this assessment, and evaluations for breast cancer were conducted for each of these 24 individual compounds.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen (prospective cohort) was appropriate for the research question (incidence of breast cancer). Cox proportional hazard models and SAS 9.3 were used in this assessment. Data analysis was described.
	Metric 13:	Statistical Power	Medium	Statistical power calculations were not provided. No significant effects were observed with ethylene dichloride (1,2-dichloroethane), however, this study utilized a large cohort, approximately 112,000 individuals. Distributions of chemicals of interest suggest there were sufficient numbers of participants in exposure subgroups.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to understand precisely what has been done and to be conceptually reproducible with access to the analytic data.
	Metric 15:	Statistical Analysis	High	The statistical models that were used were identified and described. ”No apparent violation of the underlying assumption of proportional hazards was detected”.

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Study Citation:	Garcia, E., Hurley, S., Nelson, D.O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health: A Global Access Science Source 14(1):14.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	breast cancer in females
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	3014082

Domain	Metric	Rating	Comments
Additional Comments:	A group of 112,378 female participants from the California Teacher Study cohort were assessed for their estimated exposure to ambient air pollutants, including ethylene dichloride (1,2-dichloroethane), and the incidence of invasive breast cancer. Air contaminant concentrations were estimated using the US EPA NATA and the ASPEN and HEM models. The approximate median concentration of 1,2-dichloroethane is between 1E-4 and 1E-2 (estimated from Figure 1). Exposures were categorized into 5 Quintiles, and compared against Quintile 1. No significant increase in the estimated hazard rate ratio for invasive breast cancer was observed with Quintile 2-5 exposure estimates for 1,2-dichloroethane, adjusted for age and race, when compared against Quintile 1, or when further adjusted using multiple comparisons.		

Overall Quality Determination High

* No biomarkers were identified for this evaluation.

Study Citation:	Garcia, E., Hurley, S., Nelson, D.O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health: A Global Access Science Source 14(1):14.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	breast cancer in females
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	3014082

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	A total of 112,378 women were included in this study out of 133,479 eligible female participants from the California Teacher Study cohort. A full description of the cohort is provided in Bernstein et al. 2002 (HERO ID 808446). Reasons for exclusion were provided. The reported information indicates that participant selection in or out of the study and participation was not likely to be biased.
	Metric 2:	Attrition	High	112,378/133,479 participants were included in the study. Exclusions were for the purpose of the study and analysis. Exclusion criteria were documented. Included participants had completed questionnaires. The California Cancer Registry is estimated to be 99% complete.
	Metric 3:	Comparison Group	Medium	There is only indirect evidence that groups are similar. Participants were recruited from the same eligible population with the same method of ascertainment. Comparisons were provided for participants with and without breast cancer. Characteristics between these two groups were generally similar. 5 Quintiles of exposure were used, and Q2-5 were compared with Q1.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	High	The Assessment System for Population Exposure Nationwide and the Human Exposure Model are used as part of the National-Scale Air Toxics Assessment produced by the EPA and was used to estimate ambient HAP concentrations for geographic locations. Methods are described online through the US EPA Assessment Methods.
	Metric 5:	Exposure Levels	Medium	The distribution of the NATA annual ambient concentration for each compound was plotted in Figure 1 using a box plot, and 5 Quintiles were used in the analyses.
	Metric 6:	Temporality	Medium	The follow-up period was from 1995-2011, and the NATA estimates were made in 2002 because it was approximately half way between the start and end of the follow-up period. However, it is unclear whether exposures fall within relevant exposure windows for the outcome of interest.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Annual linkage between the CTS cohort and the California Cancer Registry (CCR) was used to identify cases of invasive breast cancer. The CCR is estimated to be 99% complete. The case of invasive breast cancer was defined by ICD codes.
	Metric 8:	Reporting Bias	Medium	A description of measured outcome is reported for adjustments by age and race, and effect estimates are reported with a 95% confidence interval. The measured outcomes using multiple comparisons were generally described in the text, but non-significant results were excluded from Table 3.

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Study Citation:	Garcia, E., Hurley, S., Nelson, D.O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health: A Global Access Science Source 14(1):14.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	breast cancer in females
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	3014082

Domain	Metric		Rating	Comments
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	The models were stratified by age and race. Additionally, adjustments were made for multiple comparisons among subsets of the participants (significant results reported in Table 3). Socioeconomic status (SES) of each participant was not evaluated, however, cohort SES characteristics were thought to be similar by study authors.
	Metric 10:	Covariate Characterization	Medium	Information about baseline characteristics for each participant was collected through a questionnaire. It is unknown if the questionnaire was validated.
	Metric 11:	Co-exposure Counfounding	Medium	A total of 37 compounds were identified as mammary gland carcinogens, but 13 were not included in this analysis. Thirteen compounds were excluded from the analysis due to insufficient variability (nine because they had the same value for all census tracts in the state of California; and four because they had less than 25% non-zero values). Ethylene dichloride (1,2-dichloroethane) was among the 24 compounds evaluated in this assessment, and evaluations for breast cancer were conducted for each of these 24 individual compounds.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen (prospective cohort) was appropriate for the research question (incidence of breast cancer). Cox proportional hazard models and SAS 9.3 were used in this assessment. Data analysis was described.
	Metric 13:	Statistical Power	Medium	Statistical power calculations were not provided. No significant effects were observed with ethylene dichloride (1,2-dichloroethane), however, this study utilized a large cohort, approximately 112,000 individuals. Distributions of chemicals of interest suggest there were sufficient numbers of participants in exposure subgroups.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to understand precisely what has been done and to be conceptually reproducible with access to the analytic data.
	Metric 15:	Statistical Analysis	High	The statistical models that were used were identified and described. "No apparent violation of the underlying assumption of proportional hazards was detected".

Additional Comments: A group of 112,378 female participants from the California Teacher Study cohort were assessed for their estimated exposure to ambient air pollutants, including ethylene dichloride (1,2-dichloroethane), and the incidence of invasive breast cancer. Air contaminant concentrations were estimated using the US EPA NATA and the ASPEN and HEM models. The approximate median concentration of 1,2-dichloroethane is between 1E-4 and 1E-2 (estimated from Figure 1). Exposures were categorized into 5 Quintiles, and compared against Quintile 1. No significant increase in the estimated hazard rate ratio for invasive breast cancer was observed with Quintile 2-5 exposure estimates for 1,2-dichloroethane, adjusted for age and race, when compared against Quintile 1, or when further adjusted using multiple comparisons.

Overall Quality Determination High

* No biomarkers were identified for this evaluation.

Study Citation:	Guo, P., Yokoyama, K., Piao, F., Sakai, K., Khalequzzaman, M., Kamijima, M., Nakajima, T., Kitamura, F. (2013). Sick building syndrome by indoor air pollution in Dalian, China. International Journal of Environmental Research and Public Health 10(4):1489-1504.
Health Outcome(s):	sick building syndrome
Reported Health Effect(s):	The statistical analysis considers all subjective self-reported symptoms together (not segregated by health outcome) as a group health outcome –sick building syndrome. The study compared two conditions for each studied chemical: combined self-reported symptoms to no symptoms. Therefore, only one form 3 was completed.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1938385

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Residents of a housing estate of 3000 homes were invited to a community meeting to explain the purpose of the study and volunteers were invited to participate. It was not reported whether these volunteers were different from the overall eligible population.
	Metric 2:	Attrition	Low	Of the 70 families that agreed to participate, questionnaires were provided by 59. Reasons of uncompleted questionnaires were not fully provided, and there was no comparison between those who participated and those who did not.
	Metric 3:	Comparison Group	Low	The overall description of the analysis sample indicated a wide range of ages and lengths of stay at the current residence. Thus it is hard to know that subjects in all exposure groups were similar. In addition, the methods of selecting participants in all exposure groups were not fully reported. The numbers of male and female smokers were reported, respectively, but the smoking status and age were not controlled in the statistical analysis.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure concentrations for each home were obtained by diffusion sampling over 24 hrs in the bedroom, kitchen, and outdoors; temperature, the vertical height of samplers, and ventilation (hours windows left open) were reported. Samples were analyzed by GC/MS. The number of samples per home is unclear. The frequency of measurements for each house was not reported.
	Metric 5:	Exposure Levels	Low	The frequency of detection was not reported, so it is difficult to ascertain the actual exposure range. In addition, the reported exposure levels were median, geometric mean, and 95% CI, so they are inadequate to develop an exposure-response estimate.
	Metric 6:	Temporality	Uninformative	For 1,2-dichloroethane, the study evaluated self-reported symptoms in the past (”since they moved into their flats”) and their association with sampling conducted during the study; thus, exposure was measured after the outcome.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Low	Participants provided self-reported symptoms using a questionnaire. Study authors cited a previous study, Kamijima et al., 2005 (in Japanese, HERO ID 1598645) for further details on the questionnaire. It was not clear whether the questionnaire was validated.

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Study Citation:	Guo, P., Yokoyama, K., Piao, F., Sakai, K., Khalequzzaman, M., Kamijima, M., Nakajima, T., Kitamura, F. (2013). Sick building syndrome by indoor air pollution in Dalian, China. International Journal of Environmental Research and Public Health 10(4):1489-1504.
Health Outcome(s):	sick building syndrome
Reported Health Effect(s):	The statistical analysis considers all subjective self-reported symptoms together (not segregated by health outcome) as a group health outcome –sick building syndrome. The study compared two conditions for each studied chemical: combined self-reported symptoms to no symptoms. Therefore, only one form 3 was completed.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1938385

Domain	Metric		Rating	Comments
	Metric 8:	Reporting Bias	Low	The study only mentioned subjective symptoms in the abstract or methods. The abstract and method sections did not report the specific symptoms included in the questionnaire or whether the questionnaire was open-ended for symptoms. The questionnaire was cited to Kamijima et al. 2005 (in Japanese).
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	Comparisons were made separately by sex. The distribution of age and time spent living in residence differed greatly between those reporting symptoms and those not reporting symptoms. Smoking was indicated but not controlled for in the analysis. In short, the statistical analysis did not consider these three potential confounders, age, time spent living in residence, and smoking.
	Metric 10:	Covariate Characterization	Low	Covariates were presumably evaluated via a questionnaire that was cited to Kamijima et al. 2005 (in Japanese).
	Metric 11:	Co-exposure Counfounding	Low	The analysis did not account for other exposures. A number of other VOCs, HCHO, and NO2 were measured in the homes. The concentrations of several other VOCs and HCHO were much higher (5-30x) than 1,2-dichloroethane and may also be associated with these symptoms.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Low	The study design is best characterized as cross-sectional. Only one analysis to compare exposure concentrations between those with and without symptoms was adjusted for a confounder, sex, via stratification. Other potential confounders were not adjusted for. Study authors combine responses for symptoms reported before and during the sampling period in one statistical analysis, which may not reflect the relationship between symptoms and contaminants' exposure at each period.
	Metric 13:	Statistical Power	Medium	Statistical power was not reported. The number of participants was sufficient to detect a difference in median concentration between those with and without symptoms.
	Metric 14:	Reproducibility of Analyses	Medium	Study presents sufficient description of analysis (statistical methods) to be conceptually reproducible with access to the raw data.
	Metric 15:	Statistical Analysis	Low	Study uses a Wilcoxon's rank sum test to compare exposure concentrations in persons with and without symptoms; test for equal variance is not reported.

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Study Citation:	Guo, P., Yokoyama, K., Piao, F., Sakai, K., Khalequzzaman, M., Kamijima, M., Nakajima, T., Kitamura, F. (2013). Sick building syndrome by indoor air pollution in Dalian, China. International Journal of Environmental Research and Public Health 10(4):1489-1504.
Health Outcome(s):	sick building syndrome
Reported Health Effect(s):	The statistical analysis considers all subjective self-reported symptoms together (not segregated by health outcome) as a group health outcome –sick building syndrome. The study compared two conditions for each studied chemical: combined self-reported symptoms to no symptoms. Therefore, only one form 3 was completed.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1938385

Domain	Metric	Rating	Comments
Additional Comments:	Concentrations of VOCs (including 1,2-dichloroethane), HCHO, and NO2 were measured in the 59 homes of families that agreed to participate after being informed of the nature of the study. Participants completed questionnaires asking about symptoms since they moved into the homes and the concentrations of selected compounds were compared among men and women reporting any symptoms vs no symptoms. Concentrations of 1,2-dichloroethane in homes of people with symptoms were higher than in homes without. p-Dichlorobenzene was measured in the homes as well, but median concentration was <DL and no further analysis was made. Unacceptable due to selection bias, lack of confounding control, inadequate outcome characterization, and lack of temporality.		

Overall Quality Determination — Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Kernan, G.J., Ji, B.T., Dosemeci, M., Silverman, D.T., Balbus, J., Zahm, S.H. (1999). Occupational risk factors for pancreatic cancer: A case-control study based on death certificates from 24 U.S. states. American Journal of Industrial Medicine 36(2):260-270.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Death from pancreatic cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	194820

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	The National Cancer Institute, National Institute of Occupational Safety and Health, and the National Center for Health Statistics reviewed death certificates from 24 states to select cases from those that had died from pancreatic cancer and matched controls. Controls with cause of death related to the outcome of interest (i.e. pancreatic diseases) were excluded from the study. All key elements of the study design were reported.
	Metric 2:	Attrition	Medium	There was no direct evidence of subject loss or exclusion of subgroups from analyses. The authors provide the total number of cases and controls in the analysis. Case and control data were taken from a registry. It can be assumed that the data are complete for each subject.
	Metric 3:	Comparison Group	High	Controls were selected from the same pool of death certificates from 24 states that cases were selected from. Controls with cause of death related to the outcome of interest were eliminated. Differences in baseline characteristics were controlled for via matching, stratification, and adjustment.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure was assessed via occupation and industry data on death certificates. A job matrix was further applied to assess the likely levels of exposure. Probability and intensity of exposure were estimated across four levels for each occupation. Only employment captured on the death certificate could be considered. The exposure assessment needs exposure information before the job listed on the death certificates.
	Metric 5:	Exposure Levels	Medium	The study offers 4 levels of estimated probability and intensity of exposure (referent, low, medium, high).
	Metric 6:	Temporality	Medium	Exposure was determined by occupational and industry codes on death certificates and indicate that exposure would precede disease, however, the timing and latency period is less clear.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Causes of mortality were determined from death certificates for both cases and controls. Death certificates were drawn from death registries of participating states (n=24). Causes of death were coded using ICD-9 codes, and pancreatic cancer was identified as ICD 157.
	Metric 8:	Reporting Bias	Medium	Measured outcomes, effect estimates and confidence intervals are reported. Number of exposed cases is reported for each analysis, however the number of controls (exposed and unexposed) are not reported for analyses.

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Study Citation:	Kernan, G.J., Ji, B.T., Dosemeci, M., Silverman, D.T., Balbus, J., Zahm, S.H. (1999). Occupational risk factors for pancreatic cancer: A case-control study based on death certificates from 24 U.S. states. American Journal of Industrial Medicine 36(2):260-270.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Death from pancreatic cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	194820

Domain	Metric		Rating	Comments
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Potential confounders were accounted for in the following ways: matching (five year age group, state, race, and gender); adjustment in models (age, marital status, metropolitan, and residential status); and stratification (race and gender). Smoking was not included as a confounder.
	Metric 10:	Covariate Characterization	Medium	Data used to assess potential confounders was derived from death certificates, an adequate measure. However, no information about cigarette smoking and other lifestyle factors were available for adjustment in the analysis.
	Metric 11:	Co-exposure Counfounding	Medium	The variety of industries considered in the analysis diminishes concerns about co-exposures.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The case-control study design and statistical analysis methods were appropriate to assess the exposures/outcome of interest.
	Metric 13:	Statistical Power	Medium	This study had an adequate sample size to detect an effect (n for cases = 63,097; n for controls = 252,386).
	Metric 14:	Reproducibility of Analyses	Medium	The description of analysis was sufficient and would be reproducible.
	Metric 15:	Statistical Analysis	High	The model to calculate risk estimates was transparent.

Additional Comments: This case-control study examined the risk of death from pancreatic cancer in different occupational settings. Exposure was solely assessed using occupation/industry at time of death (reported on death certificate) and the application of a job matrix assessing likely levels of exposure for different positions. This means of estimating exposure may not fully represent a participant's exposure history. Additionally, the number of impacted participants (exposed cases) was inadequate to perform quality analyses for some exposure levels.

Overall Quality Determination High

* No biomarkers were identified for this evaluation.

Study Citation:	Kernan, G.J., Ji, B.T., Dosemeci, M., Silverman, D.T., Balbus, J., Zahm, S.H. (1999). Occupational risk factors for pancreatic cancer: A case-control study based on death certificates from 24 U.S. states. American Journal of Industrial Medicine 36(2):260-270.
Health Outcome(s):	Endocrine
Reported Health Effect(s):	Death from pancreatic cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	194820

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	The National Cancer Institute, National Institute of Occupational Safety and Health, and the National Center for Health Statistics reviewed death certificates from 24 states to select cases from those that had died from pancreatic cancer and matched controls. Controls with cause of death related to the outcome of interest (i.e. pancreatic diseases) were excluded from the study. All key elements of the study design were reported.
	Metric 2:	Attrition	Medium	There was no direct evidence of subject loss or exclusion of subgroups from analyses. The authors provide the total number of cases and controls in the analysis. Case and control data were taken from a registry. It can be assumed that the data are complete for each subject.
	Metric 3:	Comparison Group	High	Controls were selected from the same pool of death certificates from 24 states that cases were selected from. Controls with cause of death related to the outcome of interest were eliminated. Differences in baseline characteristics were controlled for via matching, stratification, and adjustment.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure was assessed via occupation and industry data on death certificates. A job matrix was further applied to assess the likely levels of exposure. Probability and intensity of exposure were estimated across four levels for each occupation. Only employment captured on the death certificate could be considered. The exposure assessment needs exposure information before the job listed on the death certificates.
	Metric 5:	Exposure Levels	Medium	The study offers 4 levels of estimated probability and intensity of exposure (referent, low, medium, high).
	Metric 6:	Temporality	Medium	Exposure was determined by occupational and industry codes on death certificates and indicate that exposure would precede disease, however, the timing and latency period is less clear.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Causes of mortality were determined from death certificates for both cases and controls. Death certificates were drawn from death registries of participating states (n=24). Causes of death were coded using ICD-9 codes, and pancreatic cancer was identified as ICD 157.
	Metric 8:	Reporting Bias	Medium	Measured outcomes, effect estimates and confidence intervals are reported. Number of exposed cases is reported for each analysis, however the number of controls (exposed and unexposed) are not reported for analyses.
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Kernan, G.J., Ji, B.T., Dosemeci, M., Silverman, D.T., Balbus, J., Zahm, S.H. (1999). Occupational risk factors for pancreatic cancer: A case-control study based on death certificates from 24 U.S. states. American Journal of Industrial Medicine 36(2):260-270.
Health Outcome(s):	Endocrine
Reported Health Effect(s):	Death from pancreatic cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	194820

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Medium	Potential confounders were accounted for in the following ways: matching (five year age group, state, race, and gender); adjustment in models (age, marital status, metropolitan, and residential status); and stratification (race and gender). Smoking was not included as a confounder.
	Metric 10:	Covariate Characterization	Medium	Data used to assess potential confounders was derived from death certificates, an adequate measure. However, no information about cigarette smoking and other lifestyle factors were available for adjustment in the analysis.
	Metric 11:	Co-exposure Counfounding	Medium	The variety of industries considered in the analysis diminishes concerns about co-exposures.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The case-control study design and statistical analysis methods were appropriate to assess the exposures/outcome of interest.
	Metric 13:	Statistical Power	Medium	This study had an adequate sample size to detect an effect (n for cases = 63,097; n for controls = 252,386).
	Metric 14:	Reproducibility of Analyses	Medium	The description of analysis was sufficient and would be reproducible.
	Metric 15:	Statistical Analysis	High	The model to calculate risk estimates was transparent.

Additional Comments: This case-control study examined the risk of death from pancreatic cancer in different occupational settings. Exposure was solely assessed using occupation/industry at time of death (reported on death certificate) and the application of a job matrix assessing likely levels of exposure for different positions. This means of estimating exposure may not fully represent a participant's exposure history. Additionally, the number of impacted participants (exposed cases) was inadequate to perform quality analyses for some exposure levels.

Overall Quality Determination High

* No biomarkers were identified for this evaluation.

Study Citation:	Niehoff, N.M., Gammon, M.D., Keil, A.P., Nichols, H.B., Engel, L.S., Sandler, D.P., White, A.J. (2019). Airborne mammary carcinogens and breast cancer risk in the Sister Study. Environment International 130:104897.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Breast cancer diagnosis (overall), tumor characteristics, and estrogen receptor positive (ER+) invasive breast cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5440630

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	Data from the Sister Study were used. The Sister Study is "a prospective cohort of 50,884 women from across the US who were ages 35–74 at enrollment (Sandler et al., 2017). Participants were recruited from 2003 to 2009 using a national advertising campaign in English and Spanish. Women were eligible for the Sister Study if they had a sister who had been diagnosed with breast cancer, but no prior breast cancer themselves."Exclusions from the study occurred for the following reasons:-breast cancer diagnosed before enrollment was complete, or did not have follow-up information (n = 163)-Residential address couldn't be geocoded (n = 1003, < 2%) - This is a small perecentage, but all of those who were excluded for this reason were from Puerto Rico, West Virginia, Missouri, or Oklahoma.Key elements of the study design are reported. There is some potential for selection bias, but based on the small percentage of those eligible who were excluded, participation was not likely to be substantially biased.
	Metric 2:	Attrition	High	Response rates in the overall Sister study remained over 91% over follow-up. Reasons for non-response were not reported, and characteristics of those lost to follow up were not reported or compared with those included, but 9% loss to follow-up is minimal.
	Metric 3:	Comparison Group	High	Differences in baseline characteristics of groups were considered as potential confounding variables.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	The EPA NATA database of census-tract level modeled air toxics data was used. The study authors note the potential for exposure misclassification: "Concentrations at the census tract level do not fully account for variation in an individual's daily activities that could lead to higher or lower exposure, and all women within a census tract are assigned the same concentration."
	Metric 5:	Exposure Levels	Medium	There were five quintiles of exposure, so there was a sufficient range and distribution of exposure.
	Metric 6:	Temporality	Medium	This is a prospective cohort study.Exposure data from 2005 were chosen because they represented the middle of the enrollment period (2003-2009).The study reported that "94% of women enrolled in 2005 or later, and thus the exposure assessment primarily predated enrollment for the majority of Sister Study participants."The six percent of women who had the potential to have the outcome before exposure was measured in 2005 are a concern. But sensitivity analyses were used to assess whether the associations changed when restricted to those who enrolled in 2005 or later.The authors note that the study is making assumptions about the relevant exposure windows - therefore the exposure window is not certain.

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Study Citation:	Niehoff, N.M., Gammon, M.D., Keil, A.P., Nichols, H.B., Engel, L.S., Sandler, D.P., White, A.J. (2019). Airborne mammary carcinogens and breast cancer risk in the Sister Study. Environment International 130:104897.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Breast cancer diagnosis (overall), tumor characteristics, and estrogen receptor positive (ER+) invasive breast cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5440630

Domain	Metric		Rating	Comments
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Women who reported a breast cancer diagnosis on the annual health updates or follow-up questionnaires were asked to provide additional diagnosis information, and to grant permission for the study to obtain medical records and pathology reports. Medical records were obtained for 81% of breast cancer diagnoses. Agreement between self-reported breast cancers and medical records was high (positive predictive value > 99%) (Sandler et al., 2017), so self-report was used when medical records were not available. Tumor characteristics (stage; histology; and estrogen receptor (ER) status) were abstracted from medical records, or self-reported.
	Metric 8:	Reporting Bias	High	A description of measured outcomes is reported. Effect estimates are reported with confidence intervals.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Covariates considered included age, race, BMI, residence type, education, and smoking status. Potential confounders were identified using DAGs and literature review. Appropriate considerations were made for potential confounders.
	Metric 10:	Covariate Characterization	Medium	”Most covariates were assessed by self-report at the baseline interview.””At baseline, women completed a computer-assisted telephone interview and written questionnaires.”Previous publications might describe whether the questionnaires were validated, but validation was not specified in this publication.
	Metric 11:	Co-exposure Counfounding	Medium	Co-exposures to other air pollutants were assessed, but at the census tract level.Multipollutant classification trees were used, which might provide useful qualitative information.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design (large prospective cohort) and analysis method (Cox proportional hazard single and multi-pollutant models accounting for potential confounders) were appropriate to assess the association between exposure and disease.
	Metric 13:	Statistical Power	Medium	The study had an adequate sample size (1975 cancer cases) and follow-up time (mean=8.4 years).
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to be conceptually reproducible.

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Study Citation:	Niehoff, N.M., Gammon, M.D., Keil, A.P., Nichols, H.B., Engel, L.S., Sandler, D.P., White, A.J. (2019). Airborne mammary carcinogens and breast cancer risk in the Sister Study. Environment International 130:104897.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Breast cancer diagnosis (overall), tumor characteristics, and estrogen receptor positive (ER+) invasive breast cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5440630

Domain	Metric	Rating	Comments
	Metric 15: Statistical Analysis	High	Hazard ratios and 95% confidence intervals (CIs) are reported "comparing index categories of exposure to exposures below the first quintile using Cox proportional hazards regression, with age as the time scale." The method of calculating the hazard ratios is transparent. The authors reported that "the proportional hazards assumption was evaluated by conducting a Wald test for an interaction between the continuous form of the air toxic measure and time." Censoring times and times at-risk are described.

Additional Comments: This was a well-conducted study of a large prospective cohort, but the measurement of exposure at the census-tract rather than the individual level is a limitation.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Sobel, W., Bond, G.G., Skowronski, B.J., Brownson, P.J., Cook, R.R. (1987). A soft tissue sarcoma case control study in a large multi-chemical manufacturing facility. Chemosphere 16(8-9):2095-2099.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	soft-tissue sarcoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1357737

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	From a pool of > 37,000 subjects who worked at least 1 year at chemical company between January 1940-December 1979, the study identified 14 people who died due to soft-cell sarcoma (via death certificate, medical records, or histopathology report). Referents were matched 9:1 with cases (126 matched controls).
	Metric 2:	Attrition	High	There was minimal subject exclusion from the analysis sample; one case could not be matched to controls and was excluded from analysis.
	Metric 3:	Comparison Group	High	Cases and controls were recruited from the same eligible population within the same time frame and matched on sex, race, year of birth and year of hire. Both cases and controls had to have worked ≥1 yr at the plant during the study period.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Work histories for cases and referents were coded to determine an individual's potential exposure to chemical of interest and reviewed by an industrial hygienist blinded to case status.
	Metric 5:	Exposure Levels	Low	Exposure was considered dichotomous, ever exposed or never exposed. There is no quantitative information on exposure levels or range of exposures.
	Metric 6:	Temporality	Low	Temporality of exposure and outcome is established. It is unclear if the interval between exposure and outcome is sufficient for soft tissue sarcoma outcomes.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	The soft-tissue sarcoma outcome was assessed by information provided by death certificates, medical records, and histopathology reports, but study authors did not report the proportions determined by each method.
	Metric 8:	Reporting Bias	High	All outcomes outlined were reported. Authors reported the number of cases and controls in the table. Maximum likelihood estimate ORs with respective 95 % confidence intervals were reported.
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Sobel, W., Bond, G.G., Skowronski, B.J., Brownson, P.J., Cook, R.R. (1987). A soft tissue sarcoma case control study in a large multi-chemical manufacturing facility. Chemosphere 16(8-9):2095-2099.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	soft-tissue sarcoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1357737

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Low	Controls were matched with cases on age, sex, year of hire and survival information. There is indirect evidence that the considerations were made to identify potential confounders through evaluation of medical records of cases and controls (various heritable syndromes, family history of cancer, history of lymphedema, steroids, throrotrast, foreign body implants, chronic extensive scarring, radiation therapy, and immunological defects). Identified confounders between cases and controls were not reported and it is unclear if adjustments for these confounders were included in the final analyses.
	Metric 10:	Covariate Characterization	High	Potential covariates were assessed through evaluation of work histories and medical records.
	Metric 11:	Co-exposure Counfounding	Low	The study documented 13 chemicals, known to be associated with soft-tissue sarcoma (according to NTP, 1983) that were used at the manufacturing facility at some point since 1940. The authors note that some individuals were exposed to multiple chemicals during their employment history and were counted multiple times in the analysis for different chemical exposures. Co-exposures to chemicals to not appear to be adjusted for in analysis.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Low	The study design was adequate to assess the association between exposure and the outcome of interest (soft-tissue sarcoma). The study authors noted they used programs developed by Rothman and Boice to calculate odds ratios with CI intervals; the statistical methods are not further described. The page containing the Rothman and Boice reference appears to be missing from the PDF (or the citation is missing).
	Metric 13:	Statistical Power	Low	Statistical power was not calculated. For 1,2-dichloroethane, there was one case and 6 controls included in the analysis, which was not adequate to detect and effect.
	Metric 14:	Reproducibility of Analyses	Low	The study calculated odd ratios, and 95% CIs were calculated using point estimates and chi from hypothesis testing. The study authors noted they used programs developed by Rothman and Boice to calculate odds ratios with 95% CIs; the statistical methods are not further described and there was no reference for the programs cited.
	Metric 15:	Statistical Analysis	Low	A description of analyses/assumptions was not reported.

Additional Comments: A case-control study of workers at a chemical production facility who worked at least 1 year between January 1940-December 1979 (n=37,000) investigated the incidence of deaths due to soft-tissue sarcoma. The study identified 14 people who died due to soft-tissue sarcoma (through death certificate, medical records, or histopathology reports). Cases were matched to controls based on sex, race, year of birth and year of hire. 13 chemicals, including 1,2-dichloroethane, associated with soft-tissue sarcoma were used at the facility; it does not appear that co-exposures were adjusted for in the analysis. Odds ratios and corresponding CIs were calculated. No significant association was found between exposure to 1,2-DCE and soft-tissue sarcoma.

Overall Quality Determination Medium

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Study Citation:	Sobel, W., Bond, G.G., Skowronski, B.J., Brownson, P.J., Cook, R.R. (1987). A soft tissue sarcoma case control study in a large multi-chemical manufacturing facility. Chemosphere 16(8-9):2095-2099.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	soft-tissue sarcoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1357737

Domain	Metric	Rating	Comments

* No biomarkers were identified for this evaluation.

Study Citation:	Sobel, W., Bond, G.G., Skowronski, B.J., Brownson, P.J., Cook, R.R. (1987). A soft tissue sarcoma case control study in a large multi-chemical manufacturing facility. Chemosphere 16(8-9):2095-2099.
Health Outcome(s):	Skin and Connective Tissue
Reported Health Effect(s):	soft-tissue sarcoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1357737

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	From a pool of > 37,000 subjects who worked at least 1 year at chemical company between January 1940-December 1979, the study identified 14 people who died due to soft-cell sarcoma (via death certificate, medical records, or histopathology report). Referents were matched 9:1 with cases (126 matched controls).
	Metric 2:	Attrition	High	There was minimal subject exclusion from the analysis sample; one case could not be matched to controls and was excluded from analysis.
	Metric 3:	Comparison Group	High	Cases and controls were recruited from the same eligible population within the same time frame and matched on sex, race, year of birth and year of hire. Both cases and controls had to have worked ≥1 yr at the plant during the study period.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Work histories for cases and referents were coded to determine an individual's potential exposure to chemical of interest and reviewed by an industrial hygienist blinded to case status.
	Metric 5:	Exposure Levels	Low	Exposure was considered dichotomous, ever exposed or never exposed. There is no quantitative information on exposure levels or range of exposures.
	Metric 6:	Temporality	Low	Temporality of exposure and outcome is established. It is unclear if the interval between exposure and outcome is sufficient for soft tissue sarcoma outcomes.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	The soft-tissue sarcoma outcome was assessed by information provided by death certificates, medical records, and histopathology reports, but study authors did not report the proportions determined by each method.
	Metric 8:	Reporting Bias	High	All outcomes outlined were reported. Authors reported the number of cases and controls in the table. Maximum likelihood estimate ORs with respective confidence intervals were reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	Controls were matched with cases on age, sex, year of hire and survival information. There is indirect evidence that that considerations were made to identify potential confounders through evaluation of medical records of cases and controls (various heritable syndromes, family history of cancer, history of lymphedema, steroids, throrotrast, foreign body implants, chronic extensive scarring, radiation therapy, and immunological defects). Identified confounders between cases and controls were not reported and it is unclear if adjustments for these confounders were included in the final analyses.

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Study Citation:	Sobel, W., Bond, G.G., Skowronski, B.J., Brownson, P.J., Cook, R.R. (1987). A soft tissue sarcoma case control study in a large multi-chemical manufacturing facility. Chemosphere 16(8-9):2095-2099.
Health Outcome(s):	Skin and Connective Tissue
Reported Health Effect(s):	soft-tissue sarcoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1357737

Domain	Metric		Rating	Comments
	Metric 10:	Covariate Characterization	High	Potential covariates were assessed through evaluation of work histories and medical records.
	Metric 11:	Co-exposure Counfounding	Low	The study documented 13 chemicals, known to be associated with soft-tissue sarcoma (according to NTP, 1983) that were used at the manufacturing facility at some point since 1940. The authors note that some individuals were exposed to multiple chemicals during their employment history and were counted multiple times in the analysis for different chemical exposures. Co-exposures to chemicals to not appear to be adjusted for in analysis.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Low	The study design was adequate to assess the association between exposure and the outcome of interest (soft-tissue sarcoma). The study authors noted they used programs developed by Rothman and Boice to calculate odds ratios with (95% CIs; the statistical methods are not further described. The page containing the Rothman and Boice reference appears to be missing from the PDF (or the citation is missing).
	Metric 13:	Statistical Power	Low	Statistical power was not calculated. For 1,2-dichloroethane, there was one case and 6 controls included in the analysis, which was not adequate to detect and effect.
	Metric 14:	Reproducibility of Analyses	Low	The study calculated odd ratios, and 95% CIs were calculated using point estimates and chi from hypothesis testing. The study authors noted they used programs developed by Rothman and Boice to calculate odds ratios with CI intervals; the statistical methods are not further described and there was no reference for the programs cited.
	Metric 15:	Statistical Analysis	Low	A description of analyses/assumptions was not reported.

Additional Comments: A case-control study of workers at a chemical production facility who worked at least 1 year between January 1940-December 1979 (n=37,000) investigated the incidence of deaths due to soft-tissue sarcoma. The study identified 14 people who died due to soft-tissue sarcoma (through death certificate, medical records, or histopathology reports). Cases were matched to controls based on sex, race, year of birth and year of hire. 13 chemicals, including 1,2-dichloroethane, associated with soft-tissue sarcoma were used at the facility; it does not appear that co-exposures were adjusted for in the analysis. Odds ratios and corresponding CIs were calculated. No significant association was found between exposure to 1,2-DCE and soft-tissue sarcoma.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Teta, M. J., Ott, M. G., Schnatter, A. R. (1991). An update of mortality due to brain neoplasms and other causes among employees of a petrochemical facility. Journal of Occupational Medicine 33(1):45-51.
Health Outcome(s):	Mortality
Reported Health Effect(s):	all cause mortality, gastrointestinal cancer mortality, respiratory system cancer mortality, kidney and other urinary organ cancer mortality, skin cancer mortality, brain cancer mortality, lymphatic and hematopoietic tissue cancer mortality, benign neoplasm mortality, heart disease mortality, and liver cirrhosis mortality.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200633, 1629047
HERO ID:	200633

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	The facility was described in some detail. All male employees working for one day or more between 1941 and 1983 were included. There may be some healthy worker effect in this population.
	Metric 2:	Attrition	High	Study authors reported that vital status was complete for 99% of the population, and death certificates were obtained for 99% of decedents.
	Metric 3:	Comparison Group	High	SMRs were calculated using age-, race-, and calendar year-specific mortality rates of males in the United States. All included employees were male.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	All employees were treated as exposed. Table 4 indicates that relatively few employees were employed in areas designated as 1,2-DCA work areas. There is potential for substantial exposure misclassification.
	Metric 5:	Exposure Levels	Low	All employed individuals were categorized as exposed, and the reference population was described as unexposed. This represents two levels of exposure. The distribution of exposure within the employed population is unclear.
	Metric 6:	Temporality	Medium	Employees were followed from 1950 (or date of first hire) through 1983. The relevant timing of exposure is not entirely clear; however, this represents a sufficiently long period of follow-up.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Mortality was tracked using company records, Social Security Administration records, and the National Death Index. Specific ICD codes and use of a nosologist were not described, but there was no evidence to suggest the method had poor validity.
	Metric 8:	Reporting Bias	High	SMRs were provided with confidence intervals in addition to observed and expected cases. The authors state they did not carry out regional specific SMRs due to the higher prevalence of neoplasms in the surrounding area.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	SMRs were restricted to males. Rates were age-, race-, and calendar period-specific. No consideration was made for smoking.
	Metric 10:	Covariate Characterization	Medium	Demographic information was obtained from employment records. This was not a validated method, but there was no evidence to suggest it was an invalid method.

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Study Citation:	Teta, M. J., Ott, M. G., Schnatter, A. R. (1991). An update of mortality due to brain neoplasms and other causes among employees of a petrochemical facility. Journal of Occupational Medicine 33(1):45-51.
Health Outcome(s):	Mortality
Reported Health Effect(s):	all cause mortality, gastrointestinal cancer mortality, respiratory system cancer mortality, kidney and other urinary organ cancer mortality, skin cancer mortality, brain cancer mortality, lymphatic and hematopoietic tissue cancer mortality, benign neoplasm mortality, heart disease mortality, and liver cirrhosis mortality.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200633, 1629047
HERO ID:	200633

Domain	Metric		Rating	Comments
	Metric 11:	Co-exposure Counfounding	Low	Several other occupational exposures linked to cancer mortality were present, including vinyl chloride, butanol, and other petrochemicals.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	This study design was appropriate for the research question. Authors utilized retrospective occupational cohort data to determine standardized mortality rates for cancer-specific mortalities.
	Metric 13:	Statistical Power	Medium	While power was not calculated, there were over 1350 deaths from 7849 employees which was adequate to detect robust effect estimates.
	Metric 14:	Reproducibility of Analyses	Low	Most details were provided; however, ICD codes used to determine and group cancer mortality diagnoses were not provided.
	Metric 15:	Statistical Analysis	High	No issues identified.

Additional Comments: This study utilized an occupational cohort to retrospectively evaluate elevated rates of cancer mortality among petrochemical plant workers. There were numerous potentially hazardous chemicals mentioned in the plant description which may lead to co-exposure. Additionally, it appears that only a moderate portion of workers may have been exposed to 1,2-DCA or worked in 1,2-DCA areas which may lead to some exposure misclassification and limit the study's ability to inform hazard on 1,2-DCA.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Cases in this case-control study were former Union Carbide Corporation (UCC) chemical plant employees in Texas City, Texas. Cases were identified through death certificate searches and tumor registries, and may have included individuals formerly employed at UCC whose cause of death was unknown to the company. Additionally, control deaths were stated to be pulled from corporate employee benefits department and through locally published obituary notices routinely screened by the medical department - it is possible to assume that cases were identified in a similar manner. The study identified cases of brain tumors by searching death certificates primarily, although tumor registries throughout the state of Texas were also searched. The study clarifies that it is possible that some cases were not found if they survived or died due to another cause - while this is likely to have impacted selection, there is no evidence that this would be differential by exposure status. Overall, there is limited information on the source population of workers from which cases were identified.
	Metric 2:	Attrition	Medium	Attrition is not discussed in the study, and outcome data appear to be complete. There was a large proportion of missing exposure data (roughly 50%) due to workers being employed in roles such as maintenance, where exposure to any chemical is possible but unknown. Analyses were run separately where these ”unknown” individuals were a) treated as exposed, b) treated as unexposed, or c) treated as unknown and thus excluded. The study only presents results for when these individuals were excluded but specifies that the first scenario resulted in increased exposure estimates for controls relative to cases.

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Study Citation:	Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
	Metric 3:	Comparison Group	Medium	The study identifies two series of control groups, selected from all former Union Carbide Corporation (UCC) employees. However, the total number of employees is not stated. Only those who were deceased were used as controls since they had known causes of death and could thus be verified as non-brain tumors. One group of controls excluded employees whose cause of death was due to any malignant neoplasm to allow for the possibility that a general chemical carcinogen may have been associated with cancers of other sites. The other group of controls included deaths from all causes; this included malignant neoplasms other than brain tumors. Both control groups had 80 male employees randomly selected from 450 deceased employees known to the company in June 1979. Control deaths were stated to be pulled from corporate employee benefits department and through locally published obituary notices routinely screened by the medical department - it is possible to assume that cases were identified in a similar manner. The study reports that cases were slightly more likely to have been employed for less than 10 years than controls - the study attributes this in part to the fact that employees whose deaths were known to the company were more likely to have worked for longer - regardless the mean number of years employed was similar between cases and controls. However, cases were more likely to have been terminated from their job for reasons other than death, disability, or retirement (quitting, being fired, etc.), were generally younger at hire, and were less likely to survive to their 70th birthday. None of these factors are controlled for in statistical analyses - however, since controls and cases were pulled from the same population, there is indirect evidence that the groups were similar.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was determined based on official employment records. Records included job title and department assignment codes for each employment from date of hire to date of termination. For each unique department code, UCC and NIOSH industrial hygienists identified principal chemicals used or produced at any time in the history of the plant and correlated those with individual departments. This assessment was not performed on a year-by-year basis due to concerns for recall bias for longer-term employees where less detailed records were kept. An employee was categorized as ”exposed” to 1,2-dichloroethane if they ever worked in a department associated with that chemical. An ”unknown” exposure group was also created to account for employees who had only worked in departments for which no specific chemical could be identified.
	Metric 5:	Exposure Levels	Low	The study does not report any quantitative information and only splits exposure into ”exposed”, ”unexposed”, and ”unknown”.
	Metric 6:	Temporality	High	In this study exposure is confirmed to occur before the outcome is measured. The study reports latency periods, with subjects dichotomized into less than 15 years of latency or more than 15 years of latency. The majority of cases and controls had a latency of greater than 15 years, which is sufficiently long for brain tumors.

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Domain	Metric		Rating	Comments
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Cases were identified through death certificate searches and partially through tumor registries in the state of Texas. Case validation was performed by NIOSH, and 5 different levels of confirmation were reported: 1) tissue specimen interpreted by the Armed Forces Institute of Pathology; 2) autopsy report; 3) histopathology report; 4) clinical diagnosis from hospital record; 5) dearth certificate diagnosis. Codes 1-3 were considered to be ”confirmed” cases of brain tumors, while 4-5 were considered unconfirmed. 5/21 cases were only evaluated using ”unconfirmed methods”, meaning there is likely a high amount of accuracy in roughly 75% of cases. While no case validation is reported for controls, the study specifies that only controls who had died and thus could be confirmed to be non-brain tumors were included.
	Metric 8:	Reporting Bias	Medium	All primary and secondary outcomes that are outlined in the methods are reported in the results. However, the only statistical outcome of their analysis were unadjusted p-values that were not reported and were just described qualitatively.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	The only statistical analysis performed were Mantel-Haenszel chi-squared tests, which did not allow for confounder adjustment. The study does not present a distribution of potential confounders by exposure status but by case/control status. Several variables, such as reason for termination, age at hire, and age at death were significantly different between cases and controls and were not accounted for in statistical modeling. The study explains that these differences are not likely to have any epidemiologic significance and appear to be relatively small differences.
	Metric 10:	Covariate Characterization	Medium	While the study does not explain where they obtained covariate information, it is reasonable to assume that they gathered the information from company records.
	Metric 11:	Co-exposure Counfounding	Low	The study assesses a wide range of other potential occupational co-exposures. While these co-exposures are not adjusted for in any statistical models, effect estimates are presented separately for benzene, diethyl sulfate, ethylene oxide, and vinyl chloride. The distribution of co-exposures across cases and controls is demonstrated to be mostly balanced by comparing proportions of exposed/unexposed between cases and controls. The only notable instance of imbalance is for benzene, where 11.1% of cases were exposed whereas 37.9% of all controls and 19.2% of non-neoplasm related controls were exposed.
Domain 5: Analysis				

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Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	The study chose a case-control design, which was appropriate to study the rare disease of brain tumors and its association with occupational exposures. The only statistical analysis conducted is a Mantzel-Haenszel chi-squared test, but there is no reason to suggest that this would be inappropriate.
	Metric 13:	Statistical Power	Medium	The study does not calculate statistical power, but the number of cases (n=21) and controls (n=80 in each analysis) is likely sufficient to detect an effect.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to understand what was done and could be reproduced given access to the analytic data.
	Metric 15:	Statistical Analysis	High	The only statistical analysis conducted is a Mantel-Haenszel chi-squared test, and all assumptions were met. The statistical process is transparent.

Additional Comments: This case-control study pulled deceased former employees of the Union Carbide Corporation in Texas City, Texas. The study examined dichotomous exposure to a wide range of occupational exposures, including 1,2-dichloroethane, in relation to brain tumor cases. There is no quantitative estimate of exposure. The only statistical analysis in the study is a Mantel-Haenszel chi-squared test statistic and no statistically significant differences in exposure between cases and controls were observed. The fact that there are no effect estimates, no adjustment for confounders, and no quantitative exposure estimates limits the usefulness of this paper.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Cases in this case-control study were former Union Carbide Corporation (UCC) chemical plant employees in Texas City, Texas. Cases were identified through death certificate searches and tumor registries, and may have included individuals formerly employed at UCC whose cause of death was unknown to the company. Additionally, control deaths were stated to be pulled from corporate employee benefits department and through locally published obituary notices routinely screened by the medical department - it is possible to assume that cases were identified in a similar manner. The study identified cases of brain tumors by searching death certificates primarily, although tumor registries throughout the state of Texas were also searched. The study clarifies that it is possible that some cases were not found if they survived or died due to another cause - while this is likely to have impacted selection, there is no evidence that this would be differential by exposure status. Overall, there is limited information on the source population of workers from which cases were identified.
	Metric 2:	Attrition	Medium	Attrition is not discussed in the study, and outcome data appear to be complete. There was a large proportion of missing exposure data (roughly 50%) due to workers being employed in roles such as maintenance, where exposure to any chemical is possible but unknown. Analyses were run separately where these ”unknown” individuals were a) treated as exposed, b) treated as unexposed, or c) treated as unknown and thus excluded. The study only presents results for when these individuals were excluded but specifies that the first scenario resulted in increased exposure estimates for controls relative to cases.

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Domain	Metric		Rating	Comments
	Metric 3:	Comparison Group	Medium	The study identifies two series of control groups, selected from all former Union Carbide Corporation (UCC) employees. However, the total number of employees is not stated. Only those who were deceased were used as controls since they had known causes of death and could thus be verified as non-brain tumors. One group of controls excluded employees whose cause of death was due to any malignant neoplasm to allow for the possibility that a general chemical carcinogen may have been associated with cancers of other sites. The other group of controls included deaths from all causes; this included malignant neoplasms other than brain tumors. Both control groups had 80 male employees randomly selected from 450 deceased employees known to the company in June 1979. Control deaths were stated to be pulled from corporate employee benefits department and through locally published obituary notices routinely screened by the medical department - it is possible to assume that cases were identified in a similar manner. The study reports that cases were slightly more likely to have been employed for less than 10 years than controls - the study attributes this in part to the fact that employees whose deaths were known to the company were more likely to have worked for longer - regardless the mean number of years employed was similar between cases and controls. However, cases were more likely to have been terminated from their job for reasons other than death, disability, or retirement (quitting, being fired, etc.), were generally younger at hire, and were less likely to survive to their 70th birthday. None of these factors are controlled for in statistical analyses - however, since controls and cases were pulled from the same population, there is indirect evidence that the groups were similar.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was determined based on official employment records. Records included job title and department assignment codes for each employment from date of hire to date of termination. For each unique department code, UCC and NIOSH industrial hygienists identified principal chemicals used or produced at any time in the history of the plant and correlated those with individual departments. This assessment was not performed on a year-by-year basis due to concerns for recall bias for longer-term employees where less detailed records were kept. An employee was categorized as ”exposed” to 1,2-dichloroethane if they ever worked in a department associated with that chemical. An ”unknown” exposure group was also created to account for employees who had only worked in departments for which no specific chemical could be identified.
	Metric 5:	Exposure Levels	Low	The study does not report any quantitative information and only splits exposure into ”exposed”, ”unexposed”, and ”unknown”.
	Metric 6:	Temporality	High	In this study exposure is confirmed to occur before the outcome is measured. The study reports latency periods, with subjects dichotomized into less than 15 years of latency or more than 15 years of latency. The majority of cases and controls had a latency of greater than 15 years, which is sufficiently long for brain tumors.

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Linked HERO ID(s):	No linked references.
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Domain	Metric		Rating	Comments
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Cases were identified through death certificate searches and partially through tumor registries in the state of Texas. Case validation was performed by NIOSH, and 5 different levels of confirmation were reported: 1) tissue specimen interpreted by the Armed Forces Institute of Pathology; 2) autopsy report; 3) histopathology report; 4) clinical diagnosis from hospital record; 5) dearth certificate diagnosis. Codes 1-3 were considered to be ”confirmed” cases of brain tumors, while 4-5 were considered unconfirmed. 5/21 cases were only evaluated using ”unconfirmed methods”, meaning there is likely a high amount of accuracy in roughly 75% of cases. While no case validation is reported for controls, the study specifies that only controls who had died and thus could be confirmed to be non-brain tumors were included.
	Metric 8:	Reporting Bias	Medium	All primary and secondary outcomes that are outlined in the methods are reported in the results. However, the only statistical outcome of their analysis were unadjusted p-values that were not reported and were just described qualitatively.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	The only statistical analysis performed were Mantel-Haenszel chi-squared tests, which did not allow for confounder adjustment. The study does not present a distribution of potential confounders by exposure status but by case/control status. Several variables, such as reason for termination, age at hire, and age at death were significantly different between cases and controls and were not accounted for in statistical modeling. The study explains that these differences are not likely to have any epidemiologic significance and appear to be relatively small differences.
	Metric 10:	Covariate Characterization	Medium	While the study does not explain where they obtained covariate information, it is reasonable to assume that they gathered the information from company records.
	Metric 11:	Co-exposure Counfounding	Low	The study assesses a wide range of other potential occupational co-exposures. While these co-exposures are not adjusted for in any statistical models, effect estimates are presented separately for benzene, diethyl sulfate, ethylene oxide, and vinyl chloride. The distribution of co-exposures across cases and controls is demonstrated to be mostly balanced by comparing proportions of exposed/unexposed between cases and controls. The only notable instance of imbalance is for benzene, where 11.1% of cases were exposed whereas 37.9% of all controls and 19.2% of non-neoplasm related controls were exposed.
Domain 5: Analysis				

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Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	The study chose a case-control design, which was appropriate to study the rare disease of brain tumors and its association with occupational exposures. The only statistical analysis conducted is a Mantzel-Haenszel chi-squared test, but there is no reason to suggest that this would be inappropriate.
	Metric 13:	Statistical Power	Medium	The study does not calculate statistical power, but the number of cases (n=21) and controls (n=80 in each analysis) is likely sufficient to detect an effect.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to understand what was done and could be reproduced given access to the analytic data.
	Metric 15:	Statistical Analysis	High	The only statistical analysis conducted is a Mantel-Haenszel chi-squared test, and all assumptions were met. The statistical process is transparent.

Additional Comments: This case-control study pulled deceased former employees of the Union Carbide Corporation in Texas City, Texas. The study examined dichotomous exposure to a wide range of occupational exposures, including 1,2-dichloroethane, in relation to brain tumor cases. There is no quantitative estimate of exposure. The only statistical analysis in the study is a Mantel-Haenszel chi-squared test statistic and no statistically significant differences in exposure between cases and controls were observed. The fact that there are no effect estimates, no adjustment for confounders, and no quantitative exposure estimates limits the usefulness of this paper.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	Urinary system cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	Urinary system cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	Urinary system cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Immune/Hematological
Reported Health Effect(s):	Lymphatic and hematopoietic tissue cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Health Outcome(s):	Immune/Hematological
Reported Health Effect(s):	Lymphatic and hematopoietic tissue cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
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Domain	Metric		Rating	Comments
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	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
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	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Immune/Hematological
Reported Health Effect(s):	Lymphatic and hematopoietic tissue cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Other cancers (not specified)
Reported Health Effect(s):	Other cancers (not specified)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Other cancers (not specified)
Reported Health Effect(s):	Other cancers (not specified)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Other cancers (not specified)
Reported Health Effect(s):	Other cancers (not specified)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Mortality
Reported Health Effect(s):	All-cause mortality
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Vital status was tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Medium	Death rates among unit employees were compared to death rates in the U.S. population adjusted for age and gender. Demographics of the exposed workers are not provided; therefore, it is not clear whether additional adjustment for race may have been appropriate. No justification is provided for the choice of the entire U.S. population as the comparison group. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis. Additional analyses are conducted limiting workers to those with the greatest likelihood of exposure (i.e., those working in jobs with high likelihood of contact with chemicals for more than a year, those working for the full year of 1979 during which chemical exposures were most frequently reported); these smaller groups are also compared to the unexposed general population.
	Metric 6:	Temporality	High	Temporality was established due to the longitudinal design and the use of mortality as the outcome. Exposures occurred between 1979 and 1987 and follow-up for vital status was conducted through 2003.
Domain 3: Outcome Assessment				

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Mortality
Reported Health Effect(s):	All-cause mortality
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Medium	The study did not provide information on how mortality was assessed either in the exposed population or in the comparison population; use of death certificates is implied but not stated.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected deaths are reported, but SIRs and 95% confidence intervals are not provided.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Comparisons of observed versus expected deaths were adjusted for age and gender. Demographics of the exposed workers are not provided; therefore, it is not clear whether additional adjustment for race may have been appropriate.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records or death records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed deaths among a population of exposed workers compared to expected deaths among the U.S. population, adjusted for age and gender.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected deaths; no SIR was provided. Expected death rates were adjusted for age and gender.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Mortality
Reported Health Effect(s):	All-cause mortality
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	All cancer (excluding non-melanoma skin cancer), digestive system cancer, colorectal cancer, respiratory cancer, prostate cancer, urinary system cancer, lymphatic and hematopoietic tissue cancer, other cancers (not specified)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	All cancer (excluding non-melanoma skin cancer), digestive system cancer, colorectal cancer, respiratory cancer, prostate cancer, urinary system cancer, lymphatic and hematopoietic tissue cancer, other cancers (not specified)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	All cancer (excluding non-melanoma skin cancer), digestive system cancer, colorectal cancer, respiratory cancer, prostate cancer, urinary system cancer, lymphatic and hematopoietic tissue cancer, other cancers (not specified)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Gastrointestinal
Reported Health Effect(s):	Digestive system cancer, colorectal cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Health Outcome(s):	Gastrointestinal
Reported Health Effect(s):	Digestive system cancer, colorectal cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Health Outcome(s):	Gastrointestinal
Reported Health Effect(s):	Digestive system cancer, colorectal cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Lung/Respiratory
Reported Health Effect(s):	Respiratory cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Lung/Respiratory
Reported Health Effect(s):	Respiratory cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Lung/Respiratory
Reported Health Effect(s):	Respiratory cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Prostate cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Prostate cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Prostate cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Male workers who had ever been assigned to the chlorohydrin unit between 1 January 1940 and 31 December 1967 at Union Carbide's South Charleston plant were enrolled and matched to the US National Death Index. Status on 5 workers could not be identified. Information on how workers were matched to death index was not specified.
	Metric 2:	Attrition	Medium	Rate of inclusion/participation was very high, as records were able to be matched for 98% of participants. Medium rating given because information on how participants whose vital status was not known was not specified.
	Metric 3:	Comparison Group	Uninformative	Unacceptable rating given because SMRs were calculated based on expected deaths from a reference population matched on sex, but not age.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Exposure was assessed based on duration of work in the plant. No information is provided on exposure levels, and a JEM was not used.
	Metric 5:	Exposure Levels	Uninformative	No information provided on levels of exposure.
	Metric 6:	Temporality	High	Temporality is well established; person-years stopped accumulating in 1967 and outcome was assessed beginning at that time.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar period, and interval since assignments, but distribution of these covariates was not reported.
	Metric 10:	Covariate Characterization	Medium	Information on covariate characterization not provided, but the selected covariates (age, calendar period, and interval since assignments) were likely extracted from employee records and unlikely to be largely problematic
	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.

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Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Study design was appropriate for the research method. Statistical methods were also appropriate.
	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.
	Metric 14:	Reproducibility of Analyses	Medium	Methods are well-enough described that study could be adequately reproduced.
	Metric 15:	Statistical Analysis	High	SMRs calculated based on US general population mortality for white males through 1988. RRs were ”evaluated over levels of duration of assignment to the chlorohydrin unit, stratified by age, calendar year, and interval since first assignment to the chlorohydrin unit”.

Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Male workers who had ever been assigned to the chlorohydrin unit between 1 January 1940 and 31 December 1967 at Union Carbide's South Charleston plant were enrolled and matched to the US National Death Index. Status on 5 workers could not be identified. Information on how workers were matched to death index was not specified.
	Metric 2:	Attrition	Medium	Rate of inclusion/participation was very high, as records were able to be matched for 98% of participants. Medium rating given because information on how participants whose vital status was not known was not specified.
	Metric 3:	Comparison Group	Uninformative	Unacceptable rating given because SMRs were calculated based on expected deaths from a reference population matched on sex, but not age.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Exposure was assessed based on duration of work in the plant. No information is provided on exposure levels, and a JEM was not used.
	Metric 5:	Exposure Levels	Uninformative	No information provided on levels of exposure.
	Metric 6:	Temporality	High	Temporality is well established; person-years stopped accumulating in 1967 and outcome was assessed beginning at that time.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar period, and interval since assignments, but distribution of these covariates was not reported.
	Metric 10:	Covariate Characterization	Medium	Information on covariate characterization not provided, but the selected covariates (age, calendar period, and interval since assignments) were likely extracted from employee records and unlikely to be largely problematic
	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.
Domain 5: Analysis				

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Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Study design was appropriate for the research method. Statistical methods were also appropriate.
	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.
	Metric 14:	Reproducibility of Analyses	Medium	Methods are well-enough described that study could be adequately reproduced.
	Metric 15:	Statistical Analysis	High	SMRs calculated based on US general population mortality for white males through 1988. RRs were ”evaluated over levels of duration of assignment to the chlorohydrin unit, stratified by age, calendar year, and interval since first assignment to the chlorohydrin unit”.

Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Male workers who had ever been assigned to the chlorohydrin unit between 1 January 1940 and 31 December 1967 at Union Carbide's South Charleston plant were enrolled and matched to the US National Death Index. Status on 5 workers could not be identified. Information on how workers were matched to death index was not specified.
	Metric 2:	Attrition	Medium	Rate of inclusion/participation was very high, as records were able to be matched for 98% of participants. Medium rating given because information on how participants whose vital status was not known was not specified.
	Metric 3:	Comparison Group	Uninformative	Unacceptable rating given because SMRs were calculated based on expected deaths from a reference population matched on sex, but not age.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Exposure was assessed based on duration of work in the plant. No information is provided on exposure levels, and a JEM was not used.
	Metric 5:	Exposure Levels	Uninformative	No information provided on levels of exposure.
	Metric 6:	Temporality	High	Temporality is well established; person-years stopped accumulating in 1967 and outcome was assessed beginning at that time.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar period, and interval since assignments, but distribution of these covariates was not reported.
	Metric 10:	Covariate Characterization	Medium	Information on covariate characterization not provided, but the selected covariates (age, calendar period, and interval since assignments) were likely extracted from employee records and unlikely to be largely problematic
	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.
Domain 5: Analysis				

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Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Study design was appropriate for the research method. Statistical methods were also appropriate.
	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.
	Metric 14:	Reproducibility of Analyses	Medium	Methods are well-enough described that study could be adequately reproduced.
	Metric 15:	Statistical Analysis	High	SMRs calculated based on US general population mortality for white males through 1988. RRs were ”evaluated over levels of duration of assignment to the chlorohydrin unit, stratified by age, calendar year, and interval since first assignment to the chlorohydrin unit”.

Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
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Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
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Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Male workers who had ever been assigned to the chlorohydrin unit between 1 January 1940 and 31 December 1967 at Union Carbide's South Charleston plant were enrolled and matched to the US National Death Index. Status on 5 workers could not be identified. Information on how workers were matched to death index was not specified.
	Metric 2:	Attrition	Medium	Rate of inclusion/participation was very high, as records were able to be matched for 98% of participants. Medium rating given because information on how participants whose vital status was not known was not specified.
	Metric 3:	Comparison Group	Uninformative	Unacceptable rating given because SMRs were calculated based on expected deaths from a reference population matched on sex, but not age.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Exposure was assessed based on duration of work in the plant. No information is provided on exposure levels, and a JEM was not used.
	Metric 5:	Exposure Levels	Uninformative	No information provided on levels of exposure.
	Metric 6:	Temporality	High	Temporality is well established; person-years stopped accumulating in 1967 and outcome was assessed beginning at that time.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar period, and interval since assignments, but distribution of these covariates was not reported.
	Metric 10:	Covariate Characterization	Medium	Information on covariate characterization not provided, but the selected covariates (age, calendar period, and interval since assignments) were likely extracted from employee records and unlikely to be largely problematic
	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.
Domain 5: Analysis				

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Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Study design was appropriate for the research method. Statistical methods were also appropriate.
	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.
	Metric 14:	Reproducibility of Analyses	Medium	Methods are well-enough described that study could be adequately reproduced.
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Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
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Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Male workers who had ever been assigned to the chlorohydrin unit between 1 January 1940 and 31 December 1967 at Union Carbide's South Charleston plant were enrolled and matched to the US National Death Index. Status on 5 workers could not be identified. Information on how workers were matched to death index was not specified.
	Metric 2:	Attrition	Medium	Rate of inclusion/participation was very high, as records were able to be matched for 98% of participants. Medium rating given because information on how participants whose vital status was not known was not specified.
	Metric 3:	Comparison Group	Uninformative	Unacceptable rating given because SMRs were calculated based on expected deaths from a reference population matched on sex, but not age.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Exposure was assessed based on duration of work in the plant. No information is provided on exposure levels, and a JEM was not used.
	Metric 5:	Exposure Levels	Uninformative	No information provided on levels of exposure.
	Metric 6:	Temporality	High	Temporality is well established; person-years stopped accumulating in 1967 and outcome was assessed beginning at that time.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar period, and interval since assignments, but distribution of these covariates was not reported.
	Metric 10:	Covariate Characterization	Medium	Information on covariate characterization not provided, but the selected covariates (age, calendar period, and interval since assignments) were likely extracted from employee records and unlikely to be largely problematic
	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.
Domain 5: Analysis				

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Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Study design was appropriate for the research method. Statistical methods were also appropriate.
	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.
	Metric 14:	Reproducibility of Analyses	Medium	Methods are well-enough described that study could be adequately reproduced.
	Metric 15:	Statistical Analysis	High	SMRs calculated based on US general population mortality for white males through 1988. RRs were ”evaluated over levels of duration of assignment to the chlorohydrin unit, stratified by age, calendar year, and interval since first assignment to the chlorohydrin unit”.

Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
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Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Male workers who had ever been assigned to the chlorohydrin unit between 1 January 1940 and 31 December 1967 at Union Carbide's South Charleston plant were enrolled and matched to the US National Death Index. Status on 5 workers could not be identified. Information on how workers were matched to death index was not specified.
	Metric 2:	Attrition	Medium	Rate of inclusion/participation was very high, as records were able to be matched for 98% of participants. Medium rating given because information on how participants whose vital status was not known was not specified.
	Metric 3:	Comparison Group	Uninformative	Unacceptable rating given because SMRs were calculated based on expected deaths from a reference population matched on sex, but not age.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Exposure was assessed based on duration of work in the plant. No information is provided on exposure levels, and a JEM was not used.
	Metric 5:	Exposure Levels	Uninformative	No information provided on levels of exposure.
	Metric 6:	Temporality	High	Temporality is well established; person-years stopped accumulating in 1967 and outcome was assessed beginning at that time.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar period, and interval since assignments, but distribution of these covariates was not reported.
	Metric 10:	Covariate Characterization	Medium	Information on covariate characterization not provided, but the selected covariates (age, calendar period, and interval since assignments) were likely extracted from employee records and unlikely to be largely problematic
	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.
Domain 5: Analysis				

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Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Study design was appropriate for the research method. Statistical methods were also appropriate.
	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.
	Metric 14:	Reproducibility of Analyses	Medium	Methods are well-enough described that study could be adequately reproduced.
	Metric 15:	Statistical Analysis	High	SMRs calculated based on US general population mortality for white males through 1988. RRs were ”evaluated over levels of duration of assignment to the chlorohydrin unit, stratified by age, calendar year, and interval since first assignment to the chlorohydrin unit”.

Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
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Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Male workers who had ever been assigned to the chlorohydrin unit between 1 January 1940 and 31 December 1967 at Union Carbide's South Charleston plant were enrolled and matched to the US National Death Index. Status on 5 workers could not be identified. Information on how workers were matched to death index was not specified.
	Metric 2:	Attrition	Medium	Rate of inclusion/participation was very high, as records were able to be matched for 98% of participants. Medium rating given because information on how participants whose vital status was not known was not specified.
	Metric 3:	Comparison Group	Uninformative	Unacceptable rating given because SMRs were calculated based on expected deaths from a reference population matched on sex, but not age.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Exposure was assessed based on duration of work in the plant. No information is provided on exposure levels, and a JEM was not used.
	Metric 5:	Exposure Levels	Uninformative	No information provided on levels of exposure.
	Metric 6:	Temporality	High	Temporality is well established; person-years stopped accumulating in 1967 and outcome was assessed beginning at that time.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar period, and interval since assignments, but distribution of these covariates was not reported.
	Metric 10:	Covariate Characterization	Medium	Information on covariate characterization not provided, but the selected covariates (age, calendar period, and interval since assignments) were likely extracted from employee records and unlikely to be largely problematic
	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.
Domain 5: Analysis				

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Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Study design was appropriate for the research method. Statistical methods were also appropriate.
	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.
	Metric 14:	Reproducibility of Analyses	Medium	Methods are well-enough described that study could be adequately reproduced.
	Metric 15:	Statistical Analysis	High	SMRs calculated based on US general population mortality for white males through 1988. RRs were ”evaluated over levels of duration of assignment to the chlorohydrin unit, stratified by age, calendar year, and interval since first assignment to the chlorohydrin unit”.

Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
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Linked HERO ID(s):	200224, 5447107
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Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Male workers who had ever been assigned to the chlorohydrin unit between 1 January 1940 and 31 December 1967 at Union Carbide's South Charleston plant were enrolled and matched to the US National Death Index. Status on 5 workers could not be identified. Information on how workers were matched to death index was not specified.
	Metric 2:	Attrition	Medium	Rate of inclusion/participation was very high, as records were able to be matched for 98% of participants. Medium rating given because information on how participants whose vital status was not known was not specified.
	Metric 3:	Comparison Group	Uninformative	Unacceptable rating given because SMRs were calculated based on expected deaths from a reference population matched on sex, but not age.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Exposure was assessed based on duration of work in the plant. No information is provided on exposure levels, and a JEM was not used.
	Metric 5:	Exposure Levels	Uninformative	No information provided on levels of exposure.
	Metric 6:	Temporality	High	Temporality is well established; person-years stopped accumulating in 1967 and outcome was assessed beginning at that time.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar period, and interval since assignments, but distribution of these covariates was not reported.
	Metric 10:	Covariate Characterization	Medium	Information on covariate characterization not provided, but the selected covariates (age, calendar period, and interval since assignments) were likely extracted from employee records and unlikely to be largely problematic
	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.
Domain 5: Analysis				

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Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
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Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Study design was appropriate for the research method. Statistical methods were also appropriate.
	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.
	Metric 14:	Reproducibility of Analyses	Medium	Methods are well-enough described that study could be adequately reproduced.
	Metric 15:	Statistical Analysis	High	SMRs calculated based on US general population mortality for white males through 1988. RRs were ”evaluated over levels of duration of assignment to the chlorohydrin unit, stratified by age, calendar year, and interval since first assignment to the chlorohydrin unit”.

Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Bove, F. J. (1996). Public drinking water contamination and birthweight, prematurity, fetal deaths, and birth defects. Toxicology and Industrial Health 12(2):255-266.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	200239

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	This cross-sectional study (n=80,938) included all registered singleton live births and fetal deaths (>20 weeks' gestation) in 1985-88 in 75 New Jersey towns located in 4 counties with "some" water supplies contaminated with substances of interest and where: (i) residents were "mostly" served by public water systems; and (ii) births occurred "mostly" in state. Estimated proportions of residents served by public water systems, and of pregnancies/births captured, were not described. However, the inclusion of all eligible registered births, fetal deaths, and birth defects, as well as the selection of towns without knowledge of birth outcome prevalence, limited the likelihood of selection bias.
	Metric 2:	Attrition	Medium	All registered births and fetal deaths were included. Attrition due to missing values for multiple variables was not quantified and is therefore uncertain. However, attrition was likely modest as the proportion of missing values for individual variables was relatively low: (i) ~6% of subjects were excluded from analyses of outcomes such as preterm birth due to invalid or missing gestational ages; and (ii) other covariates evaluated as confounders had up to 4.9% missing values.
	Metric 3:	Comparison Group	High	After excluding plural pregnancies and chromosomal abnormalities, all registered live births during the study period in the areas included without the outcomes of interest were included in the comparison group. This comprehensive approach limited the potential for bias. Chromosomal abnormalities were not included as outcomes as they were not hypothesized to be associated with the exposures under study but were appropriately excluded given their uncertain etiology.
Domain 2: Exposure Characterization				

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Study Citation:	Bove, F. J. (1996). Public drinking water contamination and birthweight, prematurity, fetal deaths, and birth defects. Toxicology and Industrial Health 12(2):255-266.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	200239

Domain	Metric		Rating	Comments
	Metric 4:	Measurement of Exposure	Medium	Along with several other contaminants, residential drinking water exposure to 1,2-dichloroethane (as well as 1,1,1-trichloroethane and 'total dichloroethylenes') – was assigned based on maternal town of residence at birth. Exposure estimates were calculated using the average of water company sampling reports during the first trimester (for birth defects and fetal death) or the duration of pregnancy (for other outcomes). Detection limits and data availability were not specified in detail but were described as below 1 ppb, with reporting compliance >85%. A minimum of 1 sample per 6-month interval was required; variability in the number of measures available across water systems and towns was not described. Additional sources of measurement error included: changes in residence during pregnancy; water from alternate sources (ex. private wells, bottles, workplaces); variability in residential contaminant levels vs measured samples; unknown levels of tap water intake; and errors in estimated dermal and inhalation exposure while bathing or showering. While the extent of exposure misclassification is uncertain, there is no evidence to suggest it was differential rather than random.
	Metric 5:	Exposure Levels	Medium	Due to the high proportion of measures below detection limits, analyses relating exposure to health outcomes used only 2 categories for each of the chlorinated solvents of interest: cutoffs close to detection limits were used to define elevated exposure. Proportions defined as having elevated exposure was low (1.8% had 1,1-dichloroethylene ≥1 ppb). An important concern is that relatively low levels of exposure to these contaminants from sources other than residential drinking water, for which data were not available, could potentially have resulted in considerable misclassification.
	Metric 6:	Temporality	High	Exposure levels were assigned based on contaminant exposures estimated during: (i) the first trimester for analyses of birth defects and fetal deaths; and (ii) the duration of pregnancy for other pregnancy outcomes.

Domain 3: Outcome Assessment

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Study Citation:	Bove, F. J. (1996). Public drinking water contamination and birthweight, prematurity, fetal deaths, and birth defects. Toxicology and Industrial Health 12(2):255-266.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	200239

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcomes included measures of birthweight (continuous among term births, low term birthweight, very low birthweight), prematurity, fetal death, and congenital anomalies in live births or fetal deaths. The anomalies analyzed included defects of the central nervous system, neural tube, oral cleft, total cardiac, major cardiac, ventricular septum, and any surveillance defect excluding chromosomal defects. All outcomes were identified using birth certificates, fetal death certificates (>20 weeks' gestation), and the NJ congenital birth defect registry (ICD codes provided). These registry data are likely to be sufficiently valid for late pregnancy outcomes. However, their limited ability to capture early pregnancy losses is a weakness. The sample included only 594 fetal deaths (less than 1% of the >80,0000 sample). Typical estimates are that 10-20%, of recognized pregnancies ending in losses. Moreover, developmental defects contributing to early pregnancy losses were also not captured. A further limitation is that that potentially etiologically heterogeneous preterm birth types were analyzed together, as these data did not distinguish premature rupture of membranes vs idiopathic prematurity.
	Metric 8:	Reporting Bias	Medium	Models were constructed only for contaminants with associations > 1.0, and tables included only associations with odds ratios ≥1.5. No clear rationale was provided. Several positive odds ratios below the 1.5 cutoff were described in the results text (without confidence intervals), but no null/negative odds ratios were presented or described.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Potential confounding by maternal race, education, parity, and prior pregnancy loss, along with infant sex (for birth outcomes) and adequacy of prenatal care, was examined. Gestational age was addressed by analyzing birthweight among full term births, term low birth weight, and small size for gestational age. Only fully adjusted models were presented. In a companion case-control study (with low participation rates), adjustment for other variables not available on birth certificates (ex. maternal smoking, occupational exposures, medical history, and gestational weight gain) did not influence associations with other studied contaminants. This separate study reduces concerns for important confounding bias, but confounding cannot be ruled out.
	Metric 10:	Covariate Characterization	Medium	Data on covariates came from registry data: birth certificates, fetal death certificates, and the NJ congenital birth defects registry.
	Metric 11:	Co-exposure Counfounding	Medium	Co-exposure confounding by drinking water trihalomethane concentrations was evaluated. There was no evidence to suggest substantial confounding by this or other co-exposures.
Domain 5: Analysis				

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Study Citation:	Bove, F. J. (1996). Public drinking water contamination and birthweight, prematurity, fetal deaths, and birth defects. Toxicology and Industrial Health 12(2):255-266.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	200239

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Methods were appropriate. The study used logistic regression models to estimate odds ratios and confidence intervals for dichotomous outcomes, and linear regression for analysis of continuous birth weight.
	Metric 13:	Statistical Power	Medium	Statistical power was likely to have been limited as a consequence of the small proportion of the sample defined as having "elevated" residential water concentrations of the chemicals of interest. The range of exposure examined was limited, as cutoffs for elevated levels were close to the detection limits of 1 ppb. In addition, for most birth defect outcomes, fewer than 10 cases had elevated exposure.
	Metric 14:	Reproducibility of Analyses	Medium	The authors clearly described steps used to estimate exposure-outcome associations, including exposure category cutoffs and criteria for confounding. However, many results were not shown as tables included odds ratios ≥1.5.
	Metric 15:	Statistical Analysis	High	The authors estimated coefficients, odds ratios and 95% confidence intervals using adequate methods. Confounding was based on 15% change-in-estimate comparing nested models. Effect modification (ex by infant sex) was not evaluated as there was no a priori evidence to suggest such analyses at that time.

Additional Comments: This study analyzed the association between estimated residential drinking water concentrations of several chlorinated solvents including 1,2-dichloroethane (as well as 1,1,1-trichloroethane; ∑[trans-1,2-dichloroethylene and 1,1-dichloroethylene]) and pregnancy outcomes (size at birth, prematurity, fetal deaths, and congenital birth defects). The sample included more than 80,000 births during 1985-88 for residents of 75 towns in NJ using public water system records to estimate exposure during gestation, and registry data (birth certificate, fetal death certificates for pregnancies >20 weeks, state birth defect registry) to characterize outcomes. Strengths included the large sample size and inclusion of all eligible registered births and fetal deaths in the study period. A critical concern is the inability to capture early fetal deaths and any related malformations (1% of the sample had fetal deaths vs typical estimates of >10%). An important limitation was the low percentage of the sample with detectable (> 1ppb) concentrations of these contaminants (<1% to 6.2%). Small numbers for birth defect outcomes also limited power. Exposure misclassification (ex. drinking water from wells/ work/ bottles, changes in residence, exposure from other sources) is also a concern. However, such misclassification was likely non-differential, and thus more likely to under- vs. to over-estimate associations.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Bove, F. J., Fulcomer, M. C., Klotz, J. B., Esmart, J., Dufficy, E. M., Savrin, J. E. (1995). Public drinking water contamination and birth outcomes. American Journal of Epidemiology 141(9):850-862.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	194932

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	This semi-ecological study (n=80,938) included all registered singleton live births and fetal deaths (>20 weeks) in 1985-88 in 75 New Jersey towns located in 4 counties with "some" water supplies contaminated with substances of interest and where: (i) residents were "mostly" served by public water systems; and (ii) births occurred "mostly" in state. Estimated proportions of residents served by public water systems, and of pregnancies/births captured, were not described. However, the inclusion of all eligible registered births, fetal deaths, and birth defects, as well as the selection of towns without knowledge of birth outcome prevalence, limited the likelihood of selection bias.
	Metric 2:	Attrition	Medium	All registered births and fetal deaths were included. Attrition due to missing values for multiple variables was not quantified and is therefore uncertain. However, attrition was likely modest as the proportion of missing values for individual variables was relatively low: (i) ~6% of subjects were excluded from analyses of outcomes such as preterm birth due to invalid or missing gestational ages; and (ii) other covariates evaluated as confounders had up to 4.9% missing values.
	Metric 3:	Comparison Group	High	After excluding plural pregnancies and chromosomal abnormalities, all registered live births during the study period in the areas included without the outcomes of interest were included in the comparison group. This comprehensive approach limited the potential for bias. Chromosomal abnormalities were not included as outcomes as they were not hypothesized to be associated with the exposures under study but were appropriately excluded given their uncertain etiology.
Domain 2: Exposure Characterization				

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Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	194932

Domain	Metric		Rating	Comments
	Metric 4:	Measurement of Exposure	Medium	Along with several other contaminants, residential drinking water exposure to 1,2-dichloroethane (as well as 1,1,1-trichloroethane and 'total dichloroethylenes') was assigned based on maternal town of residence at birth. Exposure estimates were calculated using the average of water company sampling reports during the first trimester (for birth defects and fetal death) or the duration of pregnancy (for other outcomes). Detection limits and data availability were not specified in detail but were described as below 1 ppb, with reporting compliance >85%. A minimum of 1 sample per 6-month interval was required; variability in the number of measures available across water systems and towns was not described. Additional sources of measurement error included: changes in residence during pregnancy; water from alternate sources (ex. private wells, bottles, workplaces); variability in residential contaminant levels vs measured samples; unknown levels of tap water intake; and errors in estimated dermal and inhalation exposure while bathing or showering. While the extent of exposure misclassification is uncertain, there is no evidence to suggest it was differential rather than random.
	Metric 5:	Exposure Levels	Low	Due to the high proportion of measures below detection limits, analyses relating exposure to health outcomes used only 2 categories for each of the three chemicals of interest: cutoffs close to detection limits were used to define elevated exposure. Proportions defined as having elevated exposure were low (1.8% had 1,1-dichloroethylene ≥1 ppb). An important concern is that relatively low levels of exposure to this contaminant from sources other than residential drinking water, for which data were not available, could potentially have resulted in considerable misclassification.
	Metric 6:	Temporality	High	Exposure levels were assigned based on contaminant exposures estimated during: (i) the first trimester for analyses of birth defects and fetal deaths; and (ii) the duration of pregnancy for other pregnancy outcomes.

Domain 3: Outcome Assessment

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Study Citation:	Bove, F. J., Fulcomer, M. C., Klotz, J. B., Esmart, J., Dufficy, E. M., Savrin, J. E. (1995). Public drinking water contamination and birth outcomes. American Journal of Epidemiology 141(9):850-862.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	194932

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcomes included measures of birthweight (continuous among term births, low term birthweight, very low birthweight), prematurity, fetal death, and congenital anomalies in live births or fetal deaths. The anomalies analyzed included defects of the central nervous system, neural tube, oral cleft, total cardiac, major cardiac, ventricular septum, and any surveillance defect excluding chromosomal defects. All outcomes were identified using birth certificates, fetal death certificates (>20 weeks' gestation), and the NJ congenital birth defect registry (ICD codes provided). These registry data are likely to be sufficiently valid for late pregnancy outcomes. However, their limited ability to capture early pregnancy losses is a weakness. The sample included only 594 fetal deaths (less than 1% of the >80,0000 sample). Typical estimates are that 10-20%, of recognized pregnancies ending in losses. Moreover, developmental defects contributing to early pregnancy losses were also not captured. A further limitation is that that potentially etiologically heterogeneous preterm birth types were analyzed together, as these data did not distinguish premature rupture of membranes vs idiopathic prematurity.
	Metric 8:	Reporting Bias	Low	Models were constructed only for contaminants with associations > 1.0, and tables included only associations with odds ratios ≥1.5. No clear rationale was provided. Several positive odds ratios below the 1.5 cutoff were described in the results text (without confidence intervals), but no null/negative odds ratios were presented or described.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Potential confounding by maternal race, education, parity, and prior pregnancy loss, along with infant sex (for birth outcomes) and adequacy of prenatal care, was examined. Gestational age was addressed by analyzing birthweight among full term births, term low birth weight, and small size for gestational age. Only fully adjusted models were presented. In a companion case-control study (with low participation rates), adjustment for other variables not available on birth certificates (ex. maternal smoking, occupational exposures, medical history, and gestational weight gain) did not influence associations with other studied contaminants. This separate study reduces concerns for important confounding bias, but confounding cannot be ruled out.
	Metric 10:	Covariate Characterization	Medium	Data on covariates came from registry data: birth certificates, fetal death certificates, and the NJ congenital birth defects registry.
	Metric 11:	Co-exposure Counfounding	Medium	Co-exposure confounding by drinking water trihalomethane concentrations was evaluated. There was no evidence to suggest substantial confounding by this or other co-exposures.
Domain 5: Analysis				

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Study Citation:	Bove, F. J., Fulcomer, M. C., Klotz, J. B., Esmart, J., Dufficy, E. M., Savrin, J. E. (1995). Public drinking water contamination and birth outcomes. American Journal of Epidemiology 141(9):850-862.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	194932

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Methods were appropriate. The study used logistic regression models to estimate odds ratios and confidence intervals for dichotomous outcomes, and linear regression for analysis of continuous birth weight.
	Metric 13:	Statistical Power	Low	Statistical power was likely to have been limited as a consequence of the small proportion of the sample defined as having "elevated" residential water concentrations of the chemicals of interest. The range of exposure examined was limited, as cutoffs for elevated levels were close to the detection limits of 1 ppb. In addition, for most birth defect outcomes, fewer than 10 cases had elevated exposure. However, the authors emphasized the magnitude of associations rather than statistical significance and presented multiple confidence intervals to aid interpretation of the precision of estimates (50%, 90% and 99%).
	Metric 14:	Reproducibility of Analyses	Medium	The authors clearly described steps used to estimate exposure-outcome associations, including exposure category cutoffs and criteria for confounding. However, many results were not shown as tables included odds ratios ≥1.5.
	Metric 15:	Statistical Analysis	High	The authors estimated coefficients, odds ratios and confidence intervals using adequate methods. Confounding was based on 15% change-in-estimate comparing nested models. Effect modification (ex by infant sex) was not evaluated as there was no a priori evidence to suggest such analyses at that time.

Additional Comments: This study analyzed the association between estimated residential drinking water concentrations of several chlorinated solvents including 1,2-dichloroethane (as well as 1,1,1-trichloroethane and the ∑[trans-1,2-dichloroethylene & 1,1-dichloroethylene]) and pregnancy outcomes (size at birth, prematurity, fetal deaths, and congenital birth defects). The sample included more than 80,000 births during 1985-88 for residents of 75 towns in NJ using public water system records to estimate exposure during gestation, and registry data (birth certificate, fetal death certificates for pregnancies >20 weeks' gestation, state birth defect registry) to characterize outcomes. Strengths included the large sample size and inclusion of all eligible registered births and fetal deaths in the study period. A critical concern is the inability to capture early fetal deaths and any related malformations (1% of the sample had fetal deaths vs typical estimates of >10%). An important limitation was the low percentage of the sample with detectable (> 1ppb) concentrations of this solvent (<2%), which likely limited power. Small numbers for birth defect outcomes also limited power. Exposure misclassification (ex. drinking water from wells/ work/ bottles, changes in residence, exposure from other sources) is also a concern. However, such misclassification was likely non-differential, and thus more likely to under- vs. to over-estimate associations.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Bowler, R.M., Gysens, S., Hartney, C. (2003). Neuropsychological effects of ethylene dichloride exposure. NeuroToxicology 24(4-5):553-562.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Wechsler Adult Intelligence Scale III (WAIS-III), Wechsler Memory Scale III (WMS-III), Boston Naming Test (BNT), Trail Making Test (TMT), Stroop Color-Word Test, Grooved Pegboard, Dynamometer, Wide Range Achievement Test (WRAT), Finger tapping, Beck Anxiety Index, Beck Depression Index, Symptom Checklist-90 (SCL-90).
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	200241

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Uninformative	221 workers that had been exposed to 1,2-DCE in the Southern United States were initially included. Exclusion criteria were provided, including the number of individuals excluded for each reason. The study authors note that those initially included in the analysis sample were referred by physicians after neurological complaints were documented. Detailed criteria for referral were not provided. Referral-based recruitment of neurological cases will likely result in an analysis sample with an exposure-outcome distribution that is not representative of the eligible population (i.e., contamination site clean-up workers).
	Metric 2:	Attrition	Medium	There was moderate subject loss. Reasons for exclusion from the analysis sample are provided, and only those with complete information were included in the analysis.
	Metric 3:	Comparison Group	Low	Impairment scores were compared to normative data from manuals and/or a "demographically similar control group" cited to Bowler et al. (2001). The controls from this study appeared similar (albeit somewhat older) than 1,2-DCE-exposed workers and reported no prior chemical exposure.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	A job-exposure matrix was not considered plausible; variables considered as surrogates of exposure were obtained from interviews. This method is expected to have poor validity because it relies on workers' recall of subjective events and their frequency (e.g., contact with water); workers (who are taking part in a lawsuit) may overestimate their exposure.
	Metric 5:	Exposure Levels	Low	Two levels of exposure (exposed and not exposed) were used to evaluate neurophysiological effects.
	Metric 6:	Temporality	Medium	Exposures primarily occurred between 1993 and 1995 and neurophysiological effects were evaluated in 2000. Temporality is established, but it is unclear whether exposures fall within relevant exposure windows for the outcome of interest.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Neurophysiological effects were evaluated using a number of standardized tests, including (but not limited to) the Wechsler Adult Intelligence Scale (WAIS-III), the Wechsler Memory Scale (WMS-III), and the Symptom Checklist 90-Revised (SCL90-R). There was no information whether tests were performed using the same methods for exposed and referent groups (e.g., timing and order of tests).

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Study Citation:	Bowler, R.M., Gysens, S., Hartney, C. (2003). Neuropsychological effects of ethylene dichloride exposure. NeuroToxicology 24(4-5):553-562.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Wechsler Adult Intelligence Scale III (WAIS-III), Wechsler Memory Scale III (WMS-III), Boston Naming Test (BNT), Trail Making Test (TMT), Stroop Color-Word Test, Grooved Pegboard, Dynamometer, Wide Range Achievement Test (WRAT), Finger tapping, Beck Anxiety Index, Beck Depression Index, Symptom Checklist-90 (SCL-90).
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	200241

Domain	Metric		Rating	Comments
	Metric 8:	Reporting Bias	Low	Neurobehavioral outcomes mentioned in the methods were reported for 1,2-DCE-exposed workers (as mean score, standard deviation, and percentage impaired); results for controls/normative data were not shown and/or p-values from t-tests were not provided. Control data were used to define impairment (based on z-score) but these values were not reported. Data pertaining to specific exposure variables were reported in the text only; no data were shown in a table.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Normative data permitted adjustments based on age, education, and gender. The control group was "socio-demographically" similar but specific parameters used to define similarity were not indicated. Separate ANCOVA analyses on workers only were stratified by race (citation provided), and adjusted for ethnicity, age, and education. The methods for identifying and including potential confounders in the analytic approach was not described.
	Metric 10:	Covariate Characterization	Low	No description of the covariate collection method was provided. It was not clear whether the method used was valid or not.
	Metric 11:	Co-exposure Counfounding	Low	A number of workers (18%) reported current exposure to chemicals in their work environment. These potential co-exposures were not were not appropriately adjusted for in the analytical approach used.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Low	The study design was appropriate to evaluate the neurophysiological status of 1,2-DCE-exposed workers; however, statistical methods were not comprehensive.
	Metric 13:	Statistical Power	Medium	The report indicates "significant impairments" were observed on various neurophysiological tests using t-tests, and significant exposure relationships were reported based on test scores and specific exposure variables (used as surrogates of exposure). Therefore, the number of participants was sufficient to detect an effect.
	Metric 14:	Reproducibility of Analyses	Low	Tests were scored according to relevant manuals; the calculation of z-scores, used in all impairment comparisons and analyses of exposure relationships, was not explained in adequate detail. The methods used to determine relationships between specific exposure variables and test scores (i.e., ANCOVA analyses) were not fully described.
	Metric 15:	Statistical Analysis	Low	Description of the ANCOVA analysis was largely not present. It is not clear whether model assumptions were met.

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Study Citation:	Bowler, R.M., Gysens, S., Hartney, C. (2003). Neuropsychological effects of ethylene dichloride exposure. NeuroToxicology 24(4-5):553-562.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Wechsler Adult Intelligence Scale III (WAIS-III), Wechsler Memory Scale III (WMS-III), Boston Naming Test (BNT), Trail Making Test (TMT), Stroop Color-Word Test, Grooved Pegboard, Dynamometer, Wide Range Achievement Test (WRAT), Finger tapping, Beck Anxiety Index, Beck Depression Index, Symptom Checklist-90 (SCL-90).
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	200241

Domain	Metric	Rating	Comments
Additional Comments:	The study evaluated the neurobehavioral status of a group of workers with known exposure to 1,2-DCE at a clean-up site. Impairments related to processing speed, attention, cognitive flexibility, motor coordination and speed, verbal memory/fluency, vision and visual-spatial abilities, and mood were reported in exposed workers. Serious and consequential flaws are associated with the study including methods of participant selection and retention, and exposure characterization among others.		

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Brender, J.D., Shinde, M.U., Zhan, F.B., Gong, X., Langlois, P.H. (2014). Maternal residential proximity to chlorinated solvent emissions and birth defects in offspring: A case-control study. Environmental Health: A Global Access Science Source 13(1):96.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	birth defects (neural tube defects, limbs deficiencies, oral cleft defects, heart defects, spina bifida, anencephaly)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	2799700

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Participants were drawn from the Texas Birth Defects Registry (TBDR) for years 1996-2008. Controls were frequency matched from the same registry. Study authors state that neural tube cases were more likely to not be successfully geocoded which may introduce selection bias, however, the authors note that both cases and controls with addresses that could not be geocoded were similar. In spite of that, the inclusion criteria, methods of participant selection, and frequency match were reported.
	Metric 2:	Attrition	Medium	13.3% case mother addresses and 12.8% control mother addresses were unable to be geocoded, however this most likely only lowered the precision of the study and most likely does not vary based on exposure level.
	Metric 3:	Comparison Group	Medium	Controls were matched to cases and pulled from the same eligible population by year of delivery and public health service region. Other demographic factors, e.g., race was not matched in population selection. However, statistical analyses were adjusted for year of delivery, maternal age, race/ethnicity, education, and public health region of residence.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Used Emission Weighted Proximity Model to estimate exposure at a given address based on proximity to emission sources and the specific amount or type of pollutant emitted. There may be some exposure misclassification due to mothers moving away from geocoded addresses. Previous studies indicate ~67% of mothers do not move between conception and delivery.
	Metric 5:	Exposure Levels	Medium	Reports exposure as "exposure risk value" and groups the risk values into quartiles, with exposure risk values < 0 being the referent group
	Metric 6:	Temporality	Medium	The study authors estimated exposure based on residence during pregnancy and evaluated birth outcomes. Temporality is established. Previous studies indicate ~67% mothers don't move between trimester and delivery. For mothers who moved during the pregnancy, the temporality is unknown.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Outcomes determined by Texas Birth Defect Registry, checking for birth defect diagnosis. Birth certificates came from Center for Health Statistics at Texas Department of State Health Services
	Metric 8:	Reporting Bias	High	Outcome data measured and reported clearly, stratified by specific type of birth defect
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Brender, J.D., Shinde, M.U., Zhan, F.B., Gong, X., Langlois, P.H. (2014). Maternal residential proximity to chlorinated solvent emissions and birth defects in offspring: A case-control study. Environmental Health: A Global Access Science Source 13(1):96.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	birth defects (neural tube defects, limbs deficiencies, oral cleft defects, heart defects, spina bifida, anencephaly)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	2799700

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	High	Cases were frequency matched by year of delivery and public health service region. Final models were adjusted for year of delivery, public health region, maternal age (<20, 20-24, 25-29, 30-34, 35-39, >39 years), education (<12 years, 12 years, >12 years), and race/ethnicity (Whit non-Hispanic, Black non-Hispanic, Hispanic, other non-Hispanic).
	Metric 10:	Covariate Characterization	High	Used birth and death certificates for demographic information
	Metric 11:	Co-exposure Counfounding	Medium	other co-exposures were not described
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	study used logistic regression to measure association between exposure and birth defects
	Metric 13:	Statistical Power	Medium	Overall adequate number of cases and controls - some effects have low cell counts, but at least one health effect has sufficient statistical power.
	Metric 14:	Reproducibility of Analyses	Medium	Methods sufficiently detailed for reproducibility
	Metric 15:	Statistical Analysis	High	No logistic regression model assumption violations were identified.

Additional Comments: This study examined the association between proximity to several point sources of chlorinated solvents and birth defects. Exposure was assessed using EPA's Toxic Release Inventory, and birth defects were assessed using Texas birth registries. The geocoded address of mothers on day of delivery and the amount of solvent was plugged into the Emission Weighted Probability model to assign each mother an exposure risk value. Limitations include limited evidence of temporality. Additionally, elective terminations lacked a vital record, which meant only 69% of mothers with neural tube defects were geocoded. Mothers highly exposed to 1,2-dichloroethane were 1.85 times more likely to have the spina bifida birth defect than mothers who were not significantly exposed.

Overall Quality Determination High

* No biomarkers were identified for this evaluation.

Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Nested case-control design; cases selected from deaths in cohort study was described by Rinsky et al (1988; HERO 597923) (29,139 workers in Union Carbide facilities in West Virginia followed from 1940 to 1978). Vital status complete for 95% of cohort members.
	Metric 2:	Attrition	High	There was minimal exclusion of subjects/missing data, because vital status follow-up was complete for 96% of the 29,139 men in the cohort study.
	Metric 3:	Comparison Group	Medium	Controls were randomly selected in a 5:1 ratio to cases from the total employee cohort such that they were first employed in the same decade and survived to the same five-year survival period as cases. Controls survived at least to the beginning of the five-year interval in which cases died. Controls were independently selected for each of the individual disease subcategories. However, the demographic information between cases and controls were not compared in the paper.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was partially described: (1) Potential employee contact with a specific substance was determined by tracing each employee's work assignments and linking these assignment records to a separate computer file that contained a history of departmental usage for each substance; (2) Potential exposure to each chemical group was assumed on the basis of assignment o a production unit with a history of usage of any member of that chemical group. However, exposure level either based on work assignment in departments such as job exposure matrix or on the chemical levels were not presented.
	Metric 5:	Exposure Levels	Low	The range of exposure is limited. For example, exposure was presented by the duration of work in two categories: <5 years and 5+ years.
	Metric 6:	Temporality	Medium	Temporality is established, but it is unclear whether the exposures fall within the relevant exposure window. Authors used a lag time of 5 years; since controls were selected for 5 yr intervals, the effective lag time ranged from 5-9 years with an average of 7.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Case definition was based on death certificate diagnosis; but no method validation was conducted against this well-established methods.
	Metric 8:	Reporting Bias	Medium	All outcomes reported, but ORs for many analyses presented without CIs (some CIs reported in text).
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Low	There is indirect evidence that considerations were not made for potential confounders (ORs not adjusted, controls not age- or race-matched). Even though authors note that "Age-adjusted stratified analyses, which were also conducted, did not materially modify the odds ratio estimates". Also stratified examination of odds ratios were conducted to assess duration of exposure effects. However, other key confounders e.g., smoking status and race were not accounted for.
	Metric 10:	Covariate Characterization	Medium	The only potential confounder considered was age; this was presumably evaluated based on employment records (no discussion presented). Age-adjusted stratified analyses were conducted.
	Metric 11:	Co-exposure Counfounding	Low	Co-exposures were present and were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Nested case-control study design is appropriate for research question. Initial data analysis included crude odds ratio and then stratified examination of odds ratios was conducted to ass duration of exposure effect. Also, age-adjusted stratified analysis was conducted.
	Metric 13:	Statistical Power	Low	Statistical power calculations were not reported. Case numbers for each disease were low. The number of subjects was not sufficient to detect an effect of 1,2-dichloroethylene exposure.
	Metric 14:	Reproducibility of Analyses	Medium	Description was sufficient to be conceptually reproducible.
	Metric 15:	Statistical Analysis	Low	Statistical model to calculate odds ratio was not described.

Additional Comments: This nested case-control study within a cohort study is a good study design to answer the research question regarding the association between multiple chemical exposures and four cancer sites. Cases and controls are selected appropriate. However, there are several limitations in this study: (1) confounders were not all considered and adjusted for, except that age-adjusted odds ratios were conducted; (2) it is not described if co-exposures were adjusted for; (3) numbers of cancer cases for each cancer type were small, so the statistical power is limited; (4) statistical models for calculating odds ratios were not described.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Nested case-control design; cases selected from deaths in cohort study was described by Rinsky et al (1988; HERO 597923) (29,139 workers in Union Carbide facilities in West Virginia followed from 1940 to 1978). Vital status complete for 95% of cohort members.
	Metric 2:	Attrition	High	There was minimal exclusion of subjects/missing data, because vital status follow-up was complete for 96% of the 29,139 men in the cohort study.
	Metric 3:	Comparison Group	Medium	Controls were randomly selected in a 5:1 ratio to cases from the total employee cohort such that they were first employed in the same decade and survived to the same five-year survival period as cases. Controls survived at least to the beginning of the five-year interval in which cases died. Controls were independently selected for each of the individual disease subcategories. However, the demographic information between cases and controls were not compared in the paper.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was partially described: (1) Potential employee contact with a specific substance was determined by tracing each employee's work assignments and linking these assignment records to a separate computer file that contained a history of departmental usage for each substance; (2) Potential exposure to each chemical group was assumed on the basis of assignment o a production unit with a history of usage of any member of that chemical group. However, exposure level either based on work assignment in departments such as job exposure matrix or on the chemical levels were not presented.
	Metric 5:	Exposure Levels	Low	The range of exposure is limited. For example, exposure was presented by the duration of work in two categories: <5 years and 5+ years.
	Metric 6:	Temporality	Medium	Temporality is established, but it is unclear whether the exposures fall within the relevant exposure window. Authors used a lag time of 5 years; since controls were selected for 5 yr intervals, the effective lag time ranged from 5-9 years with an average of 7.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Case definition was based on death certificate diagnosis; but no method validation was conducted against this well-established methods.
	Metric 8:	Reporting Bias	Medium	All outcomes reported, but ORs for many analyses presented without CIs (some CIs reported in text).
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Low	There is indirect evidence that considerations were not made for potential confounders (ORs not adjusted, controls not age- or race-matched). Even though authors note that "Age-adjusted stratified analyses, which were also conducted, did not materially modify the odds ratio estimates". Also stratified examination of odds ratios were conducted to assess duration of exposure effects. However, other key confounders e.g., smoking status and race were not accounted for.
	Metric 10:	Covariate Characterization	Medium	The only potential confounder considered was age; this was presumably evaluated based on employment records (no discussion presented). Age-adjusted stratified analyses were conducted.
	Metric 11:	Co-exposure Counfounding	Low	Co-exposures were present and were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Nested case-control study design is appropriate for research question. Initial data analysis included crude odds ratio and then stratified examination of odds ratios was conducted to ass duration of exposure effect. Also, age-adjusted stratified analysis was conducted.
	Metric 13:	Statistical Power	Low	Statistical power calculations were not reported. Case numbers for each disease were low. The number of subjects was not sufficient to detect an effect of 1,2-dichloroethylene exposure.
	Metric 14:	Reproducibility of Analyses	Medium	Description was sufficient to be conceptually reproducible.
	Metric 15:	Statistical Analysis	Low	Statistical model to calculate odds ratio was not described.

Additional Comments: This nested case-control study within a cohort study is a good study design to answer the research question regarding the association between multiple chemical exposures and four cancer sites. Cases and controls are selected appropriate. However, there are several limitations in this study: (1) confounders were not all considered and adjusted for, except that age-adjusted odds ratios were conducted; (2) it is not described if co-exposures were adjusted for; (3) numbers of cancer cases for each cancer type were small, so the statistical power is limited; (4) statistical models for calculating odds ratios were not described.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Nested case-control design; cases selected from deaths in cohort study was described by Rinsky et al (1988; HERO 597923) (29,139 workers in Union Carbide facilities in West Virginia followed from 1940 to 1978). Vital status complete for 95% of cohort members.
	Metric 2:	Attrition	High	There was minimal exclusion of subjects/missing data, because vital status follow-up was complete for 96% of the 29,139 men in the cohort study.
	Metric 3:	Comparison Group	Medium	Controls were randomly selected in a 5:1 ratio to cases from the total employee cohort such that they were first employed in the same decade and survived to the same five-year survival period as cases. Controls survived at least to the beginning of the five-year interval in which cases died. Controls were independently selected for each of the individual disease subcategories. However, the demographic information between cases and controls were not compared in the paper.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was partially described: (1) Potential employee contact with a specific substance was determined by tracing each employee's work assignments and linking these assignment records to a separate computer file that contained a history of departmental usage for each substance; (2) Potential exposure to each chemical group was assumed on the basis of assignment o a production unit with a history of usage of any member of that chemical group. However, exposure level either based on work assignment in departments such as job exposure matrix or on the chemical levels were not presented.
	Metric 5:	Exposure Levels	Low	The range of exposure is limited. For example, exposure was presented by the duration of work in two categories: <5 years and 5+ years.
	Metric 6:	Temporality	Medium	Temporality is established, but it is unclear whether the exposures fall within the relevant exposure window. Authors used a lag time of 5 years; since controls were selected for 5 yr intervals, the effective lag time ranged from 5-9 years with an average of 7.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Case definition was based on death certificate diagnosis; but no method validation was conducted against this well-established methods.
	Metric 8:	Reporting Bias	Medium	All outcomes reported, but ORs for many analyses presented without CIs (some CIs reported in text).
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Low	There is indirect evidence that considerations were not made for potential confounders (ORs not adjusted, controls not age- or race-matched). Even though authors note that "Age-adjusted stratified analyses, which were also conducted, did not materially modify the odds ratio estimates". Also stratified examination of odds ratios were conducted to assess duration of exposure effects. However, other key confounders e.g., smoking status and race were not accounted for.
	Metric 10:	Covariate Characterization	Medium	The only potential confounder considered was age; this was presumably evaluated based on employment records (no discussion presented). Age-adjusted stratified analyses were conducted.
	Metric 11:	Co-exposure Counfounding	Low	Co-exposures were present and were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Nested case-control study design is appropriate for research question. Initial data analysis included crude odds ratio and then stratified examination of odds ratios was conducted to ass duration of exposure effect. Also, age-adjusted stratified analysis was conducted.
	Metric 13:	Statistical Power	Low	Statistical power calculations were not reported. Case numbers for each disease were low. The number of subjects was not sufficient to detect an effect of 1,2-dichloroethylene exposure.
	Metric 14:	Reproducibility of Analyses	Medium	Description was sufficient to be conceptually reproducible.
	Metric 15:	Statistical Analysis	Low	Statistical model to calculate odds ratio was not described.

Additional Comments: This nested case-control study within a cohort study is a good study design to answer the research question regarding the association between multiple chemical exposures and four cancer sites. Cases and controls are selected appropriate. However, there are several limitations in this study: (1) confounders were not all considered and adjusted for, except that age-adjusted odds ratios were conducted; (2) it is not described if co-exposures were adjusted for; (3) numbers of cancer cases for each cancer type were small, so the statistical power is limited; (4) statistical models for calculating odds ratios were not described.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Nested case-control design; cases selected from deaths in cohort study was described by Rinsky et al (1988; HERO 597923) (29,139 workers in Union Carbide facilities in West Virginia followed from 1940 to 1978). Vital status complete for 95% of cohort members.
	Metric 2:	Attrition	High	There was minimal exclusion of subjects/missing data, because vital status follow-up was complete for 96% of the 29,139 men in the cohort study.
	Metric 3:	Comparison Group	Medium	Controls were randomly selected in a 5:1 ratio to cases from the total employee cohort such that they were first employed in the same decade and survived to the same five-year survival period as cases. Controls survived at least to the beginning of the five-year interval in which cases died. Controls were independently selected for each of the individual disease subcategories. However, the demographic information between cases and controls were not compared in the paper.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was partially described: (1) Potential employee contact with a specific substance was determined by tracing each employee's work assignments and linking these assignment records to a separate computer file that contained a history of departmental usage for each substance; (2) Potential exposure to each chemical group was assumed on the basis of assignment o a production unit with a history of usage of any member of that chemical group. However, exposure level either based on work assignment in departments such as job exposure matrix or on the chemical levels were not presented.
	Metric 5:	Exposure Levels	Low	The range of exposure is limited. For example, exposure was presented by the duration of work in two categories: <5 years and 5+ years.
	Metric 6:	Temporality	Medium	Temporality is established, but it is unclear whether the exposures fall within the relevant exposure window. Authors used a lag time of 5 years; since controls were selected for 5 yr intervals, the effective lag time ranged from 5-9 years with an average of 7.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Case definition was based on death certificate diagnosis; but no method validation was conducted against this well-established methods.
	Metric 8:	Reporting Bias	Medium	All outcomes reported, but ORs for many analyses presented without CIs (some CIs reported in text).
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Low	There is indirect evidence that considerations were not made for potential confounders (ORs not adjusted, controls not age- or race-matched). Even though authors note that "Age-adjusted stratified analyses, which were also conducted, did not materially modify the odds ratio estimates". Also stratified examination of odds ratios were conducted to assess duration of exposure effects. However, other key confounders e.g., smoking status and race were not accounted for.
	Metric 10:	Covariate Characterization	Medium	The only potential confounder considered was age; this was presumably evaluated based on employment records (no discussion presented). Age-adjusted stratified analyses were conducted.
	Metric 11:	Co-exposure Counfounding	Low	Co-exposures were present and were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Nested case-control study design is appropriate for research question. Initial data analysis included crude odds ratio and then stratified examination of odds ratios was conducted to ass duration of exposure effect. Also, age-adjusted stratified analysis was conducted.
	Metric 13:	Statistical Power	Low	Statistical power calculations were not reported. Case numbers for each disease were low. The number of subjects was not sufficient to detect an effect of 1,2-dichloroethylene exposure.
	Metric 14:	Reproducibility of Analyses	Medium	Description was sufficient to be conceptually reproducible.
	Metric 15:	Statistical Analysis	Low	Statistical model to calculate odds ratio was not described.

Additional Comments: This nested case-control study within a cohort study is a good study design to answer the research question regarding the association between multiple chemical exposures and four cancer sites. Cases and controls are selected appropriate. However, there are several limitations in this study: (1) confounders were not all considered and adjusted for, except that age-adjusted odds ratios were conducted; (2) it is not described if co-exposures were adjusted for; (3) numbers of cancer cases for each cancer type were small, so the statistical power is limited; (4) statistical models for calculating odds ratios were not described.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Cheng, T.J., Huang, M.L., You, N.C., Du, C.L., Chau, T.T. (1999). Abnormal liver function in workers exposed to low levels of ethylene dichloride and vinyl chloride monomer. Journal of Occupational and Environmental Medicine 41(12):1128-1133.
Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	AST, ALT, GGT, Hepatitis B virus surface antigen (HBsAg), and anti-hepatitis C virus antibody (anti-HCV).
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	200266

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	A total of 251 male workers were included from 4 vinyl chloride monomer manufacturing plants. Other details on recruitment strategy, eligibility criteria, year of enrollment, and participation rates were not provided.
	Metric 2:	Attrition	Low	There was no indication of attrition and details on the number of eligible participants throughout the study was limited. Attrition could not be adequately assessed due to a lack of information regarding recruitment and selection.
	Metric 3:	Comparison Group	Medium	The low-EDC-low-VCM group (187 participants) was used as the comparison group, and there is indirect evidence groups are similar. Limited details were provided for setting, inclusion and exclusion criteria, and methods of participant selection.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	NIOSH recommended methods 1003 and 1007 were used for personal and area sampling, respectively. Air samples were collected, stored at 4 deg. C, and analyzed within 2 weeks of the sampling event. However, historical job changes, changes in exposure levels over time, and timing (year or days during work week) or duration of area or personal sampling were not reported.
	Metric 5:	Exposure Levels	Medium	EDC and VCM levels were reported for the different categories of jobs, which were classified into low-EDC-low-VCM, mod-EDC-low-VCM, and low-EDC-mod-VCM groups.
	Metric 6:	Temporality	High	The age of participants (mean age 33.7-40.1 years) and employment duration (mean 7.5-14.3 years) were reported, and the temporality between the exposure and outcome appears to be appropriate.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	AST, ALT, and GGT "were analyzed with a Hitachi 7050 autoanalyzer". A basis for the cutoff values used in Table 4 to determine "abnormal" AST, ALT, and GGT levels was not provided.
	Metric 8:	Reporting Bias	High	Odds ratios for abnormal liver function were provided with 95% confidence intervals, the number per exposure level, and significance when applicable.
Domain 4: Potential Confounding / Variability Control				

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Study Citation: Cheng, T.J., Huang, M.L., You, N.C., Du, C.L., Chau, T.T. (1999). Abnormal liver function in workers exposed to low levels of ethylene dichloride and vinyl chloride monomer. Journal of Occupational and Environmental Medicine 41(12):1128-1133.
Health Outcome(s): Hepatic/Liver
Reported Health Effect(s): AST, ALT, GGT, Hepatitis B virus surface antigen (HBsAg), and anti-hepatitis C virus antibody (anti-HCV).
Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s): No linked references.
HERO ID: 200266

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Medium	The study reports information on potential confounders (age, hepatitis, BMI, alcohol use, and employment duration), and controls for hepatitis, BMI and alcohol consumption in the multiple logistic regression analyses. There is indirect evidence that appropriate adjustments were made.
	Metric 10:	Covariate Characterization	Medium	An interviewer administered the questionnaires to collect information about potential confounders and occupational history.
	Metric 11:	Co-exposure Counfounding	Low	Exposure to ethylene dichloride was evaluated in a vinyl chloride monomer (VCM) manufacturing facility, and VCM was also subsequently analyzed using personal and area sampling. Results for VCM exposure concentrations were provided. VCM is also suspected to cause liver damage.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design (cohort) was appropriate to assess the outcome of interest (”markers of liver damage”). Chi-squared (X2) test and multiple logistic regression were used for statistical analyses.
	Metric 13:	Statistical Power	Medium	The number of participants was adequate to detect an effect in the exposed populations, although power calculations were not provided. There were >20 participants in each group.
	Metric 14:	Reproducibility of Analyses	Low	A description of the logistic regression analysis was provided, however, study authors do not provide information on categorization of abnormal liver function.
	Metric 15:	Statistical Analysis	High	There were no identifiable logistic regression model assumption violations.
Domain 6: Other (if applicable) Considerations for Biomarker Selection and Measurement (Lakind et al. 2014)				
	Metric 16:	Use of Biomarker of Exposure	N/A	Biomarker of exposures were not assessed.
	Metric 17:	Effect Biomarker	High	This study uses aspartate aminotransferase, alanine aminotransferase, and y-glutamyltransferase as biomarkers of effect. While these no works cited to explain their connection to liver function, all three are well-known marker of liver function. Similarly, Hepatitis B virus surface antigen and antihepatitis C virus anitbody are also well-known measures of liver function and health.
	Metric 18:	Method Sensitivity	Low	No limit of detection information is provided for any of the effect biomarkers.
	Metric 19:	Biomarker Stability	Medium	While the study does not provide a lot of information regarding biomarker storage or stability, the authors do mention that venous blood used to detect biomarkers was stored at 4 degrees C.
	Metric 20:	Sample Contamination	Medium	No specific information regarding potential sample contamination was provided.
	Metric 21:	Method Requirements	Medium	Aspartate aminotransferase, alanine aminotransferase, and y-glutamyltransferase were analyzed using a Hitachi 7050 autoanalyzer. Hepatitis B virus surface antibody and antihepatitis C virus antibody were assessed with radioimmunoassay and enzyme-linked immunosorbent assay.

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Study Citation:	Cheng, T.J., Huang, M.L., You, N.C., Du, C.L., Chau, T.T. (1999). Abnormal liver function in workers exposed to low levels of ethylene dichloride and vinyl chloride monomer. Journal of Occupational and Environmental Medicine 41(12):1128-1133.
Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	AST, ALT, GGT, Hepatitis B virus surface antigen (HBsAg), and anti-hepatitis C virus antibody (anti-HCV).
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	200266

Domain	Metric	Rating	Comments
	Metric 22: Matrix Adjustment	N/A	No information on matrix adjustment was provided/available.

Additional Comments: A group of 251 male workers from 4 vinyl chloride monomer (VCM) manufacturing plants were included in this assessment to examine if occupational exposure to VCM and ethylene dichloride (EDC) "resulted in increased risk of liver damage" by examining AST, ALT, and GGT levels in the blood. Increased ORs for abnormal AST (>37 IU/L) and ALT (>41 IU/L) in the mod-EDC-low-VCM group (0.17-333.7 ppm EDC, 0.18-0.34 ppm VCM), compared with the low-EDC-low-VCM group, was reported. Exposure levels were measured using area and personal sampling, but the timing and duration of the sampling events were not reported.

Overall Quality Determination Medium

Study Citation:	Dosemeci, M., Cocco, P., Chow, W.H. (1999). Gender differences in risk of renal cell carcinoma and occupational exposures to chlorinated aliphatic hydrocarbons. American Journal of Industrial Medicine 36(1):54-59.
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	renal cell carcinoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	4697224

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	The details of the study design were reported elsewhere (Chow et al. 1994, HERO ID 701514). Brief details about the setting, date, number of eligible participants, and control matching were reported. Reasons for exclusions/non-participation were described with details by Chow et al. (1994).
	Metric 2:	Attrition	High	For the details of the study design and attrition of study subjects, the study authors referred to another publication by Chow et al., 1994. Chow et al. (1994) mentioned that at the end of the personal interview, the respondents were given a self-administered food-frequency questionnaire. Of the subjects interviewed for the study, 632 patients (79% of 796 eligible patients) and 653 control subjects (79% of 707 eligible control subjects) returned the diet questionnaire. A number of subjects, whose responses were considered unreliable, were excluded from the analysis, including 48 patients and three control subjects who had seven or more skipped food items or had questionable data and 50 patients whose next-of-kin respondent was not a spouse. Also excluded were two patients with unknown smoking status, since smoking is a risk factor.
	Metric 3:	Comparison Group	Medium	The cases were pulled from the Minnesota Cancer Surveillance System. Controls were selected from the general population of Minnesota; controls age 20-64 years were selected through random digital dialing and controls age 65-85 years were collected from files through the Health Care Financing Administration. Controls were age- and gender-stratified and were of the same race. Characteristics of cases and controls were not provided in the text or a table.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	High	Occupational histories including the most recent and usual occupation and industry, job activities, started-year and ended-year, and part-time/full-time status were collected. Occupations and industries were coded according to the standard occupational classification (SOC) and standard industrial classification (SIC) schemes. The National Cancer Institute developed job exposure matrices (JEM) for nine individual chlorinated aliphatic hydrocarbons (CAHCs), all CAHCs-combined, and all organic solvents-combined. These JEMs were merged with assigned SOC and SIC to determine the exposure status to these chemicals for each study subject. Application of the JEM was described elsewhere (Dosemeci et al. 1994, HERO ID 632334; Gomez et al. 1994, HERO ID 702154).
	Metric 5:	Exposure Levels	Medium	Details of the application of the JEM were described elsewhere (Dosemeci et al. 1994, HERO ID 632334; Gomez et al. 1994, HERO ID 702154). Dosemeci et al. (1994) described more details about that this study assigned three levels of probability (low, medium, high) to industries and occupations for chemical exposure levels.

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Study Citation:	Dosemeci, M., Cocco, P., Chow, W.H. (1999). Gender differences in risk of renal cell carcinoma and occupational exposures to chlorinated aliphatic hydrocarbons. American Journal of Industrial Medicine 36(1):54-59.
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	renal cell carcinoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	4697224

Domain	Metric		Rating	Comments
	Metric 6:	Temporality	Medium	Occupational questionnaires identified prior exposures based on reported recent and usual occupations as well as duration of employment. Outcome status was determined from registry data. The authors note that some occupational history was incomplete which may result in some uncertainty in regard to temporality.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Cases were identified as newly diagnosed and histologically confirmed renal cell carcinoma through the Minnesota Cancer Surveillance System and information about each participant was collected using a questionnaire. Validation was not specified.
	Metric 8:	Reporting Bias	Medium	A description of measured outcomes is reported and ORs were stratified by sex. Effect estimates are reported with a confidence interval. One table showed the total numbers of men and women respectively for each chemical, but numbers of cases/controls were not reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Appropriate adjustments were made in the final analysis, including age, gender, smoking, hypertension and the use of diuretics and/or anti-hypertension drugs, and BMI. Results were stratified by sex.
	Metric 10:	Covariate Characterization	Medium	Information about participants was collected using a questionnaire, and it includes potential confounders, e.g., smoking habits. Validation was not specified.
	Metric 11:	Co-exposure Counfounding	Medium	Co-exposures were identified through the job exposure matrices. Chemicals were evaluated individually and as a group.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen (case-control) was appropriate for the research question (renal cell carcinoma risk from occupational organic solvent exposure). Logistic regression models were used to estimate the relative risk and 95% CI.
	Metric 13:	Statistical Power	Low	Statistical power calculations were not provided. No significant effects were observed with 1,2-dichloroethane. The number of participated women to calculate odds ratio was inadequate to detect an effect in the participants for other chemicals or the combined risk, because it was very low.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis was brief, but is sufficient to understand precisely what has been done and to be conceptually reproducible with access to the analytic data.
	Metric 15:	Statistical Analysis	High	Model assumptions for logistic regression were met. The odds ratios were adjusted for age, smoking, hypertension status and/or use of diuretic and/or anti-hypertension drugs, and body mass index for men and women separately.

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Study Citation:	Dosemeci, M., Cocco, P., Chow, W.H. (1999). Gender differences in risk of renal cell carcinoma and occupational exposures to chlorinated aliphatic hydrocarbons. American Journal of Industrial Medicine 36(1):54-59.
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	renal cell carcinoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	4697224

Domain	Metric	Rating	Comments
Additional Comments:	A group of 438 cases (273 men and 165 women) were selected from the Minnesota Cancer Surveillance System that had been newly diagnosed with renal cell carcinoma. Controls included 687 participants (462 men and 225 women) age- and gender- stratified that were selected from either the general population of Minnesota (age 20-64 years) or from the Health Care Financing Administration files (age 65-85). No significant increase in the risk of renal cell carcinoma was observed with exposure to 1,2-dichloroethane among men or women separately, or for all participants exposed.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Dosemeci, M., Cocco, P., Chow, W.H. (1999). Gender differences in risk of renal cell carcinoma and occupational exposures to chlorinated aliphatic hydrocarbons. American Journal of Industrial Medicine 36(1):54-59.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	renal cell carcinoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	4697224

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	The details of the study design were reported elsewhere (Chow et al. 1994, HERO ID 701514). Brief details about the setting, date, number of eligible participants, and control matching were reported. Reasons for exclusions/non-participation were described with details by Chow et al. (1994).
	Metric 2:	Attrition	Medium	For the details of the study design and attrition of study subjects, the study authors referred to another publication by Chow et al., 1994. Chow et al. (1994) mentioned that at the end of the personal interview, the respondents were given a self-administered food-frequency questionnaire. Of the subjects interviewed for the study, 632 patients (79% of 796 eligible patients) and 653 control subjects (79% of 707 eligible control subjects) returned the diet questionnaire. A number of subjects, whose responses were considered unreliable, were excluded from the analysis, including 48 patients and three control subjects who had seven or more skipped food items or had questionable data and 50 patients whose next-of-kin respondent was not a spouse. Also excluded were two patients with unknown smoking status, since smoking is a risk factor.
	Metric 3:	Comparison Group	Medium	The cases were pulled from the Minnesota Cancer Surveillance System. Controls were selected from the general population of Minnesota; controls age 20-64 years were selected through random digital dialing and controls age 65-85 years were collected from files through the Health Care Financing Administration. Controls were age- and gender-stratified and were of the same race. Characteristics of cases and controls were not provided in the text or a table.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	High	Occupational histories including the most recent and usual occupation and industry, job activities, started-year and ended-year, and part-time/full-time status were collected. Occupations and industries were coded according to the standard occupational classification (SOC) and standard industrial classification (SIC) schemes. The National Cancer Institute developed job exposure matrices (JEM) for nine individual chlorinated aliphatic hydrocarbons (CAHCs), all CAHCs-combined, and all organic solvents-combined. These JEMs were merged with assigned SOC and SIC to determine the exposure status to these chemicals for each study subject. Application of the JEM was described elsewhere (Dosemeci et al. 1994, HERO ID 632334; Gomez et al. 1994, HERO ID 702154).
	Metric 5:	Exposure Levels	Medium	Details of the application of the JEM were described elsewhere (Dosemeci et al. 1994, HERO ID 632334; Gomez et al. 1994, HERO ID 702154). Dosemeci et al. (1994) described more details about that this study assigned three levels of probability (low, medium, high) to industries and occupations for chemical exposure levels.

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Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	renal cell carcinoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	4697224

Domain	Metric		Rating	Comments
	Metric 6:	Temporality	Medium	Occupational questionnaires identified prior exposures based on reported recent and usual occupations as well as duration of employment. Outcome status was determined from registry data. The authors note that some occupational history was incomplete which may result in some uncertainty in regard to temporality.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Cases were identified as newly diagnosed and histologically confirmed renal cell carcinoma through the Minnesota Cancer Surveillance System and information about each participant was collected using a questionnaire. Validation was not specified.
	Metric 8:	Reporting Bias	Medium	A description of measured outcomes is reported and ORs were stratified by sex. Effect estimates are reported with a confidence interval. One table showed the total numbers of men and women respectively for each chemical, but numbers of cases/controls were not reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Appropriate adjustments were made in the final analysis, including age, gender, smoking, hypertension and the use of diuretics and/or anti-hypertension drugs, and BMI. Results were stratified by sex.
	Metric 10:	Covariate Characterization	Medium	Information about participants was collected using a questionnaire, and it includes potential confounders, e.g., smoking habits. Validation was not specified.
	Metric 11:	Co-exposure Counfounding	Medium	Co-exposures were identified through the job exposure matrices. Chemicals were evaluated individually and as a group.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen (case-control) was appropriate for the research question (renal cell carcinoma risk from occupational organic solvent exposure). Logistic regression models were used to estimate the relative risk and 95% CI.
	Metric 13:	Statistical Power	Low	Statistical power calculations were not provided. No significant effects were observed with 1,2-dichloroethane. The number of participated women to calculate odds ratio was inadequate to detect an effect in the participants for other chemicals or the combined risk, because it was very low.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis was brief, but is sufficient to understand precisely what has been done and to be conceptually reproducible with access to the analytic data.
	Metric 15:	Statistical Analysis	High	Model assumptions for logistic regression were met. The odds ratios were adjusted for age, smoking, hypertension status and/or use of diuretic and/or anti-hypertension drugs, and body mass index for men and women separately.

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Study Citation:	Dosemeci, M., Cocco, P., Chow, W.H. (1999). Gender differences in risk of renal cell carcinoma and occupational exposures to chlorinated aliphatic hydrocarbons. American Journal of Industrial Medicine 36(1):54-59.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	renal cell carcinoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	4697224

Domain	Metric	Rating	Comments
Additional Comments:	A group of 438 cases (273 men and 165 women) were selected from the Minnesota Cancer Surveillance System that had been newly diagnosed with renal cell carcinoma. Controls included 687 participants (462 men and 225 women) age- and gender- stratified that were selected from either the general population of Minnesota (age 20-64 years) or from the Health Care Financing Administration files (age 65-85). No significant increase in the risk of renal cell carcinoma was observed with exposure to 1,2-dichloroethane among men or women separately, or for all participants exposed.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Garcia, E., Hurley, S., Nelson, D.O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health: A Global Access Science Source 14(1):14.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	breast cancer in females
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	3014082

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	A total of 112,378 women were included in this study out of 133,479 eligible female participants from the California Teacher Study cohort. A full description of the cohort is provided in Bernstein et al. 2002 (HERO ID 808446). Reasons for exclusion were provided. The reported information indicates that participant selection in or out of the study and participation was not likely to be biased.
	Metric 2:	Attrition	High	112,378/133,479 participants were included in the study. Exclusions were for the purpose of the study and analysis. Exclusion criteria were documented. Included participants had completed questionnaires. The California Cancer Registry is estimated to be 99% complete.
	Metric 3:	Comparison Group	Medium	There is only indirect evidence that groups are similar. Participants were recruited from the same eligible population with the same method of ascertainment. Comparisons were provided for participants with and without breast cancer. Characteristics between these two groups were generally similar. 5 Quintiles of exposure were used, and Q2-5 were compared with Q1.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	High	The Assessment System for Population Exposure Nationwide and the Human Exposure Model are used as part of the National-Scale Air Toxics Assessment produced by the EPA and was used to estimate ambient HAP concentrations for geographic locations. Methods are described online through the US EPA Assessment Methods.
	Metric 5:	Exposure Levels	Medium	The distribution of the NATA annual ambient concentration for each compound was plotted in Figure 1 using a box plot, and 5 Quintiles were used in the analyses.
	Metric 6:	Temporality	Medium	The follow-up period was from 1995-2011, and the NATA estimates were made in 2002 because it was approximately half way between the start and end of the follow-up period. However, it is unclear whether exposures fall within relevant exposure windows for the outcome of interest.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Annual linkage between the CTS cohort and the California Cancer Registry (CCR) was used to identify cases of invasive breast cancer. The CCR is estimated to be 99% complete. The case of invasive breast cancer was defined by ICD codes.

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Study Citation:	Garcia, E., Hurley, S., Nelson, D.O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health: A Global Access Science Source 14(1):14.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	breast cancer in females
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	3014082

Domain	Metric		Rating	Comments
	Metric 8:	Reporting Bias	Medium	A description of measured outcome is reported for adjustments by age and race, and effect estimates are reported with a 95% confidence interval. The measured outcomes using multiple comparisons were generally described in the text, but non-significant results were excluded from Table 3.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	The models were stratified by age and race. Additionally, adjustments were made for multiple comparisons among subsets of the participants (significant results reported in Table 3). Socioeconomic status (SES) of each participant was not evaluated, however, cohort SES characteristics were thought to be similar by study authors.
	Metric 10:	Covariate Characterization	Medium	Information about baseline characteristics for each participant was collected through a questionnaire. It is unknown if the questionnaire was validated.
	Metric 11:	Co-exposure Counfounding	Medium	A total of 37 compounds were identified as mammary gland carcinogens, but 13 were not included in this analysis. Thirteen compounds were excluded from the analysis due to insufficient variability (nine because they had the same value for all census tracts in the state of California; and four because they had less than 25% non-zero values). Ethylene dichloride (1,2-dichloroethane) was among the 24 compounds evaluated in this assessment, and evaluations for breast cancer were conducted for each of these 24 individual compounds.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen (prospective cohort) was appropriate for the research question (incidence of breast cancer). Cox proportional hazard models and SAS 9.3 were used in this assessment. Data analysis was described.
	Metric 13:	Statistical Power	Medium	Statistical power calculations were not provided. No significant effects were observed with ethylene dichloride (1,2-dichloroethane), however, this study utilized a large cohort, approximately 112,000 individuals. Distributions of chemicals of interest suggest there were sufficient numbers of participants in exposure subgroups.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to understand precisely what has been done and to be conceptually reproducible with access to the analytic data.
	Metric 15:	Statistical Analysis	High	The statistical models that were used were identified and described. ”No apparent violation of the underlying assumption of proportional hazards was detected”.

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Study Citation:	Garcia, E., Hurley, S., Nelson, D.O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health: A Global Access Science Source 14(1):14.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	breast cancer in females
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	3014082

Domain	Metric	Rating	Comments
Additional Comments:	A group of 112,378 female participants from the California Teacher Study cohort were assessed for their estimated exposure to ambient air pollutants, including ethylene dichloride (1,2-dichloroethane), and the incidence of invasive breast cancer. Air contaminant concentrations were estimated using the US EPA NATA and the ASPEN and HEM models. The approximate median concentration of 1,2-dichloroethane is between 1E-4 and 1E-2 (estimated from Figure 1). Exposures were categorized into 5 Quintiles, and compared against Quintile 1. No significant increase in the estimated hazard rate ratio for invasive breast cancer was observed with Quintile 2-5 exposure estimates for 1,2-dichloroethane, adjusted for age and race, when compared against Quintile 1, or when further adjusted using multiple comparisons.		

Overall Quality Determination High

* No biomarkers were identified for this evaluation.

Study Citation:	Garcia, E., Hurley, S., Nelson, D.O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health: A Global Access Science Source 14(1):14.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	breast cancer in females
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	3014082

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	A total of 112,378 women were included in this study out of 133,479 eligible female participants from the California Teacher Study cohort. A full description of the cohort is provided in Bernstein et al. 2002 (HERO ID 808446). Reasons for exclusion were provided. The reported information indicates that participant selection in or out of the study and participation was not likely to be biased.
	Metric 2:	Attrition	High	112,378/133,479 participants were included in the study. Exclusions were for the purpose of the study and analysis. Exclusion criteria were documented. Included participants had completed questionnaires. The California Cancer Registry is estimated to be 99% complete.
	Metric 3:	Comparison Group	Medium	There is only indirect evidence that groups are similar. Participants were recruited from the same eligible population with the same method of ascertainment. Comparisons were provided for participants with and without breast cancer. Characteristics between these two groups were generally similar. 5 Quintiles of exposure were used, and Q2-5 were compared with Q1.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	High	The Assessment System for Population Exposure Nationwide and the Human Exposure Model are used as part of the National-Scale Air Toxics Assessment produced by the EPA and was used to estimate ambient HAP concentrations for geographic locations. Methods are described online through the US EPA Assessment Methods.
	Metric 5:	Exposure Levels	Medium	The distribution of the NATA annual ambient concentration for each compound was plotted in Figure 1 using a box plot, and 5 Quintiles were used in the analyses.
	Metric 6:	Temporality	Medium	The follow-up period was from 1995-2011, and the NATA estimates were made in 2002 because it was approximately half way between the start and end of the follow-up period. However, it is unclear whether exposures fall within relevant exposure windows for the outcome of interest.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Annual linkage between the CTS cohort and the California Cancer Registry (CCR) was used to identify cases of invasive breast cancer. The CCR is estimated to be 99% complete. The case of invasive breast cancer was defined by ICD codes.
	Metric 8:	Reporting Bias	Medium	A description of measured outcome is reported for adjustments by age and race, and effect estimates are reported with a 95% confidence interval. The measured outcomes using multiple comparisons were generally described in the text, but non-significant results were excluded from Table 3.

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Study Citation:	Garcia, E., Hurley, S., Nelson, D.O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health: A Global Access Science Source 14(1):14.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	breast cancer in females
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	3014082

Domain	Metric		Rating	Comments
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	The models were stratified by age and race. Additionally, adjustments were made for multiple comparisons among subsets of the participants (significant results reported in Table 3). Socioeconomic status (SES) of each participant was not evaluated, however, cohort SES characteristics were thought to be similar by study authors.
	Metric 10:	Covariate Characterization	Medium	Information about baseline characteristics for each participant was collected through a questionnaire. It is unknown if the questionnaire was validated.
	Metric 11:	Co-exposure Counfounding	Medium	A total of 37 compounds were identified as mammary gland carcinogens, but 13 were not included in this analysis. Thirteen compounds were excluded from the analysis due to insufficient variability (nine because they had the same value for all census tracts in the state of California; and four because they had less than 25% non-zero values). Ethylene dichloride (1,2-dichloroethane) was among the 24 compounds evaluated in this assessment, and evaluations for breast cancer were conducted for each of these 24 individual compounds.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen (prospective cohort) was appropriate for the research question (incidence of breast cancer). Cox proportional hazard models and SAS 9.3 were used in this assessment. Data analysis was described.
	Metric 13:	Statistical Power	Medium	Statistical power calculations were not provided. No significant effects were observed with ethylene dichloride (1,2-dichloroethane), however, this study utilized a large cohort, approximately 112,000 individuals. Distributions of chemicals of interest suggest there were sufficient numbers of participants in exposure subgroups.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to understand precisely what has been done and to be conceptually reproducible with access to the analytic data.
	Metric 15:	Statistical Analysis	High	The statistical models that were used were identified and described. ”No apparent violation of the underlying assumption of proportional hazards was detected”.

Additional Comments: A group of 112,378 female participants from the California Teacher Study cohort were assessed for their estimated exposure to ambient air pollutants, including ethylene dichloride (1,2-dichloroethane), and the incidence of invasive breast cancer. Air contaminant concentrations were estimated using the US EPA NATA and the ASPEN and HEM models. The approximate median concentration of 1,2-dichloroethane is between 1E-4 and 1E-2 (estimated from Figure 1). Exposures were categorized into 5 Quintiles, and compared against Quintile 1. No significant increase in the estimated hazard rate ratio for invasive breast cancer was observed with Quintile 2-5 exposure estimates for 1,2-dichloroethane, adjusted for age and race, when compared against Quintile 1, or when further adjusted using multiple comparisons.

Overall Quality Determination High

* No biomarkers were identified for this evaluation.

Study Citation:	Guo, P., Yokoyama, K., Piao, F., Sakai, K., Khalequzzaman, M., Kamijima, M., Nakajima, T., Kitamura, F. (2013). Sick building syndrome by indoor air pollution in Dalian, China. International Journal of Environmental Research and Public Health 10(4):1489-1504.
Health Outcome(s):	sick building syndrome
Reported Health Effect(s):	The statistical analysis considers all subjective self-reported symptoms together (not segregated by health outcome) as a group health outcome –sick building syndrome. The study compared two conditions for each studied chemical: combined self-reported symptoms to no symptoms. Therefore, only one form 3 was completed.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1938385

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Residents of a housing estate of 3000 homes were invited to a community meeting to explain the purpose of the study and volunteers were invited to participate. It was not reported whether these volunteers were different from the overall eligible population.
	Metric 2:	Attrition	Low	Of the 70 families that agreed to participate, questionnaires were provided by 59. Reasons of uncompleted questionnaires were not fully provided, and there was no comparison between those who participated and those who did not.
	Metric 3:	Comparison Group	Low	The overall description of the analysis sample indicated a wide range of ages and lengths of stay at the current residence. Thus it is hard to know that subjects in all exposure groups were similar. In addition, the methods of selecting participants in all exposure groups were not fully reported. The numbers of male and female smokers were reported, respectively, but the smoking status and age were not controlled in the statistical analysis.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure concentrations for each home were obtained by diffusion sampling over 24 hrs in the bedroom, kitchen, and outdoors; temperature, the vertical height of samplers, and ventilation (hours windows left open) were reported. Samples were analyzed by GC/MS. The number of samples per home is unclear. The frequency of measurements for each house was not reported.
	Metric 5:	Exposure Levels	Low	The frequency of detection was not reported, so it is difficult to ascertain the actual exposure range. In addition, the reported exposure levels were median, geometric mean, and 95% CI, so they are inadequate to develop an exposure-response estimate.
	Metric 6:	Temporality	Uninformative	For 1,2-dichloroethane, the study evaluated self-reported symptoms in the past (”since they moved into their flats”) and their association with sampling conducted during the study; thus, exposure was measured after the outcome.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Low	Participants provided self-reported symptoms using a questionnaire. Study authors cited a previous study, Kamijima et al., 2005 (in Japanese, HERO ID 1598645) for further details on the questionnaire. It was not clear whether the questionnaire was validated.

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Study Citation:	Guo, P., Yokoyama, K., Piao, F., Sakai, K., Khalequzzaman, M., Kamijima, M., Nakajima, T., Kitamura, F. (2013). Sick building syndrome by indoor air pollution in Dalian, China. International Journal of Environmental Research and Public Health 10(4):1489-1504.
Health Outcome(s):	sick building syndrome
Reported Health Effect(s):	The statistical analysis considers all subjective self-reported symptoms together (not segregated by health outcome) as a group health outcome –sick building syndrome. The study compared two conditions for each studied chemical: combined self-reported symptoms to no symptoms. Therefore, only one form 3 was completed.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1938385

Domain	Metric		Rating	Comments
	Metric 8:	Reporting Bias	Low	The study only mentioned subjective symptoms in the abstract or methods. The abstract and method sections did not report the specific symptoms included in the questionnaire or whether the questionnaire was open-ended for symptoms. The questionnaire was cited to Kamijima et al. 2005 (in Japanese).
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	Comparisons were made separately by sex. The distribution of age and time spent living in residence differed greatly between those reporting symptoms and those not reporting symptoms. Smoking was indicated but not controlled for in the analysis. In short, the statistical analysis did not consider these three potential confounders, age, time spent living in residence, and smoking.
	Metric 10:	Covariate Characterization	Low	Covariates were presumably evaluated via a questionnaire that was cited to Kamijima et al. 2005 (in Japanese).
	Metric 11:	Co-exposure Counfounding	Low	The analysis did not account for other exposures. A number of other VOCs, HCHO, and NO2 were measured in the homes. The concentrations of several other VOCs and HCHO were much higher (5-30x) than 1,2-dichloroethane and may also be associated with these symptoms.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Low	The study design is best characterized as cross-sectional. Only one analysis to compare exposure concentrations between those with and without symptoms was adjusted for a confounder, sex, via stratification. Other potential confounders were not adjusted for. Study authors combine responses for symptoms reported before and during the sampling period in one statistical analysis, which may not reflect the relationship between symptoms and contaminants' exposure at each period.
	Metric 13:	Statistical Power	Medium	Statistical power was not reported. The number of participants was sufficient to detect a difference in median concentration between those with and without symptoms.
	Metric 14:	Reproducibility of Analyses	Medium	Study presents sufficient description of analysis (statistical methods) to be conceptually reproducible with access to the raw data.
	Metric 15:	Statistical Analysis	Low	Study uses a Wilcoxon's rank sum test to compare exposure concentrations in persons with and without symptoms; test for equal variance is not reported.

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Study Citation:	Guo, P., Yokoyama, K., Piao, F., Sakai, K., Khalequzzaman, M., Kamijima, M., Nakajima, T., Kitamura, F. (2013). Sick building syndrome by indoor air pollution in Dalian, China. International Journal of Environmental Research and Public Health 10(4):1489-1504.
Health Outcome(s):	sick building syndrome
Reported Health Effect(s):	The statistical analysis considers all subjective self-reported symptoms together (not segregated by health outcome) as a group health outcome –sick building syndrome. The study compared two conditions for each studied chemical: combined self-reported symptoms to no symptoms. Therefore, only one form 3 was completed.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1938385

Domain	Metric	Rating	Comments
Additional Comments:	Concentrations of VOCs (including 1,2-dichloroethane), HCHO, and NO2 were measured in the 59 homes of families that agreed to participate after being informed of the nature of the study. Participants completed questionnaires asking about symptoms since they moved into the homes and the concentrations of selected compounds were compared among men and women reporting any symptoms vs no symptoms. Concentrations of 1,2-dichloroethane in homes of people with symptoms were higher than in homes without. p-Dichlorobenzene was measured in the homes as well, but median concentration was <DL and no further analysis was made. Unacceptable due to selection bias, lack of confounding control, inadequate outcome characterization, and lack of temporality.		

Overall Quality Determination — Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Kernan, G.J., Ji, B.T., Dosemeci, M., Silverman, D.T., Balbus, J., Zahm, S.H. (1999). Occupational risk factors for pancreatic cancer: A case-control study based on death certificates from 24 U.S. states. American Journal of Industrial Medicine 36(2):260-270.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Death from pancreatic cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	194820

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	The National Cancer Institute, National Institute of Occupational Safety and Health, and the National Center for Health Statistics reviewed death certificates from 24 states to select cases from those that had died from pancreatic cancer and matched controls. Controls with cause of death related to the outcome of interest (i.e. pancreatic diseases) were excluded from the study. All key elements of the study design were reported.
	Metric 2:	Attrition	Medium	There was no direct evidence of subject loss or exclusion of subgroups from analyses. The authors provide the total number of cases and controls in the analysis. Case and control data were taken from a registry. It can be assumed that the data are complete for each subject.
	Metric 3:	Comparison Group	High	Controls were selected from the same pool of death certificates from 24 states that cases were selected from. Controls with cause of death related to the outcome of interest were eliminated. Differences in baseline characteristics were controlled for via matching, stratification, and adjustment.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure was assessed via occupation and industry data on death certificates. A job matrix was further applied to assess the likely levels of exposure. Probability and intensity of exposure were estimated across four levels for each occupation. Only employment captured on the death certificate could be considered. The exposure assessment needs exposure information before the job listed on the death certificates.
	Metric 5:	Exposure Levels	Medium	The study offers 4 levels of estimated probability and intensity of exposure (referent, low, medium, high).
	Metric 6:	Temporality	Medium	Exposure was determined by occupational and industry codes on death certificates and indicate that exposure would precede disease, however, the timing and latency period is less clear.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Causes of mortality were determined from death certificates for both cases and controls. Death certificates were drawn from death registries of participating states (n=24). Causes of death were coded using ICD-9 codes, and pancreatic cancer was identified as ICD 157.
	Metric 8:	Reporting Bias	Medium	Measured outcomes, effect estimates and confidence intervals are reported. Number of exposed cases is reported for each analysis, however the number of controls (exposed and unexposed) are not reported for analyses.

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Study Citation:	Kernan, G.J., Ji, B.T., Dosemeci, M., Silverman, D.T., Balbus, J., Zahm, S.H. (1999). Occupational risk factors for pancreatic cancer: A case-control study based on death certificates from 24 U.S. states. American Journal of Industrial Medicine 36(2):260-270.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Death from pancreatic cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	194820

Domain	Metric		Rating	Comments
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Potential confounders were accounted for in the following ways: matching (five year age group, state, race, and gender); adjustment in models (age, marital status, metropolitan, and residential status); and stratification (race and gender). Smoking was not included as a confounder.
	Metric 10:	Covariate Characterization	Medium	Data used to assess potential confounders was derived from death certificates, an adequate measure. However, no information about cigarette smoking and other lifestyle factors were available for adjustment in the analysis.
	Metric 11:	Co-exposure Counfounding	Medium	The variety of industries considered in the analysis diminishes concerns about co-exposures.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The case-control study design and statistical analysis methods were appropriate to assess the exposures/outcome of interest.
	Metric 13:	Statistical Power	Medium	This study had an adequate sample size to detect an effect (n for cases = 63,097; n for controls = 252,386).
	Metric 14:	Reproducibility of Analyses	Medium	The description of analysis was sufficient and would be reproducible.
	Metric 15:	Statistical Analysis	High	The model to calculate risk estimates was transparent.

Additional Comments: This case-control study examined the risk of death from pancreatic cancer in different occupational settings. Exposure was solely assessed using occupation/industry at time of death (reported on death certificate) and the application of a job matrix assessing likely levels of exposure for different positions. This means of estimating exposure may not fully represent a participant's exposure history. Additionally, the number of impacted participants (exposed cases) was inadequate to perform quality analyses for some exposure levels.

Overall Quality Determination High

* No biomarkers were identified for this evaluation.

Study Citation:	Kernan, G.J., Ji, B.T., Dosemeci, M., Silverman, D.T., Balbus, J., Zahm, S.H. (1999). Occupational risk factors for pancreatic cancer: A case-control study based on death certificates from 24 U.S. states. American Journal of Industrial Medicine 36(2):260-270.
Health Outcome(s):	Endocrine
Reported Health Effect(s):	Death from pancreatic cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	194820

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	The National Cancer Institute, National Institute of Occupational Safety and Health, and the National Center for Health Statistics reviewed death certificates from 24 states to select cases from those that had died from pancreatic cancer and matched controls. Controls with cause of death related to the outcome of interest (i.e. pancreatic diseases) were excluded from the study. All key elements of the study design were reported.
	Metric 2:	Attrition	Medium	There was no direct evidence of subject loss or exclusion of subgroups from analyses. The authors provide the total number of cases and controls in the analysis. Case and control data were taken from a registry. It can be assumed that the data are complete for each subject.
	Metric 3:	Comparison Group	High	Controls were selected from the same pool of death certificates from 24 states that cases were selected from. Controls with cause of death related to the outcome of interest were eliminated. Differences in baseline characteristics were controlled for via matching, stratification, and adjustment.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure was assessed via occupation and industry data on death certificates. A job matrix was further applied to assess the likely levels of exposure. Probability and intensity of exposure were estimated across four levels for each occupation. Only employment captured on the death certificate could be considered. The exposure assessment needs exposure information before the job listed on the death certificates.
	Metric 5:	Exposure Levels	Medium	The study offers 4 levels of estimated probability and intensity of exposure (referent, low, medium, high).
	Metric 6:	Temporality	Medium	Exposure was determined by occupational and industry codes on death certificates and indicate that exposure would precede disease, however, the timing and latency period is less clear.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Causes of mortality were determined from death certificates for both cases and controls. Death certificates were drawn from death registries of participating states (n=24). Causes of death were coded using ICD-9 codes, and pancreatic cancer was identified as ICD 157.
	Metric 8:	Reporting Bias	Medium	Measured outcomes, effect estimates and confidence intervals are reported. Number of exposed cases is reported for each analysis, however the number of controls (exposed and unexposed) are not reported for analyses.
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Kernan, G.J., Ji, B.T., Dosemeci, M., Silverman, D.T., Balbus, J., Zahm, S.H. (1999). Occupational risk factors for pancreatic cancer: A case-control study based on death certificates from 24 U.S. states. American Journal of Industrial Medicine 36(2):260-270.
Health Outcome(s):	Endocrine
Reported Health Effect(s):	Death from pancreatic cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	194820

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Medium	Potential confounders were accounted for in the following ways: matching (five year age group, state, race, and gender); adjustment in models (age, marital status, metropolitan, and residential status); and stratification (race and gender). Smoking was not included as a confounder.
	Metric 10:	Covariate Characterization	Medium	Data used to assess potential confounders was derived from death certificates, an adequate measure. However, no information about cigarette smoking and other lifestyle factors were available for adjustment in the analysis.
	Metric 11:	Co-exposure Counfounding	Medium	The variety of industries considered in the analysis diminishes concerns about co-exposures.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The case-control study design and statistical analysis methods were appropriate to assess the exposures/outcome of interest.
	Metric 13:	Statistical Power	Medium	This study had an adequate sample size to detect an effect (n for cases = 63,097; n for controls = 252,386).
	Metric 14:	Reproducibility of Analyses	Medium	The description of analysis was sufficient and would be reproducible.
	Metric 15:	Statistical Analysis	High	The model to calculate risk estimates was transparent.

Additional Comments: This case-control study examined the risk of death from pancreatic cancer in different occupational settings. Exposure was solely assessed using occupation/industry at time of death (reported on death certificate) and the application of a job matrix assessing likely levels of exposure for different positions. This means of estimating exposure may not fully represent a participant's exposure history. Additionally, the number of impacted participants (exposed cases) was inadequate to perform quality analyses for some exposure levels.

Overall Quality Determination High

* No biomarkers were identified for this evaluation.

Study Citation:	Niehoff, N.M., Gammon, M.D., Keil, A.P., Nichols, H.B., Engel, L.S., Sandler, D.P., White, A.J. (2019). Airborne mammary carcinogens and breast cancer risk in the Sister Study. Environment International 130:104897.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Breast cancer diagnosis (overall), tumor characteristics, and estrogen receptor positive (ER+) invasive breast cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5440630

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	Data from the Sister Study were used. The Sister Study is "a prospective cohort of 50,884 women from across the US who were ages 35–74 at enrollment (Sandler et al., 2017). Participants were recruited from 2003 to 2009 using a national advertising campaign in English and Spanish. Women were eligible for the Sister Study if they had a sister who had been diagnosed with breast cancer, but no prior breast cancer themselves."Exclusions from the study occurred for the following reasons:-breast cancer diagnosed before enrollment was complete, or did not have follow-up information (n = 163)-Residential address couldn't be geocoded (n = 1003, < 2%) - This is a small perecentage, but all of those who were excluded for this reason were from Puerto Rico, West Virginia, Missouri, or Oklahoma.Key elements of the study design are reported. There is some potential for selection bias, but based on the small percentage of those eligible who were excluded, participation was not likely to be substantially biased.
	Metric 2:	Attrition	High	Response rates in the overall Sister study remained over 91% over follow-up. Reasons for non-response were not reported, and characteristics of those lost to follow up were not reported or compared with those included, but 9% loss to follow-up is minimal.
	Metric 3:	Comparison Group	High	Differences in baseline characteristics of groups were considered as potential confounding variables.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	The EPA NATA database of census-tract level modeled air toxics data was used. The study authors note the potential for exposure misclassification: "Concentrations at the census tract level do not fully account for variation in an individual's daily activities that could lead to higher or lower exposure, and all women within a census tract are assigned the same concentration."
	Metric 5:	Exposure Levels	Medium	There were five quintiles of exposure, so there was a sufficient range and distribution of exposure.
	Metric 6:	Temporality	Medium	This is a prospective cohort study.Exposure data from 2005 were chosen because they represented the middle of the enrollment period (2003-2009).The study reported that "94% of women enrolled in 2005 or later, and thus the exposure assessment primarily predated enrollment for the majority of Sister Study participants."The six percent of women who had the potential to have the outcome before exposure was measured in 2005 are a concern. But sensitivity analyses were used to assess whether the associations changed when restricted to those who enrolled in 2005 or later.The authors note that the study is making assumptions about the relevant exposure windows - therefore the exposure window is not certain.

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Study Citation:	Niehoff, N.M., Gammon, M.D., Keil, A.P., Nichols, H.B., Engel, L.S., Sandler, D.P., White, A.J. (2019). Airborne mammary carcinogens and breast cancer risk in the Sister Study. Environment International 130:104897.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Breast cancer diagnosis (overall), tumor characteristics, and estrogen receptor positive (ER+) invasive breast cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5440630

Domain	Metric		Rating	Comments
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Women who reported a breast cancer diagnosis on the annual health updates or follow-up questionnaires were asked to provide additional diagnosis information, and to grant permission for the study to obtain medical records and pathology reports. Medical records were obtained for 81% of breast cancer diagnoses. Agreement between self-reported breast cancers and medical records was high (positive predictive value > 99%) (Sandler et al., 2017), so self-report was used when medical records were not available. Tumor characteristics (stage; histology; and estrogen receptor (ER) status) were abstracted from medical records, or self-reported.
	Metric 8:	Reporting Bias	High	A description of measured outcomes is reported. Effect estimates are reported with confidence intervals.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Covariates considered included age, race, BMI, residence type, education, and smoking status. Potential confounders were identified using DAGs and literature review. Appropriate considerations were made for potential confounders.
	Metric 10:	Covariate Characterization	Medium	”Most covariates were assessed by self-report at the baseline interview.””At baseline, women completed a computer-assisted telephone interview and written questionnaires.”Previous publications might describe whether the questionnaires were validated, but validation was not specified in this publication.
	Metric 11:	Co-exposure Counfounding	Medium	Co-exposures to other air pollutants were assessed, but at the census tract level.Multipollutant classification trees were used, which might provide useful qualitative information.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design (large prospective cohort) and analysis method (Cox proportional hazard single and multi-pollutant models accounting for potential confounders) were appropriate to assess the association between exposure and disease.
	Metric 13:	Statistical Power	Medium	The study had an adequate sample size (1975 cancer cases) and follow-up time (mean=8.4 years).
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to be conceptually reproducible.

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Study Citation:	Niehoff, N.M., Gammon, M.D., Keil, A.P., Nichols, H.B., Engel, L.S., Sandler, D.P., White, A.J. (2019). Airborne mammary carcinogens and breast cancer risk in the Sister Study. Environment International 130:104897.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Breast cancer diagnosis (overall), tumor characteristics, and estrogen receptor positive (ER+) invasive breast cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5440630

Domain	Metric	Rating	Comments
	Metric 15: Statistical Analysis	High	Hazard ratios and 95% confidence intervals (CIs) are reported "comparing index categories of exposure to exposures below the first quintile using Cox proportional hazards regression, with age as the time scale." The method of calculating the hazard ratios is transparent. The authors reported that "the proportional hazards assumption was evaluated by conducting a Wald test for an interaction between the continuous form of the air toxic measure and time." Censoring times and times at-risk are described.

Additional Comments: This was a well-conducted study of a large prospective cohort, but the measurement of exposure at the census-tract rather than the individual level is a limitation.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Sobel, W., Bond, G.G., Skowronski, B.J., Brownson, P.J., Cook, R.R. (1987). A soft tissue sarcoma case control study in a large multi-chemical manufacturing facility. Chemosphere 16(8-9):2095-2099.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	soft-tissue sarcoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1357737

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	From a pool of > 37,000 subjects who worked at least 1 year at chemical company between January 1940-December 1979, the study identified 14 people who died due to soft-cell sarcoma (via death certificate, medical records, or histopathology report). Referents were matched 9:1 with cases (126 matched controls).
	Metric 2:	Attrition	High	There was minimal subject exclusion from the analysis sample; one case could not be matched to controls and was excluded from analysis.
	Metric 3:	Comparison Group	High	Cases and controls were recruited from the same eligible population within the same time frame and matched on sex, race, year of birth and year of hire. Both cases and controls had to have worked ≥1 yr at the plant during the study period.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Work histories for cases and referents were coded to determine an individual's potential exposure to chemical of interest and reviewed by an industrial hygienist blinded to case status.
	Metric 5:	Exposure Levels	Low	Exposure was considered dichotomous, ever exposed or never exposed. There is no quantitative information on exposure levels or range of exposures.
	Metric 6:	Temporality	Low	Temporality of exposure and outcome is established. It is unclear if the interval between exposure and outcome is sufficient for soft tissue sarcoma outcomes.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	The soft-tissue sarcoma outcome was assessed by information provided by death certificates, medical records, and histopathology reports, but study authors did not report the proportions determined by each method.
	Metric 8:	Reporting Bias	High	All outcomes outlined were reported. Authors reported the number of cases and controls in the table. Maximum likelihood estimate ORs with respective 95 % confidence intervals were reported.
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Sobel, W., Bond, G.G., Skowronski, B.J., Brownson, P.J., Cook, R.R. (1987). A soft tissue sarcoma case control study in a large multi-chemical manufacturing facility. Chemosphere 16(8-9):2095-2099.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	soft-tissue sarcoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1357737

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Low	Controls were matched with cases on age, sex, year of hire and survival information. There is indirect evidence that the considerations were made to identify potential confounders through evaluation of medical records of cases and controls (various heritable syndromes, family history of cancer, history of lymphedema, steroids, throrotrast, foreign body implants, chronic extensive scarring, radiation therapy, and immunological defects). Identified confounders between cases and controls were not reported and it is unclear if adjustments for these confounders were included in the final analyses.
	Metric 10:	Covariate Characterization	High	Potential covariates were assessed through evaluation of work histories and medical records.
	Metric 11:	Co-exposure Counfounding	Low	The study documented 13 chemicals, known to be associated with soft-tissue sarcoma (according to NTP, 1983) that were used at the manufacturing facility at some point since 1940. The authors note that some individuals were exposed to multiple chemicals during their employment history and were counted multiple times in the analysis for different chemical exposures. Co-exposures to chemicals to not appear to be adjusted for in analysis.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Low	The study design was adequate to assess the association between exposure and the outcome of interest (soft-tissue sarcoma). The study authors noted they used programs developed by Rothman and Boice to calculate odds ratios with CI intervals; the statistical methods are not further described. The page containing the Rothman and Boice reference appears to be missing from the PDF (or the citation is missing).
	Metric 13:	Statistical Power	Low	Statistical power was not calculated. For 1,2-dichloroethane, there was one case and 6 controls included in the analysis, which was not adequate to detect and effect.
	Metric 14:	Reproducibility of Analyses	Low	The study calculated odd ratios, and 95% CIs were calculated using point estimates and chi from hypothesis testing. The study authors noted they used programs developed by Rothman and Boice to calculate odds ratios with 95% CIs; the statistical methods are not further described and there was no reference for the programs cited.
	Metric 15:	Statistical Analysis	Low	A description of analyses/assumptions was not reported.

Additional Comments: A case-control study of workers at a chemical production facility who worked at least 1 year between January 1940-December 1979 (n=37,000) investigated the incidence of deaths due to soft-tissue sarcoma. The study identified 14 people who died due to soft-tissue sarcoma (through death certificate, medical records, or histopathology reports). Cases were matched to controls based on sex, race, year of birth and year of hire. 13 chemicals, including 1,2-dichloroethane, associated with soft-tissue sarcoma were used at the facility; it does not appear that co-exposures were adjusted for in the analysis. Odds ratios and corresponding CIs were calculated. No significant association was found between exposure to 1,2-DCE and soft-tissue sarcoma.

Overall Quality Determination Medium

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Study Citation:	Sobel, W., Bond, G.G., Skowronski, B.J., Brownson, P.J., Cook, R.R. (1987). A soft tissue sarcoma case control study in a large multi-chemical manufacturing facility. Chemosphere 16(8-9):2095-2099.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	soft-tissue sarcoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1357737

Domain	Metric	Rating	Comments

* No biomarkers were identified for this evaluation.

Study Citation:	Sobel, W., Bond, G.G., Skowronski, B.J., Brownson, P.J., Cook, R.R. (1987). A soft tissue sarcoma case control study in a large multi-chemical manufacturing facility. Chemosphere 16(8-9):2095-2099.
Health Outcome(s):	Skin and Connective Tissue
Reported Health Effect(s):	soft-tissue sarcoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1357737

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	From a pool of > 37,000 subjects who worked at least 1 year at chemical company between January 1940-December 1979, the study identified 14 people who died due to soft-cell sarcoma (via death certificate, medical records, or histopathology report). Referents were matched 9:1 with cases (126 matched controls).
	Metric 2:	Attrition	High	There was minimal subject exclusion from the analysis sample; one case could not be matched to controls and was excluded from analysis.
	Metric 3:	Comparison Group	High	Cases and controls were recruited from the same eligible population within the same time frame and matched on sex, race, year of birth and year of hire. Both cases and controls had to have worked ≥1 yr at the plant during the study period.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Work histories for cases and referents were coded to determine an individual's potential exposure to chemical of interest and reviewed by an industrial hygienist blinded to case status.
	Metric 5:	Exposure Levels	Low	Exposure was considered dichotomous, ever exposed or never exposed. There is no quantitative information on exposure levels or range of exposures.
	Metric 6:	Temporality	Low	Temporality of exposure and outcome is established. It is unclear if the interval between exposure and outcome is sufficient for soft tissue sarcoma outcomes.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	The soft-tissue sarcoma outcome was assessed by information provided by death certificates, medical records, and histopathology reports, but study authors did not report the proportions determined by each method.
	Metric 8:	Reporting Bias	High	All outcomes outlined were reported. Authors reported the number of cases and controls in the table. Maximum likelihood estimate ORs with respective confidence intervals were reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	Controls were matched with cases on age, sex, year of hire and survival information. There is indirect evidence that that considerations were made to identify potential confounders through evaluation of medical records of cases and controls (various heritable syndromes, family history of cancer, history of lymphedema, steroids, throrotrast, foreign body implants, chronic extensive scarring, radiation therapy, and immunological defects). Identified confounders between cases and controls were not reported and it is unclear if adjustments for these confounders were included in the final analyses.

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Study Citation:	Sobel, W., Bond, G.G., Skowronski, B.J., Brownson, P.J., Cook, R.R. (1987). A soft tissue sarcoma case control study in a large multi-chemical manufacturing facility. Chemosphere 16(8-9):2095-2099.
Health Outcome(s):	Skin and Connective Tissue
Reported Health Effect(s):	soft-tissue sarcoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1357737

Domain	Metric		Rating	Comments
	Metric 10:	Covariate Characterization	High	Potential covariates were assessed through evaluation of work histories and medical records.
	Metric 11:	Co-exposure Counfounding	Low	The study documented 13 chemicals, known to be associated with soft-tissue sarcoma (according to NTP, 1983) that were used at the manufacturing facility at some point since 1940. The authors note that some individuals were exposed to multiple chemicals during their employment history and were counted multiple times in the analysis for different chemical exposures. Co-exposures to chemicals to not appear to be adjusted for in analysis.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Low	The study design was adequate to assess the association between exposure and the outcome of interest (soft-tissue sarcoma). The study authors noted they used programs developed by Rothman and Boice to calculate odds ratios with (95% CIs; the statistical methods are not further described. The page containing the Rothman and Boice reference appears to be missing from the PDF (or the citation is missing).
	Metric 13:	Statistical Power	Low	Statistical power was not calculated. For 1,2-dichloroethane, there was one case and 6 controls included in the analysis, which was not adequate to detect and effect.
	Metric 14:	Reproducibility of Analyses	Low	The study calculated odd ratios, and 95% CIs were calculated using point estimates and chi from hypothesis testing. The study authors noted they used programs developed by Rothman and Boice to calculate odds ratios with CI intervals; the statistical methods are not further described and there was no reference for the programs cited.
	Metric 15:	Statistical Analysis	Low	A description of analyses/assumptions was not reported.

Additional Comments: A case-control study of workers at a chemical production facility who worked at least 1 year between January 1940-December 1979 (n=37,000) investigated the incidence of deaths due to soft-tissue sarcoma. The study identified 14 people who died due to soft-tissue sarcoma (through death certificate, medical records, or histopathology reports). Cases were matched to controls based on sex, race, year of birth and year of hire. 13 chemicals, including 1,2-dichloroethane, associated with soft-tissue sarcoma were used at the facility; it does not appear that co-exposures were adjusted for in the analysis. Odds ratios and corresponding CIs were calculated. No significant association was found between exposure to 1,2-DCE and soft-tissue sarcoma.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Teta, M. J., Ott, M. G., Schnatter, A. R. (1991). An update of mortality due to brain neoplasms and other causes among employees of a petrochemical facility. Journal of Occupational Medicine 33(1):45-51.
Health Outcome(s):	Mortality
Reported Health Effect(s):	all cause mortality, gastrointestinal cancer mortality, respiratory system cancer mortality, kidney and other urinary organ cancer mortality, skin cancer mortality, brain cancer mortality, lymphatic and hematopoietic tissue cancer mortality, benign neoplasm mortality, heart disease mortality, and liver cirrhosis mortality.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200633, 1629047
HERO ID:	200633

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	The facility was described in some detail. All male employees working for one day or more between 1941 and 1983 were included. There may be some healthy worker effect in this population.
	Metric 2:	Attrition	High	Study authors reported that vital status was complete for 99% of the population, and death certificates were obtained for 99% of decedents.
	Metric 3:	Comparison Group	High	SMRs were calculated using age-, race-, and calendar year-specific mortality rates of males in the United States. All included employees were male.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	All employees were treated as exposed. Table 4 indicates that relatively few employees were employed in areas designated as 1,2-DCA work areas. There is potential for substantial exposure misclassification.
	Metric 5:	Exposure Levels	Low	All employed individuals were categorized as exposed, and the reference population was described as unexposed. This represents two levels of exposure. The distribution of exposure within the employed population is unclear.
	Metric 6:	Temporality	Medium	Employees were followed from 1950 (or date of first hire) through 1983. The relevant timing of exposure is not entirely clear; however, this represents a sufficiently long period of follow-up.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Mortality was tracked using company records, Social Security Administration records, and the National Death Index. Specific ICD codes and use of a nosologist were not described, but there was no evidence to suggest the method had poor validity.
	Metric 8:	Reporting Bias	High	SMRs were provided with confidence intervals in addition to observed and expected cases. The authors state they did not carry out regional specific SMRs due to the higher prevalence of neoplasms in the surrounding area.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	SMRs were restricted to males. Rates were age-, race-, and calendar period-specific. No consideration was made for smoking.
	Metric 10:	Covariate Characterization	Medium	Demographic information was obtained from employment records. This was not a validated method, but there was no evidence to suggest it was an invalid method.

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Study Citation:	Teta, M. J., Ott, M. G., Schnatter, A. R. (1991). An update of mortality due to brain neoplasms and other causes among employees of a petrochemical facility. Journal of Occupational Medicine 33(1):45-51.
Health Outcome(s):	Mortality
Reported Health Effect(s):	all cause mortality, gastrointestinal cancer mortality, respiratory system cancer mortality, kidney and other urinary organ cancer mortality, skin cancer mortality, brain cancer mortality, lymphatic and hematopoietic tissue cancer mortality, benign neoplasm mortality, heart disease mortality, and liver cirrhosis mortality.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200633, 1629047
HERO ID:	200633

Domain	Metric		Rating	Comments
	Metric 11:	Co-exposure Counfounding	Low	Several other occupational exposures linked to cancer mortality were present, including vinyl chloride, butanol, and other petrochemicals.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	This study design was appropriate for the research question. Authors utilized retrospective occupational cohort data to determine standardized mortality rates for cancer-specific mortalities.
	Metric 13:	Statistical Power	Medium	While power was not calculated, there were over 1350 deaths from 7849 employees which was adequate to detect robust effect estimates.
	Metric 14:	Reproducibility of Analyses	Low	Most details were provided; however, ICD codes used to determine and group cancer mortality diagnoses were not provided.
	Metric 15:	Statistical Analysis	High	No issues identified.

Additional Comments: This study utilized an occupational cohort to retrospectively evaluate elevated rates of cancer mortality among petrochemical plant workers. There were numerous potentially hazardous chemicals mentioned in the plant description which may lead to co-exposure. Additionally, it appears that only a moderate portion of workers may have been exposed to 1,2-DCA or worked in 1,2-DCA areas which may lead to some exposure misclassification and limit the study's ability to inform hazard on 1,2-DCA.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Cases in this case-control study were former Union Carbide Corporation (UCC) chemical plant employees in Texas City, Texas. Cases were identified through death certificate searches and tumor registries, and may have included individuals formerly employed at UCC whose cause of death was unknown to the company. Additionally, control deaths were stated to be pulled from corporate employee benefits department and through locally published obituary notices routinely screened by the medical department - it is possible to assume that cases were identified in a similar manner. The study identified cases of brain tumors by searching death certificates primarily, although tumor registries throughout the state of Texas were also searched. The study clarifies that it is possible that some cases were not found if they survived or died due to another cause - while this is likely to have impacted selection, there is no evidence that this would be differential by exposure status. Overall, there is limited information on the source population of workers from which cases were identified.
	Metric 2:	Attrition	Medium	Attrition is not discussed in the study, and outcome data appear to be complete. There was a large proportion of missing exposure data (roughly 50%) due to workers being employed in roles such as maintenance, where exposure to any chemical is possible but unknown. Analyses were run separately where these ”unknown” individuals were a) treated as exposed, b) treated as unexposed, or c) treated as unknown and thus excluded. The study only presents results for when these individuals were excluded but specifies that the first scenario resulted in increased exposure estimates for controls relative to cases.

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Study Citation:	Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
	Metric 3:	Comparison Group	Medium	The study identifies two series of control groups, selected from all former Union Carbide Corporation (UCC) employees. However, the total number of employees is not stated. Only those who were deceased were used as controls since they had known causes of death and could thus be verified as non-brain tumors. One group of controls excluded employees whose cause of death was due to any malignant neoplasm to allow for the possibility that a general chemical carcinogen may have been associated with cancers of other sites. The other group of controls included deaths from all causes; this included malignant neoplasms other than brain tumors. Both control groups had 80 male employees randomly selected from 450 deceased employees known to the company in June 1979. Control deaths were stated to be pulled from corporate employee benefits department and through locally published obituary notices routinely screened by the medical department - it is possible to assume that cases were identified in a similar manner. The study reports that cases were slightly more likely to have been employed for less than 10 years than controls - the study attributes this in part to the fact that employees whose deaths were known to the company were more likely to have worked for longer - regardless the mean number of years employed was similar between cases and controls. However, cases were more likely to have been terminated from their job for reasons other than death, disability, or retirement (quitting, being fired, etc.), were generally younger at hire, and were less likely to survive to their 70th birthday. None of these factors are controlled for in statistical analyses - however, since controls and cases were pulled from the same population, there is indirect evidence that the groups were similar.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was determined based on official employment records. Records included job title and department assignment codes for each employment from date of hire to date of termination. For each unique department code, UCC and NIOSH industrial hygienists identified principal chemicals used or produced at any time in the history of the plant and correlated those with individual departments. This assessment was not performed on a year-by-year basis due to concerns for recall bias for longer-term employees where less detailed records were kept. An employee was categorized as ”exposed” to 1,2-dichloroethane if they ever worked in a department associated with that chemical. An ”unknown” exposure group was also created to account for employees who had only worked in departments for which no specific chemical could be identified.
	Metric 5:	Exposure Levels	Low	The study does not report any quantitative information and only splits exposure into ”exposed”, ”unexposed”, and ”unknown”.
	Metric 6:	Temporality	High	In this study exposure is confirmed to occur before the outcome is measured. The study reports latency periods, with subjects dichotomized into less than 15 years of latency or more than 15 years of latency. The majority of cases and controls had a latency of greater than 15 years, which is sufficiently long for brain tumors.

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Study Citation:	Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Cases were identified through death certificate searches and partially through tumor registries in the state of Texas. Case validation was performed by NIOSH, and 5 different levels of confirmation were reported: 1) tissue specimen interpreted by the Armed Forces Institute of Pathology; 2) autopsy report; 3) histopathology report; 4) clinical diagnosis from hospital record; 5) dearth certificate diagnosis. Codes 1-3 were considered to be ”confirmed” cases of brain tumors, while 4-5 were considered unconfirmed. 5/21 cases were only evaluated using ”unconfirmed methods”, meaning there is likely a high amount of accuracy in roughly 75% of cases. While no case validation is reported for controls, the study specifies that only controls who had died and thus could be confirmed to be non-brain tumors were included.
	Metric 8:	Reporting Bias	Medium	All primary and secondary outcomes that are outlined in the methods are reported in the results. However, the only statistical outcome of their analysis were unadjusted p-values that were not reported and were just described qualitatively.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	The only statistical analysis performed were Mantel-Haenszel chi-squared tests, which did not allow for confounder adjustment. The study does not present a distribution of potential confounders by exposure status but by case/control status. Several variables, such as reason for termination, age at hire, and age at death were significantly different between cases and controls and were not accounted for in statistical modeling. The study explains that these differences are not likely to have any epidemiologic significance and appear to be relatively small differences.
	Metric 10:	Covariate Characterization	Medium	While the study does not explain where they obtained covariate information, it is reasonable to assume that they gathered the information from company records.
	Metric 11:	Co-exposure Counfounding	Low	The study assesses a wide range of other potential occupational co-exposures. While these co-exposures are not adjusted for in any statistical models, effect estimates are presented separately for benzene, diethyl sulfate, ethylene oxide, and vinyl chloride. The distribution of co-exposures across cases and controls is demonstrated to be mostly balanced by comparing proportions of exposed/unexposed between cases and controls. The only notable instance of imbalance is for benzene, where 11.1% of cases were exposed whereas 37.9% of all controls and 19.2% of non-neoplasm related controls were exposed.
Domain 5: Analysis				

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Study Citation:	Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	The study chose a case-control design, which was appropriate to study the rare disease of brain tumors and its association with occupational exposures. The only statistical analysis conducted is a Mantzel-Haenszel chi-squared test, but there is no reason to suggest that this would be inappropriate.
	Metric 13:	Statistical Power	Medium	The study does not calculate statistical power, but the number of cases (n=21) and controls (n=80 in each analysis) is likely sufficient to detect an effect.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to understand what was done and could be reproduced given access to the analytic data.
	Metric 15:	Statistical Analysis	High	The only statistical analysis conducted is a Mantel-Haenszel chi-squared test, and all assumptions were met. The statistical process is transparent.

Additional Comments: This case-control study pulled deceased former employees of the Union Carbide Corporation in Texas City, Texas. The study examined dichotomous exposure to a wide range of occupational exposures, including 1,2-dichloroethane, in relation to brain tumor cases. There is no quantitative estimate of exposure. The only statistical analysis in the study is a Mantel-Haenszel chi-squared test statistic and no statistically significant differences in exposure between cases and controls were observed. The fact that there are no effect estimates, no adjustment for confounders, and no quantitative exposure estimates limits the usefulness of this paper.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Cases in this case-control study were former Union Carbide Corporation (UCC) chemical plant employees in Texas City, Texas. Cases were identified through death certificate searches and tumor registries, and may have included individuals formerly employed at UCC whose cause of death was unknown to the company. Additionally, control deaths were stated to be pulled from corporate employee benefits department and through locally published obituary notices routinely screened by the medical department - it is possible to assume that cases were identified in a similar manner. The study identified cases of brain tumors by searching death certificates primarily, although tumor registries throughout the state of Texas were also searched. The study clarifies that it is possible that some cases were not found if they survived or died due to another cause - while this is likely to have impacted selection, there is no evidence that this would be differential by exposure status. Overall, there is limited information on the source population of workers from which cases were identified.
	Metric 2:	Attrition	Medium	Attrition is not discussed in the study, and outcome data appear to be complete. There was a large proportion of missing exposure data (roughly 50%) due to workers being employed in roles such as maintenance, where exposure to any chemical is possible but unknown. Analyses were run separately where these ”unknown” individuals were a) treated as exposed, b) treated as unexposed, or c) treated as unknown and thus excluded. The study only presents results for when these individuals were excluded but specifies that the first scenario resulted in increased exposure estimates for controls relative to cases.

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Study Citation:	Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
	Metric 3:	Comparison Group	Medium	The study identifies two series of control groups, selected from all former Union Carbide Corporation (UCC) employees. However, the total number of employees is not stated. Only those who were deceased were used as controls since they had known causes of death and could thus be verified as non-brain tumors. One group of controls excluded employees whose cause of death was due to any malignant neoplasm to allow for the possibility that a general chemical carcinogen may have been associated with cancers of other sites. The other group of controls included deaths from all causes; this included malignant neoplasms other than brain tumors. Both control groups had 80 male employees randomly selected from 450 deceased employees known to the company in June 1979. Control deaths were stated to be pulled from corporate employee benefits department and through locally published obituary notices routinely screened by the medical department - it is possible to assume that cases were identified in a similar manner. The study reports that cases were slightly more likely to have been employed for less than 10 years than controls - the study attributes this in part to the fact that employees whose deaths were known to the company were more likely to have worked for longer - regardless the mean number of years employed was similar between cases and controls. However, cases were more likely to have been terminated from their job for reasons other than death, disability, or retirement (quitting, being fired, etc.), were generally younger at hire, and were less likely to survive to their 70th birthday. None of these factors are controlled for in statistical analyses - however, since controls and cases were pulled from the same population, there is indirect evidence that the groups were similar.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was determined based on official employment records. Records included job title and department assignment codes for each employment from date of hire to date of termination. For each unique department code, UCC and NIOSH industrial hygienists identified principal chemicals used or produced at any time in the history of the plant and correlated those with individual departments. This assessment was not performed on a year-by-year basis due to concerns for recall bias for longer-term employees where less detailed records were kept. An employee was categorized as ”exposed” to 1,2-dichloroethane if they ever worked in a department associated with that chemical. An ”unknown” exposure group was also created to account for employees who had only worked in departments for which no specific chemical could be identified.
	Metric 5:	Exposure Levels	Low	The study does not report any quantitative information and only splits exposure into ”exposed”, ”unexposed”, and ”unknown”.
	Metric 6:	Temporality	High	In this study exposure is confirmed to occur before the outcome is measured. The study reports latency periods, with subjects dichotomized into less than 15 years of latency or more than 15 years of latency. The majority of cases and controls had a latency of greater than 15 years, which is sufficiently long for brain tumors.

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Study Citation:	Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Cases were identified through death certificate searches and partially through tumor registries in the state of Texas. Case validation was performed by NIOSH, and 5 different levels of confirmation were reported: 1) tissue specimen interpreted by the Armed Forces Institute of Pathology; 2) autopsy report; 3) histopathology report; 4) clinical diagnosis from hospital record; 5) dearth certificate diagnosis. Codes 1-3 were considered to be ”confirmed” cases of brain tumors, while 4-5 were considered unconfirmed. 5/21 cases were only evaluated using ”unconfirmed methods”, meaning there is likely a high amount of accuracy in roughly 75% of cases. While no case validation is reported for controls, the study specifies that only controls who had died and thus could be confirmed to be non-brain tumors were included.
	Metric 8:	Reporting Bias	Medium	All primary and secondary outcomes that are outlined in the methods are reported in the results. However, the only statistical outcome of their analysis were unadjusted p-values that were not reported and were just described qualitatively.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	The only statistical analysis performed were Mantel-Haenszel chi-squared tests, which did not allow for confounder adjustment. The study does not present a distribution of potential confounders by exposure status but by case/control status. Several variables, such as reason for termination, age at hire, and age at death were significantly different between cases and controls and were not accounted for in statistical modeling. The study explains that these differences are not likely to have any epidemiologic significance and appear to be relatively small differences.
	Metric 10:	Covariate Characterization	Medium	While the study does not explain where they obtained covariate information, it is reasonable to assume that they gathered the information from company records.
	Metric 11:	Co-exposure Counfounding	Low	The study assesses a wide range of other potential occupational co-exposures. While these co-exposures are not adjusted for in any statistical models, effect estimates are presented separately for benzene, diethyl sulfate, ethylene oxide, and vinyl chloride. The distribution of co-exposures across cases and controls is demonstrated to be mostly balanced by comparing proportions of exposed/unexposed between cases and controls. The only notable instance of imbalance is for benzene, where 11.1% of cases were exposed whereas 37.9% of all controls and 19.2% of non-neoplasm related controls were exposed.
Domain 5: Analysis				

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Study Citation:	Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	The study chose a case-control design, which was appropriate to study the rare disease of brain tumors and its association with occupational exposures. The only statistical analysis conducted is a Mantzel-Haenszel chi-squared test, but there is no reason to suggest that this would be inappropriate.
	Metric 13:	Statistical Power	Medium	The study does not calculate statistical power, but the number of cases (n=21) and controls (n=80 in each analysis) is likely sufficient to detect an effect.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to understand what was done and could be reproduced given access to the analytic data.
	Metric 15:	Statistical Analysis	High	The only statistical analysis conducted is a Mantel-Haenszel chi-squared test, and all assumptions were met. The statistical process is transparent.

Additional Comments: This case-control study pulled deceased former employees of the Union Carbide Corporation in Texas City, Texas. The study examined dichotomous exposure to a wide range of occupational exposures, including 1,2-dichloroethane, in relation to brain tumor cases. There is no quantitative estimate of exposure. The only statistical analysis in the study is a Mantel-Haenszel chi-squared test statistic and no statistically significant differences in exposure between cases and controls were observed. The fact that there are no effect estimates, no adjustment for confounders, and no quantitative exposure estimates limits the usefulness of this paper.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	Urinary system cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	Urinary system cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	Urinary system cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Immune/Hematological
Reported Health Effect(s):	Lymphatic and hematopoietic tissue cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Health Outcome(s):	Immune/Hematological
Reported Health Effect(s):	Lymphatic and hematopoietic tissue cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Health Outcome(s):	Immune/Hematological
Reported Health Effect(s):	Lymphatic and hematopoietic tissue cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
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Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

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Health Outcome(s):	Other cancers (not specified)
Reported Health Effect(s):	Other cancers (not specified)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
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	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
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Domain 3: Outcome Assessment				

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Health Outcome(s):	Other cancers (not specified)
Reported Health Effect(s):	Other cancers (not specified)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
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	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Other cancers (not specified)
Reported Health Effect(s):	Other cancers (not specified)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Mortality
Reported Health Effect(s):	All-cause mortality
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Vital status was tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Medium	Death rates among unit employees were compared to death rates in the U.S. population adjusted for age and gender. Demographics of the exposed workers are not provided; therefore, it is not clear whether additional adjustment for race may have been appropriate. No justification is provided for the choice of the entire U.S. population as the comparison group. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis. Additional analyses are conducted limiting workers to those with the greatest likelihood of exposure (i.e., those working in jobs with high likelihood of contact with chemicals for more than a year, those working for the full year of 1979 during which chemical exposures were most frequently reported); these smaller groups are also compared to the unexposed general population.
	Metric 6:	Temporality	High	Temporality was established due to the longitudinal design and the use of mortality as the outcome. Exposures occurred between 1979 and 1987 and follow-up for vital status was conducted through 2003.
Domain 3: Outcome Assessment				

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Mortality
Reported Health Effect(s):	All-cause mortality
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Medium	The study did not provide information on how mortality was assessed either in the exposed population or in the comparison population; use of death certificates is implied but not stated.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected deaths are reported, but SIRs and 95% confidence intervals are not provided.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Comparisons of observed versus expected deaths were adjusted for age and gender. Demographics of the exposed workers are not provided; therefore, it is not clear whether additional adjustment for race may have been appropriate.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records or death records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed deaths among a population of exposed workers compared to expected deaths among the U.S. population, adjusted for age and gender.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected deaths; no SIR was provided. Expected death rates were adjusted for age and gender.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Mortality
Reported Health Effect(s):	All-cause mortality
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	All cancer (excluding non-melanoma skin cancer), digestive system cancer, colorectal cancer, respiratory cancer, prostate cancer, urinary system cancer, lymphatic and hematopoietic tissue cancer, other cancers (not specified)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	All cancer (excluding non-melanoma skin cancer), digestive system cancer, colorectal cancer, respiratory cancer, prostate cancer, urinary system cancer, lymphatic and hematopoietic tissue cancer, other cancers (not specified)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	All cancer (excluding non-melanoma skin cancer), digestive system cancer, colorectal cancer, respiratory cancer, prostate cancer, urinary system cancer, lymphatic and hematopoietic tissue cancer, other cancers (not specified)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Gastrointestinal
Reported Health Effect(s):	Digestive system cancer, colorectal cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Gastrointestinal
Reported Health Effect(s):	Digestive system cancer, colorectal cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Gastrointestinal
Reported Health Effect(s):	Digestive system cancer, colorectal cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Lung/Respiratory
Reported Health Effect(s):	Respiratory cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Health Outcome(s):	Lung/Respiratory
Reported Health Effect(s):	Respiratory cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Lung/Respiratory
Reported Health Effect(s):	Respiratory cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Prostate cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Prostate cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Prostate cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Male workers who had ever been assigned to the chlorohydrin unit between 1 January 1940 and 31 December 1967 at Union Carbide's South Charleston plant were enrolled and matched to the US National Death Index. Status on 5 workers could not be identified. Information on how workers were matched to death index was not specified.
	Metric 2:	Attrition	Medium	Rate of inclusion/participation was very high, as records were able to be matched for 98% of participants. Medium rating given because information on how participants whose vital status was not known was not specified.
	Metric 3:	Comparison Group	Uninformative	Unacceptable rating given because SMRs were calculated based on expected deaths from a reference population matched on sex, but not age.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Exposure was assessed based on duration of work in the plant. No information is provided on exposure levels, and a JEM was not used.
	Metric 5:	Exposure Levels	Uninformative	No information provided on levels of exposure.
	Metric 6:	Temporality	High	Temporality is well established; person-years stopped accumulating in 1967 and outcome was assessed beginning at that time.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar period, and interval since assignments, but distribution of these covariates was not reported.
	Metric 10:	Covariate Characterization	Medium	Information on covariate characterization not provided, but the selected covariates (age, calendar period, and interval since assignments) were likely extracted from employee records and unlikely to be largely problematic
	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.

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Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
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Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Study design was appropriate for the research method. Statistical methods were also appropriate.
	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.
	Metric 14:	Reproducibility of Analyses	Medium	Methods are well-enough described that study could be adequately reproduced.
	Metric 15:	Statistical Analysis	High	SMRs calculated based on US general population mortality for white males through 1988. RRs were ”evaluated over levels of duration of assignment to the chlorohydrin unit, stratified by age, calendar year, and interval since first assignment to the chlorohydrin unit”.

Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
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Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Male workers who had ever been assigned to the chlorohydrin unit between 1 January 1940 and 31 December 1967 at Union Carbide's South Charleston plant were enrolled and matched to the US National Death Index. Status on 5 workers could not be identified. Information on how workers were matched to death index was not specified.
	Metric 2:	Attrition	Medium	Rate of inclusion/participation was very high, as records were able to be matched for 98% of participants. Medium rating given because information on how participants whose vital status was not known was not specified.
	Metric 3:	Comparison Group	Uninformative	Unacceptable rating given because SMRs were calculated based on expected deaths from a reference population matched on sex, but not age.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Exposure was assessed based on duration of work in the plant. No information is provided on exposure levels, and a JEM was not used.
	Metric 5:	Exposure Levels	Uninformative	No information provided on levels of exposure.
	Metric 6:	Temporality	High	Temporality is well established; person-years stopped accumulating in 1967 and outcome was assessed beginning at that time.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar period, and interval since assignments, but distribution of these covariates was not reported.
	Metric 10:	Covariate Characterization	Medium	Information on covariate characterization not provided, but the selected covariates (age, calendar period, and interval since assignments) were likely extracted from employee records and unlikely to be largely problematic
	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.
Domain 5: Analysis				

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Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
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Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Study design was appropriate for the research method. Statistical methods were also appropriate.
	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.
	Metric 14:	Reproducibility of Analyses	Medium	Methods are well-enough described that study could be adequately reproduced.
	Metric 15:	Statistical Analysis	High	SMRs calculated based on US general population mortality for white males through 1988. RRs were ”evaluated over levels of duration of assignment to the chlorohydrin unit, stratified by age, calendar year, and interval since first assignment to the chlorohydrin unit”.

Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
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	Metric 2:	Attrition	Medium	Rate of inclusion/participation was very high, as records were able to be matched for 98% of participants. Medium rating given because information on how participants whose vital status was not known was not specified.
	Metric 3:	Comparison Group	Uninformative	Unacceptable rating given because SMRs were calculated based on expected deaths from a reference population matched on sex, but not age.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Exposure was assessed based on duration of work in the plant. No information is provided on exposure levels, and a JEM was not used.
	Metric 5:	Exposure Levels	Uninformative	No information provided on levels of exposure.
	Metric 6:	Temporality	High	Temporality is well established; person-years stopped accumulating in 1967 and outcome was assessed beginning at that time.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar period, and interval since assignments, but distribution of these covariates was not reported.
	Metric 10:	Covariate Characterization	Medium	Information on covariate characterization not provided, but the selected covariates (age, calendar period, and interval since assignments) were likely extracted from employee records and unlikely to be largely problematic
	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.
Domain 5: Analysis				

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Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Study design was appropriate for the research method. Statistical methods were also appropriate.
	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.
	Metric 14:	Reproducibility of Analyses	Medium	Methods are well-enough described that study could be adequately reproduced.
	Metric 15:	Statistical Analysis	High	SMRs calculated based on US general population mortality for white males through 1988. RRs were ”evaluated over levels of duration of assignment to the chlorohydrin unit, stratified by age, calendar year, and interval since first assignment to the chlorohydrin unit”.

Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

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Domain 1: Study Participation				
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	Metric 2:	Attrition	Medium	Rate of inclusion/participation was very high, as records were able to be matched for 98% of participants. Medium rating given because information on how participants whose vital status was not known was not specified.
	Metric 3:	Comparison Group	Uninformative	Unacceptable rating given because SMRs were calculated based on expected deaths from a reference population matched on sex, but not age.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Exposure was assessed based on duration of work in the plant. No information is provided on exposure levels, and a JEM was not used.
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	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar period, and interval since assignments, but distribution of these covariates was not reported.
	Metric 10:	Covariate Characterization	Medium	Information on covariate characterization not provided, but the selected covariates (age, calendar period, and interval since assignments) were likely extracted from employee records and unlikely to be largely problematic
	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.
Domain 5: Analysis				

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Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
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Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Study design was appropriate for the research method. Statistical methods were also appropriate.
	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.
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Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

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Domain 2: Exposure Characterization				
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Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar period, and interval since assignments, but distribution of these covariates was not reported.
	Metric 10:	Covariate Characterization	Medium	Information on covariate characterization not provided, but the selected covariates (age, calendar period, and interval since assignments) were likely extracted from employee records and unlikely to be largely problematic
	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.
Domain 5: Analysis				

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Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

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Domain 5: Analysis				

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Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

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Domain 5: Analysis				

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Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Study design was appropriate for the research method. Statistical methods were also appropriate.
	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.
	Metric 14:	Reproducibility of Analyses	Medium	Methods are well-enough described that study could be adequately reproduced.
	Metric 15:	Statistical Analysis	High	SMRs calculated based on US general population mortality for white males through 1988. RRs were ”evaluated over levels of duration of assignment to the chlorohydrin unit, stratified by age, calendar year, and interval since first assignment to the chlorohydrin unit”.

Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Male workers who had ever been assigned to the chlorohydrin unit between 1 January 1940 and 31 December 1967 at Union Carbide's South Charleston plant were enrolled and matched to the US National Death Index. Status on 5 workers could not be identified. Information on how workers were matched to death index was not specified.
	Metric 2:	Attrition	Medium	Rate of inclusion/participation was very high, as records were able to be matched for 98% of participants. Medium rating given because information on how participants whose vital status was not known was not specified.
	Metric 3:	Comparison Group	Uninformative	Unacceptable rating given because SMRs were calculated based on expected deaths from a reference population matched on sex, but not age.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Exposure was assessed based on duration of work in the plant. No information is provided on exposure levels, and a JEM was not used.
	Metric 5:	Exposure Levels	Uninformative	No information provided on levels of exposure.
	Metric 6:	Temporality	High	Temporality is well established; person-years stopped accumulating in 1967 and outcome was assessed beginning at that time.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar period, and interval since assignments, but distribution of these covariates was not reported.
	Metric 10:	Covariate Characterization	Medium	Information on covariate characterization not provided, but the selected covariates (age, calendar period, and interval since assignments) were likely extracted from employee records and unlikely to be largely problematic
	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.
Domain 5: Analysis				

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Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Study design was appropriate for the research method. Statistical methods were also appropriate.
	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.
	Metric 14:	Reproducibility of Analyses	Medium	Methods are well-enough described that study could be adequately reproduced.
	Metric 15:	Statistical Analysis	High	SMRs calculated based on US general population mortality for white males through 1988. RRs were ”evaluated over levels of duration of assignment to the chlorohydrin unit, stratified by age, calendar year, and interval since first assignment to the chlorohydrin unit”.

Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Bove, F. J. (1996). Public drinking water contamination and birthweight, prematurity, fetal deaths, and birth defects. Toxicology and Industrial Health 12(2):255-266.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	200239

Domain	Metric	Rating	Comments
Domain 1: Study Participation			
Metric 1:	Participant Selection	Medium	This cross-sectional study (n=80,938) included all registered singleton live births and fetal deaths (>20 weeks' gestation) in 1985-88 in 75 New Jersey towns located in 4 counties with "some" water supplies contaminated with substances of interest and where: (i) residents were "mostly" served by public water systems; and (ii) births occurred "mostly" in state. Estimated proportions of residents served by public water systems, and of pregnancies/births captured, were not described. However, the inclusion of all eligible registered births, fetal deaths, and birth defects, as well as the selection of towns without knowledge of birth outcome prevalence, limited the likelihood of selection bias.
Metric 2:	Attrition	Medium	All registered births and fetal deaths were included. Attrition due to missing values for multiple variables was not quantified and is therefore uncertain. However, attrition was likely modest as the proportion of missing values for individual variables was relatively low: (i) ~6% of subjects were excluded from analyses of outcomes such as preterm birth due to invalid or missing gestational ages; and (ii) other covariates evaluated as confounders had up to 4.9% missing values.
Metric 3:	Comparison Group	High	After excluding plural pregnancies and chromosomal abnormalities, all registered live births during the study period in the areas included without the outcomes of interest were included in the comparison group. This comprehensive approach limited the potential for bias. Chromosomal abnormalities were not included as outcomes as they were not hypothesized to be associated with the exposures under study but were appropriately excluded given their uncertain etiology.
Domain 2: Exposure Characterization			

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Study Citation:	Bove, F. J. (1996). Public drinking water contamination and birthweight, prematurity, fetal deaths, and birth defects. Toxicology and Industrial Health 12(2):255-266.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	200239

Domain	Metric		Rating	Comments
	Metric 4:	Measurement of Exposure	Medium	Along with several other contaminants, residential drinking water exposure to 1,2-dichloroethane (as well as 1,1,1-trichloroethane and 'total dichloroethylenes') – was assigned based on maternal town of residence at birth. Exposure estimates were calculated using the average of water company sampling reports during the first trimester (for birth defects and fetal death) or the duration of pregnancy (for other outcomes). Detection limits and data availability were not specified in detail but were described as below 1 ppb, with reporting compliance >85%. A minimum of 1 sample per 6-month interval was required; variability in the number of measures available across water systems and towns was not described. Additional sources of measurement error included: changes in residence during pregnancy; water from alternate sources (ex. private wells, bottles, workplaces); variability in residential contaminant levels vs measured samples; unknown levels of tap water intake; and errors in estimated dermal and inhalation exposure while bathing or showering. While the extent of exposure misclassification is uncertain, there is no evidence to suggest it was differential rather than random.
	Metric 5:	Exposure Levels	Medium	Due to the high proportion of measures below detection limits, analyses relating exposure to health outcomes used only 2 categories for each of the chlorinated solvents of interest: cutoffs close to detection limits were used to define elevated exposure. Proportions defined as having elevated exposure was low (1.8% had 1,1-dichloroethylene ≥1 ppb). An important concern is that relatively low levels of exposure to these contaminants from sources other than residential drinking water, for which data were not available, could potentially have resulted in considerable misclassification.
	Metric 6:	Temporality	High	Exposure levels were assigned based on contaminant exposures estimated during: (i) the first trimester for analyses of birth defects and fetal deaths; and (ii) the duration of pregnancy for other pregnancy outcomes.

Domain 3: Outcome Assessment

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Study Citation:	Bove, F. J. (1996). Public drinking water contamination and birthweight, prematurity, fetal deaths, and birth defects. Toxicology and Industrial Health 12(2):255-266.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	200239

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcomes included measures of birthweight (continuous among term births, low term birthweight, very low birthweight), prematurity, fetal death, and congenital anomalies in live births or fetal deaths. The anomalies analyzed included defects of the central nervous system, neural tube, oral cleft, total cardiac, major cardiac, ventricular septum, and any surveillance defect excluding chromosomal defects. All outcomes were identified using birth certificates, fetal death certificates (>20 weeks' gestation), and the NJ congenital birth defect registry (ICD codes provided). These registry data are likely to be sufficiently valid for late pregnancy outcomes. However, their limited ability to capture early pregnancy losses is a weakness. The sample included only 594 fetal deaths (less than 1% of the >80,0000 sample). Typical estimates are that 10-20%, of recognized pregnancies ending in losses. Moreover, developmental defects contributing to early pregnancy losses were also not captured. A further limitation is that that potentially etiologically heterogeneous preterm birth types were analyzed together, as these data did not distinguish premature rupture of membranes vs idiopathic prematurity.
	Metric 8:	Reporting Bias	Medium	Models were constructed only for contaminants with associations > 1.0, and tables included only associations with odds ratios ≥1.5. No clear rationale was provided. Several positive odds ratios below the 1.5 cutoff were described in the results text (without confidence intervals), but no null/negative odds ratios were presented or described.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Potential confounding by maternal race, education, parity, and prior pregnancy loss, along with infant sex (for birth outcomes) and adequacy of prenatal care, was examined. Gestational age was addressed by analyzing birthweight among full term births, term low birth weight, and small size for gestational age. Only fully adjusted models were presented. In a companion case-control study (with low participation rates), adjustment for other variables not available on birth certificates (ex. maternal smoking, occupational exposures, medical history, and gestational weight gain) did not influence associations with other studied contaminants. This separate study reduces concerns for important confounding bias, but confounding cannot be ruled out.
	Metric 10:	Covariate Characterization	Medium	Data on covariates came from registry data: birth certificates, fetal death certificates, and the NJ congenital birth defects registry.
	Metric 11:	Co-exposure Counfounding	Medium	Co-exposure confounding by drinking water trihalomethane concentrations was evaluated. There was no evidence to suggest substantial confounding by this or other co-exposures.
Domain 5: Analysis				

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Study Citation:	Bove, F. J. (1996). Public drinking water contamination and birthweight, prematurity, fetal deaths, and birth defects. Toxicology and Industrial Health 12(2):255-266.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	200239

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Methods were appropriate. The study used logistic regression models to estimate odds ratios and confidence intervals for dichotomous outcomes, and linear regression for analysis of continuous birth weight.
	Metric 13:	Statistical Power	Medium	Statistical power was likely to have been limited as a consequence of the small proportion of the sample defined as having "elevated" residential water concentrations of the chemicals of interest. The range of exposure examined was limited, as cutoffs for elevated levels were close to the detection limits of 1 ppb. In addition, for most birth defect outcomes, fewer than 10 cases had elevated exposure.
	Metric 14:	Reproducibility of Analyses	Medium	The authors clearly described steps used to estimate exposure-outcome associations, including exposure category cutoffs and criteria for confounding. However, many results were not shown as tables included odds ratios ≥1.5.
	Metric 15:	Statistical Analysis	High	The authors estimated coefficients, odds ratios and 95% confidence intervals using adequate methods. Confounding was based on 15% change-in-estimate comparing nested models. Effect modification (ex by infant sex) was not evaluated as there was no a priori evidence to suggest such analyses at that time.

Additional Comments: This study analyzed the association between estimated residential drinking water concentrations of several chlorinated solvents including 1,2-dichloroethane (as well as 1,1,1-trichloroethane; ∑[trans-1,2-dichloroethylene and 1,1-dichloroethylene]) and pregnancy outcomes (size at birth, prematurity, fetal deaths, and congenital birth defects). The sample included more than 80,000 births during 1985-88 for residents of 75 towns in NJ using public water system records to estimate exposure during gestation, and registry data (birth certificate, fetal death certificates for pregnancies >20 weeks, state birth defect registry) to characterize outcomes. Strengths included the large sample size and inclusion of all eligible registered births and fetal deaths in the study period. A critical concern is the inability to capture early fetal deaths and any related malformations (1% of the sample had fetal deaths vs typical estimates of >10%). An important limitation was the low percentage of the sample with detectable (> 1ppb) concentrations of these contaminants (<1% to 6.2%). Small numbers for birth defect outcomes also limited power. Exposure misclassification (ex. drinking water from wells/ work/ bottles, changes in residence, exposure from other sources) is also a concern. However, such misclassification was likely non-differential, and thus more likely to under- vs. to over-estimate associations.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Bove, F. J., Fulcomer, M. C., Klotz, J. B., Esmart, J., Dufficy, E. M., Savrin, J. E. (1995). Public drinking water contamination and birth outcomes. American Journal of Epidemiology 141(9):850-862.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	194932

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	This semi-ecological study (n=80,938) included all registered singleton live births and fetal deaths (>20 weeks) in 1985-88 in 75 New Jersey towns located in 4 counties with "some" water supplies contaminated with substances of interest and where: (i) residents were "mostly" served by public water systems; and (ii) births occurred "mostly" in state. Estimated proportions of residents served by public water systems, and of pregnancies/births captured, were not described. However, the inclusion of all eligible registered births, fetal deaths, and birth defects, as well as the selection of towns without knowledge of birth outcome prevalence, limited the likelihood of selection bias.
	Metric 2:	Attrition	Medium	All registered births and fetal deaths were included. Attrition due to missing values for multiple variables was not quantified and is therefore uncertain. However, attrition was likely modest as the proportion of missing values for individual variables was relatively low: (i) ~6% of subjects were excluded from analyses of outcomes such as preterm birth due to invalid or missing gestational ages; and (ii) other covariates evaluated as confounders had up to 4.9% missing values.
	Metric 3:	Comparison Group	High	After excluding plural pregnancies and chromosomal abnormalities, all registered live births during the study period in the areas included without the outcomes of interest were included in the comparison group. This comprehensive approach limited the potential for bias. Chromosomal abnormalities were not included as outcomes as they were not hypothesized to be associated with the exposures under study but were appropriately excluded given their uncertain etiology.
Domain 2: Exposure Characterization				

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Study Citation:	Bove, F. J., Fulcomer, M. C., Klotz, J. B., Esmart, J., Dufficy, E. M., Savrin, J. E. (1995). Public drinking water contamination and birth outcomes. American Journal of Epidemiology 141(9):850-862.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	194932

Domain	Metric		Rating	Comments
	Metric 4:	Measurement of Exposure	Medium	Along with several other contaminants, residential drinking water exposure to 1,2-dichloroethane (as well as 1,1,1-trichloroethane and 'total dichloroethylenes') was assigned based on maternal town of residence at birth. Exposure estimates were calculated using the average of water company sampling reports during the first trimester (for birth defects and fetal death) or the duration of pregnancy (for other outcomes). Detection limits and data availability were not specified in detail but were described as below 1 ppb, with reporting compliance >85%. A minimum of 1 sample per 6-month interval was required; variability in the number of measures available across water systems and towns was not described. Additional sources of measurement error included: changes in residence during pregnancy; water from alternate sources (ex. private wells, bottles, workplaces); variability in residential contaminant levels vs measured samples; unknown levels of tap water intake; and errors in estimated dermal and inhalation exposure while bathing or showering. While the extent of exposure misclassification is uncertain, there is no evidence to suggest it was differential rather than random.
	Metric 5:	Exposure Levels	Low	Due to the high proportion of measures below detection limits, analyses relating exposure to health outcomes used only 2 categories for each of the three chemicals of interest: cutoffs close to detection limits were used to define elevated exposure. Proportions defined as having elevated exposure were low (1.8% had 1,1-dichloroethylene ≥1 ppb). An important concern is that relatively low levels of exposure to this contaminant from sources other than residential drinking water, for which data were not available, could potentially have resulted in considerable misclassification.
	Metric 6:	Temporality	High	Exposure levels were assigned based on contaminant exposures estimated during: (i) the first trimester for analyses of birth defects and fetal deaths; and (ii) the duration of pregnancy for other pregnancy outcomes.

Domain 3: Outcome Assessment

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Study Citation:	Bove, F. J., Fulcomer, M. C., Klotz, J. B., Esmart, J., Dufficy, E. M., Savrin, J. E. (1995). Public drinking water contamination and birth outcomes. American Journal of Epidemiology 141(9):850-862.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	194932

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcomes included measures of birthweight (continuous among term births, low term birthweight, very low birthweight), prematurity, fetal death, and congenital anomalies in live births or fetal deaths. The anomalies analyzed included defects of the central nervous system, neural tube, oral cleft, total cardiac, major cardiac, ventricular septum, and any surveillance defect excluding chromosomal defects. All outcomes were identified using birth certificates, fetal death certificates (>20 weeks' gestation), and the NJ congenital birth defect registry (ICD codes provided). These registry data are likely to be sufficiently valid for late pregnancy outcomes. However, their limited ability to capture early pregnancy losses is a weakness. The sample included only 594 fetal deaths (less than 1% of the >80,0000 sample). Typical estimates are that 10-20%, of recognized pregnancies ending in losses. Moreover, developmental defects contributing to early pregnancy losses were also not captured. A further limitation is that that potentially etiologically heterogeneous preterm birth types were analyzed together, as these data did not distinguish premature rupture of membranes vs idiopathic prematurity.
	Metric 8:	Reporting Bias	Low	Models were constructed only for contaminants with associations > 1.0, and tables included only associations with odds ratios ≥1.5. No clear rationale was provided. Several positive odds ratios below the 1.5 cutoff were described in the results text (without confidence intervals), but no null/negative odds ratios were presented or described.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Potential confounding by maternal race, education, parity, and prior pregnancy loss, along with infant sex (for birth outcomes) and adequacy of prenatal care, was examined. Gestational age was addressed by analyzing birthweight among full term births, term low birth weight, and small size for gestational age. Only fully adjusted models were presented. In a companion case-control study (with low participation rates), adjustment for other variables not available on birth certificates (ex. maternal smoking, occupational exposures, medical history, and gestational weight gain) did not influence associations with other studied contaminants. This separate study reduces concerns for important confounding bias, but confounding cannot be ruled out.
	Metric 10:	Covariate Characterization	Medium	Data on covariates came from registry data: birth certificates, fetal death certificates, and the NJ congenital birth defects registry.
	Metric 11:	Co-exposure Counfounding	Medium	Co-exposure confounding by drinking water trihalomethane concentrations was evaluated. There was no evidence to suggest substantial confounding by this or other co-exposures.
Domain 5: Analysis				

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Study Citation:	Bove, F. J., Fulcomer, M. C., Klotz, J. B., Esmart, J., Dufficy, E. M., Savrin, J. E. (1995). Public drinking water contamination and birth outcomes. American Journal of Epidemiology 141(9):850-862.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	194932

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Methods were appropriate. The study used logistic regression models to estimate odds ratios and confidence intervals for dichotomous outcomes, and linear regression for analysis of continuous birth weight.
	Metric 13:	Statistical Power	Low	Statistical power was likely to have been limited as a consequence of the small proportion of the sample defined as having "elevated" residential water concentrations of the chemicals of interest. The range of exposure examined was limited, as cutoffs for elevated levels were close to the detection limits of 1 ppb. In addition, for most birth defect outcomes, fewer than 10 cases had elevated exposure. However, the authors emphasized the magnitude of associations rather than statistical significance and presented multiple confidence intervals to aid interpretation of the precision of estimates (50%, 90% and 99%).
	Metric 14:	Reproducibility of Analyses	Medium	The authors clearly described steps used to estimate exposure-outcome associations, including exposure category cutoffs and criteria for confounding. However, many results were not shown as tables included odds ratios ≥1.5.
	Metric 15:	Statistical Analysis	High	The authors estimated coefficients, odds ratios and confidence intervals using adequate methods. Confounding was based on 15% change-in-estimate comparing nested models. Effect modification (ex by infant sex) was not evaluated as there was no a priori evidence to suggest such analyses at that time.

Additional Comments: This study analyzed the association between estimated residential drinking water concentrations of several chlorinated solvents including 1,2-dichloroethane (as well as 1,1,1-trichloroethane and the ∑[trans-1,2-dichloroethylene & 1,1-dichloroethylene]) and pregnancy outcomes (size at birth, prematurity, fetal deaths, and congenital birth defects). The sample included more than 80,000 births during 1985-88 for residents of 75 towns in NJ using public water system records to estimate exposure during gestation, and registry data (birth certificate, fetal death certificates for pregnancies >20 weeks' gestation, state birth defect registry) to characterize outcomes. Strengths included the large sample size and inclusion of all eligible registered births and fetal deaths in the study period. A critical concern is the inability to capture early fetal deaths and any related malformations (1% of the sample had fetal deaths vs typical estimates of >10%). An important limitation was the low percentage of the sample with detectable (> 1ppb) concentrations of this solvent (<2%), which likely limited power. Small numbers for birth defect outcomes also limited power. Exposure misclassification (ex. drinking water from wells/ work/ bottles, changes in residence, exposure from other sources) is also a concern. However, such misclassification was likely non-differential, and thus more likely to under- vs. to over-estimate associations.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Bowler, R.M., Gysens, S., Hartney, C. (2003). Neuropsychological effects of ethylene dichloride exposure. NeuroToxicology 24(4-5):553-562.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Wechsler Adult Intelligence Scale III (WAIS-III), Wechsler Memory Scale III (WMS-III), Boston Naming Test (BNT), Trail Making Test (TMT), Stroop Color-Word Test, Grooved Pegboard, Dynamometer, Wide Range Achievement Test (WRAT), Finger tapping, Beck Anxiety Index, Beck Depression Index, Symptom Checklist-90 (SCL-90).
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	200241

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Uninformative	221 workers that had been exposed to 1,2-DCE in the Southern United States were initially included. Exclusion criteria were provided, including the number of individuals excluded for each reason. The study authors note that those initially included in the analysis sample were referred by physicians after neurological complaints were documented. Detailed criteria for referral were not provided. Referral-based recruitment of neurological cases will likely result in an analysis sample with an exposure-outcome distribution that is not representative of the eligible population (i.e., contamination site clean-up workers).
	Metric 2:	Attrition	Medium	There was moderate subject loss. Reasons for exclusion from the analysis sample are provided, and only those with complete information were included in the analysis.
	Metric 3:	Comparison Group	Low	Impairment scores were compared to normative data from manuals and/or a "demographically similar control group" cited to Bowler et al. (2001). The controls from this study appeared similar (albeit somewhat older) than 1,2-DCE-exposed workers and reported no prior chemical exposure.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	A job-exposure matrix was not considered plausible; variables considered as surrogates of exposure were obtained from interviews. This method is expected to have poor validity because it relies on workers' recall of subjective events and their frequency (e.g., contact with water); workers (who are taking part in a lawsuit) may overestimate their exposure.
	Metric 5:	Exposure Levels	Low	Two levels of exposure (exposed and not exposed) were used to evaluate neurophysiological effects.
	Metric 6:	Temporality	Medium	Exposures primarily occurred between 1993 and 1995 and neurophysiological effects were evaluated in 2000. Temporality is established, but it is unclear whether exposures fall within relevant exposure windows for the outcome of interest.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Neurophysiological effects were evaluated using a number of standardized tests, including (but not limited to) the Wechsler Adult Intelligence Scale (WAIS-III), the Wechsler Memory Scale (WMS-III), and the Symptom Checklist 90-Revised (SCL90-R). There was no information whether tests were performed using the same methods for exposed and referent groups (e.g., timing and order of tests).

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Study Citation:	Bowler, R.M., Gysens, S., Hartney, C. (2003). Neuropsychological effects of ethylene dichloride exposure. NeuroToxicology 24(4-5):553-562.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Wechsler Adult Intelligence Scale III (WAIS-III), Wechsler Memory Scale III (WMS-III), Boston Naming Test (BNT), Trail Making Test (TMT), Stroop Color-Word Test, Grooved Pegboard, Dynamometer, Wide Range Achievement Test (WRAT), Finger tapping, Beck Anxiety Index, Beck Depression Index, Symptom Checklist-90 (SCL-90).
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	200241

Domain	Metric		Rating	Comments
	Metric 8:	Reporting Bias	Low	Neurobehavioral outcomes mentioned in the methods were reported for 1,2-DCE-exposed workers (as mean score, standard deviation, and percentage impaired); results for controls/normative data were not shown and/or p-values from t-tests were not provided. Control data were used to define impairment (based on z-score) but these values were not reported. Data pertaining to specific exposure variables were reported in the text only; no data were shown in a table.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Normative data permitted adjustments based on age, education, and gender. The control group was "socio-demographically" similar but specific parameters used to define similarity were not indicated. Separate ANCOVA analyses on workers only were stratified by race (citation provided), and adjusted for ethnicity, age, and education. The methods for identifying and including potential confounders in the analytic approach was not described.
	Metric 10:	Covariate Characterization	Low	No description of the covariate collection method was provided. It was not clear whether the method used was valid or not.
	Metric 11:	Co-exposure Counfounding	Low	A number of workers (18%) reported current exposure to chemicals in their work environment. These potential co-exposures were not were not appropriately adjusted for in the analytical approach used.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Low	The study design was appropriate to evaluate the neurophysiological status of 1,2-DCE-exposed workers; however, statistical methods were not comprehensive.
	Metric 13:	Statistical Power	Medium	The report indicates "significant impairments" were observed on various neurophysiological tests using t-tests, and significant exposure relationships were reported based on test scores and specific exposure variables (used as surrogates of exposure). Therefore, the number of participants was sufficient to detect an effect.
	Metric 14:	Reproducibility of Analyses	Low	Tests were scored according to relevant manuals; the calculation of z-scores, used in all impairment comparisons and analyses of exposure relationships, was not explained in adequate detail. The methods used to determine relationships between specific exposure variables and test scores (i.e., ANCOVA analyses) were not fully described.
	Metric 15:	Statistical Analysis	Low	Description of the ANCOVA analysis was largely not present. It is not clear whether model assumptions were met.

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Study Citation:	Bowler, R.M., Gysens, S., Hartney, C. (2003). Neuropsychological effects of ethylene dichloride exposure. NeuroToxicology 24(4-5):553-562.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Wechsler Adult Intelligence Scale III (WAIS-III), Wechsler Memory Scale III (WMS-III), Boston Naming Test (BNT), Trail Making Test (TMT), Stroop Color-Word Test, Grooved Pegboard, Dynamometer, Wide Range Achievement Test (WRAT), Finger tapping, Beck Anxiety Index, Beck Depression Index, Symptom Checklist-90 (SCL-90).
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	200241

Domain	Metric	Rating	Comments
Additional Comments:	The study evaluated the neurobehavioral status of a group of workers with known exposure to 1,2-DCE at a clean-up site. Impairments related to processing speed, attention, cognitive flexibility, motor coordination and speed, verbal memory/fluency, vision and visual-spatial abilities, and mood were reported in exposed workers. Serious and consequential flaws are associated with the study including methods of participant selection and retention, and exposure characterization among others.		

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Brender, J.D., Shinde, M.U., Zhan, F.B., Gong, X., Langlois, P.H. (2014). Maternal residential proximity to chlorinated solvent emissions and birth defects in offspring: A case-control study. Environmental Health: A Global Access Science Source 13(1):96.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	birth defects (neural tube defects, limbs deficiencies, oral cleft defects, heart defects, spina bifida, anencephaly)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	2799700

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Participants were drawn from the Texas Birth Defects Registry (TBDR) for years 1996-2008. Controls were frequency matched from the same registry. Study authors state that neural tube cases were more likely to not be successfully geocoded which may introduce selection bias, however, the authors note that both cases and controls with addresses that could not be geocoded were similar. In spite of that, the inclusion criteria, methods of participant selection, and frequency match were reported.
	Metric 2:	Attrition	Medium	13.3% case mother addresses and 12.8% control mother addresses were unable to be geocoded, however this most likely only lowered the precision of the study and most likely does not vary based on exposure level.
	Metric 3:	Comparison Group	Medium	Controls were matched to cases and pulled from the same eligible population by year of delivery and public health service region. Other demographic factors, e.g., race was not matched in population selection. However, statistical analyses were adjusted for year of delivery, maternal age, race/ethnicity, education, and public health region of residence.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Used Emission Weighted Proximity Model to estimate exposure at a given address based on proximity to emission sources and the specific amount or type of pollutant emitted. There may be some exposure misclassification due to mothers moving away from geocoded addresses. Previous studies indicate ~67% of mothers do not move between conception and delivery.
	Metric 5:	Exposure Levels	Medium	Reports exposure as "exposure risk value" and groups the risk values into quartiles, with exposure risk values < 0 being the referent group
	Metric 6:	Temporality	Medium	The study authors estimated exposure based on residence during pregnancy and evaluated birth outcomes. Temporality is established. Previous studies indicate ~67% mothers don't move between trimester and delivery. For mothers who moved during the pregnancy, the temporality is unknown.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Outcomes determined by Texas Birth Defect Registry, checking for birth defect diagnosis. Birth certificates came from Center for Health Statistics at Texas Department of State Health Services
	Metric 8:	Reporting Bias	High	Outcome data measured and reported clearly, stratified by specific type of birth defect
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Brender, J.D., Shinde, M.U., Zhan, F.B., Gong, X., Langlois, P.H. (2014). Maternal residential proximity to chlorinated solvent emissions and birth defects in offspring: A case-control study. Environmental Health: A Global Access Science Source 13(1):96.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	birth defects (neural tube defects, limbs deficiencies, oral cleft defects, heart defects, spina bifida, anencephaly)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	2799700

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	High	Cases were frequency matched by year of delivery and public health service region. Final models were adjusted for year of delivery, public health region, maternal age (<20, 20-24, 25-29, 30-34, 35-39, >39 years), education (<12 years, 12 years, >12 years), and race/ethnicity (Whit non-Hispanic, Black non-Hispanic, Hispanic, other non-Hispanic).
	Metric 10:	Covariate Characterization	High	Used birth and death certificates for demographic information
	Metric 11:	Co-exposure Counfounding	Medium	other co-exposures were not described
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	study used logistic regression to measure association between exposure and birth defects
	Metric 13:	Statistical Power	Medium	Overall adequate number of cases and controls - some effects have low cell counts, but at least one health effect has sufficient statistical power.
	Metric 14:	Reproducibility of Analyses	Medium	Methods sufficiently detailed for reproducibility
	Metric 15:	Statistical Analysis	High	No logistic regression model assumption violations were identified.

Additional Comments: This study examined the association between proximity to several point sources of chlorinated solvents and birth defects. Exposure was assessed using EPA's Toxic Release Inventory, and birth defects were assessed using Texas birth registries. The geocoded address of mothers on day of delivery and the amount of solvent was plugged into the Emission Weighted Probability model to assign each mother an exposure risk value. Limitations include limited evidence of temporality. Additionally, elective terminations lacked a vital record, which meant only 69% of mothers with neural tube defects were geocoded. Mothers highly exposed to 1,2-dichloroethane were 1.85 times more likely to have the spina bifida birth defect than mothers who were not significantly exposed.

Overall Quality Determination High

* No biomarkers were identified for this evaluation.

Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Nested case-control design; cases selected from deaths in cohort study was described by Rinsky et al (1988; HERO 597923) (29,139 workers in Union Carbide facilities in West Virginia followed from 1940 to 1978). Vital status complete for 95% of cohort members.
	Metric 2:	Attrition	High	There was minimal exclusion of subjects/missing data, because vital status follow-up was complete for 96% of the 29,139 men in the cohort study.
	Metric 3:	Comparison Group	Medium	Controls were randomly selected in a 5:1 ratio to cases from the total employee cohort such that they were first employed in the same decade and survived to the same five-year survival period as cases. Controls survived at least to the beginning of the five-year interval in which cases died. Controls were independently selected for each of the individual disease subcategories. However, the demographic information between cases and controls were not compared in the paper.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was partially described: (1) Potential employee contact with a specific substance was determined by tracing each employee's work assignments and linking these assignment records to a separate computer file that contained a history of departmental usage for each substance; (2) Potential exposure to each chemical group was assumed on the basis of assignment o a production unit with a history of usage of any member of that chemical group. However, exposure level either based on work assignment in departments such as job exposure matrix or on the chemical levels were not presented.
	Metric 5:	Exposure Levels	Low	The range of exposure is limited. For example, exposure was presented by the duration of work in two categories: <5 years and 5+ years.
	Metric 6:	Temporality	Medium	Temporality is established, but it is unclear whether the exposures fall within the relevant exposure window. Authors used a lag time of 5 years; since controls were selected for 5 yr intervals, the effective lag time ranged from 5-9 years with an average of 7.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Case definition was based on death certificate diagnosis; but no method validation was conducted against this well-established methods.
	Metric 8:	Reporting Bias	Medium	All outcomes reported, but ORs for many analyses presented without CIs (some CIs reported in text).
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Low	There is indirect evidence that considerations were not made for potential confounders (ORs not adjusted, controls not age- or race-matched). Even though authors note that "Age-adjusted stratified analyses, which were also conducted, did not materially modify the odds ratio estimates". Also stratified examination of odds ratios were conducted to assess duration of exposure effects. However, other key confounders e.g., smoking status and race were not accounted for.
	Metric 10:	Covariate Characterization	Medium	The only potential confounder considered was age; this was presumably evaluated based on employment records (no discussion presented). Age-adjusted stratified analyses were conducted.
	Metric 11:	Co-exposure Counfounding	Low	Co-exposures were present and were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Nested case-control study design is appropriate for research question. Initial data analysis included crude odds ratio and then stratified examination of odds ratios was conducted to ass duration of exposure effect. Also, age-adjusted stratified analysis was conducted.
	Metric 13:	Statistical Power	Low	Statistical power calculations were not reported. Case numbers for each disease were low. The number of subjects was not sufficient to detect an effect of 1,2-dichloroethylene exposure.
	Metric 14:	Reproducibility of Analyses	Medium	Description was sufficient to be conceptually reproducible.
	Metric 15:	Statistical Analysis	Low	Statistical model to calculate odds ratio was not described.

Additional Comments: This nested case-control study within a cohort study is a good study design to answer the research question regarding the association between multiple chemical exposures and four cancer sites. Cases and controls are selected appropriate. However, there are several limitations in this study: (1) confounders were not all considered and adjusted for, except that age-adjusted odds ratios were conducted; (2) it is not described if co-exposures were adjusted for; (3) numbers of cancer cases for each cancer type were small, so the statistical power is limited; (4) statistical models for calculating odds ratios were not described.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Nested case-control design; cases selected from deaths in cohort study was described by Rinsky et al (1988; HERO 597923) (29,139 workers in Union Carbide facilities in West Virginia followed from 1940 to 1978). Vital status complete for 95% of cohort members.
	Metric 2:	Attrition	High	There was minimal exclusion of subjects/missing data, because vital status follow-up was complete for 96% of the 29,139 men in the cohort study.
	Metric 3:	Comparison Group	Medium	Controls were randomly selected in a 5:1 ratio to cases from the total employee cohort such that they were first employed in the same decade and survived to the same five-year survival period as cases. Controls survived at least to the beginning of the five-year interval in which cases died. Controls were independently selected for each of the individual disease subcategories. However, the demographic information between cases and controls were not compared in the paper.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was partially described: (1) Potential employee contact with a specific substance was determined by tracing each employee's work assignments and linking these assignment records to a separate computer file that contained a history of departmental usage for each substance; (2) Potential exposure to each chemical group was assumed on the basis of assignment o a production unit with a history of usage of any member of that chemical group. However, exposure level either based on work assignment in departments such as job exposure matrix or on the chemical levels were not presented.
	Metric 5:	Exposure Levels	Low	The range of exposure is limited. For example, exposure was presented by the duration of work in two categories: <5 years and 5+ years.
	Metric 6:	Temporality	Medium	Temporality is established, but it is unclear whether the exposures fall within the relevant exposure window. Authors used a lag time of 5 years; since controls were selected for 5 yr intervals, the effective lag time ranged from 5-9 years with an average of 7.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Case definition was based on death certificate diagnosis; but no method validation was conducted against this well-established methods.
	Metric 8:	Reporting Bias	Medium	All outcomes reported, but ORs for many analyses presented without CIs (some CIs reported in text).
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Low	There is indirect evidence that considerations were not made for potential confounders (ORs not adjusted, controls not age- or race-matched). Even though authors note that "Age-adjusted stratified analyses, which were also conducted, did not materially modify the odds ratio estimates". Also stratified examination of odds ratios were conducted to assess duration of exposure effects. However, other key confounders e.g., smoking status and race were not accounted for.
	Metric 10:	Covariate Characterization	Medium	The only potential confounder considered was age; this was presumably evaluated based on employment records (no discussion presented). Age-adjusted stratified analyses were conducted.
	Metric 11:	Co-exposure Counfounding	Low	Co-exposures were present and were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Nested case-control study design is appropriate for research question. Initial data analysis included crude odds ratio and then stratified examination of odds ratios was conducted to ass duration of exposure effect. Also, age-adjusted stratified analysis was conducted.
	Metric 13:	Statistical Power	Low	Statistical power calculations were not reported. Case numbers for each disease were low. The number of subjects was not sufficient to detect an effect of 1,2-dichloroethylene exposure.
	Metric 14:	Reproducibility of Analyses	Medium	Description was sufficient to be conceptually reproducible.
	Metric 15:	Statistical Analysis	Low	Statistical model to calculate odds ratio was not described.

Additional Comments: This nested case-control study within a cohort study is a good study design to answer the research question regarding the association between multiple chemical exposures and four cancer sites. Cases and controls are selected appropriate. However, there are several limitations in this study: (1) confounders were not all considered and adjusted for, except that age-adjusted odds ratios were conducted; (2) it is not described if co-exposures were adjusted for; (3) numbers of cancer cases for each cancer type were small, so the statistical power is limited; (4) statistical models for calculating odds ratios were not described.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Nested case-control design; cases selected from deaths in cohort study was described by Rinsky et al (1988; HERO 597923) (29,139 workers in Union Carbide facilities in West Virginia followed from 1940 to 1978). Vital status complete for 95% of cohort members.
	Metric 2:	Attrition	High	There was minimal exclusion of subjects/missing data, because vital status follow-up was complete for 96% of the 29,139 men in the cohort study.
	Metric 3:	Comparison Group	Medium	Controls were randomly selected in a 5:1 ratio to cases from the total employee cohort such that they were first employed in the same decade and survived to the same five-year survival period as cases. Controls survived at least to the beginning of the five-year interval in which cases died. Controls were independently selected for each of the individual disease subcategories. However, the demographic information between cases and controls were not compared in the paper.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was partially described: (1) Potential employee contact with a specific substance was determined by tracing each employee's work assignments and linking these assignment records to a separate computer file that contained a history of departmental usage for each substance; (2) Potential exposure to each chemical group was assumed on the basis of assignment o a production unit with a history of usage of any member of that chemical group. However, exposure level either based on work assignment in departments such as job exposure matrix or on the chemical levels were not presented.
	Metric 5:	Exposure Levels	Low	The range of exposure is limited. For example, exposure was presented by the duration of work in two categories: <5 years and 5+ years.
	Metric 6:	Temporality	Medium	Temporality is established, but it is unclear whether the exposures fall within the relevant exposure window. Authors used a lag time of 5 years; since controls were selected for 5 yr intervals, the effective lag time ranged from 5-9 years with an average of 7.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Case definition was based on death certificate diagnosis; but no method validation was conducted against this well-established methods.
	Metric 8:	Reporting Bias	Medium	All outcomes reported, but ORs for many analyses presented without CIs (some CIs reported in text).
Domain 4: Potential Confounding / Variability Control				

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Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Low	There is indirect evidence that considerations were not made for potential confounders (ORs not adjusted, controls not age- or race-matched). Even though authors note that "Age-adjusted stratified analyses, which were also conducted, did not materially modify the odds ratio estimates". Also stratified examination of odds ratios were conducted to assess duration of exposure effects. However, other key confounders e.g., smoking status and race were not accounted for.
	Metric 10:	Covariate Characterization	Medium	The only potential confounder considered was age; this was presumably evaluated based on employment records (no discussion presented). Age-adjusted stratified analyses were conducted.
	Metric 11:	Co-exposure Counfounding	Low	Co-exposures were present and were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Nested case-control study design is appropriate for research question. Initial data analysis included crude odds ratio and then stratified examination of odds ratios was conducted to ass duration of exposure effect. Also, age-adjusted stratified analysis was conducted.
	Metric 13:	Statistical Power	Low	Statistical power calculations were not reported. Case numbers for each disease were low. The number of subjects was not sufficient to detect an effect of 1,2-dichloroethylene exposure.
	Metric 14:	Reproducibility of Analyses	Medium	Description was sufficient to be conceptually reproducible.
	Metric 15:	Statistical Analysis	Low	Statistical model to calculate odds ratio was not described.

Additional Comments: This nested case-control study within a cohort study is a good study design to answer the research question regarding the association between multiple chemical exposures and four cancer sites. Cases and controls are selected appropriate. However, there are several limitations in this study: (1) confounders were not all considered and adjusted for, except that age-adjusted odds ratios were conducted; (2) it is not described if co-exposures were adjusted for; (3) numbers of cancer cases for each cancer type were small, so the statistical power is limited; (4) statistical models for calculating odds ratios were not described.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Nested case-control design; cases selected from deaths in cohort study was described by Rinsky et al (1988; HERO 597923) (29,139 workers in Union Carbide facilities in West Virginia followed from 1940 to 1978). Vital status complete for 95% of cohort members.
	Metric 2:	Attrition	High	There was minimal exclusion of subjects/missing data, because vital status follow-up was complete for 96% of the 29,139 men in the cohort study.
	Metric 3:	Comparison Group	Medium	Controls were randomly selected in a 5:1 ratio to cases from the total employee cohort such that they were first employed in the same decade and survived to the same five-year survival period as cases. Controls survived at least to the beginning of the five-year interval in which cases died. Controls were independently selected for each of the individual disease subcategories. However, the demographic information between cases and controls were not compared in the paper.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was partially described: (1) Potential employee contact with a specific substance was determined by tracing each employee's work assignments and linking these assignment records to a separate computer file that contained a history of departmental usage for each substance; (2) Potential exposure to each chemical group was assumed on the basis of assignment o a production unit with a history of usage of any member of that chemical group. However, exposure level either based on work assignment in departments such as job exposure matrix or on the chemical levels were not presented.
	Metric 5:	Exposure Levels	Low	The range of exposure is limited. For example, exposure was presented by the duration of work in two categories: <5 years and 5+ years.
	Metric 6:	Temporality	Medium	Temporality is established, but it is unclear whether the exposures fall within the relevant exposure window. Authors used a lag time of 5 years; since controls were selected for 5 yr intervals, the effective lag time ranged from 5-9 years with an average of 7.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Case definition was based on death certificate diagnosis; but no method validation was conducted against this well-established methods.
	Metric 8:	Reporting Bias	Medium	All outcomes reported, but ORs for many analyses presented without CIs (some CIs reported in text).
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Low	There is indirect evidence that considerations were not made for potential confounders (ORs not adjusted, controls not age- or race-matched). Even though authors note that "Age-adjusted stratified analyses, which were also conducted, did not materially modify the odds ratio estimates". Also stratified examination of odds ratios were conducted to assess duration of exposure effects. However, other key confounders e.g., smoking status and race were not accounted for.
	Metric 10:	Covariate Characterization	Medium	The only potential confounder considered was age; this was presumably evaluated based on employment records (no discussion presented). Age-adjusted stratified analyses were conducted.
	Metric 11:	Co-exposure Counfounding	Low	Co-exposures were present and were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Nested case-control study design is appropriate for research question. Initial data analysis included crude odds ratio and then stratified examination of odds ratios was conducted to ass duration of exposure effect. Also, age-adjusted stratified analysis was conducted.
	Metric 13:	Statistical Power	Low	Statistical power calculations were not reported. Case numbers for each disease were low. The number of subjects was not sufficient to detect an effect of 1,2-dichloroethylene exposure.
	Metric 14:	Reproducibility of Analyses	Medium	Description was sufficient to be conceptually reproducible.
	Metric 15:	Statistical Analysis	Low	Statistical model to calculate odds ratio was not described.

Additional Comments: This nested case-control study within a cohort study is a good study design to answer the research question regarding the association between multiple chemical exposures and four cancer sites. Cases and controls are selected appropriate. However, there are several limitations in this study: (1) confounders were not all considered and adjusted for, except that age-adjusted odds ratios were conducted; (2) it is not described if co-exposures were adjusted for; (3) numbers of cancer cases for each cancer type were small, so the statistical power is limited; (4) statistical models for calculating odds ratios were not described.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Cheng, T.J., Huang, M.L., You, N.C., Du, C.L., Chau, T.T. (1999). Abnormal liver function in workers exposed to low levels of ethylene dichloride and vinyl chloride monomer. Journal of Occupational and Environmental Medicine 41(12):1128-1133.
Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	AST, ALT, GGT, Hepatitis B virus surface antigen (HBsAg), and anti-hepatitis C virus antibody (anti-HCV).
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	200266

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	A total of 251 male workers were included from 4 vinyl chloride monomer manufacturing plants. Other details on recruitment strategy, eligibility criteria, year of enrollment, and participation rates were not provided.
	Metric 2:	Attrition	Low	There was no indication of attrition and details on the number of eligible participants throughout the study was limited. Attrition could not be adequately assessed due to a lack of information regarding recruitment and selection.
	Metric 3:	Comparison Group	Medium	The low-EDC-low-VCM group (187 participants) was used as the comparison group, and there is indirect evidence groups are similar. Limited details were provided for setting, inclusion and exclusion criteria, and methods of participant selection.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	NIOSH recommended methods 1003 and 1007 were used for personal and area sampling, respectively. Air samples were collected, stored at 4 deg. C, and analyzed within 2 weeks of the sampling event. However, historical job changes, changes in exposure levels over time, and timing (year or days during work week) or duration of area or personal sampling were not reported.
	Metric 5:	Exposure Levels	Medium	EDC and VCM levels were reported for the different categories of jobs, which were classified into low-EDC-low-VCM, mod-EDC-low-VCM, and low-EDC-mod-VCM groups.
	Metric 6:	Temporality	High	The age of participants (mean age 33.7-40.1 years) and employment duration (mean 7.5-14.3 years) were reported, and the temporality between the exposure and outcome appears to be appropriate.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	AST, ALT, and GGT "were analyzed with a Hitachi 7050 autoanalyzer". A basis for the cutoff values used in Table 4 to determine "abnormal" AST, ALT, and GGT levels was not provided.
	Metric 8:	Reporting Bias	High	Odds ratios for abnormal liver function were provided with 95% confidence intervals, the number per exposure level, and significance when applicable.
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Cheng, T.J., Huang, M.L., You, N.C., Du, C.L., Chau, T.T. (1999). Abnormal liver function in workers exposed to low levels of ethylene dichloride and vinyl chloride monomer. Journal of Occupational and Environmental Medicine 41(12):1128-1133.
Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	AST, ALT, GGT, Hepatitis B virus surface antigen (HBsAg), and anti-hepatitis C virus antibody (anti-HCV).
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	200266

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Medium	The study reports information on potential confounders (age, hepatitis, BMI, alcohol use, and employment duration), and controls for hepatitis, BMI and alcohol consumption in the multiple logistic regression analyses. There is indirect evidence that appropriate adjustments were made.
	Metric 10:	Covariate Characterization	Medium	An interviewer administered the questionnaires to collect information about potential confounders and occupational history.
	Metric 11:	Co-exposure Counfounding	Low	Exposure to ethylene dichloride was evaluated in a vinyl chloride monomer (VCM) manufacturing facility, and VCM was also subsequently analyzed using personal and area sampling. Results for VCM exposure concentrations were provided. VCM is also suspected to cause liver damage.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design (cohort) was appropriate to assess the outcome of interest (”markers of liver damage”). Chi-squared (X2) test and multiple logistic regression were used for statistical analyses.
	Metric 13:	Statistical Power	Medium	The number of participants was adequate to detect an effect in the exposed populations, although power calculations were not provided. There were >20 participants in each group.
	Metric 14:	Reproducibility of Analyses	Low	A description of the logistic regression analysis was provided, however, study authors do not provide information on categorization of abnormal liver function.
	Metric 15:	Statistical Analysis	High	There were no identifiable logistic regression model assumption violations.
Domain 6: Other (if applicable) Considerations for Biomarker Selection and Measurement (Lakind et al. 2014)				
	Metric 16:	Use of Biomarker of Exposure	N/A	Biomarker of exposures were not assessed.
	Metric 17:	Effect Biomarker	High	This study uses aspartate aminotransferase, alanine aminotransferase, and y-glutamyltransferase as biomarkers of effect. While these no works cited to explain their connection to liver function, all three are well-known marker of liver function. Similarly, Hepatitis B virus surface antigen and antihepatitis C virus anitbody are also well-known measures of liver function and health.
	Metric 18:	Method Sensitivity	Low	No limit of detection information is provided for any of the effect biomarkers.
	Metric 19:	Biomarker Stability	Medium	While the study does not provide a lot of information regarding biomarker storage or stability, the authors do mention that venous blood used to detect biomarkers was stored at 4 degrees C.
	Metric 20:	Sample Contamination	Medium	No specific information regarding potential sample contamination was provided.
	Metric 21:	Method Requirements	Medium	Aspartate aminotransferase, alanine aminotransferase, and y-glutamyltransferase were analyzed using a Hitachi 7050 autoanalyzer. Hepatitis B virus surface antibody and antihepatitis C virus antibody were assessed with radioimmunoassay and enzyme-linked immunosorbent assay.

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Study Citation:	Cheng, T.J., Huang, M.L., You, N.C., Du, C.L., Chau, T.T. (1999). Abnormal liver function in workers exposed to low levels of ethylene dichloride and vinyl chloride monomer. Journal of Occupational and Environmental Medicine 41(12):1128-1133.
Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	AST, ALT, GGT, Hepatitis B virus surface antigen (HBsAg), and anti-hepatitis C virus antibody (anti-HCV).
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	200266

Domain	Metric	Rating	Comments
	Metric 22: Matrix Adjustment	N/A	No information on matrix adjustment was provided/available.

Additional Comments: A group of 251 male workers from 4 vinyl chloride monomer (VCM) manufacturing plants were included in this assessment to examine if occupational exposure to VCM and ethylene dichloride (EDC) "resulted in increased risk of liver damage" by examining AST, ALT, and GGT levels in the blood. Increased ORs for abnormal AST (>37 IU/L) and ALT (>41 IU/L) in the mod-EDC-low-VCM group (0.17-333.7 ppm EDC, 0.18-0.34 ppm VCM), compared with the low-EDC-low-VCM group, was reported. Exposure levels were measured using area and personal sampling, but the timing and duration of the sampling events were not reported.

Overall Quality Determination Medium

Study Citation:	Dosemeci, M., Cocco, P., Chow, W.H. (1999). Gender differences in risk of renal cell carcinoma and occupational exposures to chlorinated aliphatic hydrocarbons. American Journal of Industrial Medicine 36(1):54-59.
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	renal cell carcinoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	4697224

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	The details of the study design were reported elsewhere (Chow et al. 1994, HERO ID 701514). Brief details about the setting, date, number of eligible participants, and control matching were reported. Reasons for exclusions/non-participation were described with details by Chow et al. (1994).
	Metric 2:	Attrition	High	For the details of the study design and attrition of study subjects, the study authors referred to another publication by Chow et al., 1994. Chow et al. (1994) mentioned that at the end of the personal interview, the respondents were given a self-administered food-frequency questionnaire. Of the subjects interviewed for the study, 632 patients (79% of 796 eligible patients) and 653 control subjects (79% of 707 eligible control subjects) returned the diet questionnaire. A number of subjects, whose responses were considered unreliable, were excluded from the analysis, including 48 patients and three control subjects who had seven or more skipped food items or had questionable data and 50 patients whose next-of-kin respondent was not a spouse. Also excluded were two patients with unknown smoking status, since smoking is a risk factor.
	Metric 3:	Comparison Group	Medium	The cases were pulled from the Minnesota Cancer Surveillance System. Controls were selected from the general population of Minnesota; controls age 20-64 years were selected through random digital dialing and controls age 65-85 years were collected from files through the Health Care Financing Administration. Controls were age- and gender-stratified and were of the same race. Characteristics of cases and controls were not provided in the text or a table.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	High	Occupational histories including the most recent and usual occupation and industry, job activities, started-year and ended-year, and part-time/full-time status were collected. Occupations and industries were coded according to the standard occupational classification (SOC) and standard industrial classification (SIC) schemes. The National Cancer Institute developed job exposure matrices (JEM) for nine individual chlorinated aliphatic hydrocarbons (CAHCs), all CAHCs-combined, and all organic solvents-combined. These JEMs were merged with assigned SOC and SIC to determine the exposure status to these chemicals for each study subject. Application of the JEM was described elsewhere (Dosemeci et al. 1994, HERO ID 632334; Gomez et al. 1994, HERO ID 702154).
	Metric 5:	Exposure Levels	Medium	Details of the application of the JEM were described elsewhere (Dosemeci et al. 1994, HERO ID 632334; Gomez et al. 1994, HERO ID 702154). Dosemeci et al. (1994) described more details about that this study assigned three levels of probability (low, medium, high) to industries and occupations for chemical exposure levels.

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Study Citation:	Dosemeci, M., Cocco, P., Chow, W.H. (1999). Gender differences in risk of renal cell carcinoma and occupational exposures to chlorinated aliphatic hydrocarbons. American Journal of Industrial Medicine 36(1):54-59.
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	renal cell carcinoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	4697224

Domain	Metric		Rating	Comments
	Metric 6:	Temporality	Medium	Occupational questionnaires identified prior exposures based on reported recent and usual occupations as well as duration of employment. Outcome status was determined from registry data. The authors note that some occupational history was incomplete which may result in some uncertainty in regard to temporality.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Cases were identified as newly diagnosed and histologically confirmed renal cell carcinoma through the Minnesota Cancer Surveillance System and information about each participant was collected using a questionnaire. Validation was not specified.
	Metric 8:	Reporting Bias	Medium	A description of measured outcomes is reported and ORs were stratified by sex. Effect estimates are reported with a confidence interval. One table showed the total numbers of men and women respectively for each chemical, but numbers of cases/controls were not reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Appropriate adjustments were made in the final analysis, including age, gender, smoking, hypertension and the use of diuretics and/or anti-hypertension drugs, and BMI. Results were stratified by sex.
	Metric 10:	Covariate Characterization	Medium	Information about participants was collected using a questionnaire, and it includes potential confounders, e.g., smoking habits. Validation was not specified.
	Metric 11:	Co-exposure Counfounding	Medium	Co-exposures were identified through the job exposure matrices. Chemicals were evaluated individually and as a group.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen (case-control) was appropriate for the research question (renal cell carcinoma risk from occupational organic solvent exposure). Logistic regression models were used to estimate the relative risk and 95% CI.
	Metric 13:	Statistical Power	Low	Statistical power calculations were not provided. No significant effects were observed with 1,2-dichloroethane. The number of participated women to calculate odds ratio was inadequate to detect an effect in the participants for other chemicals or the combined risk, because it was very low.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis was brief, but is sufficient to understand precisely what has been done and to be conceptually reproducible with access to the analytic data.
	Metric 15:	Statistical Analysis	High	Model assumptions for logistic regression were met. The odds ratios were adjusted for age, smoking, hypertension status and/or use of diuretic and/or anti-hypertension drugs, and body mass index for men and women separately.

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Study Citation:	Dosemeci, M., Cocco, P., Chow, W.H. (1999). Gender differences in risk of renal cell carcinoma and occupational exposures to chlorinated aliphatic hydrocarbons. American Journal of Industrial Medicine 36(1):54-59.
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	renal cell carcinoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	4697224

Domain	Metric	Rating	Comments
Additional Comments:	A group of 438 cases (273 men and 165 women) were selected from the Minnesota Cancer Surveillance System that had been newly diagnosed with renal cell carcinoma. Controls included 687 participants (462 men and 225 women) age- and gender- stratified that were selected from either the general population of Minnesota (age 20-64 years) or from the Health Care Financing Administration files (age 65-85). No significant increase in the risk of renal cell carcinoma was observed with exposure to 1,2-dichloroethane among men or women separately, or for all participants exposed.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Dosemeci, M., Cocco, P., Chow, W.H. (1999). Gender differences in risk of renal cell carcinoma and occupational exposures to chlorinated aliphatic hydrocarbons. American Journal of Industrial Medicine 36(1):54-59.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	renal cell carcinoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	4697224

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	The details of the study design were reported elsewhere (Chow et al. 1994, HERO ID 701514). Brief details about the setting, date, number of eligible participants, and control matching were reported. Reasons for exclusions/non-participation were described with details by Chow et al. (1994).
	Metric 2:	Attrition	Medium	For the details of the study design and attrition of study subjects, the study authors referred to another publication by Chow et al., 1994. Chow et al. (1994) mentioned that at the end of the personal interview, the respondents were given a self-administered food-frequency questionnaire. Of the subjects interviewed for the study, 632 patients (79% of 796 eligible patients) and 653 control subjects (79% of 707 eligible control subjects) returned the diet questionnaire. A number of subjects, whose responses were considered unreliable, were excluded from the analysis, including 48 patients and three control subjects who had seven or more skipped food items or had questionable data and 50 patients whose next-of-kin respondent was not a spouse. Also excluded were two patients with unknown smoking status, since smoking is a risk factor.
	Metric 3:	Comparison Group	Medium	The cases were pulled from the Minnesota Cancer Surveillance System. Controls were selected from the general population of Minnesota; controls age 20-64 years were selected through random digital dialing and controls age 65-85 years were collected from files through the Health Care Financing Administration. Controls were age- and gender-stratified and were of the same race. Characteristics of cases and controls were not provided in the text or a table.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	High	Occupational histories including the most recent and usual occupation and industry, job activities, started-year and ended-year, and part-time/full-time status were collected. Occupations and industries were coded according to the standard occupational classification (SOC) and standard industrial classification (SIC) schemes. The National Cancer Institute developed job exposure matrices (JEM) for nine individual chlorinated aliphatic hydrocarbons (CAHCs), all CAHCs-combined, and all organic solvents-combined. These JEMs were merged with assigned SOC and SIC to determine the exposure status to these chemicals for each study subject. Application of the JEM was described elsewhere (Dosemeci et al. 1994, HERO ID 632334; Gomez et al. 1994, HERO ID 702154).
	Metric 5:	Exposure Levels	Medium	Details of the application of the JEM were described elsewhere (Dosemeci et al. 1994, HERO ID 632334; Gomez et al. 1994, HERO ID 702154). Dosemeci et al. (1994) described more details about that this study assigned three levels of probability (low, medium, high) to industries and occupations for chemical exposure levels.

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Study Citation:	Dosemeci, M., Cocco, P., Chow, W.H. (1999). Gender differences in risk of renal cell carcinoma and occupational exposures to chlorinated aliphatic hydrocarbons. American Journal of Industrial Medicine 36(1):54-59.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	renal cell carcinoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	4697224

Domain	Metric		Rating	Comments
	Metric 6:	Temporality	Medium	Occupational questionnaires identified prior exposures based on reported recent and usual occupations as well as duration of employment. Outcome status was determined from registry data. The authors note that some occupational history was incomplete which may result in some uncertainty in regard to temporality.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Cases were identified as newly diagnosed and histologically confirmed renal cell carcinoma through the Minnesota Cancer Surveillance System and information about each participant was collected using a questionnaire. Validation was not specified.
	Metric 8:	Reporting Bias	Medium	A description of measured outcomes is reported and ORs were stratified by sex. Effect estimates are reported with a confidence interval. One table showed the total numbers of men and women respectively for each chemical, but numbers of cases/controls were not reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Appropriate adjustments were made in the final analysis, including age, gender, smoking, hypertension and the use of diuretics and/or anti-hypertension drugs, and BMI. Results were stratified by sex.
	Metric 10:	Covariate Characterization	Medium	Information about participants was collected using a questionnaire, and it includes potential confounders, e.g., smoking habits. Validation was not specified.
	Metric 11:	Co-exposure Counfounding	Medium	Co-exposures were identified through the job exposure matrices. Chemicals were evaluated individually and as a group.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen (case-control) was appropriate for the research question (renal cell carcinoma risk from occupational organic solvent exposure). Logistic regression models were used to estimate the relative risk and 95% CI.
	Metric 13:	Statistical Power	Low	Statistical power calculations were not provided. No significant effects were observed with 1,2-dichloroethane. The number of participated women to calculate odds ratio was inadequate to detect an effect in the participants for other chemicals or the combined risk, because it was very low.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis was brief, but is sufficient to understand precisely what has been done and to be conceptually reproducible with access to the analytic data.
	Metric 15:	Statistical Analysis	High	Model assumptions for logistic regression were met. The odds ratios were adjusted for age, smoking, hypertension status and/or use of diuretic and/or anti-hypertension drugs, and body mass index for men and women separately.

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Study Citation:	Dosemeci, M., Cocco, P., Chow, W.H. (1999). Gender differences in risk of renal cell carcinoma and occupational exposures to chlorinated aliphatic hydrocarbons. American Journal of Industrial Medicine 36(1):54-59.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	renal cell carcinoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	4697224

Domain	Metric	Rating	Comments
Additional Comments:	A group of 438 cases (273 men and 165 women) were selected from the Minnesota Cancer Surveillance System that had been newly diagnosed with renal cell carcinoma. Controls included 687 participants (462 men and 225 women) age- and gender- stratified that were selected from either the general population of Minnesota (age 20-64 years) or from the Health Care Financing Administration files (age 65-85). No significant increase in the risk of renal cell carcinoma was observed with exposure to 1,2-dichloroethane among men or women separately, or for all participants exposed.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Garcia, E., Hurley, S., Nelson, D.O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health: A Global Access Science Source 14(1):14.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	breast cancer in females
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	3014082

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	A total of 112,378 women were included in this study out of 133,479 eligible female participants from the California Teacher Study cohort. A full description of the cohort is provided in Bernstein et al. 2002 (HERO ID 808446). Reasons for exclusion were provided. The reported information indicates that participant selection in or out of the study and participation was not likely to be biased.
	Metric 2:	Attrition	High	112,378/133,479 participants were included in the study. Exclusions were for the purpose of the study and analysis. Exclusion criteria were documented. Included participants had completed questionnaires. The California Cancer Registry is estimated to be 99% complete.
	Metric 3:	Comparison Group	Medium	There is only indirect evidence that groups are similar. Participants were recruited from the same eligible population with the same method of ascertainment. Comparisons were provided for participants with and without breast cancer. Characteristics between these two groups were generally similar. 5 Quintiles of exposure were used, and Q2-5 were compared with Q1.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	High	The Assessment System for Population Exposure Nationwide and the Human Exposure Model are used as part of the National-Scale Air Toxics Assessment produced by the EPA and was used to estimate ambient HAP concentrations for geographic locations. Methods are described online through the US EPA Assessment Methods.
	Metric 5:	Exposure Levels	Medium	The distribution of the NATA annual ambient concentration for each compound was plotted in Figure 1 using a box plot, and 5 Quintiles were used in the analyses.
	Metric 6:	Temporality	Medium	The follow-up period was from 1995-2011, and the NATA estimates were made in 2002 because it was approximately half way between the start and end of the follow-up period. However, it is unclear whether exposures fall within relevant exposure windows for the outcome of interest.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Annual linkage between the CTS cohort and the California Cancer Registry (CCR) was used to identify cases of invasive breast cancer. The CCR is estimated to be 99% complete. The case of invasive breast cancer was defined by ICD codes.

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Study Citation:	Garcia, E., Hurley, S., Nelson, D.O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health: A Global Access Science Source 14(1):14.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	breast cancer in females
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	3014082

Domain	Metric		Rating	Comments
	Metric 8:	Reporting Bias	Medium	A description of measured outcome is reported for adjustments by age and race, and effect estimates are reported with a 95% confidence interval. The measured outcomes using multiple comparisons were generally described in the text, but non-significant results were excluded from Table 3.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	The models were stratified by age and race. Additionally, adjustments were made for multiple comparisons among subsets of the participants (significant results reported in Table 3). Socioeconomic status (SES) of each participant was not evaluated, however, cohort SES characteristics were thought to be similar by study authors.
	Metric 10:	Covariate Characterization	Medium	Information about baseline characteristics for each participant was collected through a questionnaire. It is unknown if the questionnaire was validated.
	Metric 11:	Co-exposure Counfounding	Medium	A total of 37 compounds were identified as mammary gland carcinogens, but 13 were not included in this analysis. Thirteen compounds were excluded from the analysis due to insufficient variability (nine because they had the same value for all census tracts in the state of California; and four because they had less than 25% non-zero values). Ethylene dichloride (1,2-dichloroethane) was among the 24 compounds evaluated in this assessment, and evaluations for breast cancer were conducted for each of these 24 individual compounds.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen (prospective cohort) was appropriate for the research question (incidence of breast cancer). Cox proportional hazard models and SAS 9.3 were used in this assessment. Data analysis was described.
	Metric 13:	Statistical Power	Medium	Statistical power calculations were not provided. No significant effects were observed with ethylene dichloride (1,2-dichloroethane), however, this study utilized a large cohort, approximately 112,000 individuals. Distributions of chemicals of interest suggest there were sufficient numbers of participants in exposure subgroups.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to understand precisely what has been done and to be conceptually reproducible with access to the analytic data.
	Metric 15:	Statistical Analysis	High	The statistical models that were used were identified and described. ”No apparent violation of the underlying assumption of proportional hazards was detected”.

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Study Citation:	Garcia, E., Hurley, S., Nelson, D.O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health: A Global Access Science Source 14(1):14.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	breast cancer in females
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	3014082

Domain	Metric	Rating	Comments
Additional Comments:	A group of 112,378 female participants from the California Teacher Study cohort were assessed for their estimated exposure to ambient air pollutants, including ethylene dichloride (1,2-dichloroethane), and the incidence of invasive breast cancer. Air contaminant concentrations were estimated using the US EPA NATA and the ASPEN and HEM models. The approximate median concentration of 1,2-dichloroethane is between 1E-4 and 1E-2 (estimated from Figure 1). Exposures were categorized into 5 Quintiles, and compared against Quintile 1. No significant increase in the estimated hazard rate ratio for invasive breast cancer was observed with Quintile 2-5 exposure estimates for 1,2-dichloroethane, adjusted for age and race, when compared against Quintile 1, or when further adjusted using multiple comparisons.		

Overall Quality Determination High

* No biomarkers were identified for this evaluation.

Study Citation:	Garcia, E., Hurley, S., Nelson, D.O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health: A Global Access Science Source 14(1):14.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	breast cancer in females
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	3014082

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	A total of 112,378 women were included in this study out of 133,479 eligible female participants from the California Teacher Study cohort. A full description of the cohort is provided in Bernstein et al. 2002 (HERO ID 808446). Reasons for exclusion were provided. The reported information indicates that participant selection in or out of the study and participation was not likely to be biased.
	Metric 2:	Attrition	High	112,378/133,479 participants were included in the study. Exclusions were for the purpose of the study and analysis. Exclusion criteria were documented. Included participants had completed questionnaires. The California Cancer Registry is estimated to be 99% complete.
	Metric 3:	Comparison Group	Medium	There is only indirect evidence that groups are similar. Participants were recruited from the same eligible population with the same method of ascertainment. Comparisons were provided for participants with and without breast cancer. Characteristics between these two groups were generally similar. 5 Quintiles of exposure were used, and Q2-5 were compared with Q1.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	High	The Assessment System for Population Exposure Nationwide and the Human Exposure Model are used as part of the National-Scale Air Toxics Assessment produced by the EPA and was used to estimate ambient HAP concentrations for geographic locations. Methods are described online through the US EPA Assessment Methods.
	Metric 5:	Exposure Levels	Medium	The distribution of the NATA annual ambient concentration for each compound was plotted in Figure 1 using a box plot, and 5 Quintiles were used in the analyses.
	Metric 6:	Temporality	Medium	The follow-up period was from 1995-2011, and the NATA estimates were made in 2002 because it was approximately half way between the start and end of the follow-up period. However, it is unclear whether exposures fall within relevant exposure windows for the outcome of interest.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Annual linkage between the CTS cohort and the California Cancer Registry (CCR) was used to identify cases of invasive breast cancer. The CCR is estimated to be 99% complete. The case of invasive breast cancer was defined by ICD codes.
	Metric 8:	Reporting Bias	Medium	A description of measured outcome is reported for adjustments by age and race, and effect estimates are reported with a 95% confidence interval. The measured outcomes using multiple comparisons were generally described in the text, but non-significant results were excluded from Table 3.

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Study Citation:	Garcia, E., Hurley, S., Nelson, D.O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health: A Global Access Science Source 14(1):14.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	breast cancer in females
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	3014082

Domain	Metric		Rating	Comments
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	The models were stratified by age and race. Additionally, adjustments were made for multiple comparisons among subsets of the participants (significant results reported in Table 3). Socioeconomic status (SES) of each participant was not evaluated, however, cohort SES characteristics were thought to be similar by study authors.
	Metric 10:	Covariate Characterization	Medium	Information about baseline characteristics for each participant was collected through a questionnaire. It is unknown if the questionnaire was validated.
	Metric 11:	Co-exposure Counfounding	Medium	A total of 37 compounds were identified as mammary gland carcinogens, but 13 were not included in this analysis. Thirteen compounds were excluded from the analysis due to insufficient variability (nine because they had the same value for all census tracts in the state of California; and four because they had less than 25% non-zero values). Ethylene dichloride (1,2-dichloroethane) was among the 24 compounds evaluated in this assessment, and evaluations for breast cancer were conducted for each of these 24 individual compounds.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen (prospective cohort) was appropriate for the research question (incidence of breast cancer). Cox proportional hazard models and SAS 9.3 were used in this assessment. Data analysis was described.
	Metric 13:	Statistical Power	Medium	Statistical power calculations were not provided. No significant effects were observed with ethylene dichloride (1,2-dichloroethane), however, this study utilized a large cohort, approximately 112,000 individuals. Distributions of chemicals of interest suggest there were sufficient numbers of participants in exposure subgroups.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to understand precisely what has been done and to be conceptually reproducible with access to the analytic data.
	Metric 15:	Statistical Analysis	High	The statistical models that were used were identified and described. ”No apparent violation of the underlying assumption of proportional hazards was detected”.

Additional Comments: A group of 112,378 female participants from the California Teacher Study cohort were assessed for their estimated exposure to ambient air pollutants, including ethylene dichloride (1,2-dichloroethane), and the incidence of invasive breast cancer. Air contaminant concentrations were estimated using the US EPA NATA and the ASPEN and HEM models. The approximate median concentration of 1,2-dichloroethane is between 1E-4 and 1E-2 (estimated from Figure 1). Exposures were categorized into 5 Quintiles, and compared against Quintile 1. No significant increase in the estimated hazard rate ratio for invasive breast cancer was observed with Quintile 2-5 exposure estimates for 1,2-dichloroethane, adjusted for age and race, when compared against Quintile 1, or when further adjusted using multiple comparisons.

Overall Quality Determination High

* No biomarkers were identified for this evaluation.

Study Citation:	Guo, P., Yokoyama, K., Piao, F., Sakai, K., Khalequzzaman, M., Kamijima, M., Nakajima, T., Kitamura, F. (2013). Sick building syndrome by indoor air pollution in Dalian, China. International Journal of Environmental Research and Public Health 10(4):1489-1504.
Health Outcome(s):	sick building syndrome
Reported Health Effect(s):	The statistical analysis considers all subjective self-reported symptoms together (not segregated by health outcome) as a group health outcome –sick building syndrome. The study compared two conditions for each studied chemical: combined self-reported symptoms to no symptoms. Therefore, only one form 3 was completed.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1938385

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Residents of a housing estate of 3000 homes were invited to a community meeting to explain the purpose of the study and volunteers were invited to participate. It was not reported whether these volunteers were different from the overall eligible population.
	Metric 2:	Attrition	Low	Of the 70 families that agreed to participate, questionnaires were provided by 59. Reasons of uncompleted questionnaires were not fully provided, and there was no comparison between those who participated and those who did not.
	Metric 3:	Comparison Group	Low	The overall description of the analysis sample indicated a wide range of ages and lengths of stay at the current residence. Thus it is hard to know that subjects in all exposure groups were similar. In addition, the methods of selecting participants in all exposure groups were not fully reported. The numbers of male and female smokers were reported, respectively, but the smoking status and age were not controlled in the statistical analysis.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure concentrations for each home were obtained by diffusion sampling over 24 hrs in the bedroom, kitchen, and outdoors; temperature, the vertical height of samplers, and ventilation (hours windows left open) were reported. Samples were analyzed by GC/MS. The number of samples per home is unclear. The frequency of measurements for each house was not reported.
	Metric 5:	Exposure Levels	Low	The frequency of detection was not reported, so it is difficult to ascertain the actual exposure range. In addition, the reported exposure levels were median, geometric mean, and 95% CI, so they are inadequate to develop an exposure-response estimate.
	Metric 6:	Temporality	Uninformative	For 1,2-dichloroethane, the study evaluated self-reported symptoms in the past (”since they moved into their flats”) and their association with sampling conducted during the study; thus, exposure was measured after the outcome.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Low	Participants provided self-reported symptoms using a questionnaire. Study authors cited a previous study, Kamijima et al., 2005 (in Japanese, HERO ID 1598645) for further details on the questionnaire. It was not clear whether the questionnaire was validated.

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Study Citation:	Guo, P., Yokoyama, K., Piao, F., Sakai, K., Khalequzzaman, M., Kamijima, M., Nakajima, T., Kitamura, F. (2013). Sick building syndrome by indoor air pollution in Dalian, China. International Journal of Environmental Research and Public Health 10(4):1489-1504.
Health Outcome(s):	sick building syndrome
Reported Health Effect(s):	The statistical analysis considers all subjective self-reported symptoms together (not segregated by health outcome) as a group health outcome –sick building syndrome. The study compared two conditions for each studied chemical: combined self-reported symptoms to no symptoms. Therefore, only one form 3 was completed.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1938385

Domain	Metric		Rating	Comments
	Metric 8:	Reporting Bias	Low	The study only mentioned subjective symptoms in the abstract or methods. The abstract and method sections did not report the specific symptoms included in the questionnaire or whether the questionnaire was open-ended for symptoms. The questionnaire was cited to Kamijima et al. 2005 (in Japanese).
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	Comparisons were made separately by sex. The distribution of age and time spent living in residence differed greatly between those reporting symptoms and those not reporting symptoms. Smoking was indicated but not controlled for in the analysis. In short, the statistical analysis did not consider these three potential confounders, age, time spent living in residence, and smoking.
	Metric 10:	Covariate Characterization	Low	Covariates were presumably evaluated via a questionnaire that was cited to Kamijima et al. 2005 (in Japanese).
	Metric 11:	Co-exposure Counfounding	Low	The analysis did not account for other exposures. A number of other VOCs, HCHO, and NO2 were measured in the homes. The concentrations of several other VOCs and HCHO were much higher (5-30x) than 1,2-dichloroethane and may also be associated with these symptoms.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Low	The study design is best characterized as cross-sectional. Only one analysis to compare exposure concentrations between those with and without symptoms was adjusted for a confounder, sex, via stratification. Other potential confounders were not adjusted for. Study authors combine responses for symptoms reported before and during the sampling period in one statistical analysis, which may not reflect the relationship between symptoms and contaminants' exposure at each period.
	Metric 13:	Statistical Power	Medium	Statistical power was not reported. The number of participants was sufficient to detect a difference in median concentration between those with and without symptoms.
	Metric 14:	Reproducibility of Analyses	Medium	Study presents sufficient description of analysis (statistical methods) to be conceptually reproducible with access to the raw data.
	Metric 15:	Statistical Analysis	Low	Study uses a Wilcoxon's rank sum test to compare exposure concentrations in persons with and without symptoms; test for equal variance is not reported.

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Study Citation:	Guo, P., Yokoyama, K., Piao, F., Sakai, K., Khalequzzaman, M., Kamijima, M., Nakajima, T., Kitamura, F. (2013). Sick building syndrome by indoor air pollution in Dalian, China. International Journal of Environmental Research and Public Health 10(4):1489-1504.
Health Outcome(s):	sick building syndrome
Reported Health Effect(s):	The statistical analysis considers all subjective self-reported symptoms together (not segregated by health outcome) as a group health outcome –sick building syndrome. The study compared two conditions for each studied chemical: combined self-reported symptoms to no symptoms. Therefore, only one form 3 was completed.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1938385

Domain	Metric	Rating	Comments
Additional Comments:	Concentrations of VOCs (including 1,2-dichloroethane), HCHO, and NO2 were measured in the 59 homes of families that agreed to participate after being informed of the nature of the study. Participants completed questionnaires asking about symptoms since they moved into the homes and the concentrations of selected compounds were compared among men and women reporting any symptoms vs no symptoms. Concentrations of 1,2-dichloroethane in homes of people with symptoms were higher than in homes without. p-Dichlorobenzene was measured in the homes as well, but median concentration was <DL and no further analysis was made. Unacceptable due to selection bias, lack of confounding control, inadequate outcome characterization, and lack of temporality.		

Overall Quality Determination — Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Kernan, G.J., Ji, B.T., Dosemeci, M., Silverman, D.T., Balbus, J., Zahm, S.H. (1999). Occupational risk factors for pancreatic cancer: A case-control study based on death certificates from 24 U.S. states. American Journal of Industrial Medicine 36(2):260-270.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Death from pancreatic cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	194820

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	The National Cancer Institute, National Institute of Occupational Safety and Health, and the National Center for Health Statistics reviewed death certificates from 24 states to select cases from those that had died from pancreatic cancer and matched controls. Controls with cause of death related to the outcome of interest (i.e. pancreatic diseases) were excluded from the study. All key elements of the study design were reported.
	Metric 2:	Attrition	Medium	There was no direct evidence of subject loss or exclusion of subgroups from analyses. The authors provide the total number of cases and controls in the analysis. Case and control data were taken from a registry. It can be assumed that the data are complete for each subject.
	Metric 3:	Comparison Group	High	Controls were selected from the same pool of death certificates from 24 states that cases were selected from. Controls with cause of death related to the outcome of interest were eliminated. Differences in baseline characteristics were controlled for via matching, stratification, and adjustment.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure was assessed via occupation and industry data on death certificates. A job matrix was further applied to assess the likely levels of exposure. Probability and intensity of exposure were estimated across four levels for each occupation. Only employment captured on the death certificate could be considered. The exposure assessment needs exposure information before the job listed on the death certificates.
	Metric 5:	Exposure Levels	Medium	The study offers 4 levels of estimated probability and intensity of exposure (referent, low, medium, high).
	Metric 6:	Temporality	Medium	Exposure was determined by occupational and industry codes on death certificates and indicate that exposure would precede disease, however, the timing and latency period is less clear.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Causes of mortality were determined from death certificates for both cases and controls. Death certificates were drawn from death registries of participating states (n=24). Causes of death were coded using ICD-9 codes, and pancreatic cancer was identified as ICD 157.
	Metric 8:	Reporting Bias	Medium	Measured outcomes, effect estimates and confidence intervals are reported. Number of exposed cases is reported for each analysis, however the number of controls (exposed and unexposed) are not reported for analyses.

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Study Citation:	Kernan, G.J., Ji, B.T., Dosemeci, M., Silverman, D.T., Balbus, J., Zahm, S.H. (1999). Occupational risk factors for pancreatic cancer: A case-control study based on death certificates from 24 U.S. states. American Journal of Industrial Medicine 36(2):260-270.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Death from pancreatic cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	194820

Domain	Metric		Rating	Comments
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Potential confounders were accounted for in the following ways: matching (five year age group, state, race, and gender); adjustment in models (age, marital status, metropolitan, and residential status); and stratification (race and gender). Smoking was not included as a confounder.
	Metric 10:	Covariate Characterization	Medium	Data used to assess potential confounders was derived from death certificates, an adequate measure. However, no information about cigarette smoking and other lifestyle factors were available for adjustment in the analysis.
	Metric 11:	Co-exposure Counfounding	Medium	The variety of industries considered in the analysis diminishes concerns about co-exposures.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The case-control study design and statistical analysis methods were appropriate to assess the exposures/outcome of interest.
	Metric 13:	Statistical Power	Medium	This study had an adequate sample size to detect an effect (n for cases = 63,097; n for controls = 252,386).
	Metric 14:	Reproducibility of Analyses	Medium	The description of analysis was sufficient and would be reproducible.
	Metric 15:	Statistical Analysis	High	The model to calculate risk estimates was transparent.

Additional Comments: This case-control study examined the risk of death from pancreatic cancer in different occupational settings. Exposure was solely assessed using occupation/industry at time of death (reported on death certificate) and the application of a job matrix assessing likely levels of exposure for different positions. This means of estimating exposure may not fully represent a participant's exposure history. Additionally, the number of impacted participants (exposed cases) was inadequate to perform quality analyses for some exposure levels.

Overall Quality Determination High

* No biomarkers were identified for this evaluation.

Study Citation:	Kernan, G.J., Ji, B.T., Dosemeci, M., Silverman, D.T., Balbus, J., Zahm, S.H. (1999). Occupational risk factors for pancreatic cancer: A case-control study based on death certificates from 24 U.S. states. American Journal of Industrial Medicine 36(2):260-270.
Health Outcome(s):	Endocrine
Reported Health Effect(s):	Death from pancreatic cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	194820

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	The National Cancer Institute, National Institute of Occupational Safety and Health, and the National Center for Health Statistics reviewed death certificates from 24 states to select cases from those that had died from pancreatic cancer and matched controls. Controls with cause of death related to the outcome of interest (i.e. pancreatic diseases) were excluded from the study. All key elements of the study design were reported.
	Metric 2:	Attrition	Medium	There was no direct evidence of subject loss or exclusion of subgroups from analyses. The authors provide the total number of cases and controls in the analysis. Case and control data were taken from a registry. It can be assumed that the data are complete for each subject.
	Metric 3:	Comparison Group	High	Controls were selected from the same pool of death certificates from 24 states that cases were selected from. Controls with cause of death related to the outcome of interest were eliminated. Differences in baseline characteristics were controlled for via matching, stratification, and adjustment.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure was assessed via occupation and industry data on death certificates. A job matrix was further applied to assess the likely levels of exposure. Probability and intensity of exposure were estimated across four levels for each occupation. Only employment captured on the death certificate could be considered. The exposure assessment needs exposure information before the job listed on the death certificates.
	Metric 5:	Exposure Levels	Medium	The study offers 4 levels of estimated probability and intensity of exposure (referent, low, medium, high).
	Metric 6:	Temporality	Medium	Exposure was determined by occupational and industry codes on death certificates and indicate that exposure would precede disease, however, the timing and latency period is less clear.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Causes of mortality were determined from death certificates for both cases and controls. Death certificates were drawn from death registries of participating states (n=24). Causes of death were coded using ICD-9 codes, and pancreatic cancer was identified as ICD 157.
	Metric 8:	Reporting Bias	Medium	Measured outcomes, effect estimates and confidence intervals are reported. Number of exposed cases is reported for each analysis, however the number of controls (exposed and unexposed) are not reported for analyses.
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Kernan, G.J., Ji, B.T., Dosemeci, M., Silverman, D.T., Balbus, J., Zahm, S.H. (1999). Occupational risk factors for pancreatic cancer: A case-control study based on death certificates from 24 U.S. states. American Journal of Industrial Medicine 36(2):260-270.
Health Outcome(s):	Endocrine
Reported Health Effect(s):	Death from pancreatic cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	194820

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Medium	Potential confounders were accounted for in the following ways: matching (five year age group, state, race, and gender); adjustment in models (age, marital status, metropolitan, and residential status); and stratification (race and gender). Smoking was not included as a confounder.
	Metric 10:	Covariate Characterization	Medium	Data used to assess potential confounders was derived from death certificates, an adequate measure. However, no information about cigarette smoking and other lifestyle factors were available for adjustment in the analysis.
	Metric 11:	Co-exposure Counfounding	Medium	The variety of industries considered in the analysis diminishes concerns about co-exposures.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The case-control study design and statistical analysis methods were appropriate to assess the exposures/outcome of interest.
	Metric 13:	Statistical Power	Medium	This study had an adequate sample size to detect an effect (n for cases = 63,097; n for controls = 252,386).
	Metric 14:	Reproducibility of Analyses	Medium	The description of analysis was sufficient and would be reproducible.
	Metric 15:	Statistical Analysis	High	The model to calculate risk estimates was transparent.

Additional Comments: This case-control study examined the risk of death from pancreatic cancer in different occupational settings. Exposure was solely assessed using occupation/industry at time of death (reported on death certificate) and the application of a job matrix assessing likely levels of exposure for different positions. This means of estimating exposure may not fully represent a participant's exposure history. Additionally, the number of impacted participants (exposed cases) was inadequate to perform quality analyses for some exposure levels.

Overall Quality Determination High

* No biomarkers were identified for this evaluation.

Study Citation:	Niehoff, N.M., Gammon, M.D., Keil, A.P., Nichols, H.B., Engel, L.S., Sandler, D.P., White, A.J. (2019). Airborne mammary carcinogens and breast cancer risk in the Sister Study. Environment International 130:104897.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Breast cancer diagnosis (overall), tumor characteristics, and estrogen receptor positive (ER+) invasive breast cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5440630

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	Data from the Sister Study were used. The Sister Study is "a prospective cohort of 50,884 women from across the US who were ages 35–74 at enrollment (Sandler et al., 2017). Participants were recruited from 2003 to 2009 using a national advertising campaign in English and Spanish. Women were eligible for the Sister Study if they had a sister who had been diagnosed with breast cancer, but no prior breast cancer themselves."Exclusions from the study occurred for the following reasons:-breast cancer diagnosed before enrollment was complete, or did not have follow-up information (n = 163)-Residential address couldn't be geocoded (n = 1003, < 2%) - This is a small perecentage, but all of those who were excluded for this reason were from Puerto Rico, West Virginia, Missouri, or Oklahoma.Key elements of the study design are reported. There is some potential for selection bias, but based on the small percentage of those eligible who were excluded, participation was not likely to be substantially biased.
	Metric 2:	Attrition	High	Response rates in the overall Sister study remained over 91% over follow-up. Reasons for non-response were not reported, and characteristics of those lost to follow up were not reported or compared with those included, but 9% loss to follow-up is minimal.
	Metric 3:	Comparison Group	High	Differences in baseline characteristics of groups were considered as potential confounding variables.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	The EPA NATA database of census-tract level modeled air toxics data was used. The study authors note the potential for exposure misclassification: "Concentrations at the census tract level do not fully account for variation in an individual's daily activities that could lead to higher or lower exposure, and all women within a census tract are assigned the same concentration."
	Metric 5:	Exposure Levels	Medium	There were five quintiles of exposure, so there was a sufficient range and distribution of exposure.
	Metric 6:	Temporality	Medium	This is a prospective cohort study.Exposure data from 2005 were chosen because they represented the middle of the enrollment period (2003-2009).The study reported that "94% of women enrolled in 2005 or later, and thus the exposure assessment primarily predated enrollment for the majority of Sister Study participants."The six percent of women who had the potential to have the outcome before exposure was measured in 2005 are a concern. But sensitivity analyses were used to assess whether the associations changed when restricted to those who enrolled in 2005 or later.The authors note that the study is making assumptions about the relevant exposure windows - therefore the exposure window is not certain.

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Study Citation:	Niehoff, N.M., Gammon, M.D., Keil, A.P., Nichols, H.B., Engel, L.S., Sandler, D.P., White, A.J. (2019). Airborne mammary carcinogens and breast cancer risk in the Sister Study. Environment International 130:104897.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Breast cancer diagnosis (overall), tumor characteristics, and estrogen receptor positive (ER+) invasive breast cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5440630

Domain	Metric		Rating	Comments
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Women who reported a breast cancer diagnosis on the annual health updates or follow-up questionnaires were asked to provide additional diagnosis information, and to grant permission for the study to obtain medical records and pathology reports. Medical records were obtained for 81% of breast cancer diagnoses. Agreement between self-reported breast cancers and medical records was high (positive predictive value > 99%) (Sandler et al., 2017), so self-report was used when medical records were not available. Tumor characteristics (stage; histology; and estrogen receptor (ER) status) were abstracted from medical records, or self-reported.
	Metric 8:	Reporting Bias	High	A description of measured outcomes is reported. Effect estimates are reported with confidence intervals.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Covariates considered included age, race, BMI, residence type, education, and smoking status. Potential confounders were identified using DAGs and literature review. Appropriate considerations were made for potential confounders.
	Metric 10:	Covariate Characterization	Medium	”Most covariates were assessed by self-report at the baseline interview.””At baseline, women completed a computer-assisted telephone interview and written questionnaires.”Previous publications might describe whether the questionnaires were validated, but validation was not specified in this publication.
	Metric 11:	Co-exposure Counfounding	Medium	Co-exposures to other air pollutants were assessed, but at the census tract level.Multipollutant classification trees were used, which might provide useful qualitative information.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design (large prospective cohort) and analysis method (Cox proportional hazard single and multi-pollutant models accounting for potential confounders) were appropriate to assess the association between exposure and disease.
	Metric 13:	Statistical Power	Medium	The study had an adequate sample size (1975 cancer cases) and follow-up time (mean=8.4 years).
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to be conceptually reproducible.

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Study Citation:	Niehoff, N.M., Gammon, M.D., Keil, A.P., Nichols, H.B., Engel, L.S., Sandler, D.P., White, A.J. (2019). Airborne mammary carcinogens and breast cancer risk in the Sister Study. Environment International 130:104897.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Breast cancer diagnosis (overall), tumor characteristics, and estrogen receptor positive (ER+) invasive breast cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5440630

Domain	Metric	Rating	Comments
	Metric 15: Statistical Analysis	High	Hazard ratios and 95% confidence intervals (CIs) are reported "comparing index categories of exposure to exposures below the first quintile using Cox proportional hazards regression, with age as the time scale." The method of calculating the hazard ratios is transparent. The authors reported that "the proportional hazards assumption was evaluated by conducting a Wald test for an interaction between the continuous form of the air toxic measure and time." Censoring times and times at-risk are described.

Additional Comments: This was a well-conducted study of a large prospective cohort, but the measurement of exposure at the census-tract rather than the individual level is a limitation.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Sobel, W., Bond, G.G., Skowronski, B.J., Brownson, P.J., Cook, R.R. (1987). A soft tissue sarcoma case control study in a large multi-chemical manufacturing facility. Chemosphere 16(8-9):2095-2099.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	soft-tissue sarcoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1357737

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	From a pool of > 37,000 subjects who worked at least 1 year at chemical company between January 1940-December 1979, the study identified 14 people who died due to soft-cell sarcoma (via death certificate, medical records, or histopathology report). Referents were matched 9:1 with cases (126 matched controls).
	Metric 2:	Attrition	High	There was minimal subject exclusion from the analysis sample; one case could not be matched to controls and was excluded from analysis.
	Metric 3:	Comparison Group	High	Cases and controls were recruited from the same eligible population within the same time frame and matched on sex, race, year of birth and year of hire. Both cases and controls had to have worked ≥1 yr at the plant during the study period.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Work histories for cases and referents were coded to determine an individual's potential exposure to chemical of interest and reviewed by an industrial hygienist blinded to case status.
	Metric 5:	Exposure Levels	Low	Exposure was considered dichotomous, ever exposed or never exposed. There is no quantitative information on exposure levels or range of exposures.
	Metric 6:	Temporality	Low	Temporality of exposure and outcome is established. It is unclear if the interval between exposure and outcome is sufficient for soft tissue sarcoma outcomes.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	The soft-tissue sarcoma outcome was assessed by information provided by death certificates, medical records, and histopathology reports, but study authors did not report the proportions determined by each method.
	Metric 8:	Reporting Bias	High	All outcomes outlined were reported. Authors reported the number of cases and controls in the table. Maximum likelihood estimate ORs with respective 95 % confidence intervals were reported.
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Sobel, W., Bond, G.G., Skowronski, B.J., Brownson, P.J., Cook, R.R. (1987). A soft tissue sarcoma case control study in a large multi-chemical manufacturing facility. Chemosphere 16(8-9):2095-2099.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	soft-tissue sarcoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1357737

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Low	Controls were matched with cases on age, sex, year of hire and survival information. There is indirect evidence that the considerations were made to identify potential confounders through evaluation of medical records of cases and controls (various heritable syndromes, family history of cancer, history of lymphedema, steroids, throrotrast, foreign body implants, chronic extensive scarring, radiation therapy, and immunological defects). Identified confounders between cases and controls were not reported and it is unclear if adjustments for these confounders were included in the final analyses.
	Metric 10:	Covariate Characterization	High	Potential covariates were assessed through evaluation of work histories and medical records.
	Metric 11:	Co-exposure Counfounding	Low	The study documented 13 chemicals, known to be associated with soft-tissue sarcoma (according to NTP, 1983) that were used at the manufacturing facility at some point since 1940. The authors note that some individuals were exposed to multiple chemicals during their employment history and were counted multiple times in the analysis for different chemical exposures. Co-exposures to chemicals to not appear to be adjusted for in analysis.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Low	The study design was adequate to assess the association between exposure and the outcome of interest (soft-tissue sarcoma). The study authors noted they used programs developed by Rothman and Boice to calculate odds ratios with CI intervals; the statistical methods are not further described. The page containing the Rothman and Boice reference appears to be missing from the PDF (or the citation is missing).
	Metric 13:	Statistical Power	Low	Statistical power was not calculated. For 1,2-dichloroethane, there was one case and 6 controls included in the analysis, which was not adequate to detect and effect.
	Metric 14:	Reproducibility of Analyses	Low	The study calculated odd ratios, and 95% CIs were calculated using point estimates and chi from hypothesis testing. The study authors noted they used programs developed by Rothman and Boice to calculate odds ratios with 95% CIs; the statistical methods are not further described and there was no reference for the programs cited.
	Metric 15:	Statistical Analysis	Low	A description of analyses/assumptions was not reported.

Additional Comments: A case-control study of workers at a chemical production facility who worked at least 1 year between January 1940-December 1979 (n=37,000) investigated the incidence of deaths due to soft-tissue sarcoma. The study identified 14 people who died due to soft-tissue sarcoma (through death certificate, medical records, or histopathology reports). Cases were matched to controls based on sex, race, year of birth and year of hire. 13 chemicals, including 1,2-dichloroethane, associated with soft-tissue sarcoma were used at the facility; it does not appear that co-exposures were adjusted for in the analysis. Odds ratios and corresponding CIs were calculated. No significant association was found between exposure to 1,2-DCE and soft-tissue sarcoma.

Overall Quality Determination Medium

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Study Citation:	Sobel, W., Bond, G.G., Skowronski, B.J., Brownson, P.J., Cook, R.R. (1987). A soft tissue sarcoma case control study in a large multi-chemical manufacturing facility. Chemosphere 16(8-9):2095-2099.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	soft-tissue sarcoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1357737

Domain	Metric	Rating	Comments

* No biomarkers were identified for this evaluation.

Study Citation:	Sobel, W., Bond, G.G., Skowronski, B.J., Brownson, P.J., Cook, R.R. (1987). A soft tissue sarcoma case control study in a large multi-chemical manufacturing facility. Chemosphere 16(8-9):2095-2099.
Health Outcome(s):	Skin and Connective Tissue
Reported Health Effect(s):	soft-tissue sarcoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1357737

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	From a pool of > 37,000 subjects who worked at least 1 year at chemical company between January 1940-December 1979, the study identified 14 people who died due to soft-cell sarcoma (via death certificate, medical records, or histopathology report). Referents were matched 9:1 with cases (126 matched controls).
	Metric 2:	Attrition	High	There was minimal subject exclusion from the analysis sample; one case could not be matched to controls and was excluded from analysis.
	Metric 3:	Comparison Group	High	Cases and controls were recruited from the same eligible population within the same time frame and matched on sex, race, year of birth and year of hire. Both cases and controls had to have worked ≥1 yr at the plant during the study period.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Work histories for cases and referents were coded to determine an individual's potential exposure to chemical of interest and reviewed by an industrial hygienist blinded to case status.
	Metric 5:	Exposure Levels	Low	Exposure was considered dichotomous, ever exposed or never exposed. There is no quantitative information on exposure levels or range of exposures.
	Metric 6:	Temporality	Low	Temporality of exposure and outcome is established. It is unclear if the interval between exposure and outcome is sufficient for soft tissue sarcoma outcomes.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	The soft-tissue sarcoma outcome was assessed by information provided by death certificates, medical records, and histopathology reports, but study authors did not report the proportions determined by each method.
	Metric 8:	Reporting Bias	High	All outcomes outlined were reported. Authors reported the number of cases and controls in the table. Maximum likelihood estimate ORs with respective confidence intervals were reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	Controls were matched with cases on age, sex, year of hire and survival information. There is indirect evidence that that considerations were made to identify potential confounders through evaluation of medical records of cases and controls (various heritable syndromes, family history of cancer, history of lymphedema, steroids, throrotrast, foreign body implants, chronic extensive scarring, radiation therapy, and immunological defects). Identified confounders between cases and controls were not reported and it is unclear if adjustments for these confounders were included in the final analyses.

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Study Citation:	Sobel, W., Bond, G.G., Skowronski, B.J., Brownson, P.J., Cook, R.R. (1987). A soft tissue sarcoma case control study in a large multi-chemical manufacturing facility. Chemosphere 16(8-9):2095-2099.
Health Outcome(s):	Skin and Connective Tissue
Reported Health Effect(s):	soft-tissue sarcoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1357737

Domain	Metric		Rating	Comments
	Metric 10:	Covariate Characterization	High	Potential covariates were assessed through evaluation of work histories and medical records.
	Metric 11:	Co-exposure Counfounding	Low	The study documented 13 chemicals, known to be associated with soft-tissue sarcoma (according to NTP, 1983) that were used at the manufacturing facility at some point since 1940. The authors note that some individuals were exposed to multiple chemicals during their employment history and were counted multiple times in the analysis for different chemical exposures. Co-exposures to chemicals to not appear to be adjusted for in analysis.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Low	The study design was adequate to assess the association between exposure and the outcome of interest (soft-tissue sarcoma). The study authors noted they used programs developed by Rothman and Boice to calculate odds ratios with (95% CIs; the statistical methods are not further described. The page containing the Rothman and Boice reference appears to be missing from the PDF (or the citation is missing).
	Metric 13:	Statistical Power	Low	Statistical power was not calculated. For 1,2-dichloroethane, there was one case and 6 controls included in the analysis, which was not adequate to detect and effect.
	Metric 14:	Reproducibility of Analyses	Low	The study calculated odd ratios, and 95% CIs were calculated using point estimates and chi from hypothesis testing. The study authors noted they used programs developed by Rothman and Boice to calculate odds ratios with CI intervals; the statistical methods are not further described and there was no reference for the programs cited.
	Metric 15:	Statistical Analysis	Low	A description of analyses/assumptions was not reported.

Additional Comments: A case-control study of workers at a chemical production facility who worked at least 1 year between January 1940-December 1979 (n=37,000) investigated the incidence of deaths due to soft-tissue sarcoma. The study identified 14 people who died due to soft-tissue sarcoma (through death certificate, medical records, or histopathology reports). Cases were matched to controls based on sex, race, year of birth and year of hire. 13 chemicals, including 1,2-dichloroethane, associated with soft-tissue sarcoma were used at the facility; it does not appear that co-exposures were adjusted for in the analysis. Odds ratios and corresponding CIs were calculated. No significant association was found between exposure to 1,2-DCE and soft-tissue sarcoma.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Teta, M. J., Ott, M. G., Schnatter, A. R. (1991). An update of mortality due to brain neoplasms and other causes among employees of a petrochemical facility. Journal of Occupational Medicine 33(1):45-51.
Health Outcome(s):	Mortality
Reported Health Effect(s):	all cause mortality, gastrointestinal cancer mortality, respiratory system cancer mortality, kidney and other urinary organ cancer mortality, skin cancer mortality, brain cancer mortality, lymphatic and hematopoietic tissue cancer mortality, benign neoplasm mortality, heart disease mortality, and liver cirrhosis mortality.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200633, 1629047
HERO ID:	200633

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	The facility was described in some detail. All male employees working for one day or more between 1941 and 1983 were included. There may be some healthy worker effect in this population.
	Metric 2:	Attrition	High	Study authors reported that vital status was complete for 99% of the population, and death certificates were obtained for 99% of decedents.
	Metric 3:	Comparison Group	High	SMRs were calculated using age-, race-, and calendar year-specific mortality rates of males in the United States. All included employees were male.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	All employees were treated as exposed. Table 4 indicates that relatively few employees were employed in areas designated as 1,2-DCA work areas. There is potential for substantial exposure misclassification.
	Metric 5:	Exposure Levels	Low	All employed individuals were categorized as exposed, and the reference population was described as unexposed. This represents two levels of exposure. The distribution of exposure within the employed population is unclear.
	Metric 6:	Temporality	Medium	Employees were followed from 1950 (or date of first hire) through 1983. The relevant timing of exposure is not entirely clear; however, this represents a sufficiently long period of follow-up.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Mortality was tracked using company records, Social Security Administration records, and the National Death Index. Specific ICD codes and use of a nosologist were not described, but there was no evidence to suggest the method had poor validity.
	Metric 8:	Reporting Bias	High	SMRs were provided with confidence intervals in addition to observed and expected cases. The authors state they did not carry out regional specific SMRs due to the higher prevalence of neoplasms in the surrounding area.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	SMRs were restricted to males. Rates were age-, race-, and calendar period-specific. No consideration was made for smoking.
	Metric 10:	Covariate Characterization	Medium	Demographic information was obtained from employment records. This was not a validated method, but there was no evidence to suggest it was an invalid method.

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Study Citation:	Teta, M. J., Ott, M. G., Schnatter, A. R. (1991). An update of mortality due to brain neoplasms and other causes among employees of a petrochemical facility. Journal of Occupational Medicine 33(1):45-51.
Health Outcome(s):	Mortality
Reported Health Effect(s):	all cause mortality, gastrointestinal cancer mortality, respiratory system cancer mortality, kidney and other urinary organ cancer mortality, skin cancer mortality, brain cancer mortality, lymphatic and hematopoietic tissue cancer mortality, benign neoplasm mortality, heart disease mortality, and liver cirrhosis mortality.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200633, 1629047
HERO ID:	200633

Domain	Metric		Rating	Comments
	Metric 11:	Co-exposure Counfounding	Low	Several other occupational exposures linked to cancer mortality were present, including vinyl chloride, butanol, and other petrochemicals.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	This study design was appropriate for the research question. Authors utilized retrospective occupational cohort data to determine standardized mortality rates for cancer-specific mortalities.
	Metric 13:	Statistical Power	Medium	While power was not calculated, there were over 1350 deaths from 7849 employees which was adequate to detect robust effect estimates.
	Metric 14:	Reproducibility of Analyses	Low	Most details were provided; however, ICD codes used to determine and group cancer mortality diagnoses were not provided.
	Metric 15:	Statistical Analysis	High	No issues identified.

Additional Comments: This study utilized an occupational cohort to retrospectively evaluate elevated rates of cancer mortality among petrochemical plant workers. There were numerous potentially hazardous chemicals mentioned in the plant description which may lead to co-exposure. Additionally, it appears that only a moderate portion of workers may have been exposed to 1,2-DCA or worked in 1,2-DCA areas which may lead to some exposure misclassification and limit the study's ability to inform hazard on 1,2-DCA.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Cases in this case-control study were former Union Carbide Corporation (UCC) chemical plant employees in Texas City, Texas. Cases were identified through death certificate searches and tumor registries, and may have included individuals formerly employed at UCC whose cause of death was unknown to the company. Additionally, control deaths were stated to be pulled from corporate employee benefits department and through locally published obituary notices routinely screened by the medical department - it is possible to assume that cases were identified in a similar manner. The study identified cases of brain tumors by searching death certificates primarily, although tumor registries throughout the state of Texas were also searched. The study clarifies that it is possible that some cases were not found if they survived or died due to another cause - while this is likely to have impacted selection, there is no evidence that this would be differential by exposure status. Overall, there is limited information on the source population of workers from which cases were identified.
	Metric 2:	Attrition	Medium	Attrition is not discussed in the study, and outcome data appear to be complete. There was a large proportion of missing exposure data (roughly 50%) due to workers being employed in roles such as maintenance, where exposure to any chemical is possible but unknown. Analyses were run separately where these ”unknown” individuals were a) treated as exposed, b) treated as unexposed, or c) treated as unknown and thus excluded. The study only presents results for when these individuals were excluded but specifies that the first scenario resulted in increased exposure estimates for controls relative to cases.

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Study Citation:	Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
	Metric 3:	Comparison Group	Medium	The study identifies two series of control groups, selected from all former Union Carbide Corporation (UCC) employees. However, the total number of employees is not stated. Only those who were deceased were used as controls since they had known causes of death and could thus be verified as non-brain tumors. One group of controls excluded employees whose cause of death was due to any malignant neoplasm to allow for the possibility that a general chemical carcinogen may have been associated with cancers of other sites. The other group of controls included deaths from all causes; this included malignant neoplasms other than brain tumors. Both control groups had 80 male employees randomly selected from 450 deceased employees known to the company in June 1979. Control deaths were stated to be pulled from corporate employee benefits department and through locally published obituary notices routinely screened by the medical department - it is possible to assume that cases were identified in a similar manner. The study reports that cases were slightly more likely to have been employed for less than 10 years than controls - the study attributes this in part to the fact that employees whose deaths were known to the company were more likely to have worked for longer - regardless the mean number of years employed was similar between cases and controls. However, cases were more likely to have been terminated from their job for reasons other than death, disability, or retirement (quitting, being fired, etc.), were generally younger at hire, and were less likely to survive to their 70th birthday. None of these factors are controlled for in statistical analyses - however, since controls and cases were pulled from the same population, there is indirect evidence that the groups were similar.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was determined based on official employment records. Records included job title and department assignment codes for each employment from date of hire to date of termination. For each unique department code, UCC and NIOSH industrial hygienists identified principal chemicals used or produced at any time in the history of the plant and correlated those with individual departments. This assessment was not performed on a year-by-year basis due to concerns for recall bias for longer-term employees where less detailed records were kept. An employee was categorized as ”exposed” to 1,2-dichloroethane if they ever worked in a department associated with that chemical. An ”unknown” exposure group was also created to account for employees who had only worked in departments for which no specific chemical could be identified.
	Metric 5:	Exposure Levels	Low	The study does not report any quantitative information and only splits exposure into ”exposed”, ”unexposed”, and ”unknown”.
	Metric 6:	Temporality	High	In this study exposure is confirmed to occur before the outcome is measured. The study reports latency periods, with subjects dichotomized into less than 15 years of latency or more than 15 years of latency. The majority of cases and controls had a latency of greater than 15 years, which is sufficiently long for brain tumors.

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Study Citation:	Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Cases were identified through death certificate searches and partially through tumor registries in the state of Texas. Case validation was performed by NIOSH, and 5 different levels of confirmation were reported: 1) tissue specimen interpreted by the Armed Forces Institute of Pathology; 2) autopsy report; 3) histopathology report; 4) clinical diagnosis from hospital record; 5) dearth certificate diagnosis. Codes 1-3 were considered to be ”confirmed” cases of brain tumors, while 4-5 were considered unconfirmed. 5/21 cases were only evaluated using ”unconfirmed methods”, meaning there is likely a high amount of accuracy in roughly 75% of cases. While no case validation is reported for controls, the study specifies that only controls who had died and thus could be confirmed to be non-brain tumors were included.
	Metric 8:	Reporting Bias	Medium	All primary and secondary outcomes that are outlined in the methods are reported in the results. However, the only statistical outcome of their analysis were unadjusted p-values that were not reported and were just described qualitatively.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	The only statistical analysis performed were Mantel-Haenszel chi-squared tests, which did not allow for confounder adjustment. The study does not present a distribution of potential confounders by exposure status but by case/control status. Several variables, such as reason for termination, age at hire, and age at death were significantly different between cases and controls and were not accounted for in statistical modeling. The study explains that these differences are not likely to have any epidemiologic significance and appear to be relatively small differences.
	Metric 10:	Covariate Characterization	Medium	While the study does not explain where they obtained covariate information, it is reasonable to assume that they gathered the information from company records.
	Metric 11:	Co-exposure Counfounding	Low	The study assesses a wide range of other potential occupational co-exposures. While these co-exposures are not adjusted for in any statistical models, effect estimates are presented separately for benzene, diethyl sulfate, ethylene oxide, and vinyl chloride. The distribution of co-exposures across cases and controls is demonstrated to be mostly balanced by comparing proportions of exposed/unexposed between cases and controls. The only notable instance of imbalance is for benzene, where 11.1% of cases were exposed whereas 37.9% of all controls and 19.2% of non-neoplasm related controls were exposed.
Domain 5: Analysis				

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Study Citation:	Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	The study chose a case-control design, which was appropriate to study the rare disease of brain tumors and its association with occupational exposures. The only statistical analysis conducted is a Mantzel-Haenszel chi-squared test, but there is no reason to suggest that this would be inappropriate.
	Metric 13:	Statistical Power	Medium	The study does not calculate statistical power, but the number of cases (n=21) and controls (n=80 in each analysis) is likely sufficient to detect an effect.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to understand what was done and could be reproduced given access to the analytic data.
	Metric 15:	Statistical Analysis	High	The only statistical analysis conducted is a Mantel-Haenszel chi-squared test, and all assumptions were met. The statistical process is transparent.

Additional Comments: This case-control study pulled deceased former employees of the Union Carbide Corporation in Texas City, Texas. The study examined dichotomous exposure to a wide range of occupational exposures, including 1,2-dichloroethane, in relation to brain tumor cases. There is no quantitative estimate of exposure. The only statistical analysis in the study is a Mantel-Haenszel chi-squared test statistic and no statistically significant differences in exposure between cases and controls were observed. The fact that there are no effect estimates, no adjustment for confounders, and no quantitative exposure estimates limits the usefulness of this paper.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Cases in this case-control study were former Union Carbide Corporation (UCC) chemical plant employees in Texas City, Texas. Cases were identified through death certificate searches and tumor registries, and may have included individuals formerly employed at UCC whose cause of death was unknown to the company. Additionally, control deaths were stated to be pulled from corporate employee benefits department and through locally published obituary notices routinely screened by the medical department - it is possible to assume that cases were identified in a similar manner. The study identified cases of brain tumors by searching death certificates primarily, although tumor registries throughout the state of Texas were also searched. The study clarifies that it is possible that some cases were not found if they survived or died due to another cause - while this is likely to have impacted selection, there is no evidence that this would be differential by exposure status. Overall, there is limited information on the source population of workers from which cases were identified.
	Metric 2:	Attrition	Medium	Attrition is not discussed in the study, and outcome data appear to be complete. There was a large proportion of missing exposure data (roughly 50%) due to workers being employed in roles such as maintenance, where exposure to any chemical is possible but unknown. Analyses were run separately where these ”unknown” individuals were a) treated as exposed, b) treated as unexposed, or c) treated as unknown and thus excluded. The study only presents results for when these individuals were excluded but specifies that the first scenario resulted in increased exposure estimates for controls relative to cases.

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Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
	Metric 3:	Comparison Group	Medium	The study identifies two series of control groups, selected from all former Union Carbide Corporation (UCC) employees. However, the total number of employees is not stated. Only those who were deceased were used as controls since they had known causes of death and could thus be verified as non-brain tumors. One group of controls excluded employees whose cause of death was due to any malignant neoplasm to allow for the possibility that a general chemical carcinogen may have been associated with cancers of other sites. The other group of controls included deaths from all causes; this included malignant neoplasms other than brain tumors. Both control groups had 80 male employees randomly selected from 450 deceased employees known to the company in June 1979. Control deaths were stated to be pulled from corporate employee benefits department and through locally published obituary notices routinely screened by the medical department - it is possible to assume that cases were identified in a similar manner. The study reports that cases were slightly more likely to have been employed for less than 10 years than controls - the study attributes this in part to the fact that employees whose deaths were known to the company were more likely to have worked for longer - regardless the mean number of years employed was similar between cases and controls. However, cases were more likely to have been terminated from their job for reasons other than death, disability, or retirement (quitting, being fired, etc.), were generally younger at hire, and were less likely to survive to their 70th birthday. None of these factors are controlled for in statistical analyses - however, since controls and cases were pulled from the same population, there is indirect evidence that the groups were similar.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was determined based on official employment records. Records included job title and department assignment codes for each employment from date of hire to date of termination. For each unique department code, UCC and NIOSH industrial hygienists identified principal chemicals used or produced at any time in the history of the plant and correlated those with individual departments. This assessment was not performed on a year-by-year basis due to concerns for recall bias for longer-term employees where less detailed records were kept. An employee was categorized as ”exposed” to 1,2-dichloroethane if they ever worked in a department associated with that chemical. An ”unknown” exposure group was also created to account for employees who had only worked in departments for which no specific chemical could be identified.
	Metric 5:	Exposure Levels	Low	The study does not report any quantitative information and only splits exposure into ”exposed”, ”unexposed”, and ”unknown”.
	Metric 6:	Temporality	High	In this study exposure is confirmed to occur before the outcome is measured. The study reports latency periods, with subjects dichotomized into less than 15 years of latency or more than 15 years of latency. The majority of cases and controls had a latency of greater than 15 years, which is sufficiently long for brain tumors.

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Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Cases were identified through death certificate searches and partially through tumor registries in the state of Texas. Case validation was performed by NIOSH, and 5 different levels of confirmation were reported: 1) tissue specimen interpreted by the Armed Forces Institute of Pathology; 2) autopsy report; 3) histopathology report; 4) clinical diagnosis from hospital record; 5) dearth certificate diagnosis. Codes 1-3 were considered to be ”confirmed” cases of brain tumors, while 4-5 were considered unconfirmed. 5/21 cases were only evaluated using ”unconfirmed methods”, meaning there is likely a high amount of accuracy in roughly 75% of cases. While no case validation is reported for controls, the study specifies that only controls who had died and thus could be confirmed to be non-brain tumors were included.
	Metric 8:	Reporting Bias	Medium	All primary and secondary outcomes that are outlined in the methods are reported in the results. However, the only statistical outcome of their analysis were unadjusted p-values that were not reported and were just described qualitatively.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	The only statistical analysis performed were Mantel-Haenszel chi-squared tests, which did not allow for confounder adjustment. The study does not present a distribution of potential confounders by exposure status but by case/control status. Several variables, such as reason for termination, age at hire, and age at death were significantly different between cases and controls and were not accounted for in statistical modeling. The study explains that these differences are not likely to have any epidemiologic significance and appear to be relatively small differences.
	Metric 10:	Covariate Characterization	Medium	While the study does not explain where they obtained covariate information, it is reasonable to assume that they gathered the information from company records.
	Metric 11:	Co-exposure Counfounding	Low	The study assesses a wide range of other potential occupational co-exposures. While these co-exposures are not adjusted for in any statistical models, effect estimates are presented separately for benzene, diethyl sulfate, ethylene oxide, and vinyl chloride. The distribution of co-exposures across cases and controls is demonstrated to be mostly balanced by comparing proportions of exposed/unexposed between cases and controls. The only notable instance of imbalance is for benzene, where 11.1% of cases were exposed whereas 37.9% of all controls and 19.2% of non-neoplasm related controls were exposed.
Domain 5: Analysis				

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Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	The study chose a case-control design, which was appropriate to study the rare disease of brain tumors and its association with occupational exposures. The only statistical analysis conducted is a Mantzel-Haenszel chi-squared test, but there is no reason to suggest that this would be inappropriate.
	Metric 13:	Statistical Power	Medium	The study does not calculate statistical power, but the number of cases (n=21) and controls (n=80 in each analysis) is likely sufficient to detect an effect.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to understand what was done and could be reproduced given access to the analytic data.
	Metric 15:	Statistical Analysis	High	The only statistical analysis conducted is a Mantel-Haenszel chi-squared test, and all assumptions were met. The statistical process is transparent.

Additional Comments: This case-control study pulled deceased former employees of the Union Carbide Corporation in Texas City, Texas. The study examined dichotomous exposure to a wide range of occupational exposures, including 1,2-dichloroethane, in relation to brain tumor cases. There is no quantitative estimate of exposure. The only statistical analysis in the study is a Mantel-Haenszel chi-squared test statistic and no statistically significant differences in exposure between cases and controls were observed. The fact that there are no effect estimates, no adjustment for confounders, and no quantitative exposure estimates limits the usefulness of this paper.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	Urinary system cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	Urinary system cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	Urinary system cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Immune/Hematological
Reported Health Effect(s):	Lymphatic and hematopoietic tissue cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Immune/Hematological
Reported Health Effect(s):	Lymphatic and hematopoietic tissue cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Immune/Hematological
Reported Health Effect(s):	Lymphatic and hematopoietic tissue cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Other cancers (not specified)
Reported Health Effect(s):	Other cancers (not specified)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Other cancers (not specified)
Reported Health Effect(s):	Other cancers (not specified)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Other cancers (not specified)
Reported Health Effect(s):	Other cancers (not specified)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Mortality
Reported Health Effect(s):	All-cause mortality
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Vital status was tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Medium	Death rates among unit employees were compared to death rates in the U.S. population adjusted for age and gender. Demographics of the exposed workers are not provided; therefore, it is not clear whether additional adjustment for race may have been appropriate. No justification is provided for the choice of the entire U.S. population as the comparison group. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis. Additional analyses are conducted limiting workers to those with the greatest likelihood of exposure (i.e., those working in jobs with high likelihood of contact with chemicals for more than a year, those working for the full year of 1979 during which chemical exposures were most frequently reported); these smaller groups are also compared to the unexposed general population.
	Metric 6:	Temporality	High	Temporality was established due to the longitudinal design and the use of mortality as the outcome. Exposures occurred between 1979 and 1987 and follow-up for vital status was conducted through 2003.
Domain 3: Outcome Assessment				

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Mortality
Reported Health Effect(s):	All-cause mortality
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Medium	The study did not provide information on how mortality was assessed either in the exposed population or in the comparison population; use of death certificates is implied but not stated.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected deaths are reported, but SIRs and 95% confidence intervals are not provided.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Comparisons of observed versus expected deaths were adjusted for age and gender. Demographics of the exposed workers are not provided; therefore, it is not clear whether additional adjustment for race may have been appropriate.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records or death records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed deaths among a population of exposed workers compared to expected deaths among the U.S. population, adjusted for age and gender.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected deaths; no SIR was provided. Expected death rates were adjusted for age and gender.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Mortality
Reported Health Effect(s):	All-cause mortality
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	All cancer (excluding non-melanoma skin cancer), digestive system cancer, colorectal cancer, respiratory cancer, prostate cancer, urinary system cancer, lymphatic and hematopoietic tissue cancer, other cancers (not specified)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
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	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	All cancer (excluding non-melanoma skin cancer), digestive system cancer, colorectal cancer, respiratory cancer, prostate cancer, urinary system cancer, lymphatic and hematopoietic tissue cancer, other cancers (not specified)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	All cancer (excluding non-melanoma skin cancer), digestive system cancer, colorectal cancer, respiratory cancer, prostate cancer, urinary system cancer, lymphatic and hematopoietic tissue cancer, other cancers (not specified)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Gastrointestinal
Reported Health Effect(s):	Digestive system cancer, colorectal cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Gastrointestinal
Reported Health Effect(s):	Digestive system cancer, colorectal cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Gastrointestinal
Reported Health Effect(s):	Digestive system cancer, colorectal cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Lung/Respiratory
Reported Health Effect(s):	Respiratory cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Lung/Respiratory
Reported Health Effect(s):	Respiratory cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Lung/Respiratory
Reported Health Effect(s):	Respiratory cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Prostate cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Prostate cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Prostate cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Male workers who had ever been assigned to the chlorohydrin unit between 1 January 1940 and 31 December 1967 at Union Carbide's South Charleston plant were enrolled and matched to the US National Death Index. Status on 5 workers could not be identified. Information on how workers were matched to death index was not specified.
	Metric 2:	Attrition	Medium	Rate of inclusion/participation was very high, as records were able to be matched for 98% of participants. Medium rating given because information on how participants whose vital status was not known was not specified.
	Metric 3:	Comparison Group	Uninformative	Unacceptable rating given because SMRs were calculated based on expected deaths from a reference population matched on sex, but not age.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Exposure was assessed based on duration of work in the plant. No information is provided on exposure levels, and a JEM was not used.
	Metric 5:	Exposure Levels	Uninformative	No information provided on levels of exposure.
	Metric 6:	Temporality	High	Temporality is well established; person-years stopped accumulating in 1967 and outcome was assessed beginning at that time.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar period, and interval since assignments, but distribution of these covariates was not reported.
	Metric 10:	Covariate Characterization	Medium	Information on covariate characterization not provided, but the selected covariates (age, calendar period, and interval since assignments) were likely extracted from employee records and unlikely to be largely problematic
	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.

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Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Study design was appropriate for the research method. Statistical methods were also appropriate.
	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.
	Metric 14:	Reproducibility of Analyses	Medium	Methods are well-enough described that study could be adequately reproduced.
	Metric 15:	Statistical Analysis	High	SMRs calculated based on US general population mortality for white males through 1988. RRs were "evaluated over levels of duration of assignment to the chlorohydrin unit, stratified by age, calendar year, and interval since first assignment to the chlorohydrin unit".

Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Male workers who had ever been assigned to the chlorohydrin unit between 1 January 1940 and 31 December 1967 at Union Carbide's South Charleston plant were enrolled and matched to the US National Death Index. Status on 5 workers could not be identified. Information on how workers were matched to death index was not specified.
	Metric 2:	Attrition	Medium	Rate of inclusion/participation was very high, as records were able to be matched for 98% of participants. Medium rating given because information on how participants whose vital status was not known was not specified.
	Metric 3:	Comparison Group	Uninformative	Unacceptable rating given because SMRs were calculated based on expected deaths from a reference population matched on sex, but not age.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Exposure was assessed based on duration of work in the plant. No information is provided on exposure levels, and a JEM was not used.
	Metric 5:	Exposure Levels	Uninformative	No information provided on levels of exposure.
	Metric 6:	Temporality	High	Temporality is well established; person-years stopped accumulating in 1967 and outcome was assessed beginning at that time.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar period, and interval since assignments, but distribution of these covariates was not reported.
	Metric 10:	Covariate Characterization	Medium	Information on covariate characterization not provided, but the selected covariates (age, calendar period, and interval since assignments) were likely extracted from employee records and unlikely to be largely problematic
	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.
Domain 5: Analysis				

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Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Study design was appropriate for the research method. Statistical methods were also appropriate.
	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.
	Metric 14:	Reproducibility of Analyses	Medium	Methods are well-enough described that study could be adequately reproduced.
	Metric 15:	Statistical Analysis	High	SMRs calculated based on US general population mortality for white males through 1988. RRs were ”evaluated over levels of duration of assignment to the chlorohydrin unit, stratified by age, calendar year, and interval since first assignment to the chlorohydrin unit”.

Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

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Linked HERO ID(s):	200224, 5447107
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Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Male workers who had ever been assigned to the chlorohydrin unit between 1 January 1940 and 31 December 1967 at Union Carbide's South Charleston plant were enrolled and matched to the US National Death Index. Status on 5 workers could not be identified. Information on how workers were matched to death index was not specified.
	Metric 2:	Attrition	Medium	Rate of inclusion/participation was very high, as records were able to be matched for 98% of participants. Medium rating given because information on how participants whose vital status was not known was not specified.
	Metric 3:	Comparison Group	Uninformative	Unacceptable rating given because SMRs were calculated based on expected deaths from a reference population matched on sex, but not age.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Exposure was assessed based on duration of work in the plant. No information is provided on exposure levels, and a JEM was not used.
	Metric 5:	Exposure Levels	Uninformative	No information provided on levels of exposure.
	Metric 6:	Temporality	High	Temporality is well established; person-years stopped accumulating in 1967 and outcome was assessed beginning at that time.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar period, and interval since assignments, but distribution of these covariates was not reported.
	Metric 10:	Covariate Characterization	Medium	Information on covariate characterization not provided, but the selected covariates (age, calendar period, and interval since assignments) were likely extracted from employee records and unlikely to be largely problematic
	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.
Domain 5: Analysis				

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Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
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	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.
	Metric 14:	Reproducibility of Analyses	Medium	Methods are well-enough described that study could be adequately reproduced.
	Metric 15:	Statistical Analysis	High	SMRs calculated based on US general population mortality for white males through 1988. RRs were ”evaluated over levels of duration of assignment to the chlorohydrin unit, stratified by age, calendar year, and interval since first assignment to the chlorohydrin unit”.

Additional Comments: None

Overall Quality Determination Uninformative

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	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.
Domain 4: Potential Confounding / Variability Control				
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Domain 5: Analysis				

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Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Study design was appropriate for the research method. Statistical methods were also appropriate.
	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.
	Metric 14:	Reproducibility of Analyses	Medium	Methods are well-enough described that study could be adequately reproduced.
	Metric 15:	Statistical Analysis	High	SMRs calculated based on US general population mortality for white males through 1988. RRs were ”evaluated over levels of duration of assignment to the chlorohydrin unit, stratified by age, calendar year, and interval since first assignment to the chlorohydrin unit”.

Additional Comments: None

Overall Quality Determination Uninformative

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Domain 5: Analysis				

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Additional Comments: None

Overall Quality Determination Uninformative

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Domain 5: Analysis				

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Additional Comments: None

Overall Quality Determination Uninformative

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Domain 1: Study Participation				
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Domain 5: Analysis				

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Additional Comments: None

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Domain 5: Analysis				

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Domain	Metric		Rating	Comments
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Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Bove, F. J. (1996). Public drinking water contamination and birthweight, prematurity, fetal deaths, and birth defects. Toxicology and Industrial Health 12(2):255-266.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	200239

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	This cross-sectional study (n=80,938) included all registered singleton live births and fetal deaths (>20 weeks' gestation) in 1985-88 in 75 New Jersey towns located in 4 counties with "some" water supplies contaminated with substances of interest and where: (i) residents were "mostly" served by public water systems; and (ii) births occurred "mostly" in state. Estimated proportions of residents served by public water systems, and of pregnancies/births captured, were not described. However, the inclusion of all eligible registered births, fetal deaths, and birth defects, as well as the selection of towns without knowledge of birth outcome prevalence, limited the likelihood of selection bias.
	Metric 2:	Attrition	Medium	All registered births and fetal deaths were included. Attrition due to missing values for multiple variables was not quantified and is therefore uncertain. However, attrition was likely modest as the proportion of missing values for individual variables was relatively low: (i) ~6% of subjects were excluded from analyses of outcomes such as preterm birth due to invalid or missing gestational ages; and (ii) other covariates evaluated as confounders had up to 4.9% missing values.
	Metric 3:	Comparison Group	High	After excluding plural pregnancies and chromosomal abnormalities, all registered live births during the study period in the areas included without the outcomes of interest were included in the comparison group. This comprehensive approach limited the potential for bias. Chromosomal abnormalities were not included as outcomes as they were not hypothesized to be associated with the exposures under study but were appropriately excluded given their uncertain etiology.
Domain 2: Exposure Characterization				

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Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
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Domain	Metric		Rating	Comments
	Metric 4:	Measurement of Exposure	Medium	Along with several other contaminants, residential drinking water exposure to 1,2-dichloroethane (as well as 1,1,1-trichloroethane and 'total dichloroethylenes') – was assigned based on maternal town of residence at birth. Exposure estimates were calculated using the average of water company sampling reports during the first trimester (for birth defects and fetal death) or the duration of pregnancy (for other outcomes). Detection limits and data availability were not specified in detail but were described as below 1 ppb, with reporting compliance >85%. A minimum of 1 sample per 6-month interval was required; variability in the number of measures available across water systems and towns was not described. Additional sources of measurement error included: changes in residence during pregnancy; water from alternate sources (ex. private wells, bottles, workplaces); variability in residential contaminant levels vs measured samples; unknown levels of tap water intake; and errors in estimated dermal and inhalation exposure while bathing or showering. While the extent of exposure misclassification is uncertain, there is no evidence to suggest it was differential rather than random.
	Metric 5:	Exposure Levels	Medium	Due to the high proportion of measures below detection limits, analyses relating exposure to health outcomes used only 2 categories for each of the chlorinated solvents of interest: cutoffs close to detection limits were used to define elevated exposure. Proportions defined as having elevated exposure was low (1.8% had 1,1-dichloroethylene ≥1 ppb). An important concern is that relatively low levels of exposure to these contaminants from sources other than residential drinking water, for which data were not available, could potentially have resulted in considerable misclassification.
	Metric 6:	Temporality	High	Exposure levels were assigned based on contaminant exposures estimated during: (i) the first trimester for analyses of birth defects and fetal deaths; and (ii) the duration of pregnancy for other pregnancy outcomes.

Domain 3: Outcome Assessment

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Study Citation:	Bove, F. J. (1996). Public drinking water contamination and birthweight, prematurity, fetal deaths, and birth defects. Toxicology and Industrial Health 12(2):255-266.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	200239

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcomes included measures of birthweight (continuous among term births, low term birthweight, very low birthweight), prematurity, fetal death, and congenital anomalies in live births or fetal deaths. The anomalies analyzed included defects of the central nervous system, neural tube, oral cleft, total cardiac, major cardiac, ventricular septum, and any surveillance defect excluding chromosomal defects. All outcomes were identified using birth certificates, fetal death certificates (>20 weeks' gestation), and the NJ congenital birth defect registry (ICD codes provided). These registry data are likely to be sufficiently valid for late pregnancy outcomes. However, their limited ability to capture early pregnancy losses is a weakness. The sample included only 594 fetal deaths (less than 1% of the >80,0000 sample). Typical estimates are that 10-20%, of recognized pregnancies ending in losses. Moreover, developmental defects contributing to early pregnancy losses were also not captured. A further limitation is that that potentially etiologically heterogeneous preterm birth types were analyzed together, as these data did not distinguish premature rupture of membranes vs idiopathic prematurity.
	Metric 8:	Reporting Bias	Medium	Models were constructed only for contaminants with associations > 1.0, and tables included only associations with odds ratios ≥1.5. No clear rationale was provided. Several positive odds ratios below the 1.5 cutoff were described in the results text (without confidence intervals), but no null/negative odds ratios were presented or described.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Potential confounding by maternal race, education, parity, and prior pregnancy loss, along with infant sex (for birth outcomes) and adequacy of prenatal care, was examined. Gestational age was addressed by analyzing birthweight among full term births, term low birth weight, and small size for gestational age. Only fully adjusted models were presented. In a companion case-control study (with low participation rates), adjustment for other variables not available on birth certificates (ex. maternal smoking, occupational exposures, medical history, and gestational weight gain) did not influence associations with other studied contaminants. This separate study reduces concerns for important confounding bias, but confounding cannot be ruled out.
	Metric 10:	Covariate Characterization	Medium	Data on covariates came from registry data: birth certificates, fetal death certificates, and the NJ congenital birth defects registry.
	Metric 11:	Co-exposure Counfounding	Medium	Co-exposure confounding by drinking water trihalomethane concentrations was evaluated. There was no evidence to suggest substantial confounding by this or other co-exposures.
Domain 5: Analysis				

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Study Citation:	Bove, F. J. (1996). Public drinking water contamination and birthweight, prematurity, fetal deaths, and birth defects. Toxicology and Industrial Health 12(2):255-266.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	200239

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Methods were appropriate. The study used logistic regression models to estimate odds ratios and confidence intervals for dichotomous outcomes, and linear regression for analysis of continuous birth weight.
	Metric 13:	Statistical Power	Medium	Statistical power was likely to have been limited as a consequence of the small proportion of the sample defined as having "elevated" residential water concentrations of the chemicals of interest. The range of exposure examined was limited, as cutoffs for elevated levels were close to the detection limits of 1 ppb. In addition, for most birth defect outcomes, fewer than 10 cases had elevated exposure.
	Metric 14:	Reproducibility of Analyses	Medium	The authors clearly described steps used to estimate exposure-outcome associations, including exposure category cutoffs and criteria for confounding. However, many results were not shown as tables included odds ratios ≥1.5.
	Metric 15:	Statistical Analysis	High	The authors estimated coefficients, odds ratios and 95% confidence intervals using adequate methods. Confounding was based on 15% change-in-estimate comparing nested models. Effect modification (ex by infant sex) was not evaluated as there was no a priori evidence to suggest such analyses at that time.

Additional Comments: This study analyzed the association between estimated residential drinking water concentrations of several chlorinated solvents including 1,2-dichloroethane (as well as 1,1,1-trichloroethane; ∑[trans-1,2-dichloroethylene and 1,1-dichloroethylene]) and pregnancy outcomes (size at birth, prematurity, fetal deaths, and congenital birth defects). The sample included more than 80,000 births during 1985-88 for residents of 75 towns in NJ using public water system records to estimate exposure during gestation, and registry data (birth certificate, fetal death certificates for pregnancies >20 weeks, state birth defect registry) to characterize outcomes. Strengths included the large sample size and inclusion of all eligible registered births and fetal deaths in the study period. A critical concern is the inability to capture early fetal deaths and any related malformations (1% of the sample had fetal deaths vs typical estimates of >10%). An important limitation was the low percentage of the sample with detectable (> 1ppb) concentrations of these contaminants (<1% to 6.2%). Small numbers for birth defect outcomes also limited power. Exposure misclassification (ex. drinking water from wells/ work/ bottles, changes in residence, exposure from other sources) is also a concern. However, such misclassification was likely non-differential, and thus more likely to under- vs. to over-estimate associations.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Bove, F. J., Fulcomer, M. C., Klotz, J. B., Esmart, J., Dufficy, E. M., Savrin, J. E. (1995). Public drinking water contamination and birth outcomes. American Journal of Epidemiology 141(9):850-862.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	194932

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	This semi-ecological study (n=80,938) included all registered singleton live births and fetal deaths (>20 weeks) in 1985-88 in 75 New Jersey towns located in 4 counties with "some" water supplies contaminated with substances of interest and where: (i) residents were "mostly" served by public water systems; and (ii) births occurred "mostly" in state. Estimated proportions of residents served by public water systems, and of pregnancies/births captured, were not described. However, the inclusion of all eligible registered births, fetal deaths, and birth defects, as well as the selection of towns without knowledge of birth outcome prevalence, limited the likelihood of selection bias.
	Metric 2:	Attrition	Medium	All registered births and fetal deaths were included. Attrition due to missing values for multiple variables was not quantified and is therefore uncertain. However, attrition was likely modest as the proportion of missing values for individual variables was relatively low: (i) ~6% of subjects were excluded from analyses of outcomes such as preterm birth due to invalid or missing gestational ages; and (ii) other covariates evaluated as confounders had up to 4.9% missing values.
	Metric 3:	Comparison Group	High	After excluding plural pregnancies and chromosomal abnormalities, all registered live births during the study period in the areas included without the outcomes of interest were included in the comparison group. This comprehensive approach limited the potential for bias. Chromosomal abnormalities were not included as outcomes as they were not hypothesized to be associated with the exposures under study but were appropriately excluded given their uncertain etiology.
Domain 2: Exposure Characterization				

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Study Citation:	Bove, F. J., Fulcomer, M. C., Klotz, J. B., Esmart, J., Dufficy, E. M., Savrin, J. E. (1995). Public drinking water contamination and birth outcomes. American Journal of Epidemiology 141(9):850-862.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	194932

Domain	Metric		Rating	Comments
	Metric 4:	Measurement of Exposure	Medium	Along with several other contaminants, residential drinking water exposure to 1,2-dichloroethane (as well as 1,1,1-trichloroethane and 'total dichloroethylenes') was assigned based on maternal town of residence at birth. Exposure estimates were calculated using the average of water company sampling reports during the first trimester (for birth defects and fetal death) or the duration of pregnancy (for other outcomes). Detection limits and data availability were not specified in detail but were described as below 1 ppb, with reporting compliance >85%. A minimum of 1 sample per 6-month interval was required; variability in the number of measures available across water systems and towns was not described. Additional sources of measurement error included: changes in residence during pregnancy; water from alternate sources (ex. private wells, bottles, workplaces); variability in residential contaminant levels vs measured samples; unknown levels of tap water intake; and errors in estimated dermal and inhalation exposure while bathing or showering. While the extent of exposure misclassification is uncertain, there is no evidence to suggest it was differential rather than random.
	Metric 5:	Exposure Levels	Low	Due to the high proportion of measures below detection limits, analyses relating exposure to health outcomes used only 2 categories for each of the three chemicals of interest: cutoffs close to detection limits were used to define elevated exposure. Proportions defined as having elevated exposure were low (1.8% had 1,1-dichloroethylene ≥1 ppb). An important concern is that relatively low levels of exposure to this contaminant from sources other than residential drinking water, for which data were not available, could potentially have resulted in considerable misclassification.
	Metric 6:	Temporality	High	Exposure levels were assigned based on contaminant exposures estimated during: (i) the first trimester for analyses of birth defects and fetal deaths; and (ii) the duration of pregnancy for other pregnancy outcomes.

Domain 3: Outcome Assessment

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Study Citation:	Bove, F. J., Fulcomer, M. C., Klotz, J. B., Esmart, J., Dufficy, E. M., Savrin, J. E. (1995). Public drinking water contamination and birth outcomes. American Journal of Epidemiology 141(9):850-862.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	194932

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcomes included measures of birthweight (continuous among term births, low term birthweight, very low birthweight), prematurity, fetal death, and congenital anomalies in live births or fetal deaths. The anomalies analyzed included defects of the central nervous system, neural tube, oral cleft, total cardiac, major cardiac, ventricular septum, and any surveillance defect excluding chromosomal defects. All outcomes were identified using birth certificates, fetal death certificates (>20 weeks' gestation), and the NJ congenital birth defect registry (ICD codes provided). These registry data are likely to be sufficiently valid for late pregnancy outcomes. However, their limited ability to capture early pregnancy losses is a weakness. The sample included only 594 fetal deaths (less than 1% of the >80,0000 sample). Typical estimates are that 10-20%, of recognized pregnancies ending in losses. Moreover, developmental defects contributing to early pregnancy losses were also not captured. A further limitation is that that potentially etiologically heterogeneous preterm birth types were analyzed together, as these data did not distinguish premature rupture of membranes vs idiopathic prematurity.
	Metric 8:	Reporting Bias	Low	Models were constructed only for contaminants with associations > 1.0, and tables included only associations with odds ratios ≥1.5. No clear rationale was provided. Several positive odds ratios below the 1.5 cutoff were described in the results text (without confidence intervals), but no null/negative odds ratios were presented or described.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Potential confounding by maternal race, education, parity, and prior pregnancy loss, along with infant sex (for birth outcomes) and adequacy of prenatal care, was examined. Gestational age was addressed by analyzing birthweight among full term births, term low birth weight, and small size for gestational age. Only fully adjusted models were presented. In a companion case-control study (with low participation rates), adjustment for other variables not available on birth certificates (ex. maternal smoking, occupational exposures, medical history, and gestational weight gain) did not influence associations with other studied contaminants. This separate study reduces concerns for important confounding bias, but confounding cannot be ruled out.
	Metric 10:	Covariate Characterization	Medium	Data on covariates came from registry data: birth certificates, fetal death certificates, and the NJ congenital birth defects registry.
	Metric 11:	Co-exposure Counfounding	Medium	Co-exposure confounding by drinking water trihalomethane concentrations was evaluated. There was no evidence to suggest substantial confounding by this or other co-exposures.
Domain 5: Analysis				

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Study Citation:	Bove, F. J., Fulcomer, M. C., Klotz, J. B., Esmart, J., Dufficy, E. M., Savrin, J. E. (1995). Public drinking water contamination and birth outcomes. American Journal of Epidemiology 141(9):850-862.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	194932

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Methods were appropriate. The study used logistic regression models to estimate odds ratios and confidence intervals for dichotomous outcomes, and linear regression for analysis of continuous birth weight.
	Metric 13:	Statistical Power	Low	Statistical power was likely to have been limited as a consequence of the small proportion of the sample defined as having "elevated" residential water concentrations of the chemicals of interest. The range of exposure examined was limited, as cutoffs for elevated levels were close to the detection limits of 1 ppb. In addition, for most birth defect outcomes, fewer than 10 cases had elevated exposure. However, the authors emphasized the magnitude of associations rather than statistical significance and presented multiple confidence intervals to aid interpretation of the precision of estimates (50%, 90% and 99%).
	Metric 14:	Reproducibility of Analyses	Medium	The authors clearly described steps used to estimate exposure-outcome associations, including exposure category cutoffs and criteria for confounding. However, many results were not shown as tables included odds ratios ≥1.5.
	Metric 15:	Statistical Analysis	High	The authors estimated coefficients, odds ratios and confidence intervals using adequate methods. Confounding was based on 15% change-in-estimate comparing nested models. Effect modification (ex by infant sex) was not evaluated as there was no a priori evidence to suggest such analyses at that time.

Additional Comments: This study analyzed the association between estimated residential drinking water concentrations of several chlorinated solvents including 1,2-dichloroethane (as well as 1,1,1-trichloroethane and the ∑[trans-1,2-dichloroethylene & 1,1-dichloroethylene]) and pregnancy outcomes (size at birth, prematurity, fetal deaths, and congenital birth defects). The sample included more than 80,000 births during 1985-88 for residents of 75 towns in NJ using public water system records to estimate exposure during gestation, and registry data (birth certificate, fetal death certificates for pregnancies >20 weeks' gestation, state birth defect registry) to characterize outcomes. Strengths included the large sample size and inclusion of all eligible registered births and fetal deaths in the study period. A critical concern is the inability to capture early fetal deaths and any related malformations (1% of the sample had fetal deaths vs typical estimates of >10%). An important limitation was the low percentage of the sample with detectable (> 1ppb) concentrations of this solvent (<2%), which likely limited power. Small numbers for birth defect outcomes also limited power. Exposure misclassification (ex. drinking water from wells/ work/ bottles, changes in residence, exposure from other sources) is also a concern. However, such misclassification was likely non-differential, and thus more likely to under- vs. to over-estimate associations.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Bowler, R.M., Gysens, S., Hartney, C. (2003). Neuropsychological effects of ethylene dichloride exposure. NeuroToxicology 24(4-5):553-562.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Wechsler Adult Intelligence Scale III (WAIS-III), Wechsler Memory Scale III (WMS-III), Boston Naming Test (BNT), Trail Making Test (TMT), Stroop Color-Word Test, Grooved Pegboard, Dynamometer, Wide Range Achievement Test (WRAT), Finger tapping, Beck Anxiety Index, Beck Depression Index, Symptom Checklist-90 (SCL-90).
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	200241

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Uninformative	221 workers that had been exposed to 1,2-DCE in the Southern United States were initially included. Exclusion criteria were provided, including the number of individuals excluded for each reason. The study authors note that those initially included in the analysis sample were referred by physicians after neurological complaints were documented. Detailed criteria for referral were not provided. Referral-based recruitment of neurological cases will likely result in an analysis sample with an exposure-outcome distribution that is not representative of the eligible population (i.e., contamination site clean-up workers).
	Metric 2:	Attrition	Medium	There was moderate subject loss. Reasons for exclusion from the analysis sample are provided, and only those with complete information were included in the analysis.
	Metric 3:	Comparison Group	Low	Impairment scores were compared to normative data from manuals and/or a "demographically similar control group" cited to Bowler et al. (2001). The controls from this study appeared similar (albeit somewhat older) than 1,2-DCE-exposed workers and reported no prior chemical exposure.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	A job-exposure matrix was not considered plausible; variables considered as surrogates of exposure were obtained from interviews. This method is expected to have poor validity because it relies on workers' recall of subjective events and their frequency (e.g., contact with water); workers (who are taking part in a lawsuit) may overestimate their exposure.
	Metric 5:	Exposure Levels	Low	Two levels of exposure (exposed and not exposed) were used to evaluate neurophysiological effects.
	Metric 6:	Temporality	Medium	Exposures primarily occurred between 1993 and 1995 and neurophysiological effects were evaluated in 2000. Temporality is established, but it is unclear whether exposures fall within relevant exposure windows for the outcome of interest.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Neurophysiological effects were evaluated using a number of standardized tests, including (but not limited to) the Wechsler Adult Intelligence Scale (WAIS-III), the Wechsler Memory Scale (WMS-III), and the Symptom Checklist 90-Revised (SCL90-R). There was no information whether tests were performed using the same methods for exposed and referent groups (e.g., timing and order of tests).

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Study Citation:	Bowler, R.M., Gysens, S., Hartney, C. (2003). Neuropsychological effects of ethylene dichloride exposure. NeuroToxicology 24(4-5):553-562.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Wechsler Adult Intelligence Scale III (WAIS-III), Wechsler Memory Scale III (WMS-III), Boston Naming Test (BNT), Trail Making Test (TMT), Stroop Color-Word Test, Grooved Pegboard, Dynamometer, Wide Range Achievement Test (WRAT), Finger tapping, Beck Anxiety Index, Beck Depression Index, Symptom Checklist-90 (SCL-90).
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	200241

Domain	Metric		Rating	Comments
	Metric 8:	Reporting Bias	Low	Neurobehavioral outcomes mentioned in the methods were reported for 1,2-DCE-exposed workers (as mean score, standard deviation, and percentage impaired); results for controls/normative data were not shown and/or p-values from t-tests were not provided. Control data were used to define impairment (based on z-score) but these values were not reported. Data pertaining to specific exposure variables were reported in the text only; no data were shown in a table.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Normative data permitted adjustments based on age, education, and gender. The control group was "socio-demographically" similar but specific parameters used to define similarity were not indicated. Separate ANCOVA analyses on workers only were stratified by race (citation provided), and adjusted for ethnicity, age, and education. The methods for identifying and including potential confounders in the analytic approach was not described.
	Metric 10:	Covariate Characterization	Low	No description of the covariate collection method was provided. It was not clear whether the method used was valid or not.
	Metric 11:	Co-exposure Counfounding	Low	A number of workers (18%) reported current exposure to chemicals in their work environment. These potential co-exposures were not were not appropriately adjusted for in the analytical approach used.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Low	The study design was appropriate to evaluate the neurophysiological status of 1,2-DCE-exposed workers; however, statistical methods were not comprehensive.
	Metric 13:	Statistical Power	Medium	The report indicates "significant impairments" were observed on various neurophysiological tests using t-tests, and significant exposure relationships were reported based on test scores and specific exposure variables (used as surrogates of exposure). Therefore, the number of participants was sufficient to detect an effect.
	Metric 14:	Reproducibility of Analyses	Low	Tests were scored according to relevant manuals; the calculation of z-scores, used in all impairment comparisons and analyses of exposure relationships, was not explained in adequate detail. The methods used to determine relationships between specific exposure variables and test scores (i.e., ANCOVA analyses) were not fully described.
	Metric 15:	Statistical Analysis	Low	Description of the ANCOVA analysis was largely not present. It is not clear whether model assumptions were met.

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Study Citation:	Bowler, R.M., Gysens, S., Hartney, C. (2003). Neuropsychological effects of ethylene dichloride exposure. NeuroToxicology 24(4-5):553-562.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Wechsler Adult Intelligence Scale III (WAIS-III), Wechsler Memory Scale III (WMS-III), Boston Naming Test (BNT), Trail Making Test (TMT), Stroop Color-Word Test, Grooved Pegboard, Dynamometer, Wide Range Achievement Test (WRAT), Finger tapping, Beck Anxiety Index, Beck Depression Index, Symptom Checklist-90 (SCL-90).
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	200241

Domain	Metric	Rating	Comments
Additional Comments:	The study evaluated the neurobehavioral status of a group of workers with known exposure to 1,2-DCE at a clean-up site. Impairments related to processing speed, attention, cognitive flexibility, motor coordination and speed, verbal memory/fluency, vision and visual-spatial abilities, and mood were reported in exposed workers. Serious and consequential flaws are associated with the study including methods of participant selection and retention, and exposure characterization among others.		

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Brender, J.D., Shinde, M.U., Zhan, F.B., Gong, X., Langlois, P.H. (2014). Maternal residential proximity to chlorinated solvent emissions and birth defects in offspring: A case-control study. Environmental Health: A Global Access Science Source 13(1):96.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	birth defects (neural tube defects, limbs deficiencies, oral cleft defects, heart defects, spina bifida, anencephaly)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	2799700

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Participants were drawn from the Texas Birth Defects Registry (TBDR) for years 1996-2008. Controls were frequency matched from the same registry. Study authors state that neural tube cases were more likely to not be successfully geocoded which may introduce selection bias, however, the authors note that both cases and controls with addresses that could not be geocoded were similar. In spite of that, the inclusion criteria, methods of participant selection, and frequency match were reported.
	Metric 2:	Attrition	Medium	13.3% case mother addresses and 12.8% control mother addresses were unable to be geocoded, however this most likely only lowered the precision of the study and most likely does not vary based on exposure level.
	Metric 3:	Comparison Group	Medium	Controls were matched to cases and pulled from the same eligible population by year of delivery and public health service region. Other demographic factors, e.g., race was not matched in population selection. However, statistical analyses were adjusted for year of delivery, maternal age, race/ethnicity, education, and public health region of residence.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Used Emission Weighted Proximity Model to estimate exposure at a given address based on proximity to emission sources and the specific amount or type of pollutant emitted. There may be some exposure misclassification due to mothers moving away from geocoded addresses. Previous studies indicate ~67% of mothers do not move between conception and delivery.
	Metric 5:	Exposure Levels	Medium	Reports exposure as ”exposure risk value” and groups the risk values into quartiles, with exposure risk values < 0 being the referent group
	Metric 6:	Temporality	Medium	The study authors estimated exposure based on residence during pregnancy and evaluated birth outcomes. Temporality is established. Previous studies indicate ~67% mothers don’t move between trimester and delivery. For mothers who moved during the pregnancy, the temporality is unknown.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Outcomes determined by Texas Birth Defect Registry, checking for birth defect diagnosis. Birth certificates came from Center for Health Statistics at Texas Department of State Health Services
	Metric 8:	Reporting Bias	High	Outcome data measured and reported clearly, stratified by specific type of birth defect
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Brender, J.D., Shinde, M.U., Zhan, F.B., Gong, X., Langlois, P.H. (2014). Maternal residential proximity to chlorinated solvent emissions and birth defects in offspring: A case-control study. Environmental Health: A Global Access Science Source 13(1):96.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	birth defects (neural tube defects, limbs deficiencies, oral cleft defects, heart defects, spina bifida, anencephaly)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	2799700

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	High	Cases were frequency matched by year of delivery and public health service region. Final models were adjusted for year of delivery, public health region, maternal age (<20, 20-24, 25-29, 30-34, 35-39, >39 years), education (<12 years, 12 years, >12 years), and race/ethnicity (Whit non-Hispanic, Black non-Hispanic, Hispanic, other non-Hispanic).
	Metric 10:	Covariate Characterization	High	Used birth and death certificates for demographic information
	Metric 11:	Co-exposure Counfounding	Medium	other co-exposures were not described
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	study used logistic regression to measure association between exposure and birth defects
	Metric 13:	Statistical Power	Medium	Overall adequate number of cases and controls - some effects have low cell counts, but at least one health effect has sufficient statistical power.
	Metric 14:	Reproducibility of Analyses	Medium	Methods sufficiently detailed for reproducibility
	Metric 15:	Statistical Analysis	High	No logistic regression model assumption violations were identified.

Additional Comments: This study examined the association between proximity to several point sources of chlorinated solvents and birth defects. Exposure was assessed using EPA's Toxic Release Inventory, and birth defects were assessed using Texas birth registries. The geocoded address of mothers on day of delivery and the amount of solvent was plugged into the Emission Weighted Probability model to assign each mother an exposure risk value. Limitations include limited evidence of temporality. Additionally, elective terminations lacked a vital record, which meant only 69% of mothers with neural tube defects were geocoded. Mothers highly exposed to 1,2-dichloroethane were 1.85 times more likely to have the spina bifida birth defect than mothers who were not significantly exposed.

Overall Quality Determination High

* No biomarkers were identified for this evaluation.

Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Nested case-control design; cases selected from deaths in cohort study was described by Rinsky et al (1988; HERO 597923) (29,139 workers in Union Carbide facilities in West Virginia followed from 1940 to 1978). Vital status complete for 95% of cohort members.
	Metric 2:	Attrition	High	There was minimal exclusion of subjects/missing data, because vital status follow-up was complete for 96% of the 29,139 men in the cohort study.
	Metric 3:	Comparison Group	Medium	Controls were randomly selected in a 5:1 ratio to cases from the total employee cohort such that they were first employed in the same decade and survived to the same five-year survival period as cases. Controls survived at least to the beginning of the five-year interval in which cases died. Controls were independently selected for each of the individual disease subcategories. However, the demographic information between cases and controls were not compared in the paper.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was partially described: (1) Potential employee contact with a specific substance was determined by tracing each employee's work assignments and linking these assignment records to a separate computer file that contained a history of departmental usage for each substance; (2) Potential exposure to each chemical group was assumed on the basis of assignment o a production unit with a history of usage of any member of that chemical group. However, exposure level either based on work assignment in departments such as job exposure matrix or on the chemical levels were not presented.
	Metric 5:	Exposure Levels	Low	The range of exposure is limited. For example, exposure was presented by the duration of work in two categories: <5 years and 5+ years.
	Metric 6:	Temporality	Medium	Temporality is established, but it is unclear whether the exposures fall within the relevant exposure window. Authors used a lag time of 5 years; since controls were selected for 5 yr intervals, the effective lag time ranged from 5-9 years with an average of 7.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Case definition was based on death certificate diagnosis; but no method validation was conducted against this well-established methods.
	Metric 8:	Reporting Bias	Medium	All outcomes reported, but ORs for many analyses presented without CIs (some CIs reported in text).
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Low	There is indirect evidence that considerations were not made for potential confounders (ORs not adjusted, controls not age- or race-matched). Even though authors note that "Age-adjusted stratified analyses, which were also conducted, did not materially modify the odds ratio estimates". Also stratified examination of odds ratios were conducted to assess duration of exposure effects. However, other key confounders e.g., smoking status and race were not accounted for.
	Metric 10:	Covariate Characterization	Medium	The only potential confounder considered was age; this was presumably evaluated based on employment records (no discussion presented). Age-adjusted stratified analyses were conducted.
	Metric 11:	Co-exposure Counfounding	Low	Co-exposures were present and were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Nested case-control study design is appropriate for research question. Initial data analysis included crude odds ratio and then stratified examination of odds ratios was conducted to ass duration of exposure effect. Also, age-adjusted stratified analysis was conducted.
	Metric 13:	Statistical Power	Low	Statistical power calculations were not reported. Case numbers for each disease were low. The number of subjects was not sufficient to detect an effect of 1,2-dichloroethylene exposure.
	Metric 14:	Reproducibility of Analyses	Medium	Description was sufficient to be conceptually reproducible.
	Metric 15:	Statistical Analysis	Low	Statistical model to calculate odds ratio was not described.

Additional Comments: This nested case-control study within a cohort study is a good study design to answer the research question regarding the association between multiple chemical exposures and four cancer sites. Cases and controls are selected appropriate. However, there are several limitations in this study: (1) confounders were not all considered and adjusted for, except that age-adjusted odds ratios were conducted; (2) it is not described if co-exposures were adjusted for; (3) numbers of cancer cases for each cancer type were small, so the statistical power is limited; (4) statistical models for calculating odds ratios were not described.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Nested case-control design; cases selected from deaths in cohort study was described by Rinsky et al (1988; HERO 597923) (29,139 workers in Union Carbide facilities in West Virginia followed from 1940 to 1978). Vital status complete for 95% of cohort members.
	Metric 2:	Attrition	High	There was minimal exclusion of subjects/missing data, because vital status follow-up was complete for 96% of the 29,139 men in the cohort study.
	Metric 3:	Comparison Group	Medium	Controls were randomly selected in a 5:1 ratio to cases from the total employee cohort such that they were first employed in the same decade and survived to the same five-year survival period as cases. Controls survived at least to the beginning of the five-year interval in which cases died. Controls were independently selected for each of the individual disease subcategories. However, the demographic information between cases and controls were not compared in the paper.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was partially described: (1) Potential employee contact with a specific substance was determined by tracing each employee's work assignments and linking these assignment records to a separate computer file that contained a history of departmental usage for each substance; (2) Potential exposure to each chemical group was assumed on the basis of assignment o a production unit with a history of usage of any member of that chemical group. However, exposure level either based on work assignment in departments such as job exposure matrix or on the chemical levels were not presented.
	Metric 5:	Exposure Levels	Low	The range of exposure is limited. For example, exposure was presented by the duration of work in two categories: <5 years and 5+ years.
	Metric 6:	Temporality	Medium	Temporality is established, but it is unclear whether the exposures fall within the relevant exposure window. Authors used a lag time of 5 years; since controls were selected for 5 yr intervals, the effective lag time ranged from 5-9 years with an average of 7.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Case definition was based on death certificate diagnosis; but no method validation was conducted against this well-established methods.
	Metric 8:	Reporting Bias	Medium	All outcomes reported, but ORs for many analyses presented without CIs (some CIs reported in text).
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Low	There is indirect evidence that considerations were not made for potential confounders (ORs not adjusted, controls not age- or race-matched). Even though authors note that "Age-adjusted stratified analyses, which were also conducted, did not materially modify the odds ratio estimates". Also stratified examination of odds ratios were conducted to assess duration of exposure effects. However, other key confounders e.g., smoking status and race were not accounted for.
	Metric 10:	Covariate Characterization	Medium	The only potential confounder considered was age; this was presumably evaluated based on employment records (no discussion presented). Age-adjusted stratified analyses were conducted.
	Metric 11:	Co-exposure Counfounding	Low	Co-exposures were present and were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Nested case-control study design is appropriate for research question. Initial data analysis included crude odds ratio and then stratified examination of odds ratios was conducted to ass duration of exposure effect. Also, age-adjusted stratified analysis was conducted.
	Metric 13:	Statistical Power	Low	Statistical power calculations were not reported. Case numbers for each disease were low. The number of subjects was not sufficient to detect an effect of 1,2-dichloroethylene exposure.
	Metric 14:	Reproducibility of Analyses	Medium	Description was sufficient to be conceptually reproducible.
	Metric 15:	Statistical Analysis	Low	Statistical model to calculate odds ratio was not described.

Additional Comments: This nested case-control study within a cohort study is a good study design to answer the research question regarding the association between multiple chemical exposures and four cancer sites. Cases and controls are selected appropriate. However, there are several limitations in this study: (1) confounders were not all considered and adjusted for, except that age-adjusted odds ratios were conducted; (2) it is not described if co-exposures were adjusted for; (3) numbers of cancer cases for each cancer type were small, so the statistical power is limited; (4) statistical models for calculating odds ratios were not described.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Nested case-control design; cases selected from deaths in cohort study was described by Rinsky et al (1988; HERO 597923) (29,139 workers in Union Carbide facilities in West Virginia followed from 1940 to 1978). Vital status complete for 95% of cohort members.
	Metric 2:	Attrition	High	There was minimal exclusion of subjects/missing data, because vital status follow-up was complete for 96% of the 29,139 men in the cohort study.
	Metric 3:	Comparison Group	Medium	Controls were randomly selected in a 5:1 ratio to cases from the total employee cohort such that they were first employed in the same decade and survived to the same five-year survival period as cases. Controls survived at least to the beginning of the five-year interval in which cases died. Controls were independently selected for each of the individual disease subcategories. However, the demographic information between cases and controls were not compared in the paper.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was partially described: (1) Potential employee contact with a specific substance was determined by tracing each employee's work assignments and linking these assignment records to a separate computer file that contained a history of departmental usage for each substance; (2) Potential exposure to each chemical group was assumed on the basis of assignment o a production unit with a history of usage of any member of that chemical group. However, exposure level either based on work assignment in departments such as job exposure matrix or on the chemical levels were not presented.
	Metric 5:	Exposure Levels	Low	The range of exposure is limited. For example, exposure was presented by the duration of work in two categories: <5 years and 5+ years.
	Metric 6:	Temporality	Medium	Temporality is established, but it is unclear whether the exposures fall within the relevant exposure window. Authors used a lag time of 5 years; since controls were selected for 5 yr intervals, the effective lag time ranged from 5-9 years with an average of 7.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Case definition was based on death certificate diagnosis; but no method validation was conducted against this well-established methods.
	Metric 8:	Reporting Bias	Medium	All outcomes reported, but ORs for many analyses presented without CIs (some CIs reported in text).
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Low	There is indirect evidence that considerations were not made for potential confounders (ORs not adjusted, controls not age- or race-matched). Even though authors note that "Age-adjusted stratified analyses, which were also conducted, did not materially modify the odds ratio estimates". Also stratified examination of odds ratios were conducted to assess duration of exposure effects. However, other key confounders e.g., smoking status and race were not accounted for.
	Metric 10:	Covariate Characterization	Medium	The only potential confounder considered was age; this was presumably evaluated based on employment records (no discussion presented). Age-adjusted stratified analyses were conducted.
	Metric 11:	Co-exposure Counfounding	Low	Co-exposures were present and were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Nested case-control study design is appropriate for research question. Initial data analysis included crude odds ratio and then stratified examination of odds ratios was conducted to ass duration of exposure effect. Also, age-adjusted stratified analysis was conducted.
	Metric 13:	Statistical Power	Low	Statistical power calculations were not reported. Case numbers for each disease were low. The number of subjects was not sufficient to detect an effect of 1,2-dichloroethylene exposure.
	Metric 14:	Reproducibility of Analyses	Medium	Description was sufficient to be conceptually reproducible.
	Metric 15:	Statistical Analysis	Low	Statistical model to calculate odds ratio was not described.

Additional Comments: This nested case-control study within a cohort study is a good study design to answer the research question regarding the association between multiple chemical exposures and four cancer sites. Cases and controls are selected appropriate. However, there are several limitations in this study: (1) confounders were not all considered and adjusted for, except that age-adjusted odds ratios were conducted; (2) it is not described if co-exposures were adjusted for; (3) numbers of cancer cases for each cancer type were small, so the statistical power is limited; (4) statistical models for calculating odds ratios were not described.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Nested case-control design; cases selected from deaths in cohort study was described by Rinsky et al (1988; HERO 597923) (29,139 workers in Union Carbide facilities in West Virginia followed from 1940 to 1978). Vital status complete for 95% of cohort members.
	Metric 2:	Attrition	High	There was minimal exclusion of subjects/missing data, because vital status follow-up was complete for 96% of the 29,139 men in the cohort study.
	Metric 3:	Comparison Group	Medium	Controls were randomly selected in a 5:1 ratio to cases from the total employee cohort such that they were first employed in the same decade and survived to the same five-year survival period as cases. Controls survived at least to the beginning of the five-year interval in which cases died. Controls were independently selected for each of the individual disease subcategories. However, the demographic information between cases and controls were not compared in the paper.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was partially described: (1) Potential employee contact with a specific substance was determined by tracing each employee's work assignments and linking these assignment records to a separate computer file that contained a history of departmental usage for each substance; (2) Potential exposure to each chemical group was assumed on the basis of assignment o a production unit with a history of usage of any member of that chemical group. However, exposure level either based on work assignment in departments such as job exposure matrix or on the chemical levels were not presented.
	Metric 5:	Exposure Levels	Low	The range of exposure is limited. For example, exposure was presented by the duration of work in two categories: <5 years and 5+ years.
	Metric 6:	Temporality	Medium	Temporality is established, but it is unclear whether the exposures fall within the relevant exposure window. Authors used a lag time of 5 years; since controls were selected for 5 yr intervals, the effective lag time ranged from 5-9 years with an average of 7.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Case definition was based on death certificate diagnosis; but no method validation was conducted against this well-established methods.
	Metric 8:	Reporting Bias	Medium	All outcomes reported, but ORs for many analyses presented without CIs (some CIs reported in text).
Domain 4: Potential Confounding / Variability Control				

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Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Low	There is indirect evidence that considerations were not made for potential confounders (ORs not adjusted, controls not age- or race-matched). Even though authors note that "Age-adjusted stratified analyses, which were also conducted, did not materially modify the odds ratio estimates". Also stratified examination of odds ratios were conducted to assess duration of exposure effects. However, other key confounders e.g., smoking status and race were not accounted for.
	Metric 10:	Covariate Characterization	Medium	The only potential confounder considered was age; this was presumably evaluated based on employment records (no discussion presented). Age-adjusted stratified analyses were conducted.
	Metric 11:	Co-exposure Counfounding	Low	Co-exposures were present and were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Nested case-control study design is appropriate for research question. Initial data analysis included crude odds ratio and then stratified examination of odds ratios was conducted to ass duration of exposure effect. Also, age-adjusted stratified analysis was conducted.
	Metric 13:	Statistical Power	Low	Statistical power calculations were not reported. Case numbers for each disease were low. The number of subjects was not sufficient to detect an effect of 1,2-dichloroethylene exposure.
	Metric 14:	Reproducibility of Analyses	Medium	Description was sufficient to be conceptually reproducible.
	Metric 15:	Statistical Analysis	Low	Statistical model to calculate odds ratio was not described.

Additional Comments: This nested case-control study within a cohort study is a good study design to answer the research question regarding the association between multiple chemical exposures and four cancer sites. Cases and controls are selected appropriate. However, there are several limitations in this study: (1) confounders were not all considered and adjusted for, except that age-adjusted odds ratios were conducted; (2) it is not described if co-exposures were adjusted for; (3) numbers of cancer cases for each cancer type were small, so the statistical power is limited; (4) statistical models for calculating odds ratios were not described.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Cheng, T.J., Huang, M.L., You, N.C., Du, C.L., Chau, T.T. (1999). Abnormal liver function in workers exposed to low levels of ethylene dichloride and vinyl chloride monomer. Journal of Occupational and Environmental Medicine 41(12):1128-1133.
Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	AST, ALT, GGT, Hepatitis B virus surface antigen (HBsAg), and anti-hepatitis C virus antibody (anti-HCV).
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	200266

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	A total of 251 male workers were included from 4 vinyl chloride monomer manufacturing plants. Other details on recruitment strategy, eligibility criteria, year of enrollment, and participation rates were not provided.
	Metric 2:	Attrition	Low	There was no indication of attrition and details on the number of eligible participants throughout the study was limited. Attrition could not be adequately assessed due to a lack of information regarding recruitment and selection.
	Metric 3:	Comparison Group	Medium	The low-EDC-low-VCM group (187 participants) was used as the comparison group, and there is indirect evidence groups are similar. Limited details were provided for setting, inclusion and exclusion criteria, and methods of participant selection.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	NIOSH recommended methods 1003 and 1007 were used for personal and area sampling, respectively. Air samples were collected, stored at 4 deg. C, and analyzed within 2 weeks of the sampling event. However, historical job changes, changes in exposure levels over time, and timing (year or days during work week) or duration of area or personal sampling were not reported.
	Metric 5:	Exposure Levels	Medium	EDC and VCM levels were reported for the different categories of jobs, which were classified into low-EDC-low-VCM, mod-EDC-low-VCM, and low-EDC-mod-VCM groups.
	Metric 6:	Temporality	High	The age of participants (mean age 33.7-40.1 years) and employment duration (mean 7.5-14.3 years) were reported, and the temporality between the exposure and outcome appears to be appropriate.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	AST, ALT, and GGT "were analyzed with a Hitachi 7050 autoanalyzer". A basis for the cutoff values used in Table 4 to determine "abnormal" AST, ALT, and GGT levels was not provided.
	Metric 8:	Reporting Bias	High	Odds ratios for abnormal liver function were provided with 95% confidence intervals, the number per exposure level, and significance when applicable.
Domain 4: Potential Confounding / Variability Control				

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Study Citation: Cheng, T.J., Huang, M.L., You, N.C., Du, C.L., Chau, T.T. (1999). Abnormal liver function in workers exposed to low levels of ethylene dichloride and vinyl chloride monomer. Journal of Occupational and Environmental Medicine 41(12):1128-1133.
Health Outcome(s): Hepatic/Liver
Reported Health Effect(s): AST, ALT, GGT, Hepatitis B virus surface antigen (HBsAg), and anti-hepatitis C virus antibody (anti-HCV).
Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s): No linked references.
HERO ID: 200266

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Medium	The study reports information on potential confounders (age, hepatitis, BMI, alcohol use, and employment duration), and controls for hepatitis, BMI and alcohol consumption in the multiple logistic regression analyses. There is indirect evidence that appropriate adjustments were made.
	Metric 10:	Covariate Characterization	Medium	An interviewer administered the questionnaires to collect information about potential confounders and occupational history.
	Metric 11:	Co-exposure Counfounding	Low	Exposure to ethylene dichloride was evaluated in a vinyl chloride monomer (VCM) manufacturing facility, and VCM was also subsequently analyzed using personal and area sampling. Results for VCM exposure concentrations were provided. VCM is also suspected to cause liver damage.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design (cohort) was appropriate to assess the outcome of interest (”markers of liver damage”). Chi-squared (X2) test and multiple logistic regression were used for statistical analyses.
	Metric 13:	Statistical Power	Medium	The number of participants was adequate to detect an effect in the exposed populations, although power calculations were not provided. There were >20 participants in each group.
	Metric 14:	Reproducibility of Analyses	Low	A description of the logistic regression analysis was provided, however, study authors do not provide information on categorization of abnormal liver function.
	Metric 15:	Statistical Analysis	High	There were no identifiable logistic regression model assumption violations.
Domain 6: Other (if applicable) Considerations for Biomarker Selection and Measurement (Lakind et al. 2014)				
	Metric 16:	Use of Biomarker of Exposure	N/A	Biomarker of exposures were not assessed.
	Metric 17:	Effect Biomarker	High	This study uses aspartate aminotransferase, alanine aminotransferase, and y-glutamyltransferase as biomarkers of effect. While these no works cited to explain their connection to liver function, all three are well-known marker of liver function. Similarly, Hepatitis B virus surface antigen and antihepatitis C virus anitbody are also well-known measures of liver function and health.
	Metric 18:	Method Sensitivity	Low	No limit of detection information is provided for any of the effect biomarkers.
	Metric 19:	Biomarker Stability	Medium	While the study does not provide a lot of information regarding biomarker storage or stability, the authors do mention that venous blood used to detect biomarkers was stored at 4 degrees C.
	Metric 20:	Sample Contamination	Medium	No specific information regarding potential sample contamination was provided.
	Metric 21:	Method Requirements	Medium	Aspartate aminotransferase, alanine aminotransferase, and y-glutamyltransferase were analyzed using a Hitachi 7050 autoanalyzer. Hepatitis B virus surface antibody and antihepatitis C virus antibody were assessed with radioimmunoassay and enzyme-linked immunosorbent assay.

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Study Citation:	Cheng, T.J., Huang, M.L., You, N.C., Du, C.L., Chau, T.T. (1999). Abnormal liver function in workers exposed to low levels of ethylene dichloride and vinyl chloride monomer. Journal of Occupational and Environmental Medicine 41(12):1128-1133.
Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	AST, ALT, GGT, Hepatitis B virus surface antigen (HBsAg), and anti-hepatitis C virus antibody (anti-HCV).
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	200266

Domain	Metric	Rating	Comments
	Metric 22: Matrix Adjustment	N/A	No information on matrix adjustment was provided/available.

Additional Comments: A group of 251 male workers from 4 vinyl chloride monomer (VCM) manufacturing plants were included in this assessment to examine if occupational exposure to VCM and ethylene dichloride (EDC) "resulted in increased risk of liver damage" by examining AST, ALT, and GGT levels in the blood. Increased ORs for abnormal AST (>37 IU/L) and ALT (>41 IU/L) in the mod-EDC-low-VCM group (0.17-333.7 ppm EDC, 0.18-0.34 ppm VCM), compared with the low-EDC-low-VCM group, was reported. Exposure levels were measured using area and personal sampling, but the timing and duration of the sampling events were not reported.

Overall Quality Determination Medium

Study Citation:	Dosemeci, M., Cocco, P., Chow, W.H. (1999). Gender differences in risk of renal cell carcinoma and occupational exposures to chlorinated aliphatic hydrocarbons. American Journal of Industrial Medicine 36(1):54-59.
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	renal cell carcinoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	4697224

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	The details of the study design were reported elsewhere (Chow et al. 1994, HERO ID 701514). Brief details about the setting, date, number of eligible participants, and control matching were reported. Reasons for exclusions/non-participation were described with details by Chow et al. (1994).
	Metric 2:	Attrition	High	For the details of the study design and attrition of study subjects, the study authors referred to another publication by Chow et al., 1994. Chow et al. (1994) mentioned that at the end of the personal interview, the respondents were given a self-administered food-frequency questionnaire. Of the subjects interviewed for the study, 632 patients (79% of 796 eligible patients) and 653 control subjects (79% of 707 eligible control subjects) returned the diet questionnaire. A number of subjects, whose responses were considered unreliable, were excluded from the analysis, including 48 patients and three control subjects who had seven or more skipped food items or had questionable data and 50 patients whose next-of-kin respondent was not a spouse. Also excluded were two patients with unknown smoking status, since smoking is a risk factor.
	Metric 3:	Comparison Group	Medium	The cases were pulled from the Minnesota Cancer Surveillance System. Controls were selected from the general population of Minnesota; controls age 20-64 years were selected through random digital dialing and controls age 65-85 years were collected from files through the Health Care Financing Administration. Controls were age- and gender-stratified and were of the same race. Characteristics of cases and controls were not provided in the text or a table.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	High	Occupational histories including the most recent and usual occupation and industry, job activities, started-year and ended-year, and part-time/full-time status were collected. Occupations and industries were coded according to the standard occupational classification (SOC) and standard industrial classification (SIC) schemes. The National Cancer Institute developed job exposure matrices (JEM) for nine individual chlorinated aliphatic hydrocarbons (CAHCs), all CAHCs-combined, and all organic solvents-combined. These JEMs were merged with assigned SOC and SIC to determine the exposure status to these chemicals for each study subject. Application of the JEM was described elsewhere (Dosemeci et al. 1994, HERO ID 632334; Gomez et al. 1994, HERO ID 702154).
	Metric 5:	Exposure Levels	Medium	Details of the application of the JEM were described elsewhere (Dosemeci et al. 1994, HERO ID 632334; Gomez et al. 1994, HERO ID 702154). Dosemeci et al. (1994) described more details about that this study assigned three levels of probability (low, medium, high) to industries and occupations for chemical exposure levels.

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Study Citation:	Dosemeci, M., Cocco, P., Chow, W.H. (1999). Gender differences in risk of renal cell carcinoma and occupational exposures to chlorinated aliphatic hydrocarbons. American Journal of Industrial Medicine 36(1):54-59.
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	renal cell carcinoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	4697224

Domain	Metric		Rating	Comments
	Metric 6:	Temporality	Medium	Occupational questionnaires identified prior exposures based on reported recent and usual occupations as well as duration of employment. Outcome status was determined from registry data. The authors note that some occupational history was incomplete which may result in some uncertainty in regard to temporality.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Cases were identified as newly diagnosed and histologically confirmed renal cell carcinoma through the Minnesota Cancer Surveillance System and information about each participant was collected using a questionnaire. Validation was not specified.
	Metric 8:	Reporting Bias	Medium	A description of measured outcomes is reported and ORs were stratified by sex. Effect estimates are reported with a confidence interval. One table showed the total numbers of men and women respectively for each chemical, but numbers of cases/controls were not reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Appropriate adjustments were made in the final analysis, including age, gender, smoking, hypertension and the use of diuretics and/or anti-hypertension drugs, and BMI. Results were stratified by sex.
	Metric 10:	Covariate Characterization	Medium	Information about participants was collected using a questionnaire, and it includes potential confounders, e.g., smoking habits. Validation was not specified.
	Metric 11:	Co-exposure Counfounding	Medium	Co-exposures were identified through the job exposure matrices. Chemicals were evaluated individually and as a group.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen (case-control) was appropriate for the research question (renal cell carcinoma risk from occupational organic solvent exposure). Logistic regression models were used to estimate the relative risk and 95% CI.
	Metric 13:	Statistical Power	Low	Statistical power calculations were not provided. No significant effects were observed with 1,2-dichloroethane. The number of participated women to calculate odds ratio was inadequate to detect an effect in the participants for other chemicals or the combined risk, because it was very low.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis was brief, but is sufficient to understand precisely what has been done and to be conceptually reproducible with access to the analytic data.
	Metric 15:	Statistical Analysis	High	Model assumptions for logistic regression were met. The odds ratios were adjusted for age, smoking, hypertension status and/or use of diuretic and/or anti-hypertension drugs, and body mass index for men and women separately.

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Study Citation:	Dosemeci, M., Cocco, P., Chow, W.H. (1999). Gender differences in risk of renal cell carcinoma and occupational exposures to chlorinated aliphatic hydrocarbons. American Journal of Industrial Medicine 36(1):54-59.
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	renal cell carcinoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	4697224

Domain	Metric	Rating	Comments
Additional Comments:	A group of 438 cases (273 men and 165 women) were selected from the Minnesota Cancer Surveillance System that had been newly diagnosed with renal cell carcinoma. Controls included 687 participants (462 men and 225 women) age- and gender- stratified that were selected from either the general population of Minnesota (age 20-64 years) or from the Health Care Financing Administration files (age 65-85). No significant increase in the risk of renal cell carcinoma was observed with exposure to 1,2-dichloroethane among men or women separately, or for all participants exposed.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Dosemeci, M., Cocco, P., Chow, W.H. (1999). Gender differences in risk of renal cell carcinoma and occupational exposures to chlorinated aliphatic hydrocarbons. American Journal of Industrial Medicine 36(1):54-59.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	renal cell carcinoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	4697224

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	The details of the study design were reported elsewhere (Chow et al. 1994, HERO ID 701514). Brief details about the setting, date, number of eligible participants, and control matching were reported. Reasons for exclusions/non-participation were described with details by Chow et al. (1994).
	Metric 2:	Attrition	Medium	For the details of the study design and attrition of study subjects, the study authors referred to another publication by Chow et al., 1994. Chow et al. (1994) mentioned that at the end of the personal interview, the respondents were given a self-administered food-frequency questionnaire. Of the subjects interviewed for the study, 632 patients (79% of 796 eligible patients) and 653 control subjects (79% of 707 eligible control subjects) returned the diet questionnaire. A number of subjects, whose responses were considered unreliable, were excluded from the analysis, including 48 patients and three control subjects who had seven or more skipped food items or had questionable data and 50 patients whose next-of-kin respondent was not a spouse. Also excluded were two patients with unknown smoking status, since smoking is a risk factor.
	Metric 3:	Comparison Group	Medium	The cases were pulled from the Minnesota Cancer Surveillance System. Controls were selected from the general population of Minnesota; controls age 20-64 years were selected through random digital dialing and controls age 65-85 years were collected from files through the Health Care Financing Administration. Controls were age- and gender-stratified and were of the same race. Characteristics of cases and controls were not provided in the text or a table.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	High	Occupational histories including the most recent and usual occupation and industry, job activities, started-year and ended-year, and part-time/full-time status were collected. Occupations and industries were coded according to the standard occupational classification (SOC) and standard industrial classification (SIC) schemes. The National Cancer Institute developed job exposure matrices (JEM) for nine individual chlorinated aliphatic hydrocarbons (CAHCs), all CAHCs-combined, and all organic solvents-combined. These JEMs were merged with assigned SOC and SIC to determine the exposure status to these chemicals for each study subject. Application of the JEM was described elsewhere (Dosemeci et al. 1994, HERO ID 632334; Gomez et al. 1994, HERO ID 702154).
	Metric 5:	Exposure Levels	Medium	Details of the application of the JEM were described elsewhere (Dosemeci et al. 1994, HERO ID 632334; Gomez et al. 1994, HERO ID 702154). Dosemeci et al. (1994) described more details about that this study assigned three levels of probability (low, medium, high) to industries and occupations for chemical exposure levels.

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Study Citation:	Dosemeci, M., Cocco, P., Chow, W.H. (1999). Gender differences in risk of renal cell carcinoma and occupational exposures to chlorinated aliphatic hydrocarbons. American Journal of Industrial Medicine 36(1):54-59.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	renal cell carcinoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	4697224

Domain	Metric		Rating	Comments
	Metric 6:	Temporality	Medium	Occupational questionnaires identified prior exposures based on reported recent and usual occupations as well as duration of employment. Outcome status was determined from registry data. The authors note that some occupational history was incomplete which may result in some uncertainty in regard to temporality.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Cases were identified as newly diagnosed and histologically confirmed renal cell carcinoma through the Minnesota Cancer Surveillance System and information about each participant was collected using a questionnaire. Validation was not specified.
	Metric 8:	Reporting Bias	Medium	A description of measured outcomes is reported and ORs were stratified by sex. Effect estimates are reported with a confidence interval. One table showed the total numbers of men and women respectively for each chemical, but numbers of cases/controls were not reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Appropriate adjustments were made in the final analysis, including age, gender, smoking, hypertension and the use of diuretics and/or anti-hypertension drugs, and BMI. Results were stratified by sex.
	Metric 10:	Covariate Characterization	Medium	Information about participants was collected using a questionnaire, and it includes potential confounders, e.g., smoking habits. Validation was not specified.
	Metric 11:	Co-exposure Counfounding	Medium	Co-exposures were identified through the job exposure matrices. Chemicals were evaluated individually and as a group.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen (case-control) was appropriate for the research question (renal cell carcinoma risk from occupational organic solvent exposure). Logistic regression models were used to estimate the relative risk and 95% CI.
	Metric 13:	Statistical Power	Low	Statistical power calculations were not provided. No significant effects were observed with 1,2-dichloroethane. The number of participated women to calculate odds ratio was inadequate to detect an effect in the participants for other chemicals or the combined risk, because it was very low.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis was brief, but is sufficient to understand precisely what has been done and to be conceptually reproducible with access to the analytic data.
	Metric 15:	Statistical Analysis	High	Model assumptions for logistic regression were met. The odds ratios were adjusted for age, smoking, hypertension status and/or use of diuretic and/or anti-hypertension drugs, and body mass index for men and women separately.

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Study Citation:	Dosemeci, M., Cocco, P., Chow, W.H. (1999). Gender differences in risk of renal cell carcinoma and occupational exposures to chlorinated aliphatic hydrocarbons. American Journal of Industrial Medicine 36(1):54-59.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	renal cell carcinoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	4697224

Domain	Metric	Rating	Comments
Additional Comments:	A group of 438 cases (273 men and 165 women) were selected from the Minnesota Cancer Surveillance System that had been newly diagnosed with renal cell carcinoma. Controls included 687 participants (462 men and 225 women) age- and gender- stratified that were selected from either the general population of Minnesota (age 20-64 years) or from the Health Care Financing Administration files (age 65-85). No significant increase in the risk of renal cell carcinoma was observed with exposure to 1,2-dichloroethane among men or women separately, or for all participants exposed.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Garcia, E., Hurley, S., Nelson, D.O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health: A Global Access Science Source 14(1):14.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	breast cancer in females
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	3014082

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	A total of 112,378 women were included in this study out of 133,479 eligible female participants from the California Teacher Study cohort. A full description of the cohort is provided in Bernstein et al. 2002 (HERO ID 808446). Reasons for exclusion were provided. The reported information indicates that participant selection in or out of the study and participation was not likely to be biased.
	Metric 2:	Attrition	High	112,378/133,479 participants were included in the study. Exclusions were for the purpose of the study and analysis. Exclusion criteria were documented. Included participants had completed questionnaires. The California Cancer Registry is estimated to be 99% complete.
	Metric 3:	Comparison Group	Medium	There is only indirect evidence that groups are similar. Participants were recruited from the same eligible population with the same method of ascertainment. Comparisons were provided for participants with and without breast cancer. Characteristics between these two groups were generally similar. 5 Quintiles of exposure were used, and Q2-5 were compared with Q1.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	High	The Assessment System for Population Exposure Nationwide and the Human Exposure Model are used as part of the National-Scale Air Toxics Assessment produced by the EPA and was used to estimate ambient HAP concentrations for geographic locations. Methods are described online through the US EPA Assessment Methods.
	Metric 5:	Exposure Levels	Medium	The distribution of the NATA annual ambient concentration for each compound was plotted in Figure 1 using a box plot, and 5 Quintiles were used in the analyses.
	Metric 6:	Temporality	Medium	The follow-up period was from 1995-2011, and the NATA estimates were made in 2002 because it was approximately half way between the start and end of the follow-up period. However, it is unclear whether exposures fall within relevant exposure windows for the outcome of interest.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Annual linkage between the CTS cohort and the California Cancer Registry (CCR) was used to identify cases of invasive breast cancer. The CCR is estimated to be 99% complete. The case of invasive breast cancer was defined by ICD codes.

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Study Citation:	Garcia, E., Hurley, S., Nelson, D.O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health: A Global Access Science Source 14(1):14.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	breast cancer in females
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	3014082

Domain	Metric		Rating	Comments
	Metric 8:	Reporting Bias	Medium	A description of measured outcome is reported for adjustments by age and race, and effect estimates are reported with a 95% confidence interval. The measured outcomes using multiple comparisons were generally described in the text, but non-significant results were excluded from Table 3.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	The models were stratified by age and race. Additionally, adjustments were made for multiple comparisons among subsets of the participants (significant results reported in Table 3). Socioeconomic status (SES) of each participant was not evaluated, however, cohort SES characteristics were thought to be similar by study authors.
	Metric 10:	Covariate Characterization	Medium	Information about baseline characteristics for each participant was collected through a questionnaire. It is unknown if the questionnaire was validated.
	Metric 11:	Co-exposure Counfounding	Medium	A total of 37 compounds were identified as mammary gland carcinogens, but 13 were not included in this analysis. Thirteen compounds were excluded from the analysis due to insufficient variability (nine because they had the same value for all census tracts in the state of California; and four because they had less than 25% non-zero values). Ethylene dichloride (1,2-dichloroethane) was among the 24 compounds evaluated in this assessment, and evaluations for breast cancer were conducted for each of these 24 individual compounds.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen (prospective cohort) was appropriate for the research question (incidence of breast cancer). Cox proportional hazard models and SAS 9.3 were used in this assessment. Data analysis was described.
	Metric 13:	Statistical Power	Medium	Statistical power calculations were not provided. No significant effects were observed with ethylene dichloride (1,2-dichloroethane), however, this study utilized a large cohort, approximately 112,000 individuals. Distributions of chemicals of interest suggest there were sufficient numbers of participants in exposure subgroups.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to understand precisely what has been done and to be conceptually reproducible with access to the analytic data.
	Metric 15:	Statistical Analysis	High	The statistical models that were used were identified and described. ”No apparent violation of the underlying assumption of proportional hazards was detected”.

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Study Citation:	Garcia, E., Hurley, S., Nelson, D.O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health: A Global Access Science Source 14(1):14.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	breast cancer in females
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	3014082

Domain	Metric	Rating	Comments
Additional Comments:	A group of 112,378 female participants from the California Teacher Study cohort were assessed for their estimated exposure to ambient air pollutants, including ethylene dichloride (1,2-dichloroethane), and the incidence of invasive breast cancer. Air contaminant concentrations were estimated using the US EPA NATA and the ASPEN and HEM models. The approximate median concentration of 1,2-dichloroethane is between 1E-4 and 1E-2 (estimated from Figure 1). Exposures were categorized into 5 Quintiles, and compared against Quintile 1. No significant increase in the estimated hazard rate ratio for invasive breast cancer was observed with Quintile 2-5 exposure estimates for 1,2-dichloroethane, adjusted for age and race, when compared against Quintile 1, or when further adjusted using multiple comparisons.		

Overall Quality Determination High

* No biomarkers were identified for this evaluation.

Study Citation:	Garcia, E., Hurley, S., Nelson, D.O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health: A Global Access Science Source 14(1):14.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	breast cancer in females
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	3014082

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	A total of 112,378 women were included in this study out of 133,479 eligible female participants from the California Teacher Study cohort. A full description of the cohort is provided in Bernstein et al. 2002 (HERO ID 808446). Reasons for exclusion were provided. The reported information indicates that participant selection in or out of the study and participation was not likely to be biased.
	Metric 2:	Attrition	High	112,378/133,479 participants were included in the study. Exclusions were for the purpose of the study and analysis. Exclusion criteria were documented. Included participants had completed questionnaires. The California Cancer Registry is estimated to be 99% complete.
	Metric 3:	Comparison Group	Medium	There is only indirect evidence that groups are similar. Participants were recruited from the same eligible population with the same method of ascertainment. Comparisons were provided for participants with and without breast cancer. Characteristics between these two groups were generally similar. 5 Quintiles of exposure were used, and Q2-5 were compared with Q1.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	High	The Assessment System for Population Exposure Nationwide and the Human Exposure Model are used as part of the National-Scale Air Toxics Assessment produced by the EPA and was used to estimate ambient HAP concentrations for geographic locations. Methods are described online through the US EPA Assessment Methods.
	Metric 5:	Exposure Levels	Medium	The distribution of the NATA annual ambient concentration for each compound was plotted in Figure 1 using a box plot, and 5 Quintiles were used in the analyses.
	Metric 6:	Temporality	Medium	The follow-up period was from 1995-2011, and the NATA estimates were made in 2002 because it was approximately half way between the start and end of the follow-up period. However, it is unclear whether exposures fall within relevant exposure windows for the outcome of interest.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Annual linkage between the CTS cohort and the California Cancer Registry (CCR) was used to identify cases of invasive breast cancer. The CCR is estimated to be 99% complete. The case of invasive breast cancer was defined by ICD codes.
	Metric 8:	Reporting Bias	Medium	A description of measured outcome is reported for adjustments by age and race, and effect estimates are reported with a 95% confidence interval. The measured outcomes using multiple comparisons were generally described in the text, but non-significant results were excluded from Table 3.

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Study Citation:	Garcia, E., Hurley, S., Nelson, D.O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health: A Global Access Science Source 14(1):14.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	breast cancer in females
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	3014082

Domain	Metric		Rating	Comments
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	The models were stratified by age and race. Additionally, adjustments were made for multiple comparisons among subsets of the participants (significant results reported in Table 3). Socioeconomic status (SES) of each participant was not evaluated, however, cohort SES characteristics were thought to be similar by study authors.
	Metric 10:	Covariate Characterization	Medium	Information about baseline characteristics for each participant was collected through a questionnaire. It is unknown if the questionnaire was validated.
	Metric 11:	Co-exposure Counfounding	Medium	A total of 37 compounds were identified as mammary gland carcinogens, but 13 were not included in this analysis. Thirteen compounds were excluded from the analysis due to insufficient variability (nine because they had the same value for all census tracts in the state of California; and four because they had less than 25% non-zero values). Ethylene dichloride (1,2-dichloroethane) was among the 24 compounds evaluated in this assessment, and evaluations for breast cancer were conducted for each of these 24 individual compounds.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen (prospective cohort) was appropriate for the research question (incidence of breast cancer). Cox proportional hazard models and SAS 9.3 were used in this assessment. Data analysis was described.
	Metric 13:	Statistical Power	Medium	Statistical power calculations were not provided. No significant effects were observed with ethylene dichloride (1,2-dichloroethane), however, this study utilized a large cohort, approximately 112,000 individuals. Distributions of chemicals of interest suggest there were sufficient numbers of participants in exposure subgroups.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to understand precisely what has been done and to be conceptually reproducible with access to the analytic data.
	Metric 15:	Statistical Analysis	High	The statistical models that were used were identified and described. ”No apparent violation of the underlying assumption of proportional hazards was detected”.

Additional Comments: A group of 112,378 female participants from the California Teacher Study cohort were assessed for their estimated exposure to ambient air pollutants, including ethylene dichloride (1,2-dichloroethane), and the incidence of invasive breast cancer. Air contaminant concentrations were estimated using the US EPA NATA and the ASPEN and HEM models. The approximate median concentration of 1,2-dichloroethane is between 1E-4 and 1E-2 (estimated from Figure 1). Exposures were categorized into 5 Quintiles, and compared against Quintile 1. No significant increase in the estimated hazard rate ratio for invasive breast cancer was observed with Quintile 2-5 exposure estimates for 1,2-dichloroethane, adjusted for age and race, when compared against Quintile 1, or when further adjusted using multiple comparisons.

Overall Quality Determination High

* No biomarkers were identified for this evaluation.

Study Citation:	Guo, P., Yokoyama, K., Piao, F., Sakai, K., Khalequzzaman, M., Kamijima, M., Nakajima, T., Kitamura, F. (2013). Sick building syndrome by indoor air pollution in Dalian, China. International Journal of Environmental Research and Public Health 10(4):1489-1504.
Health Outcome(s):	sick building syndrome
Reported Health Effect(s):	The statistical analysis considers all subjective self-reported symptoms together (not segregated by health outcome) as a group health outcome –sick building syndrome. The study compared two conditions for each studied chemical: combined self-reported symptoms to no symptoms. Therefore, only one form 3 was completed.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1938385

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Residents of a housing estate of 3000 homes were invited to a community meeting to explain the purpose of the study and volunteers were invited to participate. It was not reported whether these volunteers were different from the overall eligible population.
	Metric 2:	Attrition	Low	Of the 70 families that agreed to participate, questionnaires were provided by 59. Reasons of uncompleted questionnaires were not fully provided, and there was no comparison between those who participated and those who did not.
	Metric 3:	Comparison Group	Low	The overall description of the analysis sample indicated a wide range of ages and lengths of stay at the current residence. Thus it is hard to know that subjects in all exposure groups were similar. In addition, the methods of selecting participants in all exposure groups were not fully reported. The numbers of male and female smokers were reported, respectively, but the smoking status and age were not controlled in the statistical analysis.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure concentrations for each home were obtained by diffusion sampling over 24 hrs in the bedroom, kitchen, and outdoors; temperature, the vertical height of samplers, and ventilation (hours windows left open) were reported. Samples were analyzed by GC/MS. The number of samples per home is unclear. The frequency of measurements for each house was not reported.
	Metric 5:	Exposure Levels	Low	The frequency of detection was not reported, so it is difficult to ascertain the actual exposure range. In addition, the reported exposure levels were median, geometric mean, and 95% CI, so they are inadequate to develop an exposure-response estimate.
	Metric 6:	Temporality	Uninformative	For 1,2-dichloroethane, the study evaluated self-reported symptoms in the past (”since they moved into their flats”) and their association with sampling conducted during the study; thus, exposure was measured after the outcome.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Low	Participants provided self-reported symptoms using a questionnaire. Study authors cited a previous study, Kamijima et al., 2005 (in Japanese, HERO ID 1598645) for further details on the questionnaire. It was not clear whether the questionnaire was validated.

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Study Citation:	Guo, P., Yokoyama, K., Piao, F., Sakai, K., Khalequzzaman, M., Kamijima, M., Nakajima, T., Kitamura, F. (2013). Sick building syndrome by indoor air pollution in Dalian, China. International Journal of Environmental Research and Public Health 10(4):1489-1504.
Health Outcome(s):	sick building syndrome
Reported Health Effect(s):	The statistical analysis considers all subjective self-reported symptoms together (not segregated by health outcome) as a group health outcome –sick building syndrome. The study compared two conditions for each studied chemical: combined self-reported symptoms to no symptoms. Therefore, only one form 3 was completed.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1938385

Domain	Metric		Rating	Comments
	Metric 8:	Reporting Bias	Low	The study only mentioned subjective symptoms in the abstract or methods. The abstract and method sections did not report the specific symptoms included in the questionnaire or whether the questionnaire was open-ended for symptoms. The questionnaire was cited to Kamijima et al. 2005 (in Japanese).
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	Comparisons were made separately by sex. The distribution of age and time spent living in residence differed greatly between those reporting symptoms and those not reporting symptoms. Smoking was indicated but not controlled for in the analysis. In short, the statistical analysis did not consider these three potential confounders, age, time spent living in residence, and smoking.
	Metric 10:	Covariate Characterization	Low	Covariates were presumably evaluated via a questionnaire that was cited to Kamijima et al. 2005 (in Japanese).
	Metric 11:	Co-exposure Counfounding	Low	The analysis did not account for other exposures. A number of other VOCs, HCHO, and NO2 were measured in the homes. The concentrations of several other VOCs and HCHO were much higher (5-30x) than 1,2-dichloroethane and may also be associated with these symptoms.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Low	The study design is best characterized as cross-sectional. Only one analysis to compare exposure concentrations between those with and without symptoms was adjusted for a confounder, sex, via stratification. Other potential confounders were not adjusted for. Study authors combine responses for symptoms reported before and during the sampling period in one statistical analysis, which may not reflect the relationship between symptoms and contaminants' exposure at each period.
	Metric 13:	Statistical Power	Medium	Statistical power was not reported. The number of participants was sufficient to detect a difference in median concentration between those with and without symptoms.
	Metric 14:	Reproducibility of Analyses	Medium	Study presents sufficient description of analysis (statistical methods) to be conceptually reproducible with access to the raw data.
	Metric 15:	Statistical Analysis	Low	Study uses a Wilcoxon's rank sum test to compare exposure concentrations in persons with and without symptoms; test for equal variance is not reported.

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Study Citation:	Guo, P., Yokoyama, K., Piao, F., Sakai, K., Khalequzzaman, M., Kamijima, M., Nakajima, T., Kitamura, F. (2013). Sick building syndrome by indoor air pollution in Dalian, China. International Journal of Environmental Research and Public Health 10(4):1489-1504.
Health Outcome(s):	sick building syndrome
Reported Health Effect(s):	The statistical analysis considers all subjective self-reported symptoms together (not segregated by health outcome) as a group health outcome –sick building syndrome. The study compared two conditions for each studied chemical: combined self-reported symptoms to no symptoms. Therefore, only one form 3 was completed.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1938385

Domain	Metric	Rating	Comments
Additional Comments:	Concentrations of VOCs (including 1,2-dichloroethane), HCHO, and NO2 were measured in the 59 homes of families that agreed to participate after being informed of the nature of the study. Participants completed questionnaires asking about symptoms since they moved into the homes and the concentrations of selected compounds were compared among men and women reporting any symptoms vs no symptoms. Concentrations of 1,2-dichloroethane in homes of people with symptoms were higher than in homes without. p-Dichlorobenzene was measured in the homes as well, but median concentration was <DL and no further analysis was made. Unacceptable due to selection bias, lack of confounding control, inadequate outcome characterization, and lack of temporality.		

Overall Quality Determination — Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Kernan, G.J., Ji, B.T., Dosemeci, M., Silverman, D.T., Balbus, J., Zahm, S.H. (1999). Occupational risk factors for pancreatic cancer: A case-control study based on death certificates from 24 U.S. states. American Journal of Industrial Medicine 36(2):260-270.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Death from pancreatic cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	194820

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	The National Cancer Institute, National Institute of Occupational Safety and Health, and the National Center for Health Statistics reviewed death certificates from 24 states to select cases from those that had died from pancreatic cancer and matched controls. Controls with cause of death related to the outcome of interest (i.e. pancreatic diseases) were excluded from the study. All key elements of the study design were reported.
	Metric 2:	Attrition	Medium	There was no direct evidence of subject loss or exclusion of subgroups from analyses. The authors provide the total number of cases and controls in the analysis. Case and control data were taken from a registry. It can be assumed that the data are complete for each subject.
	Metric 3:	Comparison Group	High	Controls were selected from the same pool of death certificates from 24 states that cases were selected from. Controls with cause of death related to the outcome of interest were eliminated. Differences in baseline characteristics were controlled for via matching, stratification, and adjustment.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure was assessed via occupation and industry data on death certificates. A job matrix was further applied to assess the likely levels of exposure. Probability and intensity of exposure were estimated across four levels for each occupation. Only employment captured on the death certificate could be considered. The exposure assessment needs exposure information before the job listed on the death certificates.
	Metric 5:	Exposure Levels	Medium	The study offers 4 levels of estimated probability and intensity of exposure (referent, low, medium, high).
	Metric 6:	Temporality	Medium	Exposure was determined by occupational and industry codes on death certificates and indicate that exposure would precede disease, however, the timing and latency period is less clear.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Causes of mortality were determined from death certificates for both cases and controls. Death certificates were drawn from death registries of participating states (n=24). Causes of death were coded using ICD-9 codes, and pancreatic cancer was identified as ICD 157.
	Metric 8:	Reporting Bias	Medium	Measured outcomes, effect estimates and confidence intervals are reported. Number of exposed cases is reported for each analysis, however the number of controls (exposed and unexposed) are not reported for analyses.

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Study Citation:	Kernan, G.J., Ji, B.T., Dosemeci, M., Silverman, D.T., Balbus, J., Zahm, S.H. (1999). Occupational risk factors for pancreatic cancer: A case-control study based on death certificates from 24 U.S. states. American Journal of Industrial Medicine 36(2):260-270.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Death from pancreatic cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	194820

Domain	Metric		Rating	Comments
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Potential confounders were accounted for in the following ways: matching (five year age group, state, race, and gender); adjustment in models (age, marital status, metropolitan, and residential status); and stratification (race and gender). Smoking was not included as a confounder.
	Metric 10:	Covariate Characterization	Medium	Data used to assess potential confounders was derived from death certificates, an adequate measure. However, no information about cigarette smoking and other lifestyle factors were available for adjustment in the analysis.
	Metric 11:	Co-exposure Counfounding	Medium	The variety of industries considered in the analysis diminishes concerns about co-exposures.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The case-control study design and statistical analysis methods were appropriate to assess the exposures/outcome of interest.
	Metric 13:	Statistical Power	Medium	This study had an adequate sample size to detect an effect (n for cases = 63,097; n for controls = 252,386).
	Metric 14:	Reproducibility of Analyses	Medium	The description of analysis was sufficient and would be reproducible.
	Metric 15:	Statistical Analysis	High	The model to calculate risk estimates was transparent.

Additional Comments: This case-control study examined the risk of death from pancreatic cancer in different occupational settings. Exposure was solely assessed using occupation/industry at time of death (reported on death certificate) and the application of a job matrix assessing likely levels of exposure for different positions. This means of estimating exposure may not fully represent a participant's exposure history. Additionally, the number of impacted participants (exposed cases) was inadequate to perform quality analyses for some exposure levels.

Overall Quality Determination High

* No biomarkers were identified for this evaluation.

Study Citation:	Kernan, G.J., Ji, B.T., Dosemeci, M., Silverman, D.T., Balbus, J., Zahm, S.H. (1999). Occupational risk factors for pancreatic cancer: A case-control study based on death certificates from 24 U.S. states. American Journal of Industrial Medicine 36(2):260-270.
Health Outcome(s):	Endocrine
Reported Health Effect(s):	Death from pancreatic cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	194820

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	The National Cancer Institute, National Institute of Occupational Safety and Health, and the National Center for Health Statistics reviewed death certificates from 24 states to select cases from those that had died from pancreatic cancer and matched controls. Controls with cause of death related to the outcome of interest (i.e. pancreatic diseases) were excluded from the study. All key elements of the study design were reported.
	Metric 2:	Attrition	Medium	There was no direct evidence of subject loss or exclusion of subgroups from analyses. The authors provide the total number of cases and controls in the analysis. Case and control data were taken from a registry. It can be assumed that the data are complete for each subject.
	Metric 3:	Comparison Group	High	Controls were selected from the same pool of death certificates from 24 states that cases were selected from. Controls with cause of death related to the outcome of interest were eliminated. Differences in baseline characteristics were controlled for via matching, stratification, and adjustment.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure was assessed via occupation and industry data on death certificates. A job matrix was further applied to assess the likely levels of exposure. Probability and intensity of exposure were estimated across four levels for each occupation. Only employment captured on the death certificate could be considered. The exposure assessment needs exposure information before the job listed on the death certificates.
	Metric 5:	Exposure Levels	Medium	The study offers 4 levels of estimated probability and intensity of exposure (referent, low, medium, high).
	Metric 6:	Temporality	Medium	Exposure was determined by occupational and industry codes on death certificates and indicate that exposure would precede disease, however, the timing and latency period is less clear.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Causes of mortality were determined from death certificates for both cases and controls. Death certificates were drawn from death registries of participating states (n=24). Causes of death were coded using ICD-9 codes, and pancreatic cancer was identified as ICD 157.
	Metric 8:	Reporting Bias	Medium	Measured outcomes, effect estimates and confidence intervals are reported. Number of exposed cases is reported for each analysis, however the number of controls (exposed and unexposed) are not reported for analyses.
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Kernan, G.J., Ji, B.T., Dosemeci, M., Silverman, D.T., Balbus, J., Zahm, S.H. (1999). Occupational risk factors for pancreatic cancer: A case-control study based on death certificates from 24 U.S. states. American Journal of Industrial Medicine 36(2):260-270.
Health Outcome(s):	Endocrine
Reported Health Effect(s):	Death from pancreatic cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	194820

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Medium	Potential confounders were accounted for in the following ways: matching (five year age group, state, race, and gender); adjustment in models (age, marital status, metropolitan, and residential status); and stratification (race and gender). Smoking was not included as a confounder.
	Metric 10:	Covariate Characterization	Medium	Data used to assess potential confounders was derived from death certificates, an adequate measure. However, no information about cigarette smoking and other lifestyle factors were available for adjustment in the analysis.
	Metric 11:	Co-exposure Counfounding	Medium	The variety of industries considered in the analysis diminishes concerns about co-exposures.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The case-control study design and statistical analysis methods were appropriate to assess the exposures/outcome of interest.
	Metric 13:	Statistical Power	Medium	This study had an adequate sample size to detect an effect (n for cases = 63,097; n for controls = 252,386).
	Metric 14:	Reproducibility of Analyses	Medium	The description of analysis was sufficient and would be reproducible.
	Metric 15:	Statistical Analysis	High	The model to calculate risk estimates was transparent.

Additional Comments: This case-control study examined the risk of death from pancreatic cancer in different occupational settings. Exposure was solely assessed using occupation/industry at time of death (reported on death certificate) and the application of a job matrix assessing likely levels of exposure for different positions. This means of estimating exposure may not fully represent a participant's exposure history. Additionally, the number of impacted participants (exposed cases) was inadequate to perform quality analyses for some exposure levels.

Overall Quality Determination High

* No biomarkers were identified for this evaluation.

Study Citation:	Niehoff, N.M., Gammon, M.D., Keil, A.P., Nichols, H.B., Engel, L.S., Sandler, D.P., White, A.J. (2019). Airborne mammary carcinogens and breast cancer risk in the Sister Study. Environment International 130:104897.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Breast cancer diagnosis (overall), tumor characteristics, and estrogen receptor positive (ER+) invasive breast cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5440630

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	Data from the Sister Study were used. The Sister Study is "a prospective cohort of 50,884 women from across the US who were ages 35–74 at enrollment (Sandler et al., 2017). Participants were recruited from 2003 to 2009 using a national advertising campaign in English and Spanish. Women were eligible for the Sister Study if they had a sister who had been diagnosed with breast cancer, but no prior breast cancer themselves."Exclusions from the study occurred for the following reasons:-breast cancer diagnosed before enrollment was complete, or did not have follow-up information (n = 163)-Residential address couldn't be geocoded (n = 1003, < 2%) - This is a small perecentage, but all of those who were excluded for this reason were from Puerto Rico, West Virginia, Missouri, or Oklahoma.Key elements of the study design are reported. There is some potential for selection bias, but based on the small percentage of those eligible who were excluded, participation was not likely to be substantially biased.
	Metric 2:	Attrition	High	Response rates in the overall Sister study remained over 91% over follow-up. Reasons for non-response were not reported, and characteristics of those lost to follow up were not reported or compared with those included, but 9% loss to follow-up is minimal.
	Metric 3:	Comparison Group	High	Differences in baseline characteristics of groups were considered as potential confounding variables.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	The EPA NATA database of census-tract level modeled air toxics data was used. The study authors note the potential for exposure misclassification: "Concentrations at the census tract level do not fully account for variation in an individual's daily activities that could lead to higher or lower exposure, and all women within a census tract are assigned the same concentration."
	Metric 5:	Exposure Levels	Medium	There were five quintiles of exposure, so there was a sufficient range and distribution of exposure.
	Metric 6:	Temporality	Medium	This is a prospective cohort study.Exposure data from 2005 were chosen because they represented the middle of the enrollment period (2003-2009).The study reported that "94% of women enrolled in 2005 or later, and thus the exposure assessment primarily predated enrollment for the majority of Sister Study participants."The six percent of women who had the potential to have the outcome before exposure was measured in 2005 are a concern. But sensitivity analyses were used to assess whether the associations changed when restricted to those who enrolled in 2005 or later.The authors note that the study is making assumptions about the relevant exposure windows - therefore the exposure window is not certain.

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Study Citation:	Niehoff, N.M., Gammon, M.D., Keil, A.P., Nichols, H.B., Engel, L.S., Sandler, D.P., White, A.J. (2019). Airborne mammary carcinogens and breast cancer risk in the Sister Study. Environment International 130:104897.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Breast cancer diagnosis (overall), tumor characteristics, and estrogen receptor positive (ER+) invasive breast cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5440630

Domain	Metric		Rating	Comments
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Women who reported a breast cancer diagnosis on the annual health updates or follow-up questionnaires were asked to provide additional diagnosis information, and to grant permission for the study to obtain medical records and pathology reports. Medical records were obtained for 81% of breast cancer diagnoses. Agreement between self-reported breast cancers and medical records was high (positive predictive value > 99%) (Sandler et al., 2017), so self-report was used when medical records were not available. Tumor characteristics (stage; histology; and estrogen receptor (ER) status) were abstracted from medical records, or self-reported.
	Metric 8:	Reporting Bias	High	A description of measured outcomes is reported. Effect estimates are reported with confidence intervals.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Covariates considered included age, race, BMI, residence type, education, and smoking status. Potential confounders were identified using DAGs and literature review. Appropriate considerations were made for potential confounders.
	Metric 10:	Covariate Characterization	Medium	”Most covariates were assessed by self-report at the baseline interview.””At baseline, women completed a computer-assisted telephone interview and written questionnaires.”Previous publications might describe whether the questionnaires were validated, but validation was not specified in this publication.
	Metric 11:	Co-exposure Counfounding	Medium	Co-exposures to other air pollutants were assessed, but at the census tract level.Multipollutant classification trees were used, which might provide useful qualitative information.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design (large prospective cohort) and analysis method (Cox proportional hazard single and multi-pollutant models accounting for potential confounders) were appropriate to assess the association between exposure and disease.
	Metric 13:	Statistical Power	Medium	The study had an adequate sample size (1975 cancer cases) and follow-up time (mean=8.4 years).
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to be conceptually reproducible.

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Study Citation:	Niehoff, N.M., Gammon, M.D., Keil, A.P., Nichols, H.B., Engel, L.S., Sandler, D.P., White, A.J. (2019). Airborne mammary carcinogens and breast cancer risk in the Sister Study. Environment International 130:104897.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Breast cancer diagnosis (overall), tumor characteristics, and estrogen receptor positive (ER+) invasive breast cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5440630

Domain	Metric	Rating	Comments
	Metric 15: Statistical Analysis	High	Hazard ratios and 95% confidence intervals (CIs) are reported "comparing index categories of exposure to exposures below the first quintile using Cox proportional hazards regression, with age as the time scale." The method of calculating the hazard ratios is transparent. The authors reported that "the proportional hazards assumption was evaluated by conducting a Wald test for an interaction between the continuous form of the air toxic measure and time." Censoring times and times at-risk are described.

Additional Comments: This was a well-conducted study of a large prospective cohort, but the measurement of exposure at the census-tract rather than the individual level is a limitation.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Sobel, W., Bond, G.G., Skowronski, B.J., Brownson, P.J., Cook, R.R. (1987). A soft tissue sarcoma case control study in a large multi-chemical manufacturing facility. Chemosphere 16(8-9):2095-2099.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	soft-tissue sarcoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1357737

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	From a pool of > 37,000 subjects who worked at least 1 year at chemical company between January 1940-December 1979, the study identified 14 people who died due to soft-cell sarcoma (via death certificate, medical records, or histopathology report). Referents were matched 9:1 with cases (126 matched controls).
	Metric 2:	Attrition	High	There was minimal subject exclusion from the analysis sample; one case could not be matched to controls and was excluded from analysis.
	Metric 3:	Comparison Group	High	Cases and controls were recruited from the same eligible population within the same time frame and matched on sex, race, year of birth and year of hire. Both cases and controls had to have worked ≥1 yr at the plant during the study period.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Work histories for cases and referents were coded to determine an individual's potential exposure to chemical of interest and reviewed by an industrial hygienist blinded to case status.
	Metric 5:	Exposure Levels	Low	Exposure was considered dichotomous, ever exposed or never exposed. There is no quantitative information on exposure levels or range of exposures.
	Metric 6:	Temporality	Low	Temporality of exposure and outcome is established. It is unclear if the interval between exposure and outcome is sufficient for soft tissue sarcoma outcomes.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	The soft-tissue sarcoma outcome was assessed by information provided by death certificates, medical records, and histopathology reports, but study authors did not report the proportions determined by each method.
	Metric 8:	Reporting Bias	High	All outcomes outlined were reported. Authors reported the number of cases and controls in the table. Maximum likelihood estimate ORs with respective 95 % confidence intervals were reported.
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Sobel, W., Bond, G.G., Skowronski, B.J., Brownson, P.J., Cook, R.R. (1987). A soft tissue sarcoma case control study in a large multi-chemical manufacturing facility. Chemosphere 16(8-9):2095-2099.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	soft-tissue sarcoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1357737

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Low	Controls were matched with cases on age, sex, year of hire and survival information. There is indirect evidence that the considerations were made to identify potential confounders through evaluation of medical records of cases and controls (various heritable syndromes, family history of cancer, history of lymphedema, steroids, throrotrast, foreign body implants, chronic extensive scarring, radiation therapy, and immunological defects). Identified confounders between cases and controls were not reported and it is unclear if adjustments for these confounders were included in the final analyses.
	Metric 10:	Covariate Characterization	High	Potential covariates were assessed through evaluation of work histories and medical records.
	Metric 11:	Co-exposure Counfounding	Low	The study documented 13 chemicals, known to be associated with soft-tissue sarcoma (according to NTP, 1983) that were used at the manufacturing facility at some point since 1940. The authors note that some individuals were exposed to multiple chemicals during their employment history and were counted multiple times in the analysis for different chemical exposures. Co-exposures to chemicals to not appear to be adjusted for in analysis.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Low	The study design was adequate to assess the association between exposure and the outcome of interest (soft-tissue sarcoma). The study authors noted they used programs developed by Rothman and Boice to calculate odds ratios with CI intervals; the statistical methods are not further described. The page containing the Rothman and Boice reference appears to be missing from the PDF (or the citation is missing).
	Metric 13:	Statistical Power	Low	Statistical power was not calculated. For 1,2-dichloroethane, there was one case and 6 controls included in the analysis, which was not adequate to detect and effect.
	Metric 14:	Reproducibility of Analyses	Low	The study calculated odd ratios, and 95% CIs were calculated using point estimates and chi from hypothesis testing. The study authors noted they used programs developed by Rothman and Boice to calculate odds ratios with 95% CIs; the statistical methods are not further described and there was no reference for the programs cited.
	Metric 15:	Statistical Analysis	Low	A description of analyses/assumptions was not reported.

Additional Comments: A case-control study of workers at a chemical production facility who worked at least 1 year between January 1940-December 1979 (n=37,000) investigated the incidence of deaths due to soft-tissue sarcoma. The study identified 14 people who died due to soft-tissue sarcoma (through death certificate, medical records, or histopathology reports). Cases were matched to controls based on sex, race, year of birth and year of hire. 13 chemicals, including 1,2-dichloroethane, associated with soft-tissue sarcoma were used at the facility; it does not appear that co-exposures were adjusted for in the analysis. Odds ratios and corresponding CIs were calculated. No significant association was found between exposure to 1,2-DCE and soft-tissue sarcoma.

Overall Quality Determination Medium

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Study Citation:	Sobel, W., Bond, G.G., Skowronski, B.J., Brownson, P.J., Cook, R.R. (1987). A soft tissue sarcoma case control study in a large multi-chemical manufacturing facility. Chemosphere 16(8-9):2095-2099.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	soft-tissue sarcoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1357737

Domain	Metric	Rating	Comments

* No biomarkers were identified for this evaluation.

Study Citation:	Sobel, W., Bond, G.G., Skowronski, B.J., Brownson, P.J., Cook, R.R. (1987). A soft tissue sarcoma case control study in a large multi-chemical manufacturing facility. Chemosphere 16(8-9):2095-2099.
Health Outcome(s):	Skin and Connective Tissue
Reported Health Effect(s):	soft-tissue sarcoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1357737

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	From a pool of > 37,000 subjects who worked at least 1 year at chemical company between January 1940-December 1979, the study identified 14 people who died due to soft-cell sarcoma (via death certificate, medical records, or histopathology report). Referents were matched 9:1 with cases (126 matched controls).
	Metric 2:	Attrition	High	There was minimal subject exclusion from the analysis sample; one case could not be matched to controls and was excluded from analysis.
	Metric 3:	Comparison Group	High	Cases and controls were recruited from the same eligible population within the same time frame and matched on sex, race, year of birth and year of hire. Both cases and controls had to have worked ≥1 yr at the plant during the study period.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Work histories for cases and referents were coded to determine an individual's potential exposure to chemical of interest and reviewed by an industrial hygienist blinded to case status.
	Metric 5:	Exposure Levels	Low	Exposure was considered dichotomous, ever exposed or never exposed. There is no quantitative information on exposure levels or range of exposures.
	Metric 6:	Temporality	Low	Temporality of exposure and outcome is established. It is unclear if the interval between exposure and outcome is sufficient for soft tissue sarcoma outcomes.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	The soft-tissue sarcoma outcome was assessed by information provided by death certificates, medical records, and histopathology reports, but study authors did not report the proportions determined by each method.
	Metric 8:	Reporting Bias	High	All outcomes outlined were reported. Authors reported the number of cases and controls in the table. Maximum likelihood estimate ORs with respective confidence intervals were reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	Controls were matched with cases on age, sex, year of hire and survival information. There is indirect evidence that that considerations were made to identify potential confounders through evaluation of medical records of cases and controls (various heritable syndromes, family history of cancer, history of lymphedema, steroids, throrotrast, foreign body implants, chronic extensive scarring, radiation therapy, and immunological defects). Identified confounders between cases and controls were not reported and it is unclear if adjustments for these confounders were included in the final analyses.

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Study Citation:	Sobel, W., Bond, G.G., Skowronski, B.J., Brownson, P.J., Cook, R.R. (1987). A soft tissue sarcoma case control study in a large multi-chemical manufacturing facility. Chemosphere 16(8-9):2095-2099.
Health Outcome(s):	Skin and Connective Tissue
Reported Health Effect(s):	soft-tissue sarcoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1357737

Domain	Metric		Rating	Comments
	Metric 10:	Covariate Characterization	High	Potential covariates were assessed through evaluation of work histories and medical records.
	Metric 11:	Co-exposure Counfounding	Low	The study documented 13 chemicals, known to be associated with soft-tissue sarcoma (according to NTP, 1983) that were used at the manufacturing facility at some point since 1940. The authors note that some individuals were exposed to multiple chemicals during their employment history and were counted multiple times in the analysis for different chemical exposures. Co-exposures to chemicals to not appear to be adjusted for in analysis.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Low	The study design was adequate to assess the association between exposure and the outcome of interest (soft-tissue sarcoma). The study authors noted they used programs developed by Rothman and Boice to calculate odds ratios with (95% CIs; the statistical methods are not further described. The page containing the Rothman and Boice reference appears to be missing from the PDF (or the citation is missing).
	Metric 13:	Statistical Power	Low	Statistical power was not calculated. For 1,2-dichloroethane, there was one case and 6 controls included in the analysis, which was not adequate to detect and effect.
	Metric 14:	Reproducibility of Analyses	Low	The study calculated odd ratios, and 95% CIs were calculated using point estimates and chi from hypothesis testing. The study authors noted they used programs developed by Rothman and Boice to calculate odds ratios with CI intervals; the statistical methods are not further described and there was no reference for the programs cited.
	Metric 15:	Statistical Analysis	Low	A description of analyses/assumptions was not reported.

Additional Comments: A case-control study of workers at a chemical production facility who worked at least 1 year between January 1940-December 1979 (n=37,000) investigated the incidence of deaths due to soft-tissue sarcoma. The study identified 14 people who died due to soft-tissue sarcoma (through death certificate, medical records, or histopathology reports). Cases were matched to controls based on sex, race, year of birth and year of hire. 13 chemicals, including 1,2-dichloroethane, associated with soft-tissue sarcoma were used at the facility; it does not appear that co-exposures were adjusted for in the analysis. Odds ratios and corresponding CIs were calculated. No significant association was found between exposure to 1,2-DCE and soft-tissue sarcoma.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Teta, M. J., Ott, M. G., Schnatter, A. R. (1991). An update of mortality due to brain neoplasms and other causes among employees of a petrochemical facility. Journal of Occupational Medicine 33(1):45-51.
Health Outcome(s):	Mortality
Reported Health Effect(s):	all cause mortality, gastrointestinal cancer mortality, respiratory system cancer mortality, kidney and other urinary organ cancer mortality, skin cancer mortality, brain cancer mortality, lymphatic and hematopoietic tissue cancer mortality, benign neoplasm mortality, heart disease mortality, and liver cirrhosis mortality.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200633, 1629047
HERO ID:	200633

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	The facility was described in some detail. All male employees working for one day or more between 1941 and 1983 were included. There may be some healthy worker effect in this population.
	Metric 2:	Attrition	High	Study authors reported that vital status was complete for 99% of the population, and death certificates were obtained for 99% of decedents.
	Metric 3:	Comparison Group	High	SMRs were calculated using age-, race-, and calendar year-specific mortality rates of males in the United States. All included employees were male.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	All employees were treated as exposed. Table 4 indicates that relatively few employees were employed in areas designated as 1,2-DCA work areas. There is potential for substantial exposure misclassification.
	Metric 5:	Exposure Levels	Low	All employed individuals were categorized as exposed, and the reference population was described as unexposed. This represents two levels of exposure. The distribution of exposure within the employed population is unclear.
	Metric 6:	Temporality	Medium	Employees were followed from 1950 (or date of first hire) through 1983. The relevant timing of exposure is not entirely clear; however, this represents a sufficiently long period of follow-up.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Mortality was tracked using company records, Social Security Administration records, and the National Death Index. Specific ICD codes and use of a nosologist were not described, but there was no evidence to suggest the method had poor validity.
	Metric 8:	Reporting Bias	High	SMRs were provided with confidence intervals in addition to observed and expected cases. The authors state they did not carry out regional specific SMRs due to the higher prevalence of neoplasms in the surrounding area.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	SMRs were restricted to males. Rates were age-, race-, and calendar period-specific. No consideration was made for smoking.
	Metric 10:	Covariate Characterization	Medium	Demographic information was obtained from employment records. This was not a validated method, but there was no evidence to suggest it was an invalid method.

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Study Citation:	Teta, M. J., Ott, M. G., Schnatter, A. R. (1991). An update of mortality due to brain neoplasms and other causes among employees of a petrochemical facility. Journal of Occupational Medicine 33(1):45-51.
Health Outcome(s):	Mortality
Reported Health Effect(s):	all cause mortality, gastrointestinal cancer mortality, respiratory system cancer mortality, kidney and other urinary organ cancer mortality, skin cancer mortality, brain cancer mortality, lymphatic and hematopoietic tissue cancer mortality, benign neoplasm mortality, heart disease mortality, and liver cirrhosis mortality.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200633, 1629047
HERO ID:	200633

Domain	Metric		Rating	Comments
	Metric 11:	Co-exposure Counfounding	Low	Several other occupational exposures linked to cancer mortality were present, including vinyl chloride, butanol, and other petrochemicals.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	This study design was appropriate for the research question. Authors utilized retrospective occupational cohort data to determine standardized mortality rates for cancer-specific mortalities.
	Metric 13:	Statistical Power	Medium	While power was not calculated, there were over 1350 deaths from 7849 employees which was adequate to detect robust effect estimates.
	Metric 14:	Reproducibility of Analyses	Low	Most details were provided; however, ICD codes used to determine and group cancer mortality diagnoses were not provided.
	Metric 15:	Statistical Analysis	High	No issues identified.

Additional Comments: This study utilized an occupational cohort to retrospectively evaluate elevated rates of cancer mortality among petrochemical plant workers. There were numerous potentially hazardous chemicals mentioned in the plant description which may lead to co-exposure. Additionally, it appears that only a moderate portion of workers may have been exposed to 1,2-DCA or worked in 1,2-DCA areas which may lead to some exposure misclassification and limit the study's ability to inform hazard on 1,2-DCA.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Cases in this case-control study were former Union Carbide Corporation (UCC) chemical plant employees in Texas City, Texas. Cases were identified through death certificate searches and tumor registries, and may have included individuals formerly employed at UCC whose cause of death was unknown to the company. Additionally, control deaths were stated to be pulled from corporate employee benefits department and through locally published obituary notices routinely screened by the medical department - it is possible to assume that cases were identified in a similar manner. The study identified cases of brain tumors by searching death certificates primarily, although tumor registries throughout the state of Texas were also searched. The study clarifies that it is possible that some cases were not found if they survived or died due to another cause - while this is likely to have impacted selection, there is no evidence that this would be differential by exposure status. Overall, there is limited information on the source population of workers from which cases were identified.
	Metric 2:	Attrition	Medium	Attrition is not discussed in the study, and outcome data appear to be complete. There was a large proportion of missing exposure data (roughly 50%) due to workers being employed in roles such as maintenance, where exposure to any chemical is possible but unknown. Analyses were run separately where these ”unknown” individuals were a) treated as exposed, b) treated as unexposed, or c) treated as unknown and thus excluded. The study only presents results for when these individuals were excluded but specifies that the first scenario resulted in increased exposure estimates for controls relative to cases.

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Study Citation:	Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
	Metric 3:	Comparison Group	Medium	The study identifies two series of control groups, selected from all former Union Carbide Corporation (UCC) employees. However, the total number of employees is not stated. Only those who were deceased were used as controls since they had known causes of death and could thus be verified as non-brain tumors. One group of controls excluded employees whose cause of death was due to any malignant neoplasm to allow for the possibility that a general chemical carcinogen may have been associated with cancers of other sites. The other group of controls included deaths from all causes; this included malignant neoplasms other than brain tumors. Both control groups had 80 male employees randomly selected from 450 deceased employees known to the company in June 1979. Control deaths were stated to be pulled from corporate employee benefits department and through locally published obituary notices routinely screened by the medical department - it is possible to assume that cases were identified in a similar manner. The study reports that cases were slightly more likely to have been employed for less than 10 years than controls - the study attributes this in part to the fact that employees whose deaths were known to the company were more likely to have worked for longer - regardless the mean number of years employed was similar between cases and controls. However, cases were more likely to have been terminated from their job for reasons other than death, disability, or retirement (quitting, being fired, etc.), were generally younger at hire, and were less likely to survive to their 70th birthday. None of these factors are controlled for in statistical analyses - however, since controls and cases were pulled from the same population, there is indirect evidence that the groups were similar.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was determined based on official employment records. Records included job title and department assignment codes for each employment from date of hire to date of termination. For each unique department code, UCC and NIOSH industrial hygienists identified principal chemicals used or produced at any time in the history of the plant and correlated those with individual departments. This assessment was not performed on a year-by-year basis due to concerns for recall bias for longer-term employees where less detailed records were kept. An employee was categorized as ”exposed” to 1,2-dichloroethane if they ever worked in a department associated with that chemical. An ”unknown” exposure group was also created to account for employees who had only worked in departments for which no specific chemical could be identified.
	Metric 5:	Exposure Levels	Low	The study does not report any quantitative information and only splits exposure into ”exposed”, ”unexposed”, and ”unknown”.
	Metric 6:	Temporality	High	In this study exposure is confirmed to occur before the outcome is measured. The study reports latency periods, with subjects dichotomized into less than 15 years of latency or more than 15 years of latency. The majority of cases and controls had a latency of greater than 15 years, which is sufficiently long for brain tumors.

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Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Cases were identified through death certificate searches and partially through tumor registries in the state of Texas. Case validation was performed by NIOSH, and 5 different levels of confirmation were reported: 1) tissue specimen interpreted by the Armed Forces Institute of Pathology; 2) autopsy report; 3) histopathology report; 4) clinical diagnosis from hospital record; 5) dearth certificate diagnosis. Codes 1-3 were considered to be ”confirmed” cases of brain tumors, while 4-5 were considered unconfirmed. 5/21 cases were only evaluated using ”unconfirmed methods”, meaning there is likely a high amount of accuracy in roughly 75% of cases. While no case validation is reported for controls, the study specifies that only controls who had died and thus could be confirmed to be non-brain tumors were included.
	Metric 8:	Reporting Bias	Medium	All primary and secondary outcomes that are outlined in the methods are reported in the results. However, the only statistical outcome of their analysis were unadjusted p-values that were not reported and were just described qualitatively.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	The only statistical analysis performed were Mantel-Haenszel chi-squared tests, which did not allow for confounder adjustment. The study does not present a distribution of potential confounders by exposure status but by case/control status. Several variables, such as reason for termination, age at hire, and age at death were significantly different between cases and controls and were not accounted for in statistical modeling. The study explains that these differences are not likely to have any epidemiologic significance and appear to be relatively small differences.
	Metric 10:	Covariate Characterization	Medium	While the study does not explain where they obtained covariate information, it is reasonable to assume that they gathered the information from company records.
	Metric 11:	Co-exposure Counfounding	Low	The study assesses a wide range of other potential occupational co-exposures. While these co-exposures are not adjusted for in any statistical models, effect estimates are presented separately for benzene, diethyl sulfate, ethylene oxide, and vinyl chloride. The distribution of co-exposures across cases and controls is demonstrated to be mostly balanced by comparing proportions of exposed/unexposed between cases and controls. The only notable instance of imbalance is for benzene, where 11.1% of cases were exposed whereas 37.9% of all controls and 19.2% of non-neoplasm related controls were exposed.
Domain 5: Analysis				

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Study Citation:	Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	The study chose a case-control design, which was appropriate to study the rare disease of brain tumors and its association with occupational exposures. The only statistical analysis conducted is a Mantzel-Haenszel chi-squared test, but there is no reason to suggest that this would be inappropriate.
	Metric 13:	Statistical Power	Medium	The study does not calculate statistical power, but the number of cases (n=21) and controls (n=80 in each analysis) is likely sufficient to detect an effect.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to understand what was done and could be reproduced given access to the analytic data.
	Metric 15:	Statistical Analysis	High	The only statistical analysis conducted is a Mantel-Haenszel chi-squared test, and all assumptions were met. The statistical process is transparent.

Additional Comments: This case-control study pulled deceased former employees of the Union Carbide Corporation in Texas City, Texas. The study examined dichotomous exposure to a wide range of occupational exposures, including 1,2-dichloroethane, in relation to brain tumor cases. There is no quantitative estimate of exposure. The only statistical analysis in the study is a Mantel-Haenszel chi-squared test statistic and no statistically significant differences in exposure between cases and controls were observed. The fact that there are no effect estimates, no adjustment for confounders, and no quantitative exposure estimates limits the usefulness of this paper.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Cases in this case-control study were former Union Carbide Corporation (UCC) chemical plant employees in Texas City, Texas. Cases were identified through death certificate searches and tumor registries, and may have included individuals formerly employed at UCC whose cause of death was unknown to the company. Additionally, control deaths were stated to be pulled from corporate employee benefits department and through locally published obituary notices routinely screened by the medical department - it is possible to assume that cases were identified in a similar manner. The study identified cases of brain tumors by searching death certificates primarily, although tumor registries throughout the state of Texas were also searched. The study clarifies that it is possible that some cases were not found if they survived or died due to another cause - while this is likely to have impacted selection, there is no evidence that this would be differential by exposure status. Overall, there is limited information on the source population of workers from which cases were identified.
	Metric 2:	Attrition	Medium	Attrition is not discussed in the study, and outcome data appear to be complete. There was a large proportion of missing exposure data (roughly 50%) due to workers being employed in roles such as maintenance, where exposure to any chemical is possible but unknown. Analyses were run separately where these ”unknown” individuals were a) treated as exposed, b) treated as unexposed, or c) treated as unknown and thus excluded. The study only presents results for when these individuals were excluded but specifies that the first scenario resulted in increased exposure estimates for controls relative to cases.

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Linked HERO ID(s):	No linked references.
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Domain	Metric		Rating	Comments
	Metric 3:	Comparison Group	Medium	The study identifies two series of control groups, selected from all former Union Carbide Corporation (UCC) employees. However, the total number of employees is not stated. Only those who were deceased were used as controls since they had known causes of death and could thus be verified as non-brain tumors. One group of controls excluded employees whose cause of death was due to any malignant neoplasm to allow for the possibility that a general chemical carcinogen may have been associated with cancers of other sites. The other group of controls included deaths from all causes; this included malignant neoplasms other than brain tumors. Both control groups had 80 male employees randomly selected from 450 deceased employees known to the company in June 1979. Control deaths were stated to be pulled from corporate employee benefits department and through locally published obituary notices routinely screened by the medical department - it is possible to assume that cases were identified in a similar manner. The study reports that cases were slightly more likely to have been employed for less than 10 years than controls - the study attributes this in part to the fact that employees whose deaths were known to the company were more likely to have worked for longer - regardless the mean number of years employed was similar between cases and controls. However, cases were more likely to have been terminated from their job for reasons other than death, disability, or retirement (quitting, being fired, etc.), were generally younger at hire, and were less likely to survive to their 70th birthday. None of these factors are controlled for in statistical analyses - however, since controls and cases were pulled from the same population, there is indirect evidence that the groups were similar.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was determined based on official employment records. Records included job title and department assignment codes for each employment from date of hire to date of termination. For each unique department code, UCC and NIOSH industrial hygienists identified principal chemicals used or produced at any time in the history of the plant and correlated those with individual departments. This assessment was not performed on a year-by-year basis due to concerns for recall bias for longer-term employees where less detailed records were kept. An employee was categorized as ”exposed” to 1,2-dichloroethane if they ever worked in a department associated with that chemical. An ”unknown” exposure group was also created to account for employees who had only worked in departments for which no specific chemical could be identified.
	Metric 5:	Exposure Levels	Low	The study does not report any quantitative information and only splits exposure into ”exposed”, ”unexposed”, and ”unknown”.
	Metric 6:	Temporality	High	In this study exposure is confirmed to occur before the outcome is measured. The study reports latency periods, with subjects dichotomized into less than 15 years of latency or more than 15 years of latency. The majority of cases and controls had a latency of greater than 15 years, which is sufficiently long for brain tumors.

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Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Cases were identified through death certificate searches and partially through tumor registries in the state of Texas. Case validation was performed by NIOSH, and 5 different levels of confirmation were reported: 1) tissue specimen interpreted by the Armed Forces Institute of Pathology; 2) autopsy report; 3) histopathology report; 4) clinical diagnosis from hospital record; 5) dearth certificate diagnosis. Codes 1-3 were considered to be ”confirmed” cases of brain tumors, while 4-5 were considered unconfirmed. 5/21 cases were only evaluated using ”unconfirmed methods”, meaning there is likely a high amount of accuracy in roughly 75% of cases. While no case validation is reported for controls, the study specifies that only controls who had died and thus could be confirmed to be non-brain tumors were included.
	Metric 8:	Reporting Bias	Medium	All primary and secondary outcomes that are outlined in the methods are reported in the results. However, the only statistical outcome of their analysis were unadjusted p-values that were not reported and were just described qualitatively.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	The only statistical analysis performed were Mantel-Haenszel chi-squared tests, which did not allow for confounder adjustment. The study does not present a distribution of potential confounders by exposure status but by case/control status. Several variables, such as reason for termination, age at hire, and age at death were significantly different between cases and controls and were not accounted for in statistical modeling. The study explains that these differences are not likely to have any epidemiologic significance and appear to be relatively small differences.
	Metric 10:	Covariate Characterization	Medium	While the study does not explain where they obtained covariate information, it is reasonable to assume that they gathered the information from company records.
	Metric 11:	Co-exposure Counfounding	Low	The study assesses a wide range of other potential occupational co-exposures. While these co-exposures are not adjusted for in any statistical models, effect estimates are presented separately for benzene, diethyl sulfate, ethylene oxide, and vinyl chloride. The distribution of co-exposures across cases and controls is demonstrated to be mostly balanced by comparing proportions of exposed/unexposed between cases and controls. The only notable instance of imbalance is for benzene, where 11.1% of cases were exposed whereas 37.9% of all controls and 19.2% of non-neoplasm related controls were exposed.
Domain 5: Analysis				

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Study Citation:	Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	The study chose a case-control design, which was appropriate to study the rare disease of brain tumors and its association with occupational exposures. The only statistical analysis conducted is a Mantzel-Haenszel chi-squared test, but there is no reason to suggest that this would be inappropriate.
	Metric 13:	Statistical Power	Medium	The study does not calculate statistical power, but the number of cases (n=21) and controls (n=80 in each analysis) is likely sufficient to detect an effect.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to understand what was done and could be reproduced given access to the analytic data.
	Metric 15:	Statistical Analysis	High	The only statistical analysis conducted is a Mantel-Haenszel chi-squared test, and all assumptions were met. The statistical process is transparent.

Additional Comments: This case-control study pulled deceased former employees of the Union Carbide Corporation in Texas City, Texas. The study examined dichotomous exposure to a wide range of occupational exposures, including 1,2-dichloroethane, in relation to brain tumor cases. There is no quantitative estimate of exposure. The only statistical analysis in the study is a Mantel-Haenszel chi-squared test statistic and no statistically significant differences in exposure between cases and controls were observed. The fact that there are no effect estimates, no adjustment for confounders, and no quantitative exposure estimates limits the usefulness of this paper.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	Urinary system cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	Urinary system cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	Urinary system cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Immune/Hematological
Reported Health Effect(s):	Lymphatic and hematopoietic tissue cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Immune/Hematological
Reported Health Effect(s):	Lymphatic and hematopoietic tissue cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Immune/Hematological
Reported Health Effect(s):	Lymphatic and hematopoietic tissue cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Other cancers (not specified)
Reported Health Effect(s):	Other cancers (not specified)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Other cancers (not specified)
Reported Health Effect(s):	Other cancers (not specified)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Other cancers (not specified)
Reported Health Effect(s):	Other cancers (not specified)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Mortality
Reported Health Effect(s):	All-cause mortality
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Vital status was tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Medium	Death rates among unit employees were compared to death rates in the U.S. population adjusted for age and gender. Demographics of the exposed workers are not provided; therefore, it is not clear whether additional adjustment for race may have been appropriate. No justification is provided for the choice of the entire U.S. population as the comparison group. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis. Additional analyses are conducted limiting workers to those with the greatest likelihood of exposure (i.e., those working in jobs with high likelihood of contact with chemicals for more than a year, those working for the full year of 1979 during which chemical exposures were most frequently reported); these smaller groups are also compared to the unexposed general population.
	Metric 6:	Temporality	High	Temporality was established due to the longitudinal design and the use of mortality as the outcome. Exposures occurred between 1979 and 1987 and follow-up for vital status was conducted through 2003.
Domain 3: Outcome Assessment				

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Mortality
Reported Health Effect(s):	All-cause mortality
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Medium	The study did not provide information on how mortality was assessed either in the exposed population or in the comparison population; use of death certificates is implied but not stated.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected deaths are reported, but SIRs and 95% confidence intervals are not provided.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Comparisons of observed versus expected deaths were adjusted for age and gender. Demographics of the exposed workers are not provided; therefore, it is not clear whether additional adjustment for race may have been appropriate.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records or death records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed deaths among a population of exposed workers compared to expected deaths among the U.S. population, adjusted for age and gender.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected deaths; no SIR was provided. Expected death rates were adjusted for age and gender.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Mortality
Reported Health Effect(s):	All-cause mortality
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	All cancer (excluding non-melanoma skin cancer), digestive system cancer, colorectal cancer, respiratory cancer, prostate cancer, urinary system cancer, lymphatic and hematopoietic tissue cancer, other cancers (not specified)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	All cancer (excluding non-melanoma skin cancer), digestive system cancer, colorectal cancer, respiratory cancer, prostate cancer, urinary system cancer, lymphatic and hematopoietic tissue cancer, other cancers (not specified)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	All cancer (excluding non-melanoma skin cancer), digestive system cancer, colorectal cancer, respiratory cancer, prostate cancer, urinary system cancer, lymphatic and hematopoietic tissue cancer, other cancers (not specified)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Gastrointestinal
Reported Health Effect(s):	Digestive system cancer, colorectal cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Gastrointestinal
Reported Health Effect(s):	Digestive system cancer, colorectal cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Health Outcome(s):	Gastrointestinal
Reported Health Effect(s):	Digestive system cancer, colorectal cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Lung/Respiratory
Reported Health Effect(s):	Respiratory cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Reported Health Effect(s):	Respiratory cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Health Outcome(s):	Lung/Respiratory
Reported Health Effect(s):	Respiratory cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Prostate cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Male workers who had ever been assigned to the chlorohydrin unit between 1 January 1940 and 31 December 1967 at Union Carbide's South Charleston plant were enrolled and matched to the US National Death Index. Status on 5 workers could not be identified. Information on how workers were matched to death index was not specified.
	Metric 2:	Attrition	Medium	Rate of inclusion/participation was very high, as records were able to be matched for 98% of participants. Medium rating given because information on how participants whose vital status was not known was not specified.
	Metric 3:	Comparison Group	Uninformative	Unacceptable rating given because SMRs were calculated based on expected deaths from a reference population matched on sex, but not age.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Exposure was assessed based on duration of work in the plant. No information is provided on exposure levels, and a JEM was not used.
	Metric 5:	Exposure Levels	Uninformative	No information provided on levels of exposure.
	Metric 6:	Temporality	High	Temporality is well established; person-years stopped accumulating in 1967 and outcome was assessed beginning at that time.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar period, and interval since assignments, but distribution of these covariates was not reported.
	Metric 10:	Covariate Characterization	Medium	Information on covariate characterization not provided, but the selected covariates (age, calendar period, and interval since assignments) were likely extracted from employee records and unlikely to be largely problematic
	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.

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Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Study design was appropriate for the research method. Statistical methods were also appropriate.
	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.
	Metric 14:	Reproducibility of Analyses	Medium	Methods are well-enough described that study could be adequately reproduced.
	Metric 15:	Statistical Analysis	High	SMRs calculated based on US general population mortality for white males through 1988. RRs were ”evaluated over levels of duration of assignment to the chlorohydrin unit, stratified by age, calendar year, and interval since first assignment to the chlorohydrin unit”.

Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
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Linked HERO ID(s):	200224, 5447107
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Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Male workers who had ever been assigned to the chlorohydrin unit between 1 January 1940 and 31 December 1967 at Union Carbide's South Charleston plant were enrolled and matched to the US National Death Index. Status on 5 workers could not be identified. Information on how workers were matched to death index was not specified.
	Metric 2:	Attrition	Medium	Rate of inclusion/participation was very high, as records were able to be matched for 98% of participants. Medium rating given because information on how participants whose vital status was not known was not specified.
	Metric 3:	Comparison Group	Uninformative	Unacceptable rating given because SMRs were calculated based on expected deaths from a reference population matched on sex, but not age.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Exposure was assessed based on duration of work in the plant. No information is provided on exposure levels, and a JEM was not used.
	Metric 5:	Exposure Levels	Uninformative	No information provided on levels of exposure.
	Metric 6:	Temporality	High	Temporality is well established; person-years stopped accumulating in 1967 and outcome was assessed beginning at that time.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar period, and interval since assignments, but distribution of these covariates was not reported.
	Metric 10:	Covariate Characterization	Medium	Information on covariate characterization not provided, but the selected covariates (age, calendar period, and interval since assignments) were likely extracted from employee records and unlikely to be largely problematic
	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.
Domain 5: Analysis				

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Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
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Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Study design was appropriate for the research method. Statistical methods were also appropriate.
	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.
	Metric 14:	Reproducibility of Analyses	Medium	Methods are well-enough described that study could be adequately reproduced.
	Metric 15:	Statistical Analysis	High	SMRs calculated based on US general population mortality for white males through 1988. RRs were ”evaluated over levels of duration of assignment to the chlorohydrin unit, stratified by age, calendar year, and interval since first assignment to the chlorohydrin unit”.

Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
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Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Male workers who had ever been assigned to the chlorohydrin unit between 1 January 1940 and 31 December 1967 at Union Carbide's South Charleston plant were enrolled and matched to the US National Death Index. Status on 5 workers could not be identified. Information on how workers were matched to death index was not specified.
	Metric 2:	Attrition	Medium	Rate of inclusion/participation was very high, as records were able to be matched for 98% of participants. Medium rating given because information on how participants whose vital status was not known was not specified.
	Metric 3:	Comparison Group	Uninformative	Unacceptable rating given because SMRs were calculated based on expected deaths from a reference population matched on sex, but not age.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Exposure was assessed based on duration of work in the plant. No information is provided on exposure levels, and a JEM was not used.
	Metric 5:	Exposure Levels	Uninformative	No information provided on levels of exposure.
	Metric 6:	Temporality	High	Temporality is well established; person-years stopped accumulating in 1967 and outcome was assessed beginning at that time.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar period, and interval since assignments, but distribution of these covariates was not reported.
	Metric 10:	Covariate Characterization	Medium	Information on covariate characterization not provided, but the selected covariates (age, calendar period, and interval since assignments) were likely extracted from employee records and unlikely to be largely problematic
	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.
Domain 5: Analysis				

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Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
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Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Study design was appropriate for the research method. Statistical methods were also appropriate.
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Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
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Domain	Metric		Rating	Comments
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	Metric 2:	Attrition	Medium	Rate of inclusion/participation was very high, as records were able to be matched for 98% of participants. Medium rating given because information on how participants whose vital status was not known was not specified.
	Metric 3:	Comparison Group	Uninformative	Unacceptable rating given because SMRs were calculated based on expected deaths from a reference population matched on sex, but not age.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Exposure was assessed based on duration of work in the plant. No information is provided on exposure levels, and a JEM was not used.
	Metric 5:	Exposure Levels	Uninformative	No information provided on levels of exposure.
	Metric 6:	Temporality	High	Temporality is well established; person-years stopped accumulating in 1967 and outcome was assessed beginning at that time.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar period, and interval since assignments, but distribution of these covariates was not reported.
	Metric 10:	Covariate Characterization	Medium	Information on covariate characterization not provided, but the selected covariates (age, calendar period, and interval since assignments) were likely extracted from employee records and unlikely to be largely problematic
	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.
Domain 5: Analysis				

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Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Study design was appropriate for the research method. Statistical methods were also appropriate.
	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.
	Metric 14:	Reproducibility of Analyses	Medium	Methods are well-enough described that study could be adequately reproduced.
	Metric 15:	Statistical Analysis	High	SMRs calculated based on US general population mortality for white males through 1988. RRs were ”evaluated over levels of duration of assignment to the chlorohydrin unit, stratified by age, calendar year, and interval since first assignment to the chlorohydrin unit”.

Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
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Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Male workers who had ever been assigned to the chlorohydrin unit between 1 January 1940 and 31 December 1967 at Union Carbide's South Charleston plant were enrolled and matched to the US National Death Index. Status on 5 workers could not be identified. Information on how workers were matched to death index was not specified.
	Metric 2:	Attrition	Medium	Rate of inclusion/participation was very high, as records were able to be matched for 98% of participants. Medium rating given because information on how participants whose vital status was not known was not specified.
	Metric 3:	Comparison Group	Uninformative	Unacceptable rating given because SMRs were calculated based on expected deaths from a reference population matched on sex, but not age.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Exposure was assessed based on duration of work in the plant. No information is provided on exposure levels, and a JEM was not used.
	Metric 5:	Exposure Levels	Uninformative	No information provided on levels of exposure.
	Metric 6:	Temporality	High	Temporality is well established; person-years stopped accumulating in 1967 and outcome was assessed beginning at that time.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar period, and interval since assignments, but distribution of these covariates was not reported.
	Metric 10:	Covariate Characterization	Medium	Information on covariate characterization not provided, but the selected covariates (age, calendar period, and interval since assignments) were likely extracted from employee records and unlikely to be largely problematic
	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.
Domain 5: Analysis				

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Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Study design was appropriate for the research method. Statistical methods were also appropriate.
	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.
	Metric 14:	Reproducibility of Analyses	Medium	Methods are well-enough described that study could be adequately reproduced.
	Metric 15:	Statistical Analysis	High	SMRs calculated based on US general population mortality for white males through 1988. RRs were ”evaluated over levels of duration of assignment to the chlorohydrin unit, stratified by age, calendar year, and interval since first assignment to the chlorohydrin unit”.

Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
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Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Male workers who had ever been assigned to the chlorohydrin unit between 1 January 1940 and 31 December 1967 at Union Carbide's South Charleston plant were enrolled and matched to the US National Death Index. Status on 5 workers could not be identified. Information on how workers were matched to death index was not specified.
	Metric 2:	Attrition	Medium	Rate of inclusion/participation was very high, as records were able to be matched for 98% of participants. Medium rating given because information on how participants whose vital status was not known was not specified.
	Metric 3:	Comparison Group	Uninformative	Unacceptable rating given because SMRs were calculated based on expected deaths from a reference population matched on sex, but not age.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Exposure was assessed based on duration of work in the plant. No information is provided on exposure levels, and a JEM was not used.
	Metric 5:	Exposure Levels	Uninformative	No information provided on levels of exposure.
	Metric 6:	Temporality	High	Temporality is well established; person-years stopped accumulating in 1967 and outcome was assessed beginning at that time.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar period, and interval since assignments, but distribution of these covariates was not reported.
	Metric 10:	Covariate Characterization	Medium	Information on covariate characterization not provided, but the selected covariates (age, calendar period, and interval since assignments) were likely extracted from employee records and unlikely to be largely problematic
	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.
Domain 5: Analysis				

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Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Study design was appropriate for the research method. Statistical methods were also appropriate.
	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.
	Metric 14:	Reproducibility of Analyses	Medium	Methods are well-enough described that study could be adequately reproduced.
	Metric 15:	Statistical Analysis	High	SMRs calculated based on US general population mortality for white males through 1988. RRs were ”evaluated over levels of duration of assignment to the chlorohydrin unit, stratified by age, calendar year, and interval since first assignment to the chlorohydrin unit”.

Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
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Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Male workers who had ever been assigned to the chlorohydrin unit between 1 January 1940 and 31 December 1967 at Union Carbide's South Charleston plant were enrolled and matched to the US National Death Index. Status on 5 workers could not be identified. Information on how workers were matched to death index was not specified.
	Metric 2:	Attrition	Medium	Rate of inclusion/participation was very high, as records were able to be matched for 98% of participants. Medium rating given because information on how participants whose vital status was not known was not specified.
	Metric 3:	Comparison Group	Uninformative	Unacceptable rating given because SMRs were calculated based on expected deaths from a reference population matched on sex, but not age.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Exposure was assessed based on duration of work in the plant. No information is provided on exposure levels, and a JEM was not used.
	Metric 5:	Exposure Levels	Uninformative	No information provided on levels of exposure.
	Metric 6:	Temporality	High	Temporality is well established; person-years stopped accumulating in 1967 and outcome was assessed beginning at that time.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar period, and interval since assignments, but distribution of these covariates was not reported.
	Metric 10:	Covariate Characterization	Medium	Information on covariate characterization not provided, but the selected covariates (age, calendar period, and interval since assignments) were likely extracted from employee records and unlikely to be largely problematic
	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.
Domain 5: Analysis				

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Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Study design was appropriate for the research method. Statistical methods were also appropriate.
	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.
	Metric 14:	Reproducibility of Analyses	Medium	Methods are well-enough described that study could be adequately reproduced.
	Metric 15:	Statistical Analysis	High	SMRs calculated based on US general population mortality for white males through 1988. RRs were ”evaluated over levels of duration of assignment to the chlorohydrin unit, stratified by age, calendar year, and interval since first assignment to the chlorohydrin unit”.

Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
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Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Male workers who had ever been assigned to the chlorohydrin unit between 1 January 1940 and 31 December 1967 at Union Carbide's South Charleston plant were enrolled and matched to the US National Death Index. Status on 5 workers could not be identified. Information on how workers were matched to death index was not specified.
	Metric 2:	Attrition	Medium	Rate of inclusion/participation was very high, as records were able to be matched for 98% of participants. Medium rating given because information on how participants whose vital status was not known was not specified.
	Metric 3:	Comparison Group	Uninformative	Unacceptable rating given because SMRs were calculated based on expected deaths from a reference population matched on sex, but not age.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Exposure was assessed based on duration of work in the plant. No information is provided on exposure levels, and a JEM was not used.
	Metric 5:	Exposure Levels	Uninformative	No information provided on levels of exposure.
	Metric 6:	Temporality	High	Temporality is well established; person-years stopped accumulating in 1967 and outcome was assessed beginning at that time.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar period, and interval since assignments, but distribution of these covariates was not reported.
	Metric 10:	Covariate Characterization	Medium	Information on covariate characterization not provided, but the selected covariates (age, calendar period, and interval since assignments) were likely extracted from employee records and unlikely to be largely problematic
	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.
Domain 5: Analysis				

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Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Study design was appropriate for the research method. Statistical methods were also appropriate.
	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.
	Metric 14:	Reproducibility of Analyses	Medium	Methods are well-enough described that study could be adequately reproduced.
	Metric 15:	Statistical Analysis	High	SMRs calculated based on US general population mortality for white males through 1988. RRs were ”evaluated over levels of duration of assignment to the chlorohydrin unit, stratified by age, calendar year, and interval since first assignment to the chlorohydrin unit”.

Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Bove, F. J. (1996). Public drinking water contamination and birthweight, prematurity, fetal deaths, and birth defects. Toxicology and Industrial Health 12(2):255-266.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	200239

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	This cross-sectional study (n=80,938) included all registered singleton live births and fetal deaths (>20 weeks' gestation) in 1985-88 in 75 New Jersey towns located in 4 counties with "some" water supplies contaminated with substances of interest and where: (i) residents were "mostly" served by public water systems; and (ii) births occurred "mostly" in state. Estimated proportions of residents served by public water systems, and of pregnancies/births captured, were not described. However, the inclusion of all eligible registered births, fetal deaths, and birth defects, as well as the selection of towns without knowledge of birth outcome prevalence, limited the likelihood of selection bias.
	Metric 2:	Attrition	Medium	All registered births and fetal deaths were included. Attrition due to missing values for multiple variables was not quantified and is therefore uncertain. However, attrition was likely modest as the proportion of missing values for individual variables was relatively low: (i) ~6% of subjects were excluded from analyses of outcomes such as preterm birth due to invalid or missing gestational ages; and (ii) other covariates evaluated as confounders had up to 4.9% missing values.
	Metric 3:	Comparison Group	High	After excluding plural pregnancies and chromosomal abnormalities, all registered live births during the study period in the areas included without the outcomes of interest were included in the comparison group. This comprehensive approach limited the potential for bias. Chromosomal abnormalities were not included as outcomes as they were not hypothesized to be associated with the exposures under study but were appropriately excluded given their uncertain etiology.
Domain 2: Exposure Characterization				

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Study Citation:	Bove, F. J. (1996). Public drinking water contamination and birthweight, prematurity, fetal deaths, and birth defects. Toxicology and Industrial Health 12(2):255-266.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	200239

Domain	Metric		Rating	Comments
	Metric 4:	Measurement of Exposure	Medium	Along with several other contaminants, residential drinking water exposure to 1,2-dichloroethane (as well as 1,1,1-trichloroethane and 'total dichloroethylenes') – was assigned based on maternal town of residence at birth. Exposure estimates were calculated using the average of water company sampling reports during the first trimester (for birth defects and fetal death) or the duration of pregnancy (for other outcomes). Detection limits and data availability were not specified in detail but were described as below 1 ppb, with reporting compliance >85%. A minimum of 1 sample per 6-month interval was required; variability in the number of measures available across water systems and towns was not described. Additional sources of measurement error included: changes in residence during pregnancy; water from alternate sources (ex. private wells, bottles, workplaces); variability in residential contaminant levels vs measured samples; unknown levels of tap water intake; and errors in estimated dermal and inhalation exposure while bathing or showering. While the extent of exposure misclassification is uncertain, there is no evidence to suggest it was differential rather than random.
	Metric 5:	Exposure Levels	Medium	Due to the high proportion of measures below detection limits, analyses relating exposure to health outcomes used only 2 categories for each of the chlorinated solvents of interest: cutoffs close to detection limits were used to define elevated exposure. Proportions defined as having elevated exposure was low (1.8% had 1,1-dichloroethylene ≥1 ppb). An important concern is that relatively low levels of exposure to these contaminants from sources other than residential drinking water, for which data were not available, could potentially have resulted in considerable misclassification.
	Metric 6:	Temporality	High	Exposure levels were assigned based on contaminant exposures estimated during: (i) the first trimester for analyses of birth defects and fetal deaths; and (ii) the duration of pregnancy for other pregnancy outcomes.

Domain 3: Outcome Assessment

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Study Citation:	Bove, F. J. (1996). Public drinking water contamination and birthweight, prematurity, fetal deaths, and birth defects. Toxicology and Industrial Health 12(2):255-266.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	200239

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcomes included measures of birthweight (continuous among term births, low term birthweight, very low birthweight), prematurity, fetal death, and congenital anomalies in live births or fetal deaths. The anomalies analyzed included defects of the central nervous system, neural tube, oral cleft, total cardiac, major cardiac, ventricular septum, and any surveillance defect excluding chromosomal defects. All outcomes were identified using birth certificates, fetal death certificates (>20 weeks' gestation), and the NJ congenital birth defect registry (ICD codes provided). These registry data are likely to be sufficiently valid for late pregnancy outcomes. However, their limited ability to capture early pregnancy losses is a weakness. The sample included only 594 fetal deaths (less than 1% of the >80,0000 sample). Typical estimates are that 10-20%, of recognized pregnancies ending in losses. Moreover, developmental defects contributing to early pregnancy losses were also not captured. A further limitation is that that potentially etiologically heterogeneous preterm birth types were analyzed together, as these data did not distinguish premature rupture of membranes vs idiopathic prematurity.
	Metric 8:	Reporting Bias	Medium	Models were constructed only for contaminants with associations > 1.0, and tables included only associations with odds ratios ≥1.5. No clear rationale was provided. Several positive odds ratios below the 1.5 cutoff were described in the results text (without confidence intervals), but no null/negative odds ratios were presented or described.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Potential confounding by maternal race, education, parity, and prior pregnancy loss, along with infant sex (for birth outcomes) and adequacy of prenatal care, was examined. Gestational age was addressed by analyzing birthweight among full term births, term low birth weight, and small size for gestational age. Only fully adjusted models were presented. In a companion case-control study (with low participation rates), adjustment for other variables not available on birth certificates (ex. maternal smoking, occupational exposures, medical history, and gestational weight gain) did not influence associations with other studied contaminants. This separate study reduces concerns for important confounding bias, but confounding cannot be ruled out.
	Metric 10:	Covariate Characterization	Medium	Data on covariates came from registry data: birth certificates, fetal death certificates, and the NJ congenital birth defects registry.
	Metric 11:	Co-exposure Counfounding	Medium	Co-exposure confounding by drinking water trihalomethane concentrations was evaluated. There was no evidence to suggest substantial confounding by this or other co-exposures.
Domain 5: Analysis				

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Study Citation:	Bove, F. J. (1996). Public drinking water contamination and birthweight, prematurity, fetal deaths, and birth defects. Toxicology and Industrial Health 12(2):255-266.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	200239

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Methods were appropriate. The study used logistic regression models to estimate odds ratios and confidence intervals for dichotomous outcomes, and linear regression for analysis of continuous birth weight.
	Metric 13:	Statistical Power	Medium	Statistical power was likely to have been limited as a consequence of the small proportion of the sample defined as having "elevated" residential water concentrations of the chemicals of interest. The range of exposure examined was limited, as cutoffs for elevated levels were close to the detection limits of 1 ppb. In addition, for most birth defect outcomes, fewer than 10 cases had elevated exposure.
	Metric 14:	Reproducibility of Analyses	Medium	The authors clearly described steps used to estimate exposure-outcome associations, including exposure category cutoffs and criteria for confounding. However, many results were not shown as tables included odds ratios ≥1.5.
	Metric 15:	Statistical Analysis	High	The authors estimated coefficients, odds ratios and 95% confidence intervals using adequate methods. Confounding was based on 15% change-in-estimate comparing nested models. Effect modification (ex by infant sex) was not evaluated as there was no a priori evidence to suggest such analyses at that time.

Additional Comments: This study analyzed the association between estimated residential drinking water concentrations of several chlorinated solvents including 1,2-dichloroethane (as well as 1,1,1-trichloroethane; ∑[trans-1,2-dichloroethylene and 1,1-dichloroethylene]) and pregnancy outcomes (size at birth, prematurity, fetal deaths, and congenital birth defects). The sample included more than 80,000 births during 1985-88 for residents of 75 towns in NJ using public water system records to estimate exposure during gestation, and registry data (birth certificate, fetal death certificates for pregnancies >20 weeks, state birth defect registry) to characterize outcomes. Strengths included the large sample size and inclusion of all eligible registered births and fetal deaths in the study period. A critical concern is the inability to capture early fetal deaths and any related malformations (1% of the sample had fetal deaths vs typical estimates of >10%). An important limitation was the low percentage of the sample with detectable (> 1ppb) concentrations of these contaminants (<1% to 6.2%). Small numbers for birth defect outcomes also limited power. Exposure misclassification (ex. drinking water from wells/ work/ bottles, changes in residence, exposure from other sources) is also a concern. However, such misclassification was likely non-differential, and thus more likely to under- vs. to over-estimate associations.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Bove, F. J., Fulcomer, M. C., Klotz, J. B., Esmart, J., Dufficy, E. M., Savrin, J. E. (1995). Public drinking water contamination and birth outcomes. American Journal of Epidemiology 141(9):850-862.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	194932

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	This semi-ecological study (n=80,938) included all registered singleton live births and fetal deaths (>20 weeks) in 1985-88 in 75 New Jersey towns located in 4 counties with "some" water supplies contaminated with substances of interest and where: (i) residents were "mostly" served by public water systems; and (ii) births occurred "mostly" in state. Estimated proportions of residents served by public water systems, and of pregnancies/births captured, were not described. However, the inclusion of all eligible registered births, fetal deaths, and birth defects, as well as the selection of towns without knowledge of birth outcome prevalence, limited the likelihood of selection bias.
	Metric 2:	Attrition	Medium	All registered births and fetal deaths were included. Attrition due to missing values for multiple variables was not quantified and is therefore uncertain. However, attrition was likely modest as the proportion of missing values for individual variables was relatively low: (i) ~6% of subjects were excluded from analyses of outcomes such as preterm birth due to invalid or missing gestational ages; and (ii) other covariates evaluated as confounders had up to 4.9% missing values.
	Metric 3:	Comparison Group	High	After excluding plural pregnancies and chromosomal abnormalities, all registered live births during the study period in the areas included without the outcomes of interest were included in the comparison group. This comprehensive approach limited the potential for bias. Chromosomal abnormalities were not included as outcomes as they were not hypothesized to be associated with the exposures under study but were appropriately excluded given their uncertain etiology.
Domain 2: Exposure Characterization				

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Study Citation:	Bove, F. J., Fulcomer, M. C., Klotz, J. B., Esmart, J., Dufficy, E. M., Savrin, J. E. (1995). Public drinking water contamination and birth outcomes. American Journal of Epidemiology 141(9):850-862.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	194932

Domain	Metric		Rating	Comments
	Metric 4:	Measurement of Exposure	Medium	Along with several other contaminants, residential drinking water exposure to 1,2-dichloroethane (as well as 1,1,1-trichloroethane and 'total dichloroethylenes') was assigned based on maternal town of residence at birth. Exposure estimates were calculated using the average of water company sampling reports during the first trimester (for birth defects and fetal death) or the duration of pregnancy (for other outcomes). Detection limits and data availability were not specified in detail but were described as below 1 ppb, with reporting compliance >85%. A minimum of 1 sample per 6-month interval was required; variability in the number of measures available across water systems and towns was not described. Additional sources of measurement error included: changes in residence during pregnancy; water from alternate sources (ex. private wells, bottles, workplaces); variability in residential contaminant levels vs measured samples; unknown levels of tap water intake; and errors in estimated dermal and inhalation exposure while bathing or showering. While the extent of exposure misclassification is uncertain, there is no evidence to suggest it was differential rather than random.
	Metric 5:	Exposure Levels	Low	Due to the high proportion of measures below detection limits, analyses relating exposure to health outcomes used only 2 categories for each of the three chemicals of interest: cutoffs close to detection limits were used to define elevated exposure. Proportions defined as having elevated exposure were low (1.8% had 1,1-dichloroethylene ≥1 ppb). An important concern is that relatively low levels of exposure to this contaminant from sources other than residential drinking water, for which data were not available, could potentially have resulted in considerable misclassification.
	Metric 6:	Temporality	High	Exposure levels were assigned based on contaminant exposures estimated during: (i) the first trimester for analyses of birth defects and fetal deaths; and (ii) the duration of pregnancy for other pregnancy outcomes.

Domain 3: Outcome Assessment

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Study Citation: Bove, F. J., Fulcomer, M. C., Klotz, J. B., Esmart, J., Dufficy, E. M., Savrin, J. E. (1995). Public drinking water contamination and birth outcomes. American Journal of Epidemiology 141(9):850-862.
Health Outcome(s): Reproductive/Developmental
Reported Health Effect(s): Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s): 194932, 200239
HERO ID: 194932

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcomes included measures of birthweight (continuous among term births, low term birthweight, very low birthweight), prematurity, fetal death, and congenital anomalies in live births or fetal deaths. The anomalies analyzed included defects of the central nervous system, neural tube, oral cleft, total cardiac, major cardiac, ventricular septum, and any surveillance defect excluding chromosomal defects. All outcomes were identified using birth certificates, fetal death certificates (>20 weeks' gestation), and the NJ congenital birth defect registry (ICD codes provided). These registry data are likely to be sufficiently valid for late pregnancy outcomes. However, their limited ability to capture early pregnancy losses is a weakness. The sample included only 594 fetal deaths (less than 1% of the >80,0000 sample). Typical estimates are that 10-20%, of recognized pregnancies ending in losses. Moreover, developmental defects contributing to early pregnancy losses were also not captured. A further limitation is that that potentially etiologically heterogeneous preterm birth types were analyzed together, as these data did not distinguish premature rupture of membranes vs idiopathic prematurity.
	Metric 8:	Reporting Bias	Low	Models were constructed only for contaminants with associations > 1.0, and tables included only associations with odds ratios ≥1.5. No clear rationale was provided. Several positive odds ratios below the 1.5 cutoff were described in the results text (without confidence intervals), but no null/negative odds ratios were presented or described.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Potential confounding by maternal race, education, parity, and prior pregnancy loss, along with infant sex (for birth outcomes) and adequacy of prenatal care, was examined. Gestational age was addressed by analyzing birthweight among full term births, term low birth weight, and small size for gestational age. Only fully adjusted models were presented. In a companion case-control study (with low participation rates), adjustment for other variables not available on birth certificates (ex. maternal smoking, occupational exposures, medical history, and gestational weight gain) did not influence associations with other studied contaminants. This separate study reduces concerns for important confounding bias, but confounding cannot be ruled out.
	Metric 10:	Covariate Characterization	Medium	Data on covariates came from registry data: birth certificates, fetal death certificates, and the NJ congenital birth defects registry.
	Metric 11:	Co-exposure Counfounding	Medium	Co-exposure confounding by drinking water trihalomethane concentrations was evaluated. There was no evidence to suggest substantial confounding by this or other co-exposures.
Domain 5: Analysis				

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Study Citation:	Bove, F. J., Fulcomer, M. C., Klotz, J. B., Esmart, J., Dufficy, E. M., Savrin, J. E. (1995). Public drinking water contamination and birth outcomes. American Journal of Epidemiology 141(9):850-862.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	194932

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Methods were appropriate. The study used logistic regression models to estimate odds ratios and confidence intervals for dichotomous outcomes, and linear regression for analysis of continuous birth weight.
	Metric 13:	Statistical Power	Low	Statistical power was likely to have been limited as a consequence of the small proportion of the sample defined as having "elevated" residential water concentrations of the chemicals of interest. The range of exposure examined was limited, as cutoffs for elevated levels were close to the detection limits of 1 ppb. In addition, for most birth defect outcomes, fewer than 10 cases had elevated exposure. However, the authors emphasized the magnitude of associations rather than statistical significance and presented multiple confidence intervals to aid interpretation of the precision of estimates (50%, 90% and 99%).
	Metric 14:	Reproducibility of Analyses	Medium	The authors clearly described steps used to estimate exposure-outcome associations, including exposure category cutoffs and criteria for confounding. However, many results were not shown as tables included odds ratios ≥1.5.
	Metric 15:	Statistical Analysis	High	The authors estimated coefficients, odds ratios and confidence intervals using adequate methods. Confounding was based on 15% change-in-estimate comparing nested models. Effect modification (ex by infant sex) was not evaluated as there was no a priori evidence to suggest such analyses at that time.

Additional Comments: This study analyzed the association between estimated residential drinking water concentrations of several chlorinated solvents including 1,2-dichloroethane (as well as 1,1,1-trichloroethane and the ∑[trans-1,2-dichloroethylene & 1,1-dichloroethylene]) and pregnancy outcomes (size at birth, prematurity, fetal deaths, and congenital birth defects). The sample included more than 80,000 births during 1985-88 for residents of 75 towns in NJ using public water system records to estimate exposure during gestation, and registry data (birth certificate, fetal death certificates for pregnancies >20 weeks' gestation, state birth defect registry) to characterize outcomes. Strengths included the large sample size and inclusion of all eligible registered births and fetal deaths in the study period. A critical concern is the inability to capture early fetal deaths and any related malformations (1% of the sample had fetal deaths vs typical estimates of >10%). An important limitation was the low percentage of the sample with detectable (> 1ppb) concentrations of this solvent (<2%), which likely limited power. Small numbers for birth defect outcomes also limited power. Exposure misclassification (ex. drinking water from wells/ work/ bottles, changes in residence, exposure from other sources) is also a concern. However, such misclassification was likely non-differential, and thus more likely to under- vs. to over-estimate associations.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Bowler, R.M., Gysens, S., Hartney, C. (2003). Neuropsychological effects of ethylene dichloride exposure. NeuroToxicology 24(4-5):553-562.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Wechsler Adult Intelligence Scale III (WAIS-III), Wechsler Memory Scale III (WMS-III), Boston Naming Test (BNT), Trail Making Test (TMT), Stroop Color-Word Test, Grooved Pegboard, Dynamometer, Wide Range Achievement Test (WRAT), Finger tapping, Beck Anxiety Index, Beck Depression Index, Symptom Checklist-90 (SCL-90).
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	200241

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Uninformative	221 workers that had been exposed to 1,2-DCE in the Southern United States were initially included. Exclusion criteria were provided, including the number of individuals excluded for each reason. The study authors note that those initially included in the analysis sample were referred by physicians after neurological complaints were documented. Detailed criteria for referral were not provided. Referral-based recruitment of neurological cases will likely result in an analysis sample with an exposure-outcome distribution that is not representative of the eligible population (i.e., contamination site clean-up workers).
	Metric 2:	Attrition	Medium	There was moderate subject loss. Reasons for exclusion from the analysis sample are provided, and only those with complete information were included in the analysis.
	Metric 3:	Comparison Group	Low	Impairment scores were compared to normative data from manuals and/or a "demographically similar control group" cited to Bowler et al. (2001). The controls from this study appeared similar (albeit somewhat older) than 1,2-DCE-exposed workers and reported no prior chemical exposure.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	A job-exposure matrix was not considered plausible; variables considered as surrogates of exposure were obtained from interviews. This method is expected to have poor validity because it relies on workers' recall of subjective events and their frequency (e.g., contact with water); workers (who are taking part in a lawsuit) may overestimate their exposure.
	Metric 5:	Exposure Levels	Low	Two levels of exposure (exposed and not exposed) were used to evaluate neurophysiological effects.
	Metric 6:	Temporality	Medium	Exposures primarily occurred between 1993 and 1995 and neurophysiological effects were evaluated in 2000. Temporality is established, but it is unclear whether exposures fall within relevant exposure windows for the outcome of interest.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Neurophysiological effects were evaluated using a number of standardized tests, including (but not limited to) the Wechsler Adult Intelligence Scale (WAIS-III), the Wechsler Memory Scale (WMS-III), and the Symptom Checklist 90-Revised (SCL90-R). There was no information whether tests were performed using the same methods for exposed and referent groups (e.g., timing and order of tests).

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Study Citation:	Bowler, R.M., Gysens, S., Hartney, C. (2003). Neuropsychological effects of ethylene dichloride exposure. NeuroToxicology 24(4-5):553-562.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Wechsler Adult Intelligence Scale III (WAIS-III), Wechsler Memory Scale III (WMS-III), Boston Naming Test (BNT), Trail Making Test (TMT), Stroop Color-Word Test, Grooved Pegboard, Dynamometer, Wide Range Achievement Test (WRAT), Finger tapping, Beck Anxiety Index, Beck Depression Index, Symptom Checklist-90 (SCL-90).
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	200241

Domain	Metric		Rating	Comments
	Metric 8:	Reporting Bias	Low	Neurobehavioral outcomes mentioned in the methods were reported for 1,2-DCE-exposed workers (as mean score, standard deviation, and percentage impaired); results for controls/normative data were not shown and/or p-values from t-tests were not provided. Control data were used to define impairment (based on z-score) but these values were not reported. Data pertaining to specific exposure variables were reported in the text only; no data were shown in a table.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Normative data permitted adjustments based on age, education, and gender. The control group was "socio-demographically" similar but specific parameters used to define similarity were not indicated. Separate ANCOVA analyses on workers only were stratified by race (citation provided), and adjusted for ethnicity, age, and education. The methods for identifying and including potential confounders in the analytic approach was not described.
	Metric 10:	Covariate Characterization	Low	No description of the covariate collection method was provided. It was not clear whether the method used was valid or not.
	Metric 11:	Co-exposure Counfounding	Low	A number of workers (18%) reported current exposure to chemicals in their work environment. These potential co-exposures were not were not appropriately adjusted for in the analytical approach used.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Low	The study design was appropriate to evaluate the neurophysiological status of 1,2-DCE-exposed workers; however, statistical methods were not comprehensive.
	Metric 13:	Statistical Power	Medium	The report indicates "significant impairments" were observed on various neurophysiological tests using t-tests, and significant exposure relationships were reported based on test scores and specific exposure variables (used as surrogates of exposure). Therefore, the number of participants was sufficient to detect an effect.
	Metric 14:	Reproducibility of Analyses	Low	Tests were scored according to relevant manuals; the calculation of z-scores, used in all impairment comparisons and analyses of exposure relationships, was not explained in adequate detail. The methods used to determine relationships between specific exposure variables and test scores (i.e., ANCOVA analyses) were not fully described.
	Metric 15:	Statistical Analysis	Low	Description of the ANCOVA analysis was largely not present. It is not clear whether model assumptions were met.

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Study Citation:	Bowler, R.M., Gysens, S., Hartney, C. (2003). Neuropsychological effects of ethylene dichloride exposure. NeuroToxicology 24(4-5):553-562.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Wechsler Adult Intelligence Scale III (WAIS-III), Wechsler Memory Scale III (WMS-III), Boston Naming Test (BNT), Trail Making Test (TMT), Stroop Color-Word Test, Grooved Pegboard, Dynamometer, Wide Range Achievement Test (WRAT), Finger tapping, Beck Anxiety Index, Beck Depression Index, Symptom Checklist-90 (SCL-90).
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	200241

Domain	Metric	Rating	Comments
Additional Comments:	The study evaluated the neurobehavioral status of a group of workers with known exposure to 1,2-DCE at a clean-up site. Impairments related to processing speed, attention, cognitive flexibility, motor coordination and speed, verbal memory/fluency, vision and visual-spatial abilities, and mood were reported in exposed workers. Serious and consequential flaws are associated with the study including methods of participant selection and retention, and exposure characterization among others.		

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Brender, J.D., Shinde, M.U., Zhan, F.B., Gong, X., Langlois, P.H. (2014). Maternal residential proximity to chlorinated solvent emissions and birth defects in offspring: A case-control study. Environmental Health: A Global Access Science Source 13(1):96.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	birth defects (neural tube defects, limbs deficiencies, oral cleft defects, heart defects, spina bifida, anencephaly)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	2799700

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Participants were drawn from the Texas Birth Defects Registry (TBDR) for years 1996-2008. Controls were frequency matched from the same registry. Study authors state that neural tube cases were more likely to not be successfully geocoded which may introduce selection bias, however, the authors note that both cases and controls with addresses that could not be geocoded were similar. In spite of that, the inclusion criteria, methods of participant selection, and frequency match were reported.
	Metric 2:	Attrition	Medium	13.3% case mother addresses and 12.8% control mother addresses were unable to be geocoded, however this most likely only lowered the precision of the study and most likely does not vary based on exposure level.
	Metric 3:	Comparison Group	Medium	Controls were matched to cases and pulled from the same eligible population by year of delivery and public health service region. Other demographic factors, e.g., race was not matched in population selection. However, statistical analyses were adjusted for year of delivery, maternal age, race/ethnicity, education, and public health region of residence.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Used Emission Weighted Proximity Model to estimate exposure at a given address based on proximity to emission sources and the specific amount or type of pollutant emitted. There may be some exposure misclassification due to mothers moving away from geocoded addresses. Previous studies indicate ~67% of mothers do not move between conception and delivery.
	Metric 5:	Exposure Levels	Medium	Reports exposure as ”exposure risk value” and groups the risk values into quartiles, with exposure risk values < 0 being the referent group
	Metric 6:	Temporality	Medium	The study authors estimated exposure based on residence during pregnancy and evaluated birth outcomes. Temporality is established. Previous studies indicate ~67% mothers don’t move between trimester and delivery. For mothers who moved during the pregnancy, the temporality is unknown.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Outcomes determined by Texas Birth Defect Registry, checking for birth defect diagnosis. Birth certificates came from Center for Health Statistics at Texas Department of State Health Services
	Metric 8:	Reporting Bias	High	Outcome data measured and reported clearly, stratified by specific type of birth defect
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Brender, J.D., Shinde, M.U., Zhan, F.B., Gong, X., Langlois, P.H. (2014). Maternal residential proximity to chlorinated solvent emissions and birth defects in offspring: A case-control study. Environmental Health: A Global Access Science Source 13(1):96.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	birth defects (neural tube defects, limbs deficiencies, oral cleft defects, heart defects, spina bifida, anencephaly)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	2799700

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	High	Cases were frequency matched by year of delivery and public health service region. Final models were adjusted for year of delivery, public health region, maternal age (<20, 20-24, 25-29, 30-34, 35-39, >39 years), education (<12 years, 12 years, >12 years), and race/ethnicity (Whit non-Hispanic, Black non-Hispanic, Hispanic, other non-Hispanic).
	Metric 10:	Covariate Characterization	High	Used birth and death certificates for demographic information
	Metric 11:	Co-exposure Counfounding	Medium	other co-exposures were not described
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	study used logistic regression to measure association between exposure and birth defects
	Metric 13:	Statistical Power	Medium	Overall adequate number of cases and controls - some effects have low cell counts, but at least one health effect has sufficient statistical power.
	Metric 14:	Reproducibility of Analyses	Medium	Methods sufficiently detailed for reproducibility
	Metric 15:	Statistical Analysis	High	No logistic regression model assumption violations were identified.

Additional Comments: This study examined the association between proximity to several point sources of chlorinated solvents and birth defects. Exposure was assessed using EPA's Toxic Release Inventory, and birth defects were assessed using Texas birth registries. The geocoded address of mothers on day of delivery and the amount of solvent was plugged into the Emission Weighted Probability model to assign each mother an exposure risk value. Limitations include limited evidence of temporality. Additionally, elective terminations lacked a vital record, which meant only 69% of mothers with neural tube defects were geocoded. Mothers highly exposed to 1,2-dichloroethane were 1.85 times more likely to have the spina bifida birth defect than mothers who were not significantly exposed.

Overall Quality Determination High

* No biomarkers were identified for this evaluation.

Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Nested case-control design; cases selected from deaths in cohort study was described by Rinsky et al (1988; HERO 597923) (29,139 workers in Union Carbide facilities in West Virginia followed from 1940 to 1978). Vital status complete for 95% of cohort members.
	Metric 2:	Attrition	High	There was minimal exclusion of subjects/missing data, because vital status follow-up was complete for 96% of the 29,139 men in the cohort study.
	Metric 3:	Comparison Group	Medium	Controls were randomly selected in a 5:1 ratio to cases from the total employee cohort such that they were first employed in the same decade and survived to the same five-year survival period as cases. Controls survived at least to the beginning of the five-year interval in which cases died. Controls were independently selected for each of the individual disease subcategories. However, the demographic information between cases and controls were not compared in the paper.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was partially described: (1) Potential employee contact with a specific substance was determined by tracing each employee's work assignments and linking these assignment records to a separate computer file that contained a history of departmental usage for each substance; (2) Potential exposure to each chemical group was assumed on the basis of assignment o a production unit with a history of usage of any member of that chemical group. However, exposure level either based on work assignment in departments such as job exposure matrix or on the chemical levels were not presented.
	Metric 5:	Exposure Levels	Low	The range of exposure is limited. For example, exposure was presented by the duration of work in two categories: <5 years and 5+ years.
	Metric 6:	Temporality	Medium	Temporality is established, but it is unclear whether the exposures fall within the relevant exposure window. Authors used a lag time of 5 years; since controls were selected for 5 yr intervals, the effective lag time ranged from 5-9 years with an average of 7.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Case definition was based on death certificate diagnosis; but no method validation was conducted against this well-established methods.
	Metric 8:	Reporting Bias	Medium	All outcomes reported, but ORs for many analyses presented without CIs (some CIs reported in text).
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Low	There is indirect evidence that considerations were not made for potential confounders (ORs not adjusted, controls not age- or race-matched). Even though authors note that "Age-adjusted stratified analyses, which were also conducted, did not materially modify the odds ratio estimates". Also stratified examination of odds ratios were conducted to assess duration of exposure effects. However, other key confounders e.g., smoking status and race were not accounted for.
	Metric 10:	Covariate Characterization	Medium	The only potential confounder considered was age; this was presumably evaluated based on employment records (no discussion presented). Age-adjusted stratified analyses were conducted.
	Metric 11:	Co-exposure Counfounding	Low	Co-exposures were present and were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Nested case-control study design is appropriate for research question. Initial data analysis included crude odds ratio and then stratified examination of odds ratios was conducted to ass duration of exposure effect. Also, age-adjusted stratified analysis was conducted.
	Metric 13:	Statistical Power	Low	Statistical power calculations were not reported. Case numbers for each disease were low. The number of subjects was not sufficient to detect an effect of 1,2-dichloroethylene exposure.
	Metric 14:	Reproducibility of Analyses	Medium	Description was sufficient to be conceptually reproducible.
	Metric 15:	Statistical Analysis	Low	Statistical model to calculate odds ratio was not described.

Additional Comments: This nested case-control study within a cohort study is a good study design to answer the research question regarding the association between multiple chemical exposures and four cancer sites. Cases and controls are selected appropriate. However, there are several limitations in this study: (1) confounders were not all considered and adjusted for, except that age-adjusted odds ratios were conducted; (2) it is not described if co-exposures were adjusted for; (3) numbers of cancer cases for each cancer type were small, so the statistical power is limited; (4) statistical models for calculating odds ratios were not described.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Nested case-control design; cases selected from deaths in cohort study was described by Rinsky et al (1988; HERO 597923) (29,139 workers in Union Carbide facilities in West Virginia followed from 1940 to 1978). Vital status complete for 95% of cohort members.
	Metric 2:	Attrition	High	There was minimal exclusion of subjects/missing data, because vital status follow-up was complete for 96% of the 29,139 men in the cohort study.
	Metric 3:	Comparison Group	Medium	Controls were randomly selected in a 5:1 ratio to cases from the total employee cohort such that they were first employed in the same decade and survived to the same five-year survival period as cases. Controls survived at least to the beginning of the five-year interval in which cases died. Controls were independently selected for each of the individual disease subcategories. However, the demographic information between cases and controls were not compared in the paper.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was partially described: (1) Potential employee contact with a specific substance was determined by tracing each employee's work assignments and linking these assignment records to a separate computer file that contained a history of departmental usage for each substance; (2) Potential exposure to each chemical group was assumed on the basis of assignment o a production unit with a history of usage of any member of that chemical group. However, exposure level either based on work assignment in departments such as job exposure matrix or on the chemical levels were not presented.
	Metric 5:	Exposure Levels	Low	The range of exposure is limited. For example, exposure was presented by the duration of work in two categories: <5 years and 5+ years.
	Metric 6:	Temporality	Medium	Temporality is established, but it is unclear whether the exposures fall within the relevant exposure window. Authors used a lag time of 5 years; since controls were selected for 5 yr intervals, the effective lag time ranged from 5-9 years with an average of 7.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Case definition was based on death certificate diagnosis; but no method validation was conducted against this well-established methods.
	Metric 8:	Reporting Bias	Medium	All outcomes reported, but ORs for many analyses presented without CIs (some CIs reported in text).
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Low	There is indirect evidence that considerations were not made for potential confounders (ORs not adjusted, controls not age- or race-matched). Even though authors note that "Age-adjusted stratified analyses, which were also conducted, did not materially modify the odds ratio estimates". Also stratified examination of odds ratios were conducted to assess duration of exposure effects. However, other key confounders e.g., smoking status and race were not accounted for.
	Metric 10:	Covariate Characterization	Medium	The only potential confounder considered was age; this was presumably evaluated based on employment records (no discussion presented). Age-adjusted stratified analyses were conducted.
	Metric 11:	Co-exposure Counfounding	Low	Co-exposures were present and were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Nested case-control study design is appropriate for research question. Initial data analysis included crude odds ratio and then stratified examination of odds ratios was conducted to ass duration of exposure effect. Also, age-adjusted stratified analysis was conducted.
	Metric 13:	Statistical Power	Low	Statistical power calculations were not reported. Case numbers for each disease were low. The number of subjects was not sufficient to detect an effect of 1,2-dichloroethylene exposure.
	Metric 14:	Reproducibility of Analyses	Medium	Description was sufficient to be conceptually reproducible.
	Metric 15:	Statistical Analysis	Low	Statistical model to calculate odds ratio was not described.

Additional Comments: This nested case-control study within a cohort study is a good study design to answer the research question regarding the association between multiple chemical exposures and four cancer sites. Cases and controls are selected appropriate. However, there are several limitations in this study: (1) confounders were not all considered and adjusted for, except that age-adjusted odds ratios were conducted; (2) it is not described if co-exposures were adjusted for; (3) numbers of cancer cases for each cancer type were small, so the statistical power is limited; (4) statistical models for calculating odds ratios were not described.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
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Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Nested case-control design; cases selected from deaths in cohort study was described by Rinsky et al (1988; HERO 597923) (29,139 workers in Union Carbide facilities in West Virginia followed from 1940 to 1978). Vital status complete for 95% of cohort members.
	Metric 2:	Attrition	High	There was minimal exclusion of subjects/missing data, because vital status follow-up was complete for 96% of the 29,139 men in the cohort study.
	Metric 3:	Comparison Group	Medium	Controls were randomly selected in a 5:1 ratio to cases from the total employee cohort such that they were first employed in the same decade and survived to the same five-year survival period as cases. Controls survived at least to the beginning of the five-year interval in which cases died. Controls were independently selected for each of the individual disease subcategories. However, the demographic information between cases and controls were not compared in the paper.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was partially described: (1) Potential employee contact with a specific substance was determined by tracing each employee's work assignments and linking these assignment records to a separate computer file that contained a history of departmental usage for each substance; (2) Potential exposure to each chemical group was assumed on the basis of assignment o a production unit with a history of usage of any member of that chemical group. However, exposure level either based on work assignment in departments such as job exposure matrix or on the chemical levels were not presented.
	Metric 5:	Exposure Levels	Low	The range of exposure is limited. For example, exposure was presented by the duration of work in two categories: <5 years and 5+ years.
	Metric 6:	Temporality	Medium	Temporality is established, but it is unclear whether the exposures fall within the relevant exposure window. Authors used a lag time of 5 years; since controls were selected for 5 yr intervals, the effective lag time ranged from 5-9 years with an average of 7.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Case definition was based on death certificate diagnosis; but no method validation was conducted against this well-established methods.
	Metric 8:	Reporting Bias	Medium	All outcomes reported, but ORs for many analyses presented without CIs (some CIs reported in text).
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Low	There is indirect evidence that considerations were not made for potential confounders (ORs not adjusted, controls not age- or race-matched). Even though authors note that "Age-adjusted stratified analyses, which were also conducted, did not materially modify the odds ratio estimates". Also stratified examination of odds ratios were conducted to assess duration of exposure effects. However, other key confounders e.g., smoking status and race were not accounted for.
	Metric 10:	Covariate Characterization	Medium	The only potential confounder considered was age; this was presumably evaluated based on employment records (no discussion presented). Age-adjusted stratified analyses were conducted.
	Metric 11:	Co-exposure Counfounding	Low	Co-exposures were present and were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Nested case-control study design is appropriate for research question. Initial data analysis included crude odds ratio and then stratified examination of odds ratios was conducted to ass duration of exposure effect. Also, age-adjusted stratified analysis was conducted.
	Metric 13:	Statistical Power	Low	Statistical power calculations were not reported. Case numbers for each disease were low. The number of subjects was not sufficient to detect an effect of 1,2-dichloroethylene exposure.
	Metric 14:	Reproducibility of Analyses	Medium	Description was sufficient to be conceptually reproducible.
	Metric 15:	Statistical Analysis	Low	Statistical model to calculate odds ratio was not described.

Additional Comments: This nested case-control study within a cohort study is a good study design to answer the research question regarding the association between multiple chemical exposures and four cancer sites. Cases and controls are selected appropriate. However, there are several limitations in this study: (1) confounders were not all considered and adjusted for, except that age-adjusted odds ratios were conducted; (2) it is not described if co-exposures were adjusted for; (3) numbers of cancer cases for each cancer type were small, so the statistical power is limited; (4) statistical models for calculating odds ratios were not described.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Nested case-control design; cases selected from deaths in cohort study was described by Rinsky et al (1988; HERO 597923) (29,139 workers in Union Carbide facilities in West Virginia followed from 1940 to 1978). Vital status complete for 95% of cohort members.
	Metric 2:	Attrition	High	There was minimal exclusion of subjects/missing data, because vital status follow-up was complete for 96% of the 29,139 men in the cohort study.
	Metric 3:	Comparison Group	Medium	Controls were randomly selected in a 5:1 ratio to cases from the total employee cohort such that they were first employed in the same decade and survived to the same five-year survival period as cases. Controls survived at least to the beginning of the five-year interval in which cases died. Controls were independently selected for each of the individual disease subcategories. However, the demographic information between cases and controls were not compared in the paper.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was partially described: (1) Potential employee contact with a specific substance was determined by tracing each employee's work assignments and linking these assignment records to a separate computer file that contained a history of departmental usage for each substance; (2) Potential exposure to each chemical group was assumed on the basis of assignment o a production unit with a history of usage of any member of that chemical group. However, exposure level either based on work assignment in departments such as job exposure matrix or on the chemical levels were not presented.
	Metric 5:	Exposure Levels	Low	The range of exposure is limited. For example, exposure was presented by the duration of work in two categories: <5 years and 5+ years.
	Metric 6:	Temporality	Medium	Temporality is established, but it is unclear whether the exposures fall within the relevant exposure window. Authors used a lag time of 5 years; since controls were selected for 5 yr intervals, the effective lag time ranged from 5-9 years with an average of 7.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Case definition was based on death certificate diagnosis; but no method validation was conducted against this well-established methods.
	Metric 8:	Reporting Bias	Medium	All outcomes reported, but ORs for many analyses presented without CIs (some CIs reported in text).
Domain 4: Potential Confounding / Variability Control				

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Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Low	There is indirect evidence that considerations were not made for potential confounders (ORs not adjusted, controls not age- or race-matched). Even though authors note that "Age-adjusted stratified analyses, which were also conducted, did not materially modify the odds ratio estimates". Also stratified examination of odds ratios were conducted to assess duration of exposure effects. However, other key confounders e.g., smoking status and race were not accounted for.
	Metric 10:	Covariate Characterization	Medium	The only potential confounder considered was age; this was presumably evaluated based on employment records (no discussion presented). Age-adjusted stratified analyses were conducted.
	Metric 11:	Co-exposure Counfounding	Low	Co-exposures were present and were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Nested case-control study design is appropriate for research question. Initial data analysis included crude odds ratio and then stratified examination of odds ratios was conducted to ass duration of exposure effect. Also, age-adjusted stratified analysis was conducted.
	Metric 13:	Statistical Power	Low	Statistical power calculations were not reported. Case numbers for each disease were low. The number of subjects was not sufficient to detect an effect of 1,2-dichloroethylene exposure.
	Metric 14:	Reproducibility of Analyses	Medium	Description was sufficient to be conceptually reproducible.
	Metric 15:	Statistical Analysis	Low	Statistical model to calculate odds ratio was not described.

Additional Comments: This nested case-control study within a cohort study is a good study design to answer the research question regarding the association between multiple chemical exposures and four cancer sites. Cases and controls are selected appropriate. However, there are several limitations in this study: (1) confounders were not all considered and adjusted for, except that age-adjusted odds ratios were conducted; (2) it is not described if co-exposures were adjusted for; (3) numbers of cancer cases for each cancer type were small, so the statistical power is limited; (4) statistical models for calculating odds ratios were not described.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Cheng, T.J., Huang, M.L., You, N.C., Du, C.L., Chau, T.T. (1999). Abnormal liver function in workers exposed to low levels of ethylene dichloride and vinyl chloride monomer. Journal of Occupational and Environmental Medicine 41(12):1128-1133.
Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	AST, ALT, GGT, Hepatitis B virus surface antigen (HBsAg), and anti-hepatitis C virus antibody (anti-HCV).
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	200266

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	A total of 251 male workers were included from 4 vinyl chloride monomer manufacturing plants. Other details on recruitment strategy, eligibility criteria, year of enrollment, and participation rates were not provided.
	Metric 2:	Attrition	Low	There was no indication of attrition and details on the number of eligible participants throughout the study was limited. Attrition could not be adequately assessed due to a lack of information regarding recruitment and selection.
	Metric 3:	Comparison Group	Medium	The low-EDC-low-VCM group (187 participants) was used as the comparison group, and there is indirect evidence groups are similar. Limited details were provided for setting, inclusion and exclusion criteria, and methods of participant selection.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	NIOSH recommended methods 1003 and 1007 were used for personal and area sampling, respectively. Air samples were collected, stored at 4 deg. C, and analyzed within 2 weeks of the sampling event. However, historical job changes, changes in exposure levels over time, and timing (year or days during work week) or duration of area or personal sampling were not reported.
	Metric 5:	Exposure Levels	Medium	EDC and VCM levels were reported for the different categories of jobs, which were classified into low-EDC-low-VCM, mod-EDC-low-VCM, and low-EDC-mod-VCM groups.
	Metric 6:	Temporality	High	The age of participants (mean age 33.7-40.1 years) and employment duration (mean 7.5-14.3 years) were reported, and the temporality between the exposure and outcome appears to be appropriate.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	AST, ALT, and GGT "were analyzed with a Hitachi 7050 autoanalyzer". A basis for the cutoff values used in Table 4 to determine "abnormal" AST, ALT, and GGT levels was not provided.
	Metric 8:	Reporting Bias	High	Odds ratios for abnormal liver function were provided with 95% confidence intervals, the number per exposure level, and significance when applicable.
Domain 4: Potential Confounding / Variability Control				

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Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	AST, ALT, GGT, Hepatitis B virus surface antigen (HBsAg), and anti-hepatitis C virus antibody (anti-HCV).
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	200266

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Medium	The study reports information on potential confounders (age, hepatitis, BMI, alcohol use, and employment duration), and controls for hepatitis, BMI and alcohol consumption in the multiple logistic regression analyses. There is indirect evidence that appropriate adjustments were made.
	Metric 10:	Covariate Characterization	Medium	An interviewer administered the questionnaires to collect information about potential confounders and occupational history.
	Metric 11:	Co-exposure Counfounding	Low	Exposure to ethylene dichloride was evaluated in a vinyl chloride monomer (VCM) manufacturing facility, and VCM was also subsequently analyzed using personal and area sampling. Results for VCM exposure concentrations were provided. VCM is also suspected to cause liver damage.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design (cohort) was appropriate to assess the outcome of interest (”markers of liver damage”). Chi-squared (X2) test and multiple logistic regression were used for statistical analyses.
	Metric 13:	Statistical Power	Medium	The number of participants was adequate to detect an effect in the exposed populations, although power calculations were not provided. There were >20 participants in each group.
	Metric 14:	Reproducibility of Analyses	Low	A description of the logistic regression analysis was provided, however, study authors do not provide information on categorization of abnormal liver function.
	Metric 15:	Statistical Analysis	High	There were no identifiable logistic regression model assumption violations.
Domain 6: Other (if applicable) Considerations for Biomarker Selection and Measurement (Lakind et al. 2014)				
	Metric 16:	Use of Biomarker of Exposure	N/A	Biomarker of exposures were not assessed.
	Metric 17:	Effect Biomarker	High	This study uses aspartate aminotransferase, alanine aminotransferase, and y-glutamyltransferase as biomarkers of effect. While these no works cited to explain their connection to liver function, all three are well-known marker of liver function. Similarly, Hepatitis B virus surface antigen and antihepatitis C virus anitbody are also well-known measures of liver function and health.
	Metric 18:	Method Sensitivity	Low	No limit of detection information is provided for any of the effect biomarkers.
	Metric 19:	Biomarker Stability	Medium	While the study does not provide a lot of information regarding biomarker storage or stability, the authors do mention that venous blood used to detect biomarkers was stored at 4 degrees C.
	Metric 20:	Sample Contamination	Medium	No specific information regarding potential sample contamination was provided.
	Metric 21:	Method Requirements	Medium	Aspartate aminotransferase, alanine aminotransferase, and y-glutamyltransferase were analyzed using a Hitachi 7050 autoanalyzer. Hepatitis B virus surface antibody and antihepatitis C virus antibody were assessed with radioimmunoassay and enzyme-linked immunosorbent assay.

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Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	AST, ALT, GGT, Hepatitis B virus surface antigen (HBsAg), and anti-hepatitis C virus antibody (anti-HCV).
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	200266

Domain	Metric	Rating	Comments
	Metric 22: Matrix Adjustment	N/A	No information on matrix adjustment was provided/available.

Additional Comments: A group of 251 male workers from 4 vinyl chloride monomer (VCM) manufacturing plants were included in this assessment to examine if occupational exposure to VCM and ethylene dichloride (EDC) "resulted in increased risk of liver damage" by examining AST, ALT, and GGT levels in the blood. Increased ORs for abnormal AST (>37 IU/L) and ALT (>41 IU/L) in the mod-EDC-low-VCM group (0.17-333.7 ppm EDC, 0.18-0.34 ppm VCM), compared with the low-EDC-low-VCM group, was reported. Exposure levels were measured using area and personal sampling, but the timing and duration of the sampling events were not reported.

Overall Quality Determination Medium

Study Citation:	Dosemeci, M., Cocco, P., Chow, W.H. (1999). Gender differences in risk of renal cell carcinoma and occupational exposures to chlorinated aliphatic hydrocarbons. American Journal of Industrial Medicine 36(1):54-59.
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	renal cell carcinoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	4697224

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	The details of the study design were reported elsewhere (Chow et al. 1994, HERO ID 701514). Brief details about the setting, date, number of eligible participants, and control matching were reported. Reasons for exclusions/non-participation were described with details by Chow et al. (1994).
	Metric 2:	Attrition	High	For the details of the study design and attrition of study subjects, the study authors referred to another publication by Chow et al., 1994. Chow et al. (1994) mentioned that at the end of the personal interview, the respondents were given a self-administered food-frequency questionnaire. Of the subjects interviewed for the study, 632 patients (79% of 796 eligible patients) and 653 control subjects (79% of 707 eligible control subjects) returned the diet questionnaire. A number of subjects, whose responses were considered unreliable, were excluded from the analysis, including 48 patients and three control subjects who had seven or more skipped food items or had questionable data and 50 patients whose next-of-kin respondent was not a spouse. Also excluded were two patients with unknown smoking status, since smoking is a risk factor.
	Metric 3:	Comparison Group	Medium	The cases were pulled from the Minnesota Cancer Surveillance System. Controls were selected from the general population of Minnesota; controls age 20-64 years were selected through random digital dialing and controls age 65-85 years were collected from files through the Health Care Financing Administration. Controls were age- and gender-stratified and were of the same race. Characteristics of cases and controls were not provided in the text or a table.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	High	Occupational histories including the most recent and usual occupation and industry, job activities, started-year and ended-year, and part-time/full-time status were collected. Occupations and industries were coded according to the standard occupational classification (SOC) and standard industrial classification (SIC) schemes. The National Cancer Institute developed job exposure matrices (JEM) for nine individual chlorinated aliphatic hydrocarbons (CAHCs), all CAHCs-combined, and all organic solvents-combined. These JEMs were merged with assigned SOC and SIC to determine the exposure status to these chemicals for each study subject. Application of the JEM was described elsewhere (Dosemeci et al. 1994, HERO ID 632334; Gomez et al. 1994, HERO ID 702154).
	Metric 5:	Exposure Levels	Medium	Details of the application of the JEM were described elsewhere (Dosemeci et al. 1994, HERO ID 632334; Gomez et al. 1994, HERO ID 702154). Dosemeci et al. (1994) described more details about that this study assigned three levels of probability (low, medium, high) to industries and occupations for chemical exposure levels.

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Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	renal cell carcinoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	4697224

Domain	Metric		Rating	Comments
	Metric 6:	Temporality	Medium	Occupational questionnaires identified prior exposures based on reported recent and usual occupations as well as duration of employment. Outcome status was determined from registry data. The authors note that some occupational history was incomplete which may result in some uncertainty in regard to temporality.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Cases were identified as newly diagnosed and histologically confirmed renal cell carcinoma through the Minnesota Cancer Surveillance System and information about each participant was collected using a questionnaire. Validation was not specified.
	Metric 8:	Reporting Bias	Medium	A description of measured outcomes is reported and ORs were stratified by sex. Effect estimates are reported with a confidence interval. One table showed the total numbers of men and women respectively for each chemical, but numbers of cases/controls were not reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Appropriate adjustments were made in the final analysis, including age, gender, smoking, hypertension and the use of diuretics and/or anti-hypertension drugs, and BMI. Results were stratified by sex.
	Metric 10:	Covariate Characterization	Medium	Information about participants was collected using a questionnaire, and it includes potential confounders, e.g., smoking habits. Validation was not specified.
	Metric 11:	Co-exposure Counfounding	Medium	Co-exposures were identified through the job exposure matrices. Chemicals were evaluated individually and as a group.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen (case-control) was appropriate for the research question (renal cell carcinoma risk from occupational organic solvent exposure). Logistic regression models were used to estimate the relative risk and 95% CI.
	Metric 13:	Statistical Power	Low	Statistical power calculations were not provided. No significant effects were observed with 1,2-dichloroethane. The number of participated women to calculate odds ratio was inadequate to detect an effect in the participants for other chemicals or the combined risk, because it was very low.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis was brief, but is sufficient to understand precisely what has been done and to be conceptually reproducible with access to the analytic data.
	Metric 15:	Statistical Analysis	High	Model assumptions for logistic regression were met. The odds ratios were adjusted for age, smoking, hypertension status and/or use of diuretic and/or anti-hypertension drugs, and body mass index for men and women separately.

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Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	renal cell carcinoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	4697224

Domain	Metric	Rating	Comments
Additional Comments:	A group of 438 cases (273 men and 165 women) were selected from the Minnesota Cancer Surveillance System that had been newly diagnosed with renal cell carcinoma. Controls included 687 participants (462 men and 225 women) age- and gender- stratified that were selected from either the general population of Minnesota (age 20-64 years) or from the Health Care Financing Administration files (age 65-85). No significant increase in the risk of renal cell carcinoma was observed with exposure to 1,2-dichloroethane among men or women separately, or for all participants exposed.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Dosemeci, M., Cocco, P., Chow, W.H. (1999). Gender differences in risk of renal cell carcinoma and occupational exposures to chlorinated aliphatic hydrocarbons. American Journal of Industrial Medicine 36(1):54-59.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	renal cell carcinoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	4697224

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	The details of the study design were reported elsewhere (Chow et al. 1994, HERO ID 701514). Brief details about the setting, date, number of eligible participants, and control matching were reported. Reasons for exclusions/non-participation were described with details by Chow et al. (1994).
	Metric 2:	Attrition	Medium	For the details of the study design and attrition of study subjects, the study authors referred to another publication by Chow et al., 1994. Chow et al. (1994) mentioned that at the end of the personal interview, the respondents were given a self-administered food-frequency questionnaire. Of the subjects interviewed for the study, 632 patients (79% of 796 eligible patients) and 653 control subjects (79% of 707 eligible control subjects) returned the diet questionnaire. A number of subjects, whose responses were considered unreliable, were excluded from the analysis, including 48 patients and three control subjects who had seven or more skipped food items or had questionable data and 50 patients whose next-of-kin respondent was not a spouse. Also excluded were two patients with unknown smoking status, since smoking is a risk factor.
	Metric 3:	Comparison Group	Medium	The cases were pulled from the Minnesota Cancer Surveillance System. Controls were selected from the general population of Minnesota; controls age 20-64 years were selected through random digital dialing and controls age 65-85 years were collected from files through the Health Care Financing Administration. Controls were age- and gender-stratified and were of the same race. Characteristics of cases and controls were not provided in the text or a table.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	High	Occupational histories including the most recent and usual occupation and industry, job activities, started-year and ended-year, and part-time/full-time status were collected. Occupations and industries were coded according to the standard occupational classification (SOC) and standard industrial classification (SIC) schemes. The National Cancer Institute developed job exposure matrices (JEM) for nine individual chlorinated aliphatic hydrocarbons (CAHCs), all CAHCs-combined, and all organic solvents-combined. These JEMs were merged with assigned SOC and SIC to determine the exposure status to these chemicals for each study subject. Application of the JEM was described elsewhere (Dosemeci et al. 1994, HERO ID 632334; Gomez et al. 1994, HERO ID 702154).
	Metric 5:	Exposure Levels	Medium	Details of the application of the JEM were described elsewhere (Dosemeci et al. 1994, HERO ID 632334; Gomez et al. 1994, HERO ID 702154). Dosemeci et al. (1994) described more details about that this study assigned three levels of probability (low, medium, high) to industries and occupations for chemical exposure levels.

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Study Citation:	Dosemeci, M., Cocco, P., Chow, W.H. (1999). Gender differences in risk of renal cell carcinoma and occupational exposures to chlorinated aliphatic hydrocarbons. American Journal of Industrial Medicine 36(1):54-59.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	renal cell carcinoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	4697224

Domain	Metric		Rating	Comments
	Metric 6:	Temporality	Medium	Occupational questionnaires identified prior exposures based on reported recent and usual occupations as well as duration of employment. Outcome status was determined from registry data. The authors note that some occupational history was incomplete which may result in some uncertainty in regard to temporality.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Cases were identified as newly diagnosed and histologically confirmed renal cell carcinoma through the Minnesota Cancer Surveillance System and information about each participant was collected using a questionnaire. Validation was not specified.
	Metric 8:	Reporting Bias	Medium	A description of measured outcomes is reported and ORs were stratified by sex. Effect estimates are reported with a confidence interval. One table showed the total numbers of men and women respectively for each chemical, but numbers of cases/controls were not reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Appropriate adjustments were made in the final analysis, including age, gender, smoking, hypertension and the use of diuretics and/or anti-hypertension drugs, and BMI. Results were stratified by sex.
	Metric 10:	Covariate Characterization	Medium	Information about participants was collected using a questionnaire, and it includes potential confounders, e.g., smoking habits. Validation was not specified.
	Metric 11:	Co-exposure Counfounding	Medium	Co-exposures were identified through the job exposure matrices. Chemicals were evaluated individually and as a group.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen (case-control) was appropriate for the research question (renal cell carcinoma risk from occupational organic solvent exposure). Logistic regression models were used to estimate the relative risk and 95% CI.
	Metric 13:	Statistical Power	Low	Statistical power calculations were not provided. No significant effects were observed with 1,2-dichloroethane. The number of participated women to calculate odds ratio was inadequate to detect an effect in the participants for other chemicals or the combined risk, because it was very low.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis was brief, but is sufficient to understand precisely what has been done and to be conceptually reproducible with access to the analytic data.
	Metric 15:	Statistical Analysis	High	Model assumptions for logistic regression were met. The odds ratios were adjusted for age, smoking, hypertension status and/or use of diuretic and/or anti-hypertension drugs, and body mass index for men and women separately.

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Study Citation:	Dosemeci, M., Cocco, P., Chow, W.H. (1999). Gender differences in risk of renal cell carcinoma and occupational exposures to chlorinated aliphatic hydrocarbons. American Journal of Industrial Medicine 36(1):54-59.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	renal cell carcinoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	4697224

Domain	Metric	Rating	Comments
Additional Comments:	A group of 438 cases (273 men and 165 women) were selected from the Minnesota Cancer Surveillance System that had been newly diagnosed with renal cell carcinoma. Controls included 687 participants (462 men and 225 women) age- and gender- stratified that were selected from either the general population of Minnesota (age 20-64 years) or from the Health Care Financing Administration files (age 65-85). No significant increase in the risk of renal cell carcinoma was observed with exposure to 1,2-dichloroethane among men or women separately, or for all participants exposed.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Garcia, E., Hurley, S., Nelson, D.O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health: A Global Access Science Source 14(1):14.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	breast cancer in females
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	3014082

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	A total of 112,378 women were included in this study out of 133,479 eligible female participants from the California Teacher Study cohort. A full description of the cohort is provided in Bernstein et al. 2002 (HERO ID 808446). Reasons for exclusion were provided. The reported information indicates that participant selection in or out of the study and participation was not likely to be biased.
	Metric 2:	Attrition	High	112,378/133,479 participants were included in the study. Exclusions were for the purpose of the study and analysis. Exclusion criteria were documented. Included participants had completed questionnaires. The California Cancer Registry is estimated to be 99% complete.
	Metric 3:	Comparison Group	Medium	There is only indirect evidence that groups are similar. Participants were recruited from the same eligible population with the same method of ascertainment. Comparisons were provided for participants with and without breast cancer. Characteristics between these two groups were generally similar. 5 Quintiles of exposure were used, and Q2-5 were compared with Q1.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	High	The Assessment System for Population Exposure Nationwide and the Human Exposure Model are used as part of the National-Scale Air Toxics Assessment produced by the EPA and was used to estimate ambient HAP concentrations for geographic locations. Methods are described online through the US EPA Assessment Methods.
	Metric 5:	Exposure Levels	Medium	The distribution of the NATA annual ambient concentration for each compound was plotted in Figure 1 using a box plot, and 5 Quintiles were used in the analyses.
	Metric 6:	Temporality	Medium	The follow-up period was from 1995-2011, and the NATA estimates were made in 2002 because it was approximately half way between the start and end of the follow-up period. However, it is unclear whether exposures fall within relevant exposure windows for the outcome of interest.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Annual linkage between the CTS cohort and the California Cancer Registry (CCR) was used to identify cases of invasive breast cancer. The CCR is estimated to be 99% complete. The case of invasive breast cancer was defined by ICD codes.

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Study Citation:	Garcia, E., Hurley, S., Nelson, D.O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health: A Global Access Science Source 14(1):14.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	breast cancer in females
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	3014082

Domain	Metric		Rating	Comments
	Metric 8:	Reporting Bias	Medium	A description of measured outcome is reported for adjustments by age and race, and effect estimates are reported with a 95% confidence interval. The measured outcomes using multiple comparisons were generally described in the text, but non-significant results were excluded from Table 3.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	The models were stratified by age and race. Additionally, adjustments were made for multiple comparisons among subsets of the participants (significant results reported in Table 3). Socioeconomic status (SES) of each participant was not evaluated, however, cohort SES characteristics were thought to be similar by study authors.
	Metric 10:	Covariate Characterization	Medium	Information about baseline characteristics for each participant was collected through a questionnaire. It is unknown if the questionnaire was validated.
	Metric 11:	Co-exposure Counfounding	Medium	A total of 37 compounds were identified as mammary gland carcinogens, but 13 were not included in this analysis. Thirteen compounds were excluded from the analysis due to insufficient variability (nine because they had the same value for all census tracts in the state of California; and four because they had less than 25% non-zero values). Ethylene dichloride (1,2-dichloroethane) was among the 24 compounds evaluated in this assessment, and evaluations for breast cancer were conducted for each of these 24 individual compounds.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen (prospective cohort) was appropriate for the research question (incidence of breast cancer). Cox proportional hazard models and SAS 9.3 were used in this assessment. Data analysis was described.
	Metric 13:	Statistical Power	Medium	Statistical power calculations were not provided. No significant effects were observed with ethylene dichloride (1,2-dichloroethane), however, this study utilized a large cohort, approximately 112,000 individuals. Distributions of chemicals of interest suggest there were sufficient numbers of participants in exposure subgroups.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to understand precisely what has been done and to be conceptually reproducible with access to the analytic data.
	Metric 15:	Statistical Analysis	High	The statistical models that were used were identified and described. ”No apparent violation of the underlying assumption of proportional hazards was detected”.

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Study Citation:	Garcia, E., Hurley, S., Nelson, D.O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health: A Global Access Science Source 14(1):14.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	breast cancer in females
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	3014082

Domain	Metric	Rating	Comments
Additional Comments:	A group of 112,378 female participants from the California Teacher Study cohort were assessed for their estimated exposure to ambient air pollutants, including ethylene dichloride (1,2-dichloroethane), and the incidence of invasive breast cancer. Air contaminant concentrations were estimated using the US EPA NATA and the ASPEN and HEM models. The approximate median concentration of 1,2-dichloroethane is between 1E-4 and 1E-2 (estimated from Figure 1). Exposures were categorized into 5 Quintiles, and compared against Quintile 1. No significant increase in the estimated hazard rate ratio for invasive breast cancer was observed with Quintile 2-5 exposure estimates for 1,2-dichloroethane, adjusted for age and race, when compared against Quintile 1, or when further adjusted using multiple comparisons.		

Overall Quality Determination High

* No biomarkers were identified for this evaluation.

Study Citation:	Garcia, E., Hurley, S., Nelson, D.O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health: A Global Access Science Source 14(1):14.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	breast cancer in females
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	3014082

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	A total of 112,378 women were included in this study out of 133,479 eligible female participants from the California Teacher Study cohort. A full description of the cohort is provided in Bernstein et al. 2002 (HERO ID 808446). Reasons for exclusion were provided. The reported information indicates that participant selection in or out of the study and participation was not likely to be biased.
	Metric 2:	Attrition	High	112,378/133,479 participants were included in the study. Exclusions were for the purpose of the study and analysis. Exclusion criteria were documented. Included participants had completed questionnaires. The California Cancer Registry is estimated to be 99% complete.
	Metric 3:	Comparison Group	Medium	There is only indirect evidence that groups are similar. Participants were recruited from the same eligible population with the same method of ascertainment. Comparisons were provided for participants with and without breast cancer. Characteristics between these two groups were generally similar. 5 Quintiles of exposure were used, and Q2-5 were compared with Q1.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	High	The Assessment System for Population Exposure Nationwide and the Human Exposure Model are used as part of the National-Scale Air Toxics Assessment produced by the EPA and was used to estimate ambient HAP concentrations for geographic locations. Methods are described online through the US EPA Assessment Methods.
	Metric 5:	Exposure Levels	Medium	The distribution of the NATA annual ambient concentration for each compound was plotted in Figure 1 using a box plot, and 5 Quintiles were used in the analyses.
	Metric 6:	Temporality	Medium	The follow-up period was from 1995-2011, and the NATA estimates were made in 2002 because it was approximately half way between the start and end of the follow-up period. However, it is unclear whether exposures fall within relevant exposure windows for the outcome of interest.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Annual linkage between the CTS cohort and the California Cancer Registry (CCR) was used to identify cases of invasive breast cancer. The CCR is estimated to be 99% complete. The case of invasive breast cancer was defined by ICD codes.
	Metric 8:	Reporting Bias	Medium	A description of measured outcome is reported for adjustments by age and race, and effect estimates are reported with a 95% confidence interval. The measured outcomes using multiple comparisons were generally described in the text, but non-significant results were excluded from Table 3.

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Study Citation:	Garcia, E., Hurley, S., Nelson, D.O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health: A Global Access Science Source 14(1):14.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	breast cancer in females
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	3014082

Domain	Metric		Rating	Comments
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	The models were stratified by age and race. Additionally, adjustments were made for multiple comparisons among subsets of the participants (significant results reported in Table 3). Socioeconomic status (SES) of each participant was not evaluated, however, cohort SES characteristics were thought to be similar by study authors.
	Metric 10:	Covariate Characterization	Medium	Information about baseline characteristics for each participant was collected through a questionnaire. It is unknown if the questionnaire was validated.
	Metric 11:	Co-exposure Counfounding	Medium	A total of 37 compounds were identified as mammary gland carcinogens, but 13 were not included in this analysis. Thirteen compounds were excluded from the analysis due to insufficient variability (nine because they had the same value for all census tracts in the state of California; and four because they had less than 25% non-zero values). Ethylene dichloride (1,2-dichloroethane) was among the 24 compounds evaluated in this assessment, and evaluations for breast cancer were conducted for each of these 24 individual compounds.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen (prospective cohort) was appropriate for the research question (incidence of breast cancer). Cox proportional hazard models and SAS 9.3 were used in this assessment. Data analysis was described.
	Metric 13:	Statistical Power	Medium	Statistical power calculations were not provided. No significant effects were observed with ethylene dichloride (1,2-dichloroethane), however, this study utilized a large cohort, approximately 112,000 individuals. Distributions of chemicals of interest suggest there were sufficient numbers of participants in exposure subgroups.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to understand precisely what has been done and to be conceptually reproducible with access to the analytic data.
	Metric 15:	Statistical Analysis	High	The statistical models that were used were identified and described. ”No apparent violation of the underlying assumption of proportional hazards was detected”.

Additional Comments: A group of 112,378 female participants from the California Teacher Study cohort were assessed for their estimated exposure to ambient air pollutants, including ethylene dichloride (1,2-dichloroethane), and the incidence of invasive breast cancer. Air contaminant concentrations were estimated using the US EPA NATA and the ASPEN and HEM models. The approximate median concentration of 1,2-dichloroethane is between 1E-4 and 1E-2 (estimated from Figure 1). Exposures were categorized into 5 Quintiles, and compared against Quintile 1. No significant increase in the estimated hazard rate ratio for invasive breast cancer was observed with Quintile 2-5 exposure estimates for 1,2-dichloroethane, adjusted for age and race, when compared against Quintile 1, or when further adjusted using multiple comparisons.

Overall Quality Determination High

* No biomarkers were identified for this evaluation.

Study Citation:	Guo, P., Yokoyama, K., Piao, F., Sakai, K., Khalequzzaman, M., Kamijima, M., Nakajima, T., Kitamura, F. (2013). Sick building syndrome by indoor air pollution in Dalian, China. International Journal of Environmental Research and Public Health 10(4):1489-1504.
Health Outcome(s):	sick building syndrome
Reported Health Effect(s):	The statistical analysis considers all subjective self-reported symptoms together (not segregated by health outcome) as a group health outcome –sick building syndrome. The study compared two conditions for each studied chemical: combined self-reported symptoms to no symptoms. Therefore, only one form 3 was completed.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1938385

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Residents of a housing estate of 3000 homes were invited to a community meeting to explain the purpose of the study and volunteers were invited to participate. It was not reported whether these volunteers were different from the overall eligible population.
	Metric 2:	Attrition	Low	Of the 70 families that agreed to participate, questionnaires were provided by 59. Reasons of uncompleted questionnaires were not fully provided, and there was no comparison between those who participated and those who did not.
	Metric 3:	Comparison Group	Low	The overall description of the analysis sample indicated a wide range of ages and lengths of stay at the current residence. Thus it is hard to know that subjects in all exposure groups were similar. In addition, the methods of selecting participants in all exposure groups were not fully reported. The numbers of male and female smokers were reported, respectively, but the smoking status and age were not controlled in the statistical analysis.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure concentrations for each home were obtained by diffusion sampling over 24 hrs in the bedroom, kitchen, and outdoors; temperature, the vertical height of samplers, and ventilation (hours windows left open) were reported. Samples were analyzed by GC/MS. The number of samples per home is unclear. The frequency of measurements for each house was not reported.
	Metric 5:	Exposure Levels	Low	The frequency of detection was not reported, so it is difficult to ascertain the actual exposure range. In addition, the reported exposure levels were median, geometric mean, and 95% CI, so they are inadequate to develop an exposure-response estimate.
	Metric 6:	Temporality	Uninformative	For 1,2-dichloroethane, the study evaluated self-reported symptoms in the past (”since they moved into their flats”) and their association with sampling conducted during the study; thus, exposure was measured after the outcome.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Low	Participants provided self-reported symptoms using a questionnaire. Study authors cited a previous study, Kamijima et al., 2005 (in Japanese, HERO ID 1598645) for further details on the questionnaire. It was not clear whether the questionnaire was validated.

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Study Citation:	Guo, P., Yokoyama, K., Piao, F., Sakai, K., Khalequzzaman, M., Kamijima, M., Nakajima, T., Kitamura, F. (2013). Sick building syndrome by indoor air pollution in Dalian, China. International Journal of Environmental Research and Public Health 10(4):1489-1504.
Health Outcome(s):	sick building syndrome
Reported Health Effect(s):	The statistical analysis considers all subjective self-reported symptoms together (not segregated by health outcome) as a group health outcome –sick building syndrome. The study compared two conditions for each studied chemical: combined self-reported symptoms to no symptoms. Therefore, only one form 3 was completed.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1938385

Domain	Metric		Rating	Comments
	Metric 8:	Reporting Bias	Low	The study only mentioned subjective symptoms in the abstract or methods. The abstract and method sections did not report the specific symptoms included in the questionnaire or whether the questionnaire was open-ended for symptoms. The questionnaire was cited to Kamijima et al. 2005 (in Japanese).
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	Comparisons were made separately by sex. The distribution of age and time spent living in residence differed greatly between those reporting symptoms and those not reporting symptoms. Smoking was indicated but not controlled for in the analysis. In short, the statistical analysis did not consider these three potential confounders, age, time spent living in residence, and smoking.
	Metric 10:	Covariate Characterization	Low	Covariates were presumably evaluated via a questionnaire that was cited to Kamijima et al. 2005 (in Japanese).
	Metric 11:	Co-exposure Counfounding	Low	The analysis did not account for other exposures. A number of other VOCs, HCHO, and NO2 were measured in the homes. The concentrations of several other VOCs and HCHO were much higher (5-30x) than 1,2-dichloroethane and may also be associated with these symptoms.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Low	The study design is best characterized as cross-sectional. Only one analysis to compare exposure concentrations between those with and without symptoms was adjusted for a confounder, sex, via stratification. Other potential confounders were not adjusted for. Study authors combine responses for symptoms reported before and during the sampling period in one statistical analysis, which may not reflect the relationship between symptoms and contaminants' exposure at each period.
	Metric 13:	Statistical Power	Medium	Statistical power was not reported. The number of participants was sufficient to detect a difference in median concentration between those with and without symptoms.
	Metric 14:	Reproducibility of Analyses	Medium	Study presents sufficient description of analysis (statistical methods) to be conceptually reproducible with access to the raw data.
	Metric 15:	Statistical Analysis	Low	Study uses a Wilcoxon's rank sum test to compare exposure concentrations in persons with and without symptoms; test for equal variance is not reported.

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Study Citation:	Guo, P., Yokoyama, K., Piao, F., Sakai, K., Khalequzzaman, M., Kamijima, M., Nakajima, T., Kitamura, F. (2013). Sick building syndrome by indoor air pollution in Dalian, China. International Journal of Environmental Research and Public Health 10(4):1489-1504.
Health Outcome(s):	sick building syndrome
Reported Health Effect(s):	The statistical analysis considers all subjective self-reported symptoms together (not segregated by health outcome) as a group health outcome –sick building syndrome. The study compared two conditions for each studied chemical: combined self-reported symptoms to no symptoms. Therefore, only one form 3 was completed.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1938385

Domain	Metric	Rating	Comments
Additional Comments:	Concentrations of VOCs (including 1,2-dichloroethane), HCHO, and NO2 were measured in the 59 homes of families that agreed to participate after being informed of the nature of the study. Participants completed questionnaires asking about symptoms since they moved into the homes and the concentrations of selected compounds were compared among men and women reporting any symptoms vs no symptoms. Concentrations of 1,2-dichloroethane in homes of people with symptoms were higher than in homes without. p-Dichlorobenzene was measured in the homes as well, but median concentration was <DL and no further analysis was made. Unacceptable due to selection bias, lack of confounding control, inadequate outcome characterization, and lack of temporality.		

Overall Quality Determination — Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Kernan, G.J., Ji, B.T., Dosemeci, M., Silverman, D.T., Balbus, J., Zahm, S.H. (1999). Occupational risk factors for pancreatic cancer: A case-control study based on death certificates from 24 U.S. states. American Journal of Industrial Medicine 36(2):260-270.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Death from pancreatic cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	194820

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	The National Cancer Institute, National Institute of Occupational Safety and Health, and the National Center for Health Statistics reviewed death certificates from 24 states to select cases from those that had died from pancreatic cancer and matched controls. Controls with cause of death related to the outcome of interest (i.e. pancreatic diseases) were excluded from the study. All key elements of the study design were reported.
	Metric 2:	Attrition	Medium	There was no direct evidence of subject loss or exclusion of subgroups from analyses. The authors provide the total number of cases and controls in the analysis. Case and control data were taken from a registry. It can be assumed that the data are complete for each subject.
	Metric 3:	Comparison Group	High	Controls were selected from the same pool of death certificates from 24 states that cases were selected from. Controls with cause of death related to the outcome of interest were eliminated. Differences in baseline characteristics were controlled for via matching, stratification, and adjustment.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure was assessed via occupation and industry data on death certificates. A job matrix was further applied to assess the likely levels of exposure. Probability and intensity of exposure were estimated across four levels for each occupation. Only employment captured on the death certificate could be considered. The exposure assessment needs exposure information before the job listed on the death certificates.
	Metric 5:	Exposure Levels	Medium	The study offers 4 levels of estimated probability and intensity of exposure (referent, low, medium, high).
	Metric 6:	Temporality	Medium	Exposure was determined by occupational and industry codes on death certificates and indicate that exposure would precede disease, however, the timing and latency period is less clear.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Causes of mortality were determined from death certificates for both cases and controls. Death certificates were drawn from death registries of participating states (n=24). Causes of death were coded using ICD-9 codes, and pancreatic cancer was identified as ICD 157.
	Metric 8:	Reporting Bias	Medium	Measured outcomes, effect estimates and confidence intervals are reported. Number of exposed cases is reported for each analysis, however the number of controls (exposed and unexposed) are not reported for analyses.

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Study Citation:	Kernan, G.J., Ji, B.T., Dosemeci, M., Silverman, D.T., Balbus, J., Zahm, S.H. (1999). Occupational risk factors for pancreatic cancer: A case-control study based on death certificates from 24 U.S. states. American Journal of Industrial Medicine 36(2):260-270.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Death from pancreatic cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	194820

Domain	Metric		Rating	Comments
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Potential confounders were accounted for in the following ways: matching (five year age group, state, race, and gender); adjustment in models (age, marital status, metropolitan, and residential status); and stratification (race and gender). Smoking was not included as a confounder.
	Metric 10:	Covariate Characterization	Medium	Data used to assess potential confounders was derived from death certificates, an adequate measure. However, no information about cigarette smoking and other lifestyle factors were available for adjustment in the analysis.
	Metric 11:	Co-exposure Counfounding	Medium	The variety of industries considered in the analysis diminishes concerns about co-exposures.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The case-control study design and statistical analysis methods were appropriate to assess the exposures/outcome of interest.
	Metric 13:	Statistical Power	Medium	This study had an adequate sample size to detect an effect (n for cases = 63,097; n for controls = 252,386).
	Metric 14:	Reproducibility of Analyses	Medium	The description of analysis was sufficient and would be reproducible.
	Metric 15:	Statistical Analysis	High	The model to calculate risk estimates was transparent.

Additional Comments: This case-control study examined the risk of death from pancreatic cancer in different occupational settings. Exposure was solely assessed using occupation/industry at time of death (reported on death certificate) and the application of a job matrix assessing likely levels of exposure for different positions. This means of estimating exposure may not fully represent a participant's exposure history. Additionally, the number of impacted participants (exposed cases) was inadequate to perform quality analyses for some exposure levels.

Overall Quality Determination High

* No biomarkers were identified for this evaluation.

Study Citation:	Kernan, G.J., Ji, B.T., Dosemeci, M., Silverman, D.T., Balbus, J., Zahm, S.H. (1999). Occupational risk factors for pancreatic cancer: A case-control study based on death certificates from 24 U.S. states. American Journal of Industrial Medicine 36(2):260-270.
Health Outcome(s):	Endocrine
Reported Health Effect(s):	Death from pancreatic cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	194820

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	The National Cancer Institute, National Institute of Occupational Safety and Health, and the National Center for Health Statistics reviewed death certificates from 24 states to select cases from those that had died from pancreatic cancer and matched controls. Controls with cause of death related to the outcome of interest (i.e. pancreatic diseases) were excluded from the study. All key elements of the study design were reported.
	Metric 2:	Attrition	Medium	There was no direct evidence of subject loss or exclusion of subgroups from analyses. The authors provide the total number of cases and controls in the analysis. Case and control data were taken from a registry. It can be assumed that the data are complete for each subject.
	Metric 3:	Comparison Group	High	Controls were selected from the same pool of death certificates from 24 states that cases were selected from. Controls with cause of death related to the outcome of interest were eliminated. Differences in baseline characteristics were controlled for via matching, stratification, and adjustment.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure was assessed via occupation and industry data on death certificates. A job matrix was further applied to assess the likely levels of exposure. Probability and intensity of exposure were estimated across four levels for each occupation. Only employment captured on the death certificate could be considered. The exposure assessment needs exposure information before the job listed on the death certificates.
	Metric 5:	Exposure Levels	Medium	The study offers 4 levels of estimated probability and intensity of exposure (referent, low, medium, high).
	Metric 6:	Temporality	Medium	Exposure was determined by occupational and industry codes on death certificates and indicate that exposure would precede disease, however, the timing and latency period is less clear.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Causes of mortality were determined from death certificates for both cases and controls. Death certificates were drawn from death registries of participating states (n=24). Causes of death were coded using ICD-9 codes, and pancreatic cancer was identified as ICD 157.
	Metric 8:	Reporting Bias	Medium	Measured outcomes, effect estimates and confidence intervals are reported. Number of exposed cases is reported for each analysis, however the number of controls (exposed and unexposed) are not reported for analyses.
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Kernan, G.J., Ji, B.T., Dosemeci, M., Silverman, D.T., Balbus, J., Zahm, S.H. (1999). Occupational risk factors for pancreatic cancer: A case-control study based on death certificates from 24 U.S. states. American Journal of Industrial Medicine 36(2):260-270.
Health Outcome(s):	Endocrine
Reported Health Effect(s):	Death from pancreatic cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	194820

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Medium	Potential confounders were accounted for in the following ways: matching (five year age group, state, race, and gender); adjustment in models (age, marital status, metropolitan, and residential status); and stratification (race and gender). Smoking was not included as a confounder.
	Metric 10:	Covariate Characterization	Medium	Data used to assess potential confounders was derived from death certificates, an adequate measure. However, no information about cigarette smoking and other lifestyle factors were available for adjustment in the analysis.
	Metric 11:	Co-exposure Counfounding	Medium	The variety of industries considered in the analysis diminishes concerns about co-exposures.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The case-control study design and statistical analysis methods were appropriate to assess the exposures/outcome of interest.
	Metric 13:	Statistical Power	Medium	This study had an adequate sample size to detect an effect (n for cases = 63,097; n for controls = 252,386).
	Metric 14:	Reproducibility of Analyses	Medium	The description of analysis was sufficient and would be reproducible.
	Metric 15:	Statistical Analysis	High	The model to calculate risk estimates was transparent.

Additional Comments: This case-control study examined the risk of death from pancreatic cancer in different occupational settings. Exposure was solely assessed using occupation/industry at time of death (reported on death certificate) and the application of a job matrix assessing likely levels of exposure for different positions. This means of estimating exposure may not fully represent a participant's exposure history. Additionally, the number of impacted participants (exposed cases) was inadequate to perform quality analyses for some exposure levels.

Overall Quality Determination High

* No biomarkers were identified for this evaluation.

Study Citation:	Niehoff, N.M., Gammon, M.D., Keil, A.P., Nichols, H.B., Engel, L.S., Sandler, D.P., White, A.J. (2019). Airborne mammary carcinogens and breast cancer risk in the Sister Study. Environment International 130:104897.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Breast cancer diagnosis (overall), tumor characteristics, and estrogen receptor positive (ER+) invasive breast cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5440630

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	Data from the Sister Study were used. The Sister Study is "a prospective cohort of 50,884 women from across the US who were ages 35–74 at enrollment (Sandler et al., 2017). Participants were recruited from 2003 to 2009 using a national advertising campaign in English and Spanish. Women were eligible for the Sister Study if they had a sister who had been diagnosed with breast cancer, but no prior breast cancer themselves."Exclusions from the study occurred for the following reasons:-breast cancer diagnosed before enrollment was complete, or did not have follow-up information (n = 163)-Residential address couldn't be geocoded (n = 1003, < 2%) - This is a small perecentage, but all of those who were excluded for this reason were from Puerto Rico, West Virginia, Missouri, or Oklahoma.Key elements of the study design are reported. There is some potential for selection bias, but based on the small percentage of those eligible who were excluded, participation was not likely to be substantially biased.
	Metric 2:	Attrition	High	Response rates in the overall Sister study remained over 91% over follow-up. Reasons for non-response were not reported, and characteristics of those lost to follow up were not reported or compared with those included, but 9% loss to follow-up is minimal.
	Metric 3:	Comparison Group	High	Differences in baseline characteristics of groups were considered as potential confounding variables.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	The EPA NATA database of census-tract level modeled air toxics data was used. The study authors note the potential for exposure misclassification: "Concentrations at the census tract level do not fully account for variation in an individual's daily activities that could lead to higher or lower exposure, and all women within a census tract are assigned the same concentration."
	Metric 5:	Exposure Levels	Medium	There were five quintiles of exposure, so there was a sufficient range and distribution of exposure.
	Metric 6:	Temporality	Medium	This is a prospective cohort study.Exposure data from 2005 were chosen because they represented the middle of the enrollment period (2003-2009).The study reported that "94% of women enrolled in 2005 or later, and thus the exposure assessment primarily predated enrollment for the majority of Sister Study participants."The six percent of women who had the potential to have the outcome before exposure was measured in 2005 are a concern. But sensitivity analyses were used to assess whether the associations changed when restricted to those who enrolled in 2005 or later.The authors note that the study is making assumptions about the relevant exposure windows - therefore the exposure window is not certain.

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Study Citation:	Niehoff, N.M., Gammon, M.D., Keil, A.P., Nichols, H.B., Engel, L.S., Sandler, D.P., White, A.J. (2019). Airborne mammary carcinogens and breast cancer risk in the Sister Study. Environment International 130:104897.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Breast cancer diagnosis (overall), tumor characteristics, and estrogen receptor positive (ER+) invasive breast cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5440630

Domain	Metric		Rating	Comments
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Women who reported a breast cancer diagnosis on the annual health updates or follow-up questionnaires were asked to provide additional diagnosis information, and to grant permission for the study to obtain medical records and pathology reports. Medical records were obtained for 81% of breast cancer diagnoses. Agreement between self-reported breast cancers and medical records was high (positive predictive value > 99%) (Sandler et al., 2017), so self-report was used when medical records were not available. Tumor characteristics (stage; histology; and estrogen receptor (ER) status) were abstracted from medical records, or self-reported.
	Metric 8:	Reporting Bias	High	A description of measured outcomes is reported. Effect estimates are reported with confidence intervals.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Covariates considered included age, race, BMI, residence type, education, and smoking status. Potential confounders were identified using DAGs and literature review. Appropriate considerations were made for potential confounders.
	Metric 10:	Covariate Characterization	Medium	”Most covariates were assessed by self-report at the baseline interview.””At baseline, women completed a computer-assisted telephone interview and written questionnaires.”Previous publications might describe whether the questionnaires were validated, but validation was not specified in this publication.
	Metric 11:	Co-exposure Counfounding	Medium	Co-exposures to other air pollutants were assessed, but at the census tract level.Multipollutant classification trees were used, which might provide useful qualitative information.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design (large prospective cohort) and analysis method (Cox proportional hazard single and multi-pollutant models accounting for potential confounders) were appropriate to assess the association between exposure and disease.
	Metric 13:	Statistical Power	Medium	The study had an adequate sample size (1975 cancer cases) and follow-up time (mean=8.4 years).
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to be conceptually reproducible.

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Study Citation:	Niehoff, N.M., Gammon, M.D., Keil, A.P., Nichols, H.B., Engel, L.S., Sandler, D.P., White, A.J. (2019). Airborne mammary carcinogens and breast cancer risk in the Sister Study. Environment International 130:104897.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Breast cancer diagnosis (overall), tumor characteristics, and estrogen receptor positive (ER+) invasive breast cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5440630

Domain	Metric	Rating	Comments
	Metric 15: Statistical Analysis	High	Hazard ratios and 95% confidence intervals (CIs) are reported "comparing index categories of exposure to exposures below the first quintile using Cox proportional hazards regression, with age as the time scale." The method of calculating the hazard ratios is transparent. The authors reported that "the proportional hazards assumption was evaluated by conducting a Wald test for an interaction between the continuous form of the air toxic measure and time." Censoring times and times at-risk are described.

Additional Comments: This was a well-conducted study of a large prospective cohort, but the measurement of exposure at the census-tract rather than the individual level is a limitation.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Sobel, W., Bond, G.G., Skowronski, B.J., Brownson, P.J., Cook, R.R. (1987). A soft tissue sarcoma case control study in a large multi-chemical manufacturing facility. Chemosphere 16(8-9):2095-2099.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	soft-tissue sarcoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1357737

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	From a pool of > 37,000 subjects who worked at least 1 year at chemical company between January 1940-December 1979, the study identified 14 people who died due to soft-cell sarcoma (via death certificate, medical records, or histopathology report). Referents were matched 9:1 with cases (126 matched controls).
	Metric 2:	Attrition	High	There was minimal subject exclusion from the analysis sample; one case could not be matched to controls and was excluded from analysis.
	Metric 3:	Comparison Group	High	Cases and controls were recruited from the same eligible population within the same time frame and matched on sex, race, year of birth and year of hire. Both cases and controls had to have worked ≥1 yr at the plant during the study period.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Work histories for cases and referents were coded to determine an individual's potential exposure to chemical of interest and reviewed by an industrial hygienist blinded to case status.
	Metric 5:	Exposure Levels	Low	Exposure was considered dichotomous, ever exposed or never exposed. There is no quantitative information on exposure levels or range of exposures.
	Metric 6:	Temporality	Low	Temporality of exposure and outcome is established. It is unclear if the interval between exposure and outcome is sufficient for soft tissue sarcoma outcomes.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	The soft-tissue sarcoma outcome was assessed by information provided by death certificates, medical records, and histopathology reports, but study authors did not report the proportions determined by each method.
	Metric 8:	Reporting Bias	High	All outcomes outlined were reported. Authors reported the number of cases and controls in the table. Maximum likelihood estimate ORs with respective 95 % confidence intervals were reported.
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Sobel, W., Bond, G.G., Skowronski, B.J., Brownson, P.J., Cook, R.R. (1987). A soft tissue sarcoma case control study in a large multi-chemical manufacturing facility. Chemosphere 16(8-9):2095-2099.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	soft-tissue sarcoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1357737

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Low	Controls were matched with cases on age, sex, year of hire and survival information. There is indirect evidence that the considerations were made to identify potential confounders through evaluation of medical records of cases and controls (various heritable syndromes, family history of cancer, history of lymphedema, steroids, throrotrast, foreign body implants, chronic extensive scarring, radiation therapy, and immunological defects). Identified confounders between cases and controls were not reported and it is unclear if adjustments for these confounders were included in the final analyses.
	Metric 10:	Covariate Characterization	High	Potential covariates were assessed through evaluation of work histories and medical records.
	Metric 11:	Co-exposure Counfounding	Low	The study documented 13 chemicals, known to be associated with soft-tissue sarcoma (according to NTP, 1983) that were used at the manufacturing facility at some point since 1940. The authors note that some individuals were exposed to multiple chemicals during their employment history and were counted multiple times in the analysis for different chemical exposures. Co-exposures to chemicals to not appear to be adjusted for in analysis.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Low	The study design was adequate to assess the association between exposure and the outcome of interest (soft-tissue sarcoma). The study authors noted they used programs developed by Rothman and Boice to calculate odds ratios with CI intervals; the statistical methods are not further described. The page containing the Rothman and Boice reference appears to be missing from the PDF (or the citation is missing).
	Metric 13:	Statistical Power	Low	Statistical power was not calculated. For 1,2-dichloroethane, there was one case and 6 controls included in the analysis, which was not adequate to detect and effect.
	Metric 14:	Reproducibility of Analyses	Low	The study calculated odd ratios, and 95% CIs were calculated using point estimates and chi from hypothesis testing. The study authors noted they used programs developed by Rothman and Boice to calculate odds ratios with 95% CIs; the statistical methods are not further described and there was no reference for the programs cited.
	Metric 15:	Statistical Analysis	Low	A description of analyses/assumptions was not reported.

Additional Comments: A case-control study of workers at a chemical production facility who worked at least 1 year between January 1940-December 1979 (n=37,000) investigated the incidence of deaths due to soft-tissue sarcoma. The study identified 14 people who died due to soft-tissue sarcoma (through death certificate, medical records, or histopathology reports). Cases were matched to controls based on sex, race, year of birth and year of hire. 13 chemicals, including 1,2-dichloroethane, associated with soft-tissue sarcoma were used at the facility; it does not appear that co-exposures were adjusted for in the analysis. Odds ratios and corresponding CIs were calculated. No significant association was found between exposure to 1,2-DCE and soft-tissue sarcoma.

Overall Quality Determination Medium

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Study Citation:	Sobel, W., Bond, G.G., Skowronski, B.J., Brownson, P.J., Cook, R.R. (1987). A soft tissue sarcoma case control study in a large multi-chemical manufacturing facility. Chemosphere 16(8-9):2095-2099.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	soft-tissue sarcoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1357737

Domain	Metric	Rating	Comments

* No biomarkers were identified for this evaluation.

Study Citation:	Sobel, W., Bond, G.G., Skowronski, B.J., Brownson, P.J., Cook, R.R. (1987). A soft tissue sarcoma case control study in a large multi-chemical manufacturing facility. Chemosphere 16(8-9):2095-2099.
Health Outcome(s):	Skin and Connective Tissue
Reported Health Effect(s):	soft-tissue sarcoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1357737

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	From a pool of > 37,000 subjects who worked at least 1 year at chemical company between January 1940-December 1979, the study identified 14 people who died due to soft-cell sarcoma (via death certificate, medical records, or histopathology report). Referents were matched 9:1 with cases (126 matched controls).
	Metric 2:	Attrition	High	There was minimal subject exclusion from the analysis sample; one case could not be matched to controls and was excluded from analysis.
	Metric 3:	Comparison Group	High	Cases and controls were recruited from the same eligible population within the same time frame and matched on sex, race, year of birth and year of hire. Both cases and controls had to have worked ≥1 yr at the plant during the study period.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Work histories for cases and referents were coded to determine an individual's potential exposure to chemical of interest and reviewed by an industrial hygienist blinded to case status.
	Metric 5:	Exposure Levels	Low	Exposure was considered dichotomous, ever exposed or never exposed. There is no quantitative information on exposure levels or range of exposures.
	Metric 6:	Temporality	Low	Temporality of exposure and outcome is established. It is unclear if the interval between exposure and outcome is sufficient for soft tissue sarcoma outcomes.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	The soft-tissue sarcoma outcome was assessed by information provided by death certificates, medical records, and histopathology reports, but study authors did not report the proportions determined by each method.
	Metric 8:	Reporting Bias	High	All outcomes outlined were reported. Authors reported the number of cases and controls in the table. Maximum likelihood estimate ORs with respective confidence intervals were reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	Controls were matched with cases on age, sex, year of hire and survival information. There is indirect evidence that that considerations were made to identify potential confounders through evaluation of medical records of cases and controls (various heritable syndromes, family history of cancer, history of lymphedema, steroids, throrotrast, foreign body implants, chronic extensive scarring, radiation therapy, and immunological defects). Identified confounders between cases and controls were not reported and it is unclear if adjustments for these confounders were included in the final analyses.

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Study Citation:	Sobel, W., Bond, G.G., Skowronski, B.J., Brownson, P.J., Cook, R.R. (1987). A soft tissue sarcoma case control study in a large multi-chemical manufacturing facility. Chemosphere 16(8-9):2095-2099.
Health Outcome(s):	Skin and Connective Tissue
Reported Health Effect(s):	soft-tissue sarcoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1357737

Domain	Metric		Rating	Comments
	Metric 10:	Covariate Characterization	High	Potential covariates were assessed through evaluation of work histories and medical records.
	Metric 11:	Co-exposure Counfounding	Low	The study documented 13 chemicals, known to be associated with soft-tissue sarcoma (according to NTP, 1983) that were used at the manufacturing facility at some point since 1940. The authors note that some individuals were exposed to multiple chemicals during their employment history and were counted multiple times in the analysis for different chemical exposures. Co-exposures to chemicals to not appear to be adjusted for in analysis.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Low	The study design was adequate to assess the association between exposure and the outcome of interest (soft-tissue sarcoma). The study authors noted they used programs developed by Rothman and Boice to calculate odds ratios with (95% CIs; the statistical methods are not further described. The page containing the Rothman and Boice reference appears to be missing from the PDF (or the citation is missing).
	Metric 13:	Statistical Power	Low	Statistical power was not calculated. For 1,2-dichloroethane, there was one case and 6 controls included in the analysis, which was not adequate to detect and effect.
	Metric 14:	Reproducibility of Analyses	Low	The study calculated odd ratios, and 95% CIs were calculated using point estimates and chi from hypothesis testing. The study authors noted they used programs developed by Rothman and Boice to calculate odds ratios with CI intervals; the statistical methods are not further described and there was no reference for the programs cited.
	Metric 15:	Statistical Analysis	Low	A description of analyses/assumptions was not reported.

Additional Comments: A case-control study of workers at a chemical production facility who worked at least 1 year between January 1940-December 1979 (n=37,000) investigated the incidence of deaths due to soft-tissue sarcoma. The study identified 14 people who died due to soft-tissue sarcoma (through death certificate, medical records, or histopathology reports). Cases were matched to controls based on sex, race, year of birth and year of hire. 13 chemicals, including 1,2-dichloroethane, associated with soft-tissue sarcoma were used at the facility; it does not appear that co-exposures were adjusted for in the analysis. Odds ratios and corresponding CIs were calculated. No significant association was found between exposure to 1,2-DCE and soft-tissue sarcoma.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Teta, M. J., Ott, M. G., Schnatter, A. R. (1991). An update of mortality due to brain neoplasms and other causes among employees of a petrochemical facility. Journal of Occupational Medicine 33(1):45-51.
Health Outcome(s):	Mortality
Reported Health Effect(s):	all cause mortality, gastrointestinal cancer mortality, respiratory system cancer mortality, kidney and other urinary organ cancer mortality, skin cancer mortality, brain cancer mortality, lymphatic and hematopoietic tissue cancer mortality, benign neoplasm mortality, heart disease mortality, and liver cirrhosis mortality.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200633, 1629047
HERO ID:	200633

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	The facility was described in some detail. All male employees working for one day or more between 1941 and 1983 were included. There may be some healthy worker effect in this population.
	Metric 2:	Attrition	High	Study authors reported that vital status was complete for 99% of the population, and death certificates were obtained for 99% of decedents.
	Metric 3:	Comparison Group	High	SMRs were calculated using age-, race-, and calendar year-specific mortality rates of males in the United States. All included employees were male.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	All employees were treated as exposed. Table 4 indicates that relatively few employees were employed in areas designated as 1,2-DCA work areas. There is potential for substantial exposure misclassification.
	Metric 5:	Exposure Levels	Low	All employed individuals were categorized as exposed, and the reference population was described as unexposed. This represents two levels of exposure. The distribution of exposure within the employed population is unclear.
	Metric 6:	Temporality	Medium	Employees were followed from 1950 (or date of first hire) through 1983. The relevant timing of exposure is not entirely clear; however, this represents a sufficiently long period of follow-up.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Mortality was tracked using company records, Social Security Administration records, and the National Death Index. Specific ICD codes and use of a nosologist were not described, but there was no evidence to suggest the method had poor validity.
	Metric 8:	Reporting Bias	High	SMRs were provided with confidence intervals in addition to observed and expected cases. The authors state they did not carry out regional specific SMRs due to the higher prevalence of neoplasms in the surrounding area.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	SMRs were restricted to males. Rates were age-, race-, and calendar period-specific. No consideration was made for smoking.
	Metric 10:	Covariate Characterization	Medium	Demographic information was obtained from employment records. This was not a validated method, but there was no evidence to suggest it was an invalid method.

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Study Citation:	Teta, M. J., Ott, M. G., Schnatter, A. R. (1991). An update of mortality due to brain neoplasms and other causes among employees of a petrochemical facility. Journal of Occupational Medicine 33(1):45-51.
Health Outcome(s):	Mortality
Reported Health Effect(s):	all cause mortality, gastrointestinal cancer mortality, respiratory system cancer mortality, kidney and other urinary organ cancer mortality, skin cancer mortality, brain cancer mortality, lymphatic and hematopoietic tissue cancer mortality, benign neoplasm mortality, heart disease mortality, and liver cirrhosis mortality.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200633, 1629047
HERO ID:	200633

Domain	Metric		Rating	Comments
	Metric 11:	Co-exposure Counfounding	Low	Several other occupational exposures linked to cancer mortality were present, including vinyl chloride, butanol, and other petrochemicals.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	This study design was appropriate for the research question. Authors utilized retrospective occupational cohort data to determine standardized mortality rates for cancer-specific mortalities.
	Metric 13:	Statistical Power	Medium	While power was not calculated, there were over 1350 deaths from 7849 employees which was adequate to detect robust effect estimates.
	Metric 14:	Reproducibility of Analyses	Low	Most details were provided; however, ICD codes used to determine and group cancer mortality diagnoses were not provided.
	Metric 15:	Statistical Analysis	High	No issues identified.

Additional Comments: This study utilized an occupational cohort to retrospectively evaluate elevated rates of cancer mortality among petrochemical plant workers. There were numerous potentially hazardous chemicals mentioned in the plant description which may lead to co-exposure. Additionally, it appears that only a moderate portion of workers may have been exposed to 1,2-DCA or worked in 1,2-DCA areas which may lead to some exposure misclassification and limit the study's ability to inform hazard on 1,2-DCA.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Cases in this case-control study were former Union Carbide Corporation (UCC) chemical plant employees in Texas City, Texas. Cases were identified through death certificate searches and tumor registries, and may have included individuals formerly employed at UCC whose cause of death was unknown to the company. Additionally, control deaths were stated to be pulled from corporate employee benefits department and through locally published obituary notices routinely screened by the medical department - it is possible to assume that cases were identified in a similar manner. The study identified cases of brain tumors by searching death certificates primarily, although tumor registries throughout the state of Texas were also searched. The study clarifies that it is possible that some cases were not found if they survived or died due to another cause - while this is likely to have impacted selection, there is no evidence that this would be differential by exposure status. Overall, there is limited information on the source population of workers from which cases were identified.
	Metric 2:	Attrition	Medium	Attrition is not discussed in the study, and outcome data appear to be complete. There was a large proportion of missing exposure data (roughly 50%) due to workers being employed in roles such as maintenance, where exposure to any chemical is possible but unknown. Analyses were run separately where these ”unknown” individuals were a) treated as exposed, b) treated as unexposed, or c) treated as unknown and thus excluded. The study only presents results for when these individuals were excluded but specifies that the first scenario resulted in increased exposure estimates for controls relative to cases.

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Study Citation:	Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
	Metric 3:	Comparison Group	Medium	The study identifies two series of control groups, selected from all former Union Carbide Corporation (UCC) employees. However, the total number of employees is not stated. Only those who were deceased were used as controls since they had known causes of death and could thus be verified as non-brain tumors. One group of controls excluded employees whose cause of death was due to any malignant neoplasm to allow for the possibility that a general chemical carcinogen may have been associated with cancers of other sites. The other group of controls included deaths from all causes; this included malignant neoplasms other than brain tumors. Both control groups had 80 male employees randomly selected from 450 deceased employees known to the company in June 1979. Control deaths were stated to be pulled from corporate employee benefits department and through locally published obituary notices routinely screened by the medical department - it is possible to assume that cases were identified in a similar manner. The study reports that cases were slightly more likely to have been employed for less than 10 years than controls - the study attributes this in part to the fact that employees whose deaths were known to the company were more likely to have worked for longer - regardless the mean number of years employed was similar between cases and controls. However, cases were more likely to have been terminated from their job for reasons other than death, disability, or retirement (quitting, being fired, etc.), were generally younger at hire, and were less likely to survive to their 70th birthday. None of these factors are controlled for in statistical analyses - however, since controls and cases were pulled from the same population, there is indirect evidence that the groups were similar.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was determined based on official employment records. Records included job title and department assignment codes for each employment from date of hire to date of termination. For each unique department code, UCC and NIOSH industrial hygienists identified principal chemicals used or produced at any time in the history of the plant and correlated those with individual departments. This assessment was not performed on a year-by-year basis due to concerns for recall bias for longer-term employees where less detailed records were kept. An employee was categorized as ”exposed” to 1,2-dichloroethane if they ever worked in a department associated with that chemical. An ”unknown” exposure group was also created to account for employees who had only worked in departments for which no specific chemical could be identified.
	Metric 5:	Exposure Levels	Low	The study does not report any quantitative information and only splits exposure into ”exposed”, ”unexposed”, and ”unknown”.
	Metric 6:	Temporality	High	In this study exposure is confirmed to occur before the outcome is measured. The study reports latency periods, with subjects dichotomized into less than 15 years of latency or more than 15 years of latency. The majority of cases and controls had a latency of greater than 15 years, which is sufficiently long for brain tumors.

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Study Citation:	Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Cases were identified through death certificate searches and partially through tumor registries in the state of Texas. Case validation was performed by NIOSH, and 5 different levels of confirmation were reported: 1) tissue specimen interpreted by the Armed Forces Institute of Pathology; 2) autopsy report; 3) histopathology report; 4) clinical diagnosis from hospital record; 5) dearth certificate diagnosis. Codes 1-3 were considered to be ”confirmed” cases of brain tumors, while 4-5 were considered unconfirmed. 5/21 cases were only evaluated using ”unconfirmed methods”, meaning there is likely a high amount of accuracy in roughly 75% of cases. While no case validation is reported for controls, the study specifies that only controls who had died and thus could be confirmed to be non-brain tumors were included.
	Metric 8:	Reporting Bias	Medium	All primary and secondary outcomes that are outlined in the methods are reported in the results. However, the only statistical outcome of their analysis were unadjusted p-values that were not reported and were just described qualitatively.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	The only statistical analysis performed were Mantel-Haenszel chi-squared tests, which did not allow for confounder adjustment. The study does not present a distribution of potential confounders by exposure status but by case/control status. Several variables, such as reason for termination, age at hire, and age at death were significantly different between cases and controls and were not accounted for in statistical modeling. The study explains that these differences are not likely to have any epidemiologic significance and appear to be relatively small differences.
	Metric 10:	Covariate Characterization	Medium	While the study does not explain where they obtained covariate information, it is reasonable to assume that they gathered the information from company records.
	Metric 11:	Co-exposure Counfounding	Low	The study assesses a wide range of other potential occupational co-exposures. While these co-exposures are not adjusted for in any statistical models, effect estimates are presented separately for benzene, diethyl sulfate, ethylene oxide, and vinyl chloride. The distribution of co-exposures across cases and controls is demonstrated to be mostly balanced by comparing proportions of exposed/unexposed between cases and controls. The only notable instance of imbalance is for benzene, where 11.1% of cases were exposed whereas 37.9% of all controls and 19.2% of non-neoplasm related controls were exposed.
Domain 5: Analysis				

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Study Citation:	Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	The study chose a case-control design, which was appropriate to study the rare disease of brain tumors and its association with occupational exposures. The only statistical analysis conducted is a Mantzel-Haenszel chi-squared test, but there is no reason to suggest that this would be inappropriate.
	Metric 13:	Statistical Power	Medium	The study does not calculate statistical power, but the number of cases (n=21) and controls (n=80 in each analysis) is likely sufficient to detect an effect.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to understand what was done and could be reproduced given access to the analytic data.
	Metric 15:	Statistical Analysis	High	The only statistical analysis conducted is a Mantel-Haenszel chi-squared test, and all assumptions were met. The statistical process is transparent.

Additional Comments: This case-control study pulled deceased former employees of the Union Carbide Corporation in Texas City, Texas. The study examined dichotomous exposure to a wide range of occupational exposures, including 1,2-dichloroethane, in relation to brain tumor cases. There is no quantitative estimate of exposure. The only statistical analysis in the study is a Mantel-Haenszel chi-squared test statistic and no statistically significant differences in exposure between cases and controls were observed. The fact that there are no effect estimates, no adjustment for confounders, and no quantitative exposure estimates limits the usefulness of this paper.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Cases in this case-control study were former Union Carbide Corporation (UCC) chemical plant employees in Texas City, Texas. Cases were identified through death certificate searches and tumor registries, and may have included individuals formerly employed at UCC whose cause of death was unknown to the company. Additionally, control deaths were stated to be pulled from corporate employee benefits department and through locally published obituary notices routinely screened by the medical department - it is possible to assume that cases were identified in a similar manner. The study identified cases of brain tumors by searching death certificates primarily, although tumor registries throughout the state of Texas were also searched. The study clarifies that it is possible that some cases were not found if they survived or died due to another cause - while this is likely to have impacted selection, there is no evidence that this would be differential by exposure status. Overall, there is limited information on the source population of workers from which cases were identified.
	Metric 2:	Attrition	Medium	Attrition is not discussed in the study, and outcome data appear to be complete. There was a large proportion of missing exposure data (roughly 50%) due to workers being employed in roles such as maintenance, where exposure to any chemical is possible but unknown. Analyses were run separately where these ”unknown” individuals were a) treated as exposed, b) treated as unexposed, or c) treated as unknown and thus excluded. The study only presents results for when these individuals were excluded but specifies that the first scenario resulted in increased exposure estimates for controls relative to cases.

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Study Citation:	Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
	Metric 3:	Comparison Group	Medium	The study identifies two series of control groups, selected from all former Union Carbide Corporation (UCC) employees. However, the total number of employees is not stated. Only those who were deceased were used as controls since they had known causes of death and could thus be verified as non-brain tumors. One group of controls excluded employees whose cause of death was due to any malignant neoplasm to allow for the possibility that a general chemical carcinogen may have been associated with cancers of other sites. The other group of controls included deaths from all causes; this included malignant neoplasms other than brain tumors. Both control groups had 80 male employees randomly selected from 450 deceased employees known to the company in June 1979. Control deaths were stated to be pulled from corporate employee benefits department and through locally published obituary notices routinely screened by the medical department - it is possible to assume that cases were identified in a similar manner. The study reports that cases were slightly more likely to have been employed for less than 10 years than controls - the study attributes this in part to the fact that employees whose deaths were known to the company were more likely to have worked for longer - regardless the mean number of years employed was similar between cases and controls. However, cases were more likely to have been terminated from their job for reasons other than death, disability, or retirement (quitting, being fired, etc.), were generally younger at hire, and were less likely to survive to their 70th birthday. None of these factors are controlled for in statistical analyses - however, since controls and cases were pulled from the same population, there is indirect evidence that the groups were similar.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was determined based on official employment records. Records included job title and department assignment codes for each employment from date of hire to date of termination. For each unique department code, UCC and NIOSH industrial hygienists identified principal chemicals used or produced at any time in the history of the plant and correlated those with individual departments. This assessment was not performed on a year-by-year basis due to concerns for recall bias for longer-term employees where less detailed records were kept. An employee was categorized as ”exposed” to 1,2-dichloroethane if they ever worked in a department associated with that chemical. An ”unknown” exposure group was also created to account for employees who had only worked in departments for which no specific chemical could be identified.
	Metric 5:	Exposure Levels	Low	The study does not report any quantitative information and only splits exposure into ”exposed”, ”unexposed”, and ”unknown”.
	Metric 6:	Temporality	High	In this study exposure is confirmed to occur before the outcome is measured. The study reports latency periods, with subjects dichotomized into less than 15 years of latency or more than 15 years of latency. The majority of cases and controls had a latency of greater than 15 years, which is sufficiently long for brain tumors.

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Study Citation:	Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Cases were identified through death certificate searches and partially through tumor registries in the state of Texas. Case validation was performed by NIOSH, and 5 different levels of confirmation were reported: 1) tissue specimen interpreted by the Armed Forces Institute of Pathology; 2) autopsy report; 3) histopathology report; 4) clinical diagnosis from hospital record; 5) dearth certificate diagnosis. Codes 1-3 were considered to be ”confirmed” cases of brain tumors, while 4-5 were considered unconfirmed. 5/21 cases were only evaluated using ”unconfirmed methods”, meaning there is likely a high amount of accuracy in roughly 75% of cases. While no case validation is reported for controls, the study specifies that only controls who had died and thus could be confirmed to be non-brain tumors were included.
	Metric 8:	Reporting Bias	Medium	All primary and secondary outcomes that are outlined in the methods are reported in the results. However, the only statistical outcome of their analysis were unadjusted p-values that were not reported and were just described qualitatively.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	The only statistical analysis performed were Mantel-Haenszel chi-squared tests, which did not allow for confounder adjustment. The study does not present a distribution of potential confounders by exposure status but by case/control status. Several variables, such as reason for termination, age at hire, and age at death were significantly different between cases and controls and were not accounted for in statistical modeling. The study explains that these differences are not likely to have any epidemiologic significance and appear to be relatively small differences.
	Metric 10:	Covariate Characterization	Medium	While the study does not explain where they obtained covariate information, it is reasonable to assume that they gathered the information from company records.
	Metric 11:	Co-exposure Counfounding	Low	The study assesses a wide range of other potential occupational co-exposures. While these co-exposures are not adjusted for in any statistical models, effect estimates are presented separately for benzene, diethyl sulfate, ethylene oxide, and vinyl chloride. The distribution of co-exposures across cases and controls is demonstrated to be mostly balanced by comparing proportions of exposed/unexposed between cases and controls. The only notable instance of imbalance is for benzene, where 11.1% of cases were exposed whereas 37.9% of all controls and 19.2% of non-neoplasm related controls were exposed.
Domain 5: Analysis				

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Study Citation:	Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	The study chose a case-control design, which was appropriate to study the rare disease of brain tumors and its association with occupational exposures. The only statistical analysis conducted is a Mantzel-Haenszel chi-squared test, but there is no reason to suggest that this would be inappropriate.
	Metric 13:	Statistical Power	Medium	The study does not calculate statistical power, but the number of cases (n=21) and controls (n=80 in each analysis) is likely sufficient to detect an effect.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to understand what was done and could be reproduced given access to the analytic data.
	Metric 15:	Statistical Analysis	High	The only statistical analysis conducted is a Mantel-Haenszel chi-squared test, and all assumptions were met. The statistical process is transparent.

Additional Comments: This case-control study pulled deceased former employees of the Union Carbide Corporation in Texas City, Texas. The study examined dichotomous exposure to a wide range of occupational exposures, including 1,2-dichloroethane, in relation to brain tumor cases. There is no quantitative estimate of exposure. The only statistical analysis in the study is a Mantel-Haenszel chi-squared test statistic and no statistically significant differences in exposure between cases and controls were observed. The fact that there are no effect estimates, no adjustment for confounders, and no quantitative exposure estimates limits the usefulness of this paper.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	Urinary system cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	Urinary system cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	Urinary system cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Immune/Hematological
Reported Health Effect(s):	Lymphatic and hematopoietic tissue cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Immune/Hematological
Reported Health Effect(s):	Lymphatic and hematopoietic tissue cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
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	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Health Outcome(s):	Immune/Hematological
Reported Health Effect(s):	Lymphatic and hematopoietic tissue cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Other cancers (not specified)
Reported Health Effect(s):	Other cancers (not specified)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Other cancers (not specified)
Reported Health Effect(s):	Other cancers (not specified)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Other cancers (not specified)
Reported Health Effect(s):	Other cancers (not specified)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Mortality
Reported Health Effect(s):	All-cause mortality
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Vital status was tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Medium	Death rates among unit employees were compared to death rates in the U.S. population adjusted for age and gender. Demographics of the exposed workers are not provided; therefore, it is not clear whether additional adjustment for race may have been appropriate. No justification is provided for the choice of the entire U.S. population as the comparison group. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis. Additional analyses are conducted limiting workers to those with the greatest likelihood of exposure (i.e., those working in jobs with high likelihood of contact with chemicals for more than a year, those working for the full year of 1979 during which chemical exposures were most frequently reported); these smaller groups are also compared to the unexposed general population.
	Metric 6:	Temporality	High	Temporality was established due to the longitudinal design and the use of mortality as the outcome. Exposures occurred between 1979 and 1987 and follow-up for vital status was conducted through 2003.
Domain 3: Outcome Assessment				

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Mortality
Reported Health Effect(s):	All-cause mortality
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Medium	The study did not provide information on how mortality was assessed either in the exposed population or in the comparison population; use of death certificates is implied but not stated.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected deaths are reported, but SIRs and 95% confidence intervals are not provided.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Comparisons of observed versus expected deaths were adjusted for age and gender. Demographics of the exposed workers are not provided; therefore, it is not clear whether additional adjustment for race may have been appropriate.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records or death records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed deaths among a population of exposed workers compared to expected deaths among the U.S. population, adjusted for age and gender.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected deaths; no SIR was provided. Expected death rates were adjusted for age and gender.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Mortality
Reported Health Effect(s):	All-cause mortality
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	All cancer (excluding non-melanoma skin cancer), digestive system cancer, colorectal cancer, respiratory cancer, prostate cancer, urinary system cancer, lymphatic and hematopoietic tissue cancer, other cancers (not specified)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	All cancer (excluding non-melanoma skin cancer), digestive system cancer, colorectal cancer, respiratory cancer, prostate cancer, urinary system cancer, lymphatic and hematopoietic tissue cancer, other cancers (not specified)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	All cancer (excluding non-melanoma skin cancer), digestive system cancer, colorectal cancer, respiratory cancer, prostate cancer, urinary system cancer, lymphatic and hematopoietic tissue cancer, other cancers (not specified)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Gastrointestinal
Reported Health Effect(s):	Digestive system cancer, colorectal cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Gastrointestinal
Reported Health Effect(s):	Digestive system cancer, colorectal cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Gastrointestinal
Reported Health Effect(s):	Digestive system cancer, colorectal cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Lung/Respiratory
Reported Health Effect(s):	Respiratory cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Lung/Respiratory
Reported Health Effect(s):	Respiratory cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Lung/Respiratory
Reported Health Effect(s):	Respiratory cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Prostate cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Prostate cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Male workers who had ever been assigned to the chlorohydrin unit between 1 January 1940 and 31 December 1967 at Union Carbide's South Charleston plant were enrolled and matched to the US National Death Index. Status on 5 workers could not be identified. Information on how workers were matched to death index was not specified.
	Metric 2:	Attrition	Medium	Rate of inclusion/participation was very high, as records were able to be matched for 98% of participants. Medium rating given because information on how participants whose vital status was not known was not specified.
	Metric 3:	Comparison Group	Uninformative	Unacceptable rating given because SMRs were calculated based on expected deaths from a reference population matched on sex, but not age.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Exposure was assessed based on duration of work in the plant. No information is provided on exposure levels, and a JEM was not used.
	Metric 5:	Exposure Levels	Uninformative	No information provided on levels of exposure.
	Metric 6:	Temporality	High	Temporality is well established; person-years stopped accumulating in 1967 and outcome was assessed beginning at that time.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar period, and interval since assignments, but distribution of these covariates was not reported.
	Metric 10:	Covariate Characterization	Medium	Information on covariate characterization not provided, but the selected covariates (age, calendar period, and interval since assignments) were likely extracted from employee records and unlikely to be largely problematic
	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.

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Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Study design was appropriate for the research method. Statistical methods were also appropriate.
	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.
	Metric 14:	Reproducibility of Analyses	Medium	Methods are well-enough described that study could be adequately reproduced.
	Metric 15:	Statistical Analysis	High	SMRs calculated based on US general population mortality for white males through 1988. RRs were ”evaluated over levels of duration of assignment to the chlorohydrin unit, stratified by age, calendar year, and interval since first assignment to the chlorohydrin unit”.

Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
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Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Male workers who had ever been assigned to the chlorohydrin unit between 1 January 1940 and 31 December 1967 at Union Carbide's South Charleston plant were enrolled and matched to the US National Death Index. Status on 5 workers could not be identified. Information on how workers were matched to death index was not specified.
	Metric 2:	Attrition	Medium	Rate of inclusion/participation was very high, as records were able to be matched for 98% of participants. Medium rating given because information on how participants whose vital status was not known was not specified.
	Metric 3:	Comparison Group	Uninformative	Unacceptable rating given because SMRs were calculated based on expected deaths from a reference population matched on sex, but not age.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Exposure was assessed based on duration of work in the plant. No information is provided on exposure levels, and a JEM was not used.
	Metric 5:	Exposure Levels	Uninformative	No information provided on levels of exposure.
	Metric 6:	Temporality	High	Temporality is well established; person-years stopped accumulating in 1967 and outcome was assessed beginning at that time.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar period, and interval since assignments, but distribution of these covariates was not reported.
	Metric 10:	Covariate Characterization	Medium	Information on covariate characterization not provided, but the selected covariates (age, calendar period, and interval since assignments) were likely extracted from employee records and unlikely to be largely problematic
	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.
Domain 5: Analysis				

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Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Study design was appropriate for the research method. Statistical methods were also appropriate.
	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.
	Metric 14:	Reproducibility of Analyses	Medium	Methods are well-enough described that study could be adequately reproduced.
	Metric 15:	Statistical Analysis	High	SMRs calculated based on US general population mortality for white males through 1988. RRs were ”evaluated over levels of duration of assignment to the chlorohydrin unit, stratified by age, calendar year, and interval since first assignment to the chlorohydrin unit”.

Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
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Domain 1: Study Participation				
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	Metric 2:	Attrition	Medium	Rate of inclusion/participation was very high, as records were able to be matched for 98% of participants. Medium rating given because information on how participants whose vital status was not known was not specified.
	Metric 3:	Comparison Group	Uninformative	Unacceptable rating given because SMRs were calculated based on expected deaths from a reference population matched on sex, but not age.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Exposure was assessed based on duration of work in the plant. No information is provided on exposure levels, and a JEM was not used.
	Metric 5:	Exposure Levels	Uninformative	No information provided on levels of exposure.
	Metric 6:	Temporality	High	Temporality is well established; person-years stopped accumulating in 1967 and outcome was assessed beginning at that time.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar period, and interval since assignments, but distribution of these covariates was not reported.
	Metric 10:	Covariate Characterization	Medium	Information on covariate characterization not provided, but the selected covariates (age, calendar period, and interval since assignments) were likely extracted from employee records and unlikely to be largely problematic
	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.
Domain 5: Analysis				

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Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
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HERO ID:	200224

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Study design was appropriate for the research method. Statistical methods were also appropriate.
	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.
	Metric 14:	Reproducibility of Analyses	Medium	Methods are well-enough described that study could be adequately reproduced.
	Metric 15:	Statistical Analysis	High	SMRs calculated based on US general population mortality for white males through 1988. RRs were ”evaluated over levels of duration of assignment to the chlorohydrin unit, stratified by age, calendar year, and interval since first assignment to the chlorohydrin unit”.

Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
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	Metric 2:	Attrition	Medium	Rate of inclusion/participation was very high, as records were able to be matched for 98% of participants. Medium rating given because information on how participants whose vital status was not known was not specified.
	Metric 3:	Comparison Group	Uninformative	Unacceptable rating given because SMRs were calculated based on expected deaths from a reference population matched on sex, but not age.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Exposure was assessed based on duration of work in the plant. No information is provided on exposure levels, and a JEM was not used.
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	Metric 6:	Temporality	High	Temporality is well established; person-years stopped accumulating in 1967 and outcome was assessed beginning at that time.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar period, and interval since assignments, but distribution of these covariates was not reported.
	Metric 10:	Covariate Characterization	Medium	Information on covariate characterization not provided, but the selected covariates (age, calendar period, and interval since assignments) were likely extracted from employee records and unlikely to be largely problematic
	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.
Domain 5: Analysis				

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Additional Comments: None

Overall Quality Determination Uninformative

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Domain 4: Potential Confounding / Variability Control				
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Domain 5: Analysis				

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Additional Comments: None

Overall Quality Determination Uninformative

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	Metric 3:	Comparison Group	Uninformative	Unacceptable rating given because SMRs were calculated based on expected deaths from a reference population matched on sex, but not age.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Exposure was assessed based on duration of work in the plant. No information is provided on exposure levels, and a JEM was not used.
	Metric 5:	Exposure Levels	Uninformative	No information provided on levels of exposure.
	Metric 6:	Temporality	High	Temporality is well established; person-years stopped accumulating in 1967 and outcome was assessed beginning at that time.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar period, and interval since assignments, but distribution of these covariates was not reported.
	Metric 10:	Covariate Characterization	Medium	Information on covariate characterization not provided, but the selected covariates (age, calendar period, and interval since assignments) were likely extracted from employee records and unlikely to be largely problematic
	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.
Domain 5: Analysis				

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Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Study design was appropriate for the research method. Statistical methods were also appropriate.
	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.
	Metric 14:	Reproducibility of Analyses	Medium	Methods are well-enough described that study could be adequately reproduced.
	Metric 15:	Statistical Analysis	High	SMRs calculated based on US general population mortality for white males through 1988. RRs were ”evaluated over levels of duration of assignment to the chlorohydrin unit, stratified by age, calendar year, and interval since first assignment to the chlorohydrin unit”.

Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Male workers who had ever been assigned to the chlorohydrin unit between 1 January 1940 and 31 December 1967 at Union Carbide's South Charleston plant were enrolled and matched to the US National Death Index. Status on 5 workers could not be identified. Information on how workers were matched to death index was not specified.
	Metric 2:	Attrition	Medium	Rate of inclusion/participation was very high, as records were able to be matched for 98% of participants. Medium rating given because information on how participants whose vital status was not known was not specified.
	Metric 3:	Comparison Group	Uninformative	Unacceptable rating given because SMRs were calculated based on expected deaths from a reference population matched on sex, but not age.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Exposure was assessed based on duration of work in the plant. No information is provided on exposure levels, and a JEM was not used.
	Metric 5:	Exposure Levels	Uninformative	No information provided on levels of exposure.
	Metric 6:	Temporality	High	Temporality is well established; person-years stopped accumulating in 1967 and outcome was assessed beginning at that time.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar period, and interval since assignments, but distribution of these covariates was not reported.
	Metric 10:	Covariate Characterization	Medium	Information on covariate characterization not provided, but the selected covariates (age, calendar period, and interval since assignments) were likely extracted from employee records and unlikely to be largely problematic
	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.
Domain 5: Analysis				

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Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Study design was appropriate for the research method. Statistical methods were also appropriate.
	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.
	Metric 14:	Reproducibility of Analyses	Medium	Methods are well-enough described that study could be adequately reproduced.
	Metric 15:	Statistical Analysis	High	SMRs calculated based on US general population mortality for white males through 1988. RRs were ”evaluated over levels of duration of assignment to the chlorohydrin unit, stratified by age, calendar year, and interval since first assignment to the chlorohydrin unit”.

Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Male workers who had ever been assigned to the chlorohydrin unit between 1 January 1940 and 31 December 1967 at Union Carbide's South Charleston plant were enrolled and matched to the US National Death Index. Status on 5 workers could not be identified. Information on how workers were matched to death index was not specified.
	Metric 2:	Attrition	Medium	Rate of inclusion/participation was very high, as records were able to be matched for 98% of participants. Medium rating given because information on how participants whose vital status was not known was not specified.
	Metric 3:	Comparison Group	Uninformative	Unacceptable rating given because SMRs were calculated based on expected deaths from a reference population matched on sex, but not age.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Exposure was assessed based on duration of work in the plant. No information is provided on exposure levels, and a JEM was not used.
	Metric 5:	Exposure Levels	Uninformative	No information provided on levels of exposure.
	Metric 6:	Temporality	High	Temporality is well established; person-years stopped accumulating in 1967 and outcome was assessed beginning at that time.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar period, and interval since assignments, but distribution of these covariates was not reported.
	Metric 10:	Covariate Characterization	Medium	Information on covariate characterization not provided, but the selected covariates (age, calendar period, and interval since assignments) were likely extracted from employee records and unlikely to be largely problematic
	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.
Domain 5: Analysis				

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Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Study design was appropriate for the research method. Statistical methods were also appropriate.
	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.
	Metric 14:	Reproducibility of Analyses	Medium	Methods are well-enough described that study could be adequately reproduced.
	Metric 15:	Statistical Analysis	High	SMRs calculated based on US general population mortality for white males through 1988. RRs were ”evaluated over levels of duration of assignment to the chlorohydrin unit, stratified by age, calendar year, and interval since first assignment to the chlorohydrin unit”.

Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Bove, F. J. (1996). Public drinking water contamination and birthweight, prematurity, fetal deaths, and birth defects. Toxicology and Industrial Health 12(2):255-266.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	200239

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	This cross-sectional study (n=80,938) included all registered singleton live births and fetal deaths (>20 weeks' gestation) in 1985-88 in 75 New Jersey towns located in 4 counties with "some" water supplies contaminated with substances of interest and where: (i) residents were "mostly" served by public water systems; and (ii) births occurred "mostly" in state. Estimated proportions of residents served by public water systems, and of pregnancies/births captured, were not described. However, the inclusion of all eligible registered births, fetal deaths, and birth defects, as well as the selection of towns without knowledge of birth outcome prevalence, limited the likelihood of selection bias.
	Metric 2:	Attrition	Medium	All registered births and fetal deaths were included. Attrition due to missing values for multiple variables was not quantified and is therefore uncertain. However, attrition was likely modest as the proportion of missing values for individual variables was relatively low: (i) ~6% of subjects were excluded from analyses of outcomes such as preterm birth due to invalid or missing gestational ages; and (ii) other covariates evaluated as confounders had up to 4.9% missing values.
	Metric 3:	Comparison Group	High	After excluding plural pregnancies and chromosomal abnormalities, all registered live births during the study period in the areas included without the outcomes of interest were included in the comparison group. This comprehensive approach limited the potential for bias. Chromosomal abnormalities were not included as outcomes as they were not hypothesized to be associated with the exposures under study but were appropriately excluded given their uncertain etiology.
Domain 2: Exposure Characterization				

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Study Citation:	Bove, F. J. (1996). Public drinking water contamination and birthweight, prematurity, fetal deaths, and birth defects. Toxicology and Industrial Health 12(2):255-266.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	200239

Domain	Metric		Rating	Comments
	Metric 4:	Measurement of Exposure	Medium	Along with several other contaminants, residential drinking water exposure to 1,2-dichloroethane (as well as 1,1,1-trichloroethane and 'total dichloroethylenes') – was assigned based on maternal town of residence at birth. Exposure estimates were calculated using the average of water company sampling reports during the first trimester (for birth defects and fetal death) or the duration of pregnancy (for other outcomes). Detection limits and data availability were not specified in detail but were described as below 1 ppb, with reporting compliance >85%. A minimum of 1 sample per 6-month interval was required; variability in the number of measures available across water systems and towns was not described. Additional sources of measurement error included: changes in residence during pregnancy; water from alternate sources (ex. private wells, bottles, workplaces); variability in residential contaminant levels vs measured samples; unknown levels of tap water intake; and errors in estimated dermal and inhalation exposure while bathing or showering. While the extent of exposure misclassification is uncertain, there is no evidence to suggest it was differential rather than random.
	Metric 5:	Exposure Levels	Medium	Due to the high proportion of measures below detection limits, analyses relating exposure to health outcomes used only 2 categories for each of the chlorinated solvents of interest: cutoffs close to detection limits were used to define elevated exposure. Proportions defined as having elevated exposure was low (1.8% had 1,1-dichloroethylene ≥1 ppb). An important concern is that relatively low levels of exposure to these contaminants from sources other than residential drinking water, for which data were not available, could potentially have resulted in considerable misclassification.
	Metric 6:	Temporality	High	Exposure levels were assigned based on contaminant exposures estimated during: (i) the first trimester for analyses of birth defects and fetal deaths; and (ii) the duration of pregnancy for other pregnancy outcomes.

Domain 3: Outcome Assessment

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Study Citation:	Bove, F. J. (1996). Public drinking water contamination and birthweight, prematurity, fetal deaths, and birth defects. Toxicology and Industrial Health 12(2):255-266.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	200239

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcomes included measures of birthweight (continuous among term births, low term birthweight, very low birthweight), prematurity, fetal death, and congenital anomalies in live births or fetal deaths. The anomalies analyzed included defects of the central nervous system, neural tube, oral cleft, total cardiac, major cardiac, ventricular septum, and any surveillance defect excluding chromosomal defects. All outcomes were identified using birth certificates, fetal death certificates (>20 weeks' gestation), and the NJ congenital birth defect registry (ICD codes provided). These registry data are likely to be sufficiently valid for late pregnancy outcomes. However, their limited ability to capture early pregnancy losses is a weakness. The sample included only 594 fetal deaths (less than 1% of the >80,0000 sample). Typical estimates are that 10-20%, of recognized pregnancies ending in losses. Moreover, developmental defects contributing to early pregnancy losses were also not captured. A further limitation is that that potentially etiologically heterogeneous preterm birth types were analyzed together, as these data did not distinguish premature rupture of membranes vs idiopathic prematurity.
	Metric 8:	Reporting Bias	Medium	Models were constructed only for contaminants with associations > 1.0, and tables included only associations with odds ratios ≥1.5. No clear rationale was provided. Several positive odds ratios below the 1.5 cutoff were described in the results text (without confidence intervals), but no null/negative odds ratios were presented or described.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Potential confounding by maternal race, education, parity, and prior pregnancy loss, along with infant sex (for birth outcomes) and adequacy of prenatal care, was examined. Gestational age was addressed by analyzing birthweight among full term births, term low birth weight, and small size for gestational age. Only fully adjusted models were presented. In a companion case-control study (with low participation rates), adjustment for other variables not available on birth certificates (ex. maternal smoking, occupational exposures, medical history, and gestational weight gain) did not influence associations with other studied contaminants. This separate study reduces concerns for important confounding bias, but confounding cannot be ruled out.
	Metric 10:	Covariate Characterization	Medium	Data on covariates came from registry data: birth certificates, fetal death certificates, and the NJ congenital birth defects registry.
	Metric 11:	Co-exposure Counfounding	Medium	Co-exposure confounding by drinking water trihalomethane concentrations was evaluated. There was no evidence to suggest substantial confounding by this or other co-exposures.
Domain 5: Analysis				

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Study Citation:	Bove, F. J. (1996). Public drinking water contamination and birthweight, prematurity, fetal deaths, and birth defects. Toxicology and Industrial Health 12(2):255-266.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	200239

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Methods were appropriate. The study used logistic regression models to estimate odds ratios and confidence intervals for dichotomous outcomes, and linear regression for analysis of continuous birth weight.
	Metric 13:	Statistical Power	Medium	Statistical power was likely to have been limited as a consequence of the small proportion of the sample defined as having "elevated" residential water concentrations of the chemicals of interest. The range of exposure examined was limited, as cutoffs for elevated levels were close to the detection limits of 1 ppb. In addition, for most birth defect outcomes, fewer than 10 cases had elevated exposure.
	Metric 14:	Reproducibility of Analyses	Medium	The authors clearly described steps used to estimate exposure-outcome associations, including exposure category cutoffs and criteria for confounding. However, many results were not shown as tables included odds ratios ≥1.5.
	Metric 15:	Statistical Analysis	High	The authors estimated coefficients, odds ratios and 95% confidence intervals using adequate methods. Confounding was based on 15% change-in-estimate comparing nested models. Effect modification (ex by infant sex) was not evaluated as there was no a priori evidence to suggest such analyses at that time.

Additional Comments: This study analyzed the association between estimated residential drinking water concentrations of several chlorinated solvents including 1,2-dichloroethane (as well as 1,1,1-trichloroethane; ∑[trans-1,2-dichloroethylene and 1,1-dichloroethylene]) and pregnancy outcomes (size at birth, prematurity, fetal deaths, and congenital birth defects). The sample included more than 80,000 births during 1985-88 for residents of 75 towns in NJ using public water system records to estimate exposure during gestation, and registry data (birth certificate, fetal death certificates for pregnancies >20 weeks, state birth defect registry) to characterize outcomes. Strengths included the large sample size and inclusion of all eligible registered births and fetal deaths in the study period. A critical concern is the inability to capture early fetal deaths and any related malformations (1% of the sample had fetal deaths vs typical estimates of >10%). An important limitation was the low percentage of the sample with detectable (> 1ppb) concentrations of these contaminants (<1% to 6.2%). Small numbers for birth defect outcomes also limited power. Exposure misclassification (ex. drinking water from wells/ work/ bottles, changes in residence, exposure from other sources) is also a concern. However, such misclassification was likely non-differential, and thus more likely to under- vs. to over-estimate associations.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Bove, F. J., Fulcomer, M. C., Klotz, J. B., Esmart, J., Dufficy, E. M., Savrin, J. E. (1995). Public drinking water contamination and birth outcomes. American Journal of Epidemiology 141(9):850-862.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	194932

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	This semi-ecological study (n=80,938) included all registered singleton live births and fetal deaths (>20 weeks) in 1985-88 in 75 New Jersey towns located in 4 counties with "some" water supplies contaminated with substances of interest and where: (i) residents were "mostly" served by public water systems; and (ii) births occurred "mostly" in state. Estimated proportions of residents served by public water systems, and of pregnancies/births captured, were not described. However, the inclusion of all eligible registered births, fetal deaths, and birth defects, as well as the selection of towns without knowledge of birth outcome prevalence, limited the likelihood of selection bias.
	Metric 2:	Attrition	Medium	All registered births and fetal deaths were included. Attrition due to missing values for multiple variables was not quantified and is therefore uncertain. However, attrition was likely modest as the proportion of missing values for individual variables was relatively low: (i) ~6% of subjects were excluded from analyses of outcomes such as preterm birth due to invalid or missing gestational ages; and (ii) other covariates evaluated as confounders had up to 4.9% missing values.
	Metric 3:	Comparison Group	High	After excluding plural pregnancies and chromosomal abnormalities, all registered live births during the study period in the areas included without the outcomes of interest were included in the comparison group. This comprehensive approach limited the potential for bias. Chromosomal abnormalities were not included as outcomes as they were not hypothesized to be associated with the exposures under study but were appropriately excluded given their uncertain etiology.
Domain 2: Exposure Characterization				

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Study Citation:	Bove, F. J., Fulcomer, M. C., Klotz, J. B., Esmart, J., Dufficy, E. M., Savrin, J. E. (1995). Public drinking water contamination and birth outcomes. American Journal of Epidemiology 141(9):850-862.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	194932

Domain	Metric		Rating	Comments
	Metric 4:	Measurement of Exposure	Medium	Along with several other contaminants, residential drinking water exposure to 1,2-dichloroethane (as well as 1,1,1-trichloroethane and 'total dichloroethylenes') was assigned based on maternal town of residence at birth. Exposure estimates were calculated using the average of water company sampling reports during the first trimester (for birth defects and fetal death) or the duration of pregnancy (for other outcomes). Detection limits and data availability were not specified in detail but were described as below 1 ppb, with reporting compliance >85%. A minimum of 1 sample per 6-month interval was required; variability in the number of measures available across water systems and towns was not described. Additional sources of measurement error included: changes in residence during pregnancy; water from alternate sources (ex. private wells, bottles, workplaces); variability in residential contaminant levels vs measured samples; unknown levels of tap water intake; and errors in estimated dermal and inhalation exposure while bathing or showering. While the extent of exposure misclassification is uncertain, there is no evidence to suggest it was differential rather than random.
	Metric 5:	Exposure Levels	Low	Due to the high proportion of measures below detection limits, analyses relating exposure to health outcomes used only 2 categories for each of the three chemicals of interest: cutoffs close to detection limits were used to define elevated exposure. Proportions defined as having elevated exposure were low (1.8% had 1,1-dichloroethylene ≥1 ppb). An important concern is that relatively low levels of exposure to this contaminant from sources other than residential drinking water, for which data were not available, could potentially have resulted in considerable misclassification.
	Metric 6:	Temporality	High	Exposure levels were assigned based on contaminant exposures estimated during: (i) the first trimester for analyses of birth defects and fetal deaths; and (ii) the duration of pregnancy for other pregnancy outcomes.

Domain 3: Outcome Assessment

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Study Citation:	Bove, F. J., Fulcomer, M. C., Klotz, J. B., Esmart, J., Dufficy, E. M., Savrin, J. E. (1995). Public drinking water contamination and birth outcomes. American Journal of Epidemiology 141(9):850-862.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	194932

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcomes included measures of birthweight (continuous among term births, low term birthweight, very low birthweight), prematurity, fetal death, and congenital anomalies in live births or fetal deaths. The anomalies analyzed included defects of the central nervous system, neural tube, oral cleft, total cardiac, major cardiac, ventricular septum, and any surveillance defect excluding chromosomal defects. All outcomes were identified using birth certificates, fetal death certificates (>20 weeks' gestation), and the NJ congenital birth defect registry (ICD codes provided). These registry data are likely to be sufficiently valid for late pregnancy outcomes. However, their limited ability to capture early pregnancy losses is a weakness. The sample included only 594 fetal deaths (less than 1% of the >80,0000 sample). Typical estimates are that 10-20%, of recognized pregnancies ending in losses. Moreover, developmental defects contributing to early pregnancy losses were also not captured. A further limitation is that that potentially etiologically heterogeneous preterm birth types were analyzed together, as these data did not distinguish premature rupture of membranes vs idiopathic prematurity.
	Metric 8:	Reporting Bias	Low	Models were constructed only for contaminants with associations > 1.0, and tables included only associations with odds ratios ≥1.5. No clear rationale was provided. Several positive odds ratios below the 1.5 cutoff were described in the results text (without confidence intervals), but no null/negative odds ratios were presented or described.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Potential confounding by maternal race, education, parity, and prior pregnancy loss, along with infant sex (for birth outcomes) and adequacy of prenatal care, was examined. Gestational age was addressed by analyzing birthweight among full term births, term low birth weight, and small size for gestational age. Only fully adjusted models were presented. In a companion case-control study (with low participation rates), adjustment for other variables not available on birth certificates (ex. maternal smoking, occupational exposures, medical history, and gestational weight gain) did not influence associations with other studied contaminants. This separate study reduces concerns for important confounding bias, but confounding cannot be ruled out.
	Metric 10:	Covariate Characterization	Medium	Data on covariates came from registry data: birth certificates, fetal death certificates, and the NJ congenital birth defects registry.
	Metric 11:	Co-exposure Counfounding	Medium	Co-exposure confounding by drinking water trihalomethane concentrations was evaluated. There was no evidence to suggest substantial confounding by this or other co-exposures.
Domain 5: Analysis				

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Study Citation:	Bove, F. J., Fulcomer, M. C., Klotz, J. B., Esmart, J., Dufficy, E. M., Savrin, J. E. (1995). Public drinking water contamination and birth outcomes. American Journal of Epidemiology 141(9):850-862.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	194932

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Methods were appropriate. The study used logistic regression models to estimate odds ratios and confidence intervals for dichotomous outcomes, and linear regression for analysis of continuous birth weight.
	Metric 13:	Statistical Power	Low	Statistical power was likely to have been limited as a consequence of the small proportion of the sample defined as having "elevated" residential water concentrations of the chemicals of interest. The range of exposure examined was limited, as cutoffs for elevated levels were close to the detection limits of 1 ppb. In addition, for most birth defect outcomes, fewer than 10 cases had elevated exposure. However, the authors emphasized the magnitude of associations rather than statistical significance and presented multiple confidence intervals to aid interpretation of the precision of estimates (50%, 90% and 99%).
	Metric 14:	Reproducibility of Analyses	Medium	The authors clearly described steps used to estimate exposure-outcome associations, including exposure category cutoffs and criteria for confounding. However, many results were not shown as tables included odds ratios ≥1.5.
	Metric 15:	Statistical Analysis	High	The authors estimated coefficients, odds ratios and confidence intervals using adequate methods. Confounding was based on 15% change-in-estimate comparing nested models. Effect modification (ex by infant sex) was not evaluated as there was no a priori evidence to suggest such analyses at that time.

Additional Comments: This study analyzed the association between estimated residential drinking water concentrations of several chlorinated solvents including 1,2-dichloroethane (as well as 1,1,1-trichloroethane and the ∑[trans-1,2-dichloroethylene & 1,1-dichloroethylene]) and pregnancy outcomes (size at birth, prematurity, fetal deaths, and congenital birth defects). The sample included more than 80,000 births during 1985-88 for residents of 75 towns in NJ using public water system records to estimate exposure during gestation, and registry data (birth certificate, fetal death certificates for pregnancies >20 weeks' gestation, state birth defect registry) to characterize outcomes. Strengths included the large sample size and inclusion of all eligible registered births and fetal deaths in the study period. A critical concern is the inability to capture early fetal deaths and any related malformations (1% of the sample had fetal deaths vs typical estimates of >10%). An important limitation was the low percentage of the sample with detectable (> 1ppb) concentrations of this solvent (<2%), which likely limited power. Small numbers for birth defect outcomes also limited power. Exposure misclassification (ex. drinking water from wells/ work/ bottles, changes in residence, exposure from other sources) is also a concern. However, such misclassification was likely non-differential, and thus more likely to under- vs. to over-estimate associations.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Bowler, R.M., Gysens, S., Hartney, C. (2003). Neuropsychological effects of ethylene dichloride exposure. NeuroToxicology 24(4-5):553-562.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Wechsler Adult Intelligence Scale III (WAIS-III), Wechsler Memory Scale III (WMS-III), Boston Naming Test (BNT), Trail Making Test (TMT), Stroop Color-Word Test, Grooved Pegboard, Dynamometer, Wide Range Achievement Test (WRAT), Finger tapping, Beck Anxiety Index, Beck Depression Index, Symptom Checklist-90 (SCL-90).
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	200241

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Uninformative	221 workers that had been exposed to 1,2-DCE in the Southern United States were initially included. Exclusion criteria were provided, including the number of individuals excluded for each reason. The study authors note that those initially included in the analysis sample were referred by physicians after neurological complaints were documented. Detailed criteria for referral were not provided. Referral-based recruitment of neurological cases will likely result in an analysis sample with an exposure-outcome distribution that is not representative of the eligible population (i.e., contamination site clean-up workers).
	Metric 2:	Attrition	Medium	There was moderate subject loss. Reasons for exclusion from the analysis sample are provided, and only those with complete information were included in the analysis.
	Metric 3:	Comparison Group	Low	Impairment scores were compared to normative data from manuals and/or a "demographically similar control group" cited to Bowler et al. (2001). The controls from this study appeared similar (albeit somewhat older) than 1,2-DCE-exposed workers and reported no prior chemical exposure.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	A job-exposure matrix was not considered plausible; variables considered as surrogates of exposure were obtained from interviews. This method is expected to have poor validity because it relies on workers' recall of subjective events and their frequency (e.g., contact with water); workers (who are taking part in a lawsuit) may overestimate their exposure.
	Metric 5:	Exposure Levels	Low	Two levels of exposure (exposed and not exposed) were used to evaluate neurophysiological effects.
	Metric 6:	Temporality	Medium	Exposures primarily occurred between 1993 and 1995 and neurophysiological effects were evaluated in 2000. Temporality is established, but it is unclear whether exposures fall within relevant exposure windows for the outcome of interest.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Neurophysiological effects were evaluated using a number of standardized tests, including (but not limited to) the Wechsler Adult Intelligence Scale (WAIS-III), the Wechsler Memory Scale (WMS-III), and the Symptom Checklist 90-Revised (SCL90-R). There was no information whether tests were performed using the same methods for exposed and referent groups (e.g., timing and order of tests).

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Study Citation:	Bowler, R.M., Gysens, S., Hartney, C. (2003). Neuropsychological effects of ethylene dichloride exposure. NeuroToxicology 24(4-5):553-562.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Wechsler Adult Intelligence Scale III (WAIS-III), Wechsler Memory Scale III (WMS-III), Boston Naming Test (BNT), Trail Making Test (TMT), Stroop Color-Word Test, Grooved Pegboard, Dynamometer, Wide Range Achievement Test (WRAT), Finger tapping, Beck Anxiety Index, Beck Depression Index, Symptom Checklist-90 (SCL-90).
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	200241

Domain	Metric		Rating	Comments
	Metric 8:	Reporting Bias	Low	Neurobehavioral outcomes mentioned in the methods were reported for 1,2-DCE-exposed workers (as mean score, standard deviation, and percentage impaired); results for controls/normative data were not shown and/or p-values from t-tests were not provided. Control data were used to define impairment (based on z-score) but these values were not reported. Data pertaining to specific exposure variables were reported in the text only; no data were shown in a table.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Normative data permitted adjustments based on age, education, and gender. The control group was "socio-demographically" similar but specific parameters used to define similarity were not indicated. Separate ANCOVA analyses on workers only were stratified by race (citation provided), and adjusted for ethnicity, age, and education. The methods for identifying and including potential confounders in the analytic approach was not described.
	Metric 10:	Covariate Characterization	Low	No description of the covariate collection method was provided. It was not clear whether the method used was valid or not.
	Metric 11:	Co-exposure Counfounding	Low	A number of workers (18%) reported current exposure to chemicals in their work environment. These potential co-exposures were not were not appropriately adjusted for in the analytical approach used.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Low	The study design was appropriate to evaluate the neurophysiological status of 1,2-DCE-exposed workers; however, statistical methods were not comprehensive.
	Metric 13:	Statistical Power	Medium	The report indicates "significant impairments" were observed on various neurophysiological tests using t-tests, and significant exposure relationships were reported based on test scores and specific exposure variables (used as surrogates of exposure). Therefore, the number of participants was sufficient to detect an effect.
	Metric 14:	Reproducibility of Analyses	Low	Tests were scored according to relevant manuals; the calculation of z-scores, used in all impairment comparisons and analyses of exposure relationships, was not explained in adequate detail. The methods used to determine relationships between specific exposure variables and test scores (i.e., ANCOVA analyses) were not fully described.
	Metric 15:	Statistical Analysis	Low	Description of the ANCOVA analysis was largely not present. It is not clear whether model assumptions were met.

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Study Citation:	Bowler, R.M., Gysens, S., Hartney, C. (2003). Neuropsychological effects of ethylene dichloride exposure. NeuroToxicology 24(4-5):553-562.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Wechsler Adult Intelligence Scale III (WAIS-III), Wechsler Memory Scale III (WMS-III), Boston Naming Test (BNT), Trail Making Test (TMT), Stroop Color-Word Test, Grooved Pegboard, Dynamometer, Wide Range Achievement Test (WRAT), Finger tapping, Beck Anxiety Index, Beck Depression Index, Symptom Checklist-90 (SCL-90).
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	200241

Domain	Metric	Rating	Comments
Additional Comments:	The study evaluated the neurobehavioral status of a group of workers with known exposure to 1,2-DCE at a clean-up site. Impairments related to processing speed, attention, cognitive flexibility, motor coordination and speed, verbal memory/fluency, vision and visual-spatial abilities, and mood were reported in exposed workers. Serious and consequential flaws are associated with the study including methods of participant selection and retention, and exposure characterization among others.		

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Brender, J.D., Shinde, M.U., Zhan, F.B., Gong, X., Langlois, P.H. (2014). Maternal residential proximity to chlorinated solvent emissions and birth defects in offspring: A case-control study. Environmental Health: A Global Access Science Source 13(1):96.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	birth defects (neural tube defects, limbs deficiencies, oral cleft defects, heart defects, spina bifida, anencephaly)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	2799700

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Participants were drawn from the Texas Birth Defects Registry (TBDR) for years 1996-2008. Controls were frequency matched from the same registry. Study authors state that neural tube cases were more likely to not be successfully geocoded which may introduce selection bias, however, the authors note that both cases and controls with addresses that could not be geocoded were similar. In spite of that, the inclusion criteria, methods of participant selection, and frequency match were reported.
	Metric 2:	Attrition	Medium	13.3% case mother addresses and 12.8% control mother addresses were unable to be geocoded, however this most likely only lowered the precision of the study and most likely does not vary based on exposure level.
	Metric 3:	Comparison Group	Medium	Controls were matched to cases and pulled from the same eligible population by year of delivery and public health service region. Other demographic factors, e.g., race was not matched in population selection. However, statistical analyses were adjusted for year of delivery, maternal age, race/ethnicity, education, and public health region of residence.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Used Emission Weighted Proximity Model to estimate exposure at a given address based on proximity to emission sources and the specific amount or type of pollutant emitted. There may be some exposure misclassification due to mothers moving away from geocoded addresses. Previous studies indicate ~67% of mothers do not move between conception and delivery.
	Metric 5:	Exposure Levels	Medium	Reports exposure as "exposure risk value" and groups the risk values into quartiles, with exposure risk values < 0 being the referent group
	Metric 6:	Temporality	Medium	The study authors estimated exposure based on residence during pregnancy and evaluated birth outcomes. Temporality is established. Previous studies indicate ~67% mothers don't move between trimester and delivery. For mothers who moved during the pregnancy, the temporality is unknown.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Outcomes determined by Texas Birth Defect Registry, checking for birth defect diagnosis. Birth certificates came from Center for Health Statistics at Texas Department of State Health Services
	Metric 8:	Reporting Bias	High	Outcome data measured and reported clearly, stratified by specific type of birth defect
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Brender, J.D., Shinde, M.U., Zhan, F.B., Gong, X., Langlois, P.H. (2014). Maternal residential proximity to chlorinated solvent emissions and birth defects in offspring: A case-control study. Environmental Health: A Global Access Science Source 13(1):96.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	birth defects (neural tube defects, limbs deficiencies, oral cleft defects, heart defects, spina bifida, anencephaly)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	2799700

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	High	Cases were frequency matched by year of delivery and public health service region. Final models were adjusted for year of delivery, public health region, maternal age (<20, 20-24, 25-29, 30-34, 35-39, >39 years), education (<12 years, 12 years, >12 years), and race/ethnicity (Whit non-Hispanic, Black non-Hispanic, Hispanic, other non-Hispanic).
	Metric 10:	Covariate Characterization	High	Used birth and death certificates for demographic information
	Metric 11:	Co-exposure Counfounding	Medium	other co-exposures were not described
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	study used logistic regression to measure association between exposure and birth defects
	Metric 13:	Statistical Power	Medium	Overall adequate number of cases and controls - some effects have low cell counts, but at least one health effect has sufficient statistical power.
	Metric 14:	Reproducibility of Analyses	Medium	Methods sufficiently detailed for reproducibility
	Metric 15:	Statistical Analysis	High	No logistic regression model assumption violations were identified.

Additional Comments: This study examined the association between proximity to several point sources of chlorinated solvents and birth defects. Exposure was assessed using EPA's Toxic Release Inventory, and birth defects were assessed using Texas birth registries. The geocoded address of mothers on day of delivery and the amount of solvent was plugged into the Emission Weighted Probability model to assign each mother an exposure risk value. Limitations include limited evidence of temporality. Additionally, elective terminations lacked a vital record, which meant only 69% of mothers with neural tube defects were geocoded. Mothers highly exposed to 1,2-dichloroethane were 1.85 times more likely to have the spina bifida birth defect than mothers who were not significantly exposed.

Overall Quality Determination High

* No biomarkers were identified for this evaluation.

Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Nested case-control design; cases selected from deaths in cohort study was described by Rinsky et al (1988; HERO 597923) (29,139 workers in Union Carbide facilities in West Virginia followed from 1940 to 1978). Vital status complete for 95% of cohort members.
	Metric 2:	Attrition	High	There was minimal exclusion of subjects/missing data, because vital status follow-up was complete for 96% of the 29,139 men in the cohort study.
	Metric 3:	Comparison Group	Medium	Controls were randomly selected in a 5:1 ratio to cases from the total employee cohort such that they were first employed in the same decade and survived to the same five-year survival period as cases. Controls survived at least to the beginning of the five-year interval in which cases died. Controls were independently selected for each of the individual disease subcategories. However, the demographic information between cases and controls were not compared in the paper.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was partially described: (1) Potential employee contact with a specific substance was determined by tracing each employee's work assignments and linking these assignment records to a separate computer file that contained a history of departmental usage for each substance; (2) Potential exposure to each chemical group was assumed on the basis of assignment o a production unit with a history of usage of any member of that chemical group. However, exposure level either based on work assignment in departments such as job exposure matrix or on the chemical levels were not presented.
	Metric 5:	Exposure Levels	Low	The range of exposure is limited. For example, exposure was presented by the duration of work in two categories: <5 years and 5+ years.
	Metric 6:	Temporality	Medium	Temporality is established, but it is unclear whether the exposures fall within the relevant exposure window. Authors used a lag time of 5 years; since controls were selected for 5 yr intervals, the effective lag time ranged from 5-9 years with an average of 7.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Case definition was based on death certificate diagnosis; but no method validation was conducted against this well-established methods.
	Metric 8:	Reporting Bias	Medium	All outcomes reported, but ORs for many analyses presented without CIs (some CIs reported in text).
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Low	There is indirect evidence that considerations were not made for potential confounders (ORs not adjusted, controls not age- or race-matched). Even though authors note that "Age-adjusted stratified analyses, which were also conducted, did not materially modify the odds ratio estimates". Also stratified examination of odds ratios were conducted to assess duration of exposure effects. However, other key confounders e.g., smoking status and race were not accounted for.
	Metric 10:	Covariate Characterization	Medium	The only potential confounder considered was age; this was presumably evaluated based on employment records (no discussion presented). Age-adjusted stratified analyses were conducted.
	Metric 11:	Co-exposure Counfounding	Low	Co-exposures were present and were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Nested case-control study design is appropriate for research question. Initial data analysis included crude odds ratio and then stratified examination of odds ratios was conducted to ass duration of exposure effect. Also, age-adjusted stratified analysis was conducted.
	Metric 13:	Statistical Power	Low	Statistical power calculations were not reported. Case numbers for each disease were low. The number of subjects was not sufficient to detect an effect of 1,2-dichloroethylene exposure.
	Metric 14:	Reproducibility of Analyses	Medium	Description was sufficient to be conceptually reproducible.
	Metric 15:	Statistical Analysis	Low	Statistical model to calculate odds ratio was not described.

Additional Comments: This nested case-control study within a cohort study is a good study design to answer the research question regarding the association between multiple chemical exposures and four cancer sites. Cases and controls are selected appropriate. However, there are several limitations in this study: (1) confounders were not all considered and adjusted for, except that age-adjusted odds ratios were conducted; (2) it is not described if co-exposures were adjusted for; (3) numbers of cancer cases for each cancer type were small, so the statistical power is limited; (4) statistical models for calculating odds ratios were not described.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Nested case-control design; cases selected from deaths in cohort study was described by Rinsky et al (1988; HERO 597923) (29,139 workers in Union Carbide facilities in West Virginia followed from 1940 to 1978). Vital status complete for 95% of cohort members.
	Metric 2:	Attrition	High	There was minimal exclusion of subjects/missing data, because vital status follow-up was complete for 96% of the 29,139 men in the cohort study.
	Metric 3:	Comparison Group	Medium	Controls were randomly selected in a 5:1 ratio to cases from the total employee cohort such that they were first employed in the same decade and survived to the same five-year survival period as cases. Controls survived at least to the beginning of the five-year interval in which cases died. Controls were independently selected for each of the individual disease subcategories. However, the demographic information between cases and controls were not compared in the paper.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was partially described: (1) Potential employee contact with a specific substance was determined by tracing each employee's work assignments and linking these assignment records to a separate computer file that contained a history of departmental usage for each substance; (2) Potential exposure to each chemical group was assumed on the basis of assignment o a production unit with a history of usage of any member of that chemical group. However, exposure level either based on work assignment in departments such as job exposure matrix or on the chemical levels were not presented.
	Metric 5:	Exposure Levels	Low	The range of exposure is limited. For example, exposure was presented by the duration of work in two categories: <5 years and 5+ years.
	Metric 6:	Temporality	Medium	Temporality is established, but it is unclear whether the exposures fall within the relevant exposure window. Authors used a lag time of 5 years; since controls were selected for 5 yr intervals, the effective lag time ranged from 5-9 years with an average of 7.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Case definition was based on death certificate diagnosis; but no method validation was conducted against this well-established methods.
	Metric 8:	Reporting Bias	Medium	All outcomes reported, but ORs for many analyses presented without CIs (some CIs reported in text).
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Low	There is indirect evidence that considerations were not made for potential confounders (ORs not adjusted, controls not age- or race-matched). Even though authors note that "Age-adjusted stratified analyses, which were also conducted, did not materially modify the odds ratio estimates". Also stratified examination of odds ratios were conducted to assess duration of exposure effects. However, other key confounders e.g., smoking status and race were not accounted for.
	Metric 10:	Covariate Characterization	Medium	The only potential confounder considered was age; this was presumably evaluated based on employment records (no discussion presented). Age-adjusted stratified analyses were conducted.
	Metric 11:	Co-exposure Counfounding	Low	Co-exposures were present and were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Nested case-control study design is appropriate for research question. Initial data analysis included crude odds ratio and then stratified examination of odds ratios was conducted to ass duration of exposure effect. Also, age-adjusted stratified analysis was conducted.
	Metric 13:	Statistical Power	Low	Statistical power calculations were not reported. Case numbers for each disease were low. The number of subjects was not sufficient to detect an effect of 1,2-dichloroethylene exposure.
	Metric 14:	Reproducibility of Analyses	Medium	Description was sufficient to be conceptually reproducible.
	Metric 15:	Statistical Analysis	Low	Statistical model to calculate odds ratio was not described.

Additional Comments: This nested case-control study within a cohort study is a good study design to answer the research question regarding the association between multiple chemical exposures and four cancer sites. Cases and controls are selected appropriate. However, there are several limitations in this study: (1) confounders were not all considered and adjusted for, except that age-adjusted odds ratios were conducted; (2) it is not described if co-exposures were adjusted for; (3) numbers of cancer cases for each cancer type were small, so the statistical power is limited; (4) statistical models for calculating odds ratios were not described.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
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Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Nested case-control design; cases selected from deaths in cohort study was described by Rinsky et al (1988; HERO 597923) (29,139 workers in Union Carbide facilities in West Virginia followed from 1940 to 1978). Vital status complete for 95% of cohort members.
	Metric 2:	Attrition	High	There was minimal exclusion of subjects/missing data, because vital status follow-up was complete for 96% of the 29,139 men in the cohort study.
	Metric 3:	Comparison Group	Medium	Controls were randomly selected in a 5:1 ratio to cases from the total employee cohort such that they were first employed in the same decade and survived to the same five-year survival period as cases. Controls survived at least to the beginning of the five-year interval in which cases died. Controls were independently selected for each of the individual disease subcategories. However, the demographic information between cases and controls were not compared in the paper.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was partially described: (1) Potential employee contact with a specific substance was determined by tracing each employee's work assignments and linking these assignment records to a separate computer file that contained a history of departmental usage for each substance; (2) Potential exposure to each chemical group was assumed on the basis of assignment o a production unit with a history of usage of any member of that chemical group. However, exposure level either based on work assignment in departments such as job exposure matrix or on the chemical levels were not presented.
	Metric 5:	Exposure Levels	Low	The range of exposure is limited. For example, exposure was presented by the duration of work in two categories: <5 years and 5+ years.
	Metric 6:	Temporality	Medium	Temporality is established, but it is unclear whether the exposures fall within the relevant exposure window. Authors used a lag time of 5 years; since controls were selected for 5 yr intervals, the effective lag time ranged from 5-9 years with an average of 7.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Case definition was based on death certificate diagnosis; but no method validation was conducted against this well-established methods.
	Metric 8:	Reporting Bias	Medium	All outcomes reported, but ORs for many analyses presented without CIs (some CIs reported in text).
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Low	There is indirect evidence that considerations were not made for potential confounders (ORs not adjusted, controls not age- or race-matched). Even though authors note that "Age-adjusted stratified analyses, which were also conducted, did not materially modify the odds ratio estimates". Also stratified examination of odds ratios were conducted to assess duration of exposure effects. However, other key confounders e.g., smoking status and race were not accounted for.
	Metric 10:	Covariate Characterization	Medium	The only potential confounder considered was age; this was presumably evaluated based on employment records (no discussion presented). Age-adjusted stratified analyses were conducted.
	Metric 11:	Co-exposure Counfounding	Low	Co-exposures were present and were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Nested case-control study design is appropriate for research question. Initial data analysis included crude odds ratio and then stratified examination of odds ratios was conducted to ass duration of exposure effect. Also, age-adjusted stratified analysis was conducted.
	Metric 13:	Statistical Power	Low	Statistical power calculations were not reported. Case numbers for each disease were low. The number of subjects was not sufficient to detect an effect of 1,2-dichloroethylene exposure.
	Metric 14:	Reproducibility of Analyses	Medium	Description was sufficient to be conceptually reproducible.
	Metric 15:	Statistical Analysis	Low	Statistical model to calculate odds ratio was not described.

Additional Comments: This nested case-control study within a cohort study is a good study design to answer the research question regarding the association between multiple chemical exposures and four cancer sites. Cases and controls are selected appropriate. However, there are several limitations in this study: (1) confounders were not all considered and adjusted for, except that age-adjusted odds ratios were conducted; (2) it is not described if co-exposures were adjusted for; (3) numbers of cancer cases for each cancer type were small, so the statistical power is limited; (4) statistical models for calculating odds ratios were not described.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Nested case-control design; cases selected from deaths in cohort study was described by Rinsky et al (1988; HERO 597923) (29,139 workers in Union Carbide facilities in West Virginia followed from 1940 to 1978). Vital status complete for 95% of cohort members.
	Metric 2:	Attrition	High	There was minimal exclusion of subjects/missing data, because vital status follow-up was complete for 96% of the 29,139 men in the cohort study.
	Metric 3:	Comparison Group	Medium	Controls were randomly selected in a 5:1 ratio to cases from the total employee cohort such that they were first employed in the same decade and survived to the same five-year survival period as cases. Controls survived at least to the beginning of the five-year interval in which cases died. Controls were independently selected for each of the individual disease subcategories. However, the demographic information between cases and controls were not compared in the paper.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was partially described: (1) Potential employee contact with a specific substance was determined by tracing each employee's work assignments and linking these assignment records to a separate computer file that contained a history of departmental usage for each substance; (2) Potential exposure to each chemical group was assumed on the basis of assignment o a production unit with a history of usage of any member of that chemical group. However, exposure level either based on work assignment in departments such as job exposure matrix or on the chemical levels were not presented.
	Metric 5:	Exposure Levels	Low	The range of exposure is limited. For example, exposure was presented by the duration of work in two categories: <5 years and 5+ years.
	Metric 6:	Temporality	Medium	Temporality is established, but it is unclear whether the exposures fall within the relevant exposure window. Authors used a lag time of 5 years; since controls were selected for 5 yr intervals, the effective lag time ranged from 5-9 years with an average of 7.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Case definition was based on death certificate diagnosis; but no method validation was conducted against this well-established methods.
	Metric 8:	Reporting Bias	Medium	All outcomes reported, but ORs for many analyses presented without CIs (some CIs reported in text).
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Low	There is indirect evidence that considerations were not made for potential confounders (ORs not adjusted, controls not age- or race-matched). Even though authors note that "Age-adjusted stratified analyses, which were also conducted, did not materially modify the odds ratio estimates". Also stratified examination of odds ratios were conducted to assess duration of exposure effects. However, other key confounders e.g., smoking status and race were not accounted for.
	Metric 10:	Covariate Characterization	Medium	The only potential confounder considered was age; this was presumably evaluated based on employment records (no discussion presented). Age-adjusted stratified analyses were conducted.
	Metric 11:	Co-exposure Counfounding	Low	Co-exposures were present and were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Nested case-control study design is appropriate for research question. Initial data analysis included crude odds ratio and then stratified examination of odds ratios was conducted to ass duration of exposure effect. Also, age-adjusted stratified analysis was conducted.
	Metric 13:	Statistical Power	Low	Statistical power calculations were not reported. Case numbers for each disease were low. The number of subjects was not sufficient to detect an effect of 1,2-dichloroethylene exposure.
	Metric 14:	Reproducibility of Analyses	Medium	Description was sufficient to be conceptually reproducible.
	Metric 15:	Statistical Analysis	Low	Statistical model to calculate odds ratio was not described.

Additional Comments: This nested case-control study within a cohort study is a good study design to answer the research question regarding the association between multiple chemical exposures and four cancer sites. Cases and controls are selected appropriate. However, there are several limitations in this study: (1) confounders were not all considered and adjusted for, except that age-adjusted odds ratios were conducted; (2) it is not described if co-exposures were adjusted for; (3) numbers of cancer cases for each cancer type were small, so the statistical power is limited; (4) statistical models for calculating odds ratios were not described.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Cheng, T.J., Huang, M.L., You, N.C., Du, C.L., Chau, T.T. (1999). Abnormal liver function in workers exposed to low levels of ethylene dichloride and vinyl chloride monomer. Journal of Occupational and Environmental Medicine 41(12):1128-1133.
Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	AST, ALT, GGT, Hepatitis B virus surface antigen (HBsAg), and anti-hepatitis C virus antibody (anti-HCV).
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	200266

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	A total of 251 male workers were included from 4 vinyl chloride monomer manufacturing plants. Other details on recruitment strategy, eligibility criteria, year of enrollment, and participation rates were not provided.
	Metric 2:	Attrition	Low	There was no indication of attrition and details on the number of eligible participants throughout the study was limited. Attrition could not be adequately assessed due to a lack of information regarding recruitment and selection.
	Metric 3:	Comparison Group	Medium	The low-EDC-low-VCM group (187 participants) was used as the comparison group, and there is indirect evidence groups are similar. Limited details were provided for setting, inclusion and exclusion criteria, and methods of participant selection.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	NIOSH recommended methods 1003 and 1007 were used for personal and area sampling, respectively. Air samples were collected, stored at 4 deg. C, and analyzed within 2 weeks of the sampling event. However, historical job changes, changes in exposure levels over time, and timing (year or days during work week) or duration of area or personal sampling were not reported.
	Metric 5:	Exposure Levels	Medium	EDC and VCM levels were reported for the different categories of jobs, which were classified into low-EDC-low-VCM, mod-EDC-low-VCM, and low-EDC-mod-VCM groups.
	Metric 6:	Temporality	High	The age of participants (mean age 33.7-40.1 years) and employment duration (mean 7.5-14.3 years) were reported, and the temporality between the exposure and outcome appears to be appropriate.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	AST, ALT, and GGT "were analyzed with a Hitachi 7050 autoanalyzer". A basis for the cutoff values used in Table 4 to determine "abnormal" AST, ALT, and GGT levels was not provided.
	Metric 8:	Reporting Bias	High	Odds ratios for abnormal liver function were provided with 95% confidence intervals, the number per exposure level, and significance when applicable.
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Cheng, T.J., Huang, M.L., You, N.C., Du, C.L., Chau, T.T. (1999). Abnormal liver function in workers exposed to low levels of ethylene dichloride and vinyl chloride monomer. Journal of Occupational and Environmental Medicine 41(12):1128-1133.
Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	AST, ALT, GGT, Hepatitis B virus surface antigen (HBsAg), and anti-hepatitis C virus antibody (anti-HCV).
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	200266

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Medium	The study reports information on potential confounders (age, hepatitis, BMI, alcohol use, and employment duration), and controls for hepatitis, BMI and alcohol consumption in the multiple logistic regression analyses. There is indirect evidence that appropriate adjustments were made.
	Metric 10:	Covariate Characterization	Medium	An interviewer administered the questionnaires to collect information about potential confounders and occupational history.
	Metric 11:	Co-exposure Counfounding	Low	Exposure to ethylene dichloride was evaluated in a vinyl chloride monomer (VCM) manufacturing facility, and VCM was also subsequently analyzed using personal and area sampling. Results for VCM exposure concentrations were provided. VCM is also suspected to cause liver damage.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design (cohort) was appropriate to assess the outcome of interest (”markers of liver damage”). Chi-squared (X2) test and multiple logistic regression were used for statistical analyses.
	Metric 13:	Statistical Power	Medium	The number of participants was adequate to detect an effect in the exposed populations, although power calculations were not provided. There were >20 participants in each group.
	Metric 14:	Reproducibility of Analyses	Low	A description of the logistic regression analysis was provided, however, study authors do not provide information on categorization of abnormal liver function.
	Metric 15:	Statistical Analysis	High	There were no identifiable logistic regression model assumption violations.
Domain 6: Other (if applicable) Considerations for Biomarker Selection and Measurement (Lakind et al. 2014)				
	Metric 16:	Use of Biomarker of Exposure	N/A	Biomarker of exposures were not assessed.
	Metric 17:	Effect Biomarker	High	This study uses aspartate aminotransferase, alanine aminotransferase, and y-glutamyltransferase as biomarkers of effect. While these no works cited to explain their connection to liver function, all three are well-known marker of liver function. Similarly, Hepatitis B virus surface antigen and antihepatitis C virus anitbody are also well-known measures of liver function and health.
	Metric 18:	Method Sensitivity	Low	No limit of detection information is provided for any of the effect biomarkers.
	Metric 19:	Biomarker Stability	Medium	While the study does not provide a lot of information regarding biomarker storage or stability, the authors do mention that venous blood used to detect biomarkers was stored at 4 degrees C.
	Metric 20:	Sample Contamination	Medium	No specific information regarding potential sample contamination was provided.
	Metric 21:	Method Requirements	Medium	Aspartate aminotransferase, alanine aminotransferase, and y-glutamyltransferase were analyzed using a Hitachi 7050 autoanalyzer. Hepatitis B virus surface antibody and antihepatitis C virus antibody were assessed with radioimmunoassay and enzyme-linked immunosorbent assay.

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Study Citation:	Cheng, T.J., Huang, M.L., You, N.C., Du, C.L., Chau, T.T. (1999). Abnormal liver function in workers exposed to low levels of ethylene dichloride and vinyl chloride monomer. Journal of Occupational and Environmental Medicine 41(12):1128-1133.
Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	AST, ALT, GGT, Hepatitis B virus surface antigen (HBsAg), and anti-hepatitis C virus antibody (anti-HCV).
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	200266

Domain	Metric	Rating	Comments
	Metric 22: Matrix Adjustment	N/A	No information on matrix adjustment was provided/available.

Additional Comments: A group of 251 male workers from 4 vinyl chloride monomer (VCM) manufacturing plants were included in this assessment to examine if occupational exposure to VCM and ethylene dichloride (EDC) "resulted in increased risk of liver damage" by examining AST, ALT, and GGT levels in the blood. Increased ORs for abnormal AST (>37 IU/L) and ALT (>41 IU/L) in the mod-EDC-low-VCM group (0.17-333.7 ppm EDC, 0.18-0.34 ppm VCM), compared with the low-EDC-low-VCM group, was reported. Exposure levels were measured using area and personal sampling, but the timing and duration of the sampling events were not reported.

Overall Quality Determination **Medium**

Study Citation:	Dosemeci, M., Cocco, P., Chow, W.H. (1999). Gender differences in risk of renal cell carcinoma and occupational exposures to chlorinated aliphatic hydrocarbons. American Journal of Industrial Medicine 36(1):54-59.
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	renal cell carcinoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	4697224

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	The details of the study design were reported elsewhere (Chow et al. 1994, HERO ID 701514). Brief details about the setting, date, number of eligible participants, and control matching were reported. Reasons for exclusions/non-participation were described with details by Chow et al. (1994).
	Metric 2:	Attrition	High	For the details of the study design and attrition of study subjects, the study authors referred to another publication by Chow et al., 1994. Chow et al. (1994) mentioned that at the end of the personal interview, the respondents were given a self-administered food-frequency questionnaire. Of the subjects interviewed for the study, 632 patients (79% of 796 eligible patients) and 653 control subjects (79% of 707 eligible control subjects) returned the diet questionnaire. A number of subjects, whose responses were considered unreliable, were excluded from the analysis, including 48 patients and three control subjects who had seven or more skipped food items or had questionable data and 50 patients whose next-of-kin respondent was not a spouse. Also excluded were two patients with unknown smoking status, since smoking is a risk factor.
	Metric 3:	Comparison Group	Medium	The cases were pulled from the Minnesota Cancer Surveillance System. Controls were selected from the general population of Minnesota; controls age 20-64 years were selected through random digital dialing and controls age 65-85 years were collected from files through the Health Care Financing Administration. Controls were age- and gender-stratified and were of the same race. Characteristics of cases and controls were not provided in the text or a table.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	High	Occupational histories including the most recent and usual occupation and industry, job activities, started-year and ended-year, and part-time/full-time status were collected. Occupations and industries were coded according to the standard occupational classification (SOC) and standard industrial classification (SIC) schemes. The National Cancer Institute developed job exposure matrices (JEM) for nine individual chlorinated aliphatic hydrocarbons (CAHCs), all CAHCs-combined, and all organic solvents-combined. These JEMs were merged with assigned SOC and SIC to determine the exposure status to these chemicals for each study subject. Application of the JEM was described elsewhere (Dosemeci et al. 1994, HERO ID 632334; Gomez et al. 1994, HERO ID 702154).
	Metric 5:	Exposure Levels	Medium	Details of the application of the JEM were described elsewhere (Dosemeci et al. 1994, HERO ID 632334; Gomez et al. 1994, HERO ID 702154). Dosemeci et al. (1994) described more details about that this study assigned three levels of probability (low, medium, high) to industries and occupations for chemical exposure levels.

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Study Citation:	Dosemeci, M., Cocco, P., Chow, W.H. (1999). Gender differences in risk of renal cell carcinoma and occupational exposures to chlorinated aliphatic hydrocarbons. American Journal of Industrial Medicine 36(1):54-59.
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	renal cell carcinoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	4697224

Domain	Metric		Rating	Comments
	Metric 6:	Temporality	Medium	Occupational questionnaires identified prior exposures based on reported recent and usual occupations as well as duration of employment. Outcome status was determined from registry data. The authors note that some occupational history was incomplete which may result in some uncertainty in regard to temporality.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Cases were identified as newly diagnosed and histologically confirmed renal cell carcinoma through the Minnesota Cancer Surveillance System and information about each participant was collected using a questionnaire. Validation was not specified.
	Metric 8:	Reporting Bias	Medium	A description of measured outcomes is reported and ORs were stratified by sex. Effect estimates are reported with a confidence interval. One table showed the total numbers of men and women respectively for each chemical, but numbers of cases/controls were not reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Appropriate adjustments were made in the final analysis, including age, gender, smoking, hypertension and the use of diuretics and/or anti-hypertension drugs, and BMI. Results were stratified by sex.
	Metric 10:	Covariate Characterization	Medium	Information about participants was collected using a questionnaire, and it includes potential confounders, e.g., smoking habits. Validation was not specified.
	Metric 11:	Co-exposure Counfounding	Medium	Co-exposures were identified through the job exposure matrices. Chemicals were evaluated individually and as a group.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen (case-control) was appropriate for the research question (renal cell carcinoma risk from occupational organic solvent exposure). Logistic regression models were used to estimate the relative risk and 95% CI.
	Metric 13:	Statistical Power	Low	Statistical power calculations were not provided. No significant effects were observed with 1,2-dichloroethane. The number of participated women to calculate odds ratio was inadequate to detect an effect in the participants for other chemicals or the combined risk, because it was very low.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis was brief, but is sufficient to understand precisely what has been done and to be conceptually reproducible with access to the analytic data.
	Metric 15:	Statistical Analysis	High	Model assumptions for logistic regression were met. The odds ratios were adjusted for age, smoking, hypertension status and/or use of diuretic and/or anti-hypertension drugs, and body mass index for men and women separately.

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Study Citation:	Dosemeci, M., Cocco, P., Chow, W.H. (1999). Gender differences in risk of renal cell carcinoma and occupational exposures to chlorinated aliphatic hydrocarbons. American Journal of Industrial Medicine 36(1):54-59.
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	renal cell carcinoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	4697224

Domain	Metric	Rating	Comments
Additional Comments:	A group of 438 cases (273 men and 165 women) were selected from the Minnesota Cancer Surveillance System that had been newly diagnosed with renal cell carcinoma. Controls included 687 participants (462 men and 225 women) age- and gender- stratified that were selected from either the general population of Minnesota (age 20-64 years) or from the Health Care Financing Administration files (age 65-85). No significant increase in the risk of renal cell carcinoma was observed with exposure to 1,2-dichloroethane among men or women separately, or for all participants exposed.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Dosemeci, M., Cocco, P., Chow, W.H. (1999). Gender differences in risk of renal cell carcinoma and occupational exposures to chlorinated aliphatic hydrocarbons. American Journal of Industrial Medicine 36(1):54-59.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	renal cell carcinoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	4697224

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	The details of the study design were reported elsewhere (Chow et al. 1994, HERO ID 701514). Brief details about the setting, date, number of eligible participants, and control matching were reported. Reasons for exclusions/non-participation were described with details by Chow et al. (1994).
	Metric 2:	Attrition	Medium	For the details of the study design and attrition of study subjects, the study authors referred to another publication by Chow et al., 1994. Chow et al. (1994) mentioned that at the end of the personal interview, the respondents were given a self-administered food-frequency questionnaire. Of the subjects interviewed for the study, 632 patients (79% of 796 eligible patients) and 653 control subjects (79% of 707 eligible control subjects) returned the diet questionnaire. A number of subjects, whose responses were considered unreliable, were excluded from the analysis, including 48 patients and three control subjects who had seven or more skipped food items or had questionable data and 50 patients whose next-of-kin respondent was not a spouse. Also excluded were two patients with unknown smoking status, since smoking is a risk factor.
	Metric 3:	Comparison Group	Medium	The cases were pulled from the Minnesota Cancer Surveillance System. Controls were selected from the general population of Minnesota; controls age 20-64 years were selected through random digital dialing and controls age 65-85 years were collected from files through the Health Care Financing Administration. Controls were age- and gender-stratified and were of the same race. Characteristics of cases and controls were not provided in the text or a table.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	High	Occupational histories including the most recent and usual occupation and industry, job activities, started-year and ended-year, and part-time/full-time status were collected. Occupations and industries were coded according to the standard occupational classification (SOC) and standard industrial classification (SIC) schemes. The National Cancer Institute developed job exposure matrices (JEM) for nine individual chlorinated aliphatic hydrocarbons (CAHCs), all CAHCs-combined, and all organic solvents-combined. These JEMs were merged with assigned SOC and SIC to determine the exposure status to these chemicals for each study subject. Application of the JEM was described elsewhere (Dosemeci et al. 1994, HERO ID 632334; Gomez et al. 1994, HERO ID 702154).
	Metric 5:	Exposure Levels	Medium	Details of the application of the JEM were described elsewhere (Dosemeci et al. 1994, HERO ID 632334; Gomez et al. 1994, HERO ID 702154). Dosemeci et al. (1994) described more details about that this study assigned three levels of probability (low, medium, high) to industries and occupations for chemical exposure levels.

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Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	renal cell carcinoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	4697224

Domain	Metric		Rating	Comments
	Metric 6:	Temporality	Medium	Occupational questionnaires identified prior exposures based on reported recent and usual occupations as well as duration of employment. Outcome status was determined from registry data. The authors note that some occupational history was incomplete which may result in some uncertainty in regard to temporality.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Cases were identified as newly diagnosed and histologically confirmed renal cell carcinoma through the Minnesota Cancer Surveillance System and information about each participant was collected using a questionnaire. Validation was not specified.
	Metric 8:	Reporting Bias	Medium	A description of measured outcomes is reported and ORs were stratified by sex. Effect estimates are reported with a confidence interval. One table showed the total numbers of men and women respectively for each chemical, but numbers of cases/controls were not reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Appropriate adjustments were made in the final analysis, including age, gender, smoking, hypertension and the use of diuretics and/or anti-hypertension drugs, and BMI. Results were stratified by sex.
	Metric 10:	Covariate Characterization	Medium	Information about participants was collected using a questionnaire, and it includes potential confounders, e.g., smoking habits. Validation was not specified.
	Metric 11:	Co-exposure Counfounding	Medium	Co-exposures were identified through the job exposure matrices. Chemicals were evaluated individually and as a group.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen (case-control) was appropriate for the research question (renal cell carcinoma risk from occupational organic solvent exposure). Logistic regression models were used to estimate the relative risk and 95% CI.
	Metric 13:	Statistical Power	Low	Statistical power calculations were not provided. No significant effects were observed with 1,2-dichloroethane. The number of participated women to calculate odds ratio was inadequate to detect an effect in the participants for other chemicals or the combined risk, because it was very low.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis was brief, but is sufficient to understand precisely what has been done and to be conceptually reproducible with access to the analytic data.
	Metric 15:	Statistical Analysis	High	Model assumptions for logistic regression were met. The odds ratios were adjusted for age, smoking, hypertension status and/or use of diuretic and/or anti-hypertension drugs, and body mass index for men and women separately.

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Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	renal cell carcinoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	4697224

Domain	Metric	Rating	Comments
Additional Comments:	A group of 438 cases (273 men and 165 women) were selected from the Minnesota Cancer Surveillance System that had been newly diagnosed with renal cell carcinoma. Controls included 687 participants (462 men and 225 women) age- and gender- stratified that were selected from either the general population of Minnesota (age 20-64 years) or from the Health Care Financing Administration files (age 65-85). No significant increase in the risk of renal cell carcinoma was observed with exposure to 1,2-dichloroethane among men or women separately, or for all participants exposed.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Garcia, E., Hurley, S., Nelson, D.O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health: A Global Access Science Source 14(1):14.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	breast cancer in females
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	3014082

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	A total of 112,378 women were included in this study out of 133,479 eligible female participants from the California Teacher Study cohort. A full description of the cohort is provided in Bernstein et al. 2002 (HERO ID 808446). Reasons for exclusion were provided. The reported information indicates that participant selection in or out of the study and participation was not likely to be biased.
	Metric 2:	Attrition	High	112,378/133,479 participants were included in the study. Exclusions were for the purpose of the study and analysis. Exclusion criteria were documented. Included participants had completed questionnaires. The California Cancer Registry is estimated to be 99% complete.
	Metric 3:	Comparison Group	Medium	There is only indirect evidence that groups are similar. Participants were recruited from the same eligible population with the same method of ascertainment. Comparisons were provided for participants with and without breast cancer. Characteristics between these two groups were generally similar. 5 Quintiles of exposure were used, and Q2-5 were compared with Q1.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	High	The Assessment System for Population Exposure Nationwide and the Human Exposure Model are used as part of the National-Scale Air Toxics Assessment produced by the EPA and was used to estimate ambient HAP concentrations for geographic locations. Methods are described online through the US EPA Assessment Methods.
	Metric 5:	Exposure Levels	Medium	The distribution of the NATA annual ambient concentration for each compound was plotted in Figure 1 using a box plot, and 5 Quintiles were used in the analyses.
	Metric 6:	Temporality	Medium	The follow-up period was from 1995-2011, and the NATA estimates were made in 2002 because it was approximately half way between the start and end of the follow-up period. However, it is unclear whether exposures fall within relevant exposure windows for the outcome of interest.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Annual linkage between the CTS cohort and the California Cancer Registry (CCR) was used to identify cases of invasive breast cancer. The CCR is estimated to be 99% complete. The case of invasive breast cancer was defined by ICD codes.

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Study Citation:	Garcia, E., Hurley, S., Nelson, D.O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health: A Global Access Science Source 14(1):14.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	breast cancer in females
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	3014082

Domain	Metric		Rating	Comments
	Metric 8:	Reporting Bias	Medium	A description of measured outcome is reported for adjustments by age and race, and effect estimates are reported with a 95% confidence interval. The measured outcomes using multiple comparisons were generally described in the text, but non-significant results were excluded from Table 3.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	The models were stratified by age and race. Additionally, adjustments were made for multiple comparisons among subsets of the participants (significant results reported in Table 3). Socioeconomic status (SES) of each participant was not evaluated, however, cohort SES characteristics were thought to be similar by study authors.
	Metric 10:	Covariate Characterization	Medium	Information about baseline characteristics for each participant was collected through a questionnaire. It is unknown if the questionnaire was validated.
	Metric 11:	Co-exposure Counfounding	Medium	A total of 37 compounds were identified as mammary gland carcinogens, but 13 were not included in this analysis. Thirteen compounds were excluded from the analysis due to insufficient variability (nine because they had the same value for all census tracts in the state of California; and four because they had less than 25% non-zero values). Ethylene dichloride (1,2-dichloroethane) was among the 24 compounds evaluated in this assessment, and evaluations for breast cancer were conducted for each of these 24 individual compounds.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen (prospective cohort) was appropriate for the research question (incidence of breast cancer). Cox proportional hazard models and SAS 9.3 were used in this assessment. Data analysis was described.
	Metric 13:	Statistical Power	Medium	Statistical power calculations were not provided. No significant effects were observed with ethylene dichloride (1,2-dichloroethane), however, this study utilized a large cohort, approximately 112,000 individuals. Distributions of chemicals of interest suggest there were sufficient numbers of participants in exposure subgroups.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to understand precisely what has been done and to be conceptually reproducible with access to the analytic data.
	Metric 15:	Statistical Analysis	High	The statistical models that were used were identified and described. ”No apparent violation of the underlying assumption of proportional hazards was detected”.

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Study Citation:	Garcia, E., Hurley, S., Nelson, D.O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health: A Global Access Science Source 14(1):14.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	breast cancer in females
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	3014082

Domain	Metric	Rating	Comments
Additional Comments:	A group of 112,378 female participants from the California Teacher Study cohort were assessed for their estimated exposure to ambient air pollutants, including ethylene dichloride (1,2-dichloroethane), and the incidence of invasive breast cancer. Air contaminant concentrations were estimated using the US EPA NATA and the ASPEN and HEM models. The approximate median concentration of 1,2-dichloroethane is between 1E-4 and 1E-2 (estimated from Figure 1). Exposures were categorized into 5 Quintiles, and compared against Quintile 1. No significant increase in the estimated hazard rate ratio for invasive breast cancer was observed with Quintile 2-5 exposure estimates for 1,2-dichloroethane, adjusted for age and race, when compared against Quintile 1, or when further adjusted using multiple comparisons.		

Overall Quality Determination High

* No biomarkers were identified for this evaluation.

Study Citation:	Garcia, E., Hurley, S., Nelson, D.O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health: A Global Access Science Source 14(1):14.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	breast cancer in females
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	3014082

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	A total of 112,378 women were included in this study out of 133,479 eligible female participants from the California Teacher Study cohort. A full description of the cohort is provided in Bernstein et al. 2002 (HERO ID 808446). Reasons for exclusion were provided. The reported information indicates that participant selection in or out of the study and participation was not likely to be biased.
	Metric 2:	Attrition	High	112,378/133,479 participants were included in the study. Exclusions were for the purpose of the study and analysis. Exclusion criteria were documented. Included participants had completed questionnaires. The California Cancer Registry is estimated to be 99% complete.
	Metric 3:	Comparison Group	Medium	There is only indirect evidence that groups are similar. Participants were recruited from the same eligible population with the same method of ascertainment. Comparisons were provided for participants with and without breast cancer. Characteristics between these two groups were generally similar. 5 Quintiles of exposure were used, and Q2-5 were compared with Q1.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	High	The Assessment System for Population Exposure Nationwide and the Human Exposure Model are used as part of the National-Scale Air Toxics Assessment produced by the EPA and was used to estimate ambient HAP concentrations for geographic locations. Methods are described online through the US EPA Assessment Methods.
	Metric 5:	Exposure Levels	Medium	The distribution of the NATA annual ambient concentration for each compound was plotted in Figure 1 using a box plot, and 5 Quintiles were used in the analyses.
	Metric 6:	Temporality	Medium	The follow-up period was from 1995-2011, and the NATA estimates were made in 2002 because it was approximately half way between the start and end of the follow-up period. However, it is unclear whether exposures fall within relevant exposure windows for the outcome of interest.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Annual linkage between the CTS cohort and the California Cancer Registry (CCR) was used to identify cases of invasive breast cancer. The CCR is estimated to be 99% complete. The case of invasive breast cancer was defined by ICD codes.
	Metric 8:	Reporting Bias	Medium	A description of measured outcome is reported for adjustments by age and race, and effect estimates are reported with a 95% confidence interval. The measured outcomes using multiple comparisons were generally described in the text, but non-significant results were excluded from Table 3.

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Study Citation:	Garcia, E., Hurley, S., Nelson, D.O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health: A Global Access Science Source 14(1):14.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	breast cancer in females
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	3014082

Domain	Metric		Rating	Comments
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	The models were stratified by age and race. Additionally, adjustments were made for multiple comparisons among subsets of the participants (significant results reported in Table 3). Socioeconomic status (SES) of each participant was not evaluated, however, cohort SES characteristics were thought to be similar by study authors.
	Metric 10:	Covariate Characterization	Medium	Information about baseline characteristics for each participant was collected through a questionnaire. It is unknown if the questionnaire was validated.
	Metric 11:	Co-exposure Counfounding	Medium	A total of 37 compounds were identified as mammary gland carcinogens, but 13 were not included in this analysis. Thirteen compounds were excluded from the analysis due to insufficient variability (nine because they had the same value for all census tracts in the state of California; and four because they had less than 25% non-zero values). Ethylene dichloride (1,2-dichloroethane) was among the 24 compounds evaluated in this assessment, and evaluations for breast cancer were conducted for each of these 24 individual compounds.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen (prospective cohort) was appropriate for the research question (incidence of breast cancer). Cox proportional hazard models and SAS 9.3 were used in this assessment. Data analysis was described.
	Metric 13:	Statistical Power	Medium	Statistical power calculations were not provided. No significant effects were observed with ethylene dichloride (1,2-dichloroethane), however, this study utilized a large cohort, approximately 112,000 individuals. Distributions of chemicals of interest suggest there were sufficient numbers of participants in exposure subgroups.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to understand precisely what has been done and to be conceptually reproducible with access to the analytic data.
	Metric 15:	Statistical Analysis	High	The statistical models that were used were identified and described. ”No apparent violation of the underlying assumption of proportional hazards was detected”.

Additional Comments: A group of 112,378 female participants from the California Teacher Study cohort were assessed for their estimated exposure to ambient air pollutants, including ethylene dichloride (1,2-dichloroethane), and the incidence of invasive breast cancer. Air contaminant concentrations were estimated using the US EPA NATA and the ASPEN and HEM models. The approximate median concentration of 1,2-dichloroethane is between 1E-4 and 1E-2 (estimated from Figure 1). Exposures were categorized into 5 Quintiles, and compared against Quintile 1. No significant increase in the estimated hazard rate ratio for invasive breast cancer was observed with Quintile 2-5 exposure estimates for 1,2-dichloroethane, adjusted for age and race, when compared against Quintile 1, or when further adjusted using multiple comparisons.

Overall Quality Determination High

* No biomarkers were identified for this evaluation.

Study Citation:	Guo, P., Yokoyama, K., Piao, F., Sakai, K., Khalequzzaman, M., Kamijima, M., Nakajima, T., Kitamura, F. (2013). Sick building syndrome by indoor air pollution in Dalian, China. International Journal of Environmental Research and Public Health 10(4):1489-1504.
Health Outcome(s):	sick building syndrome
Reported Health Effect(s):	The statistical analysis considers all subjective self-reported symptoms together (not segregated by health outcome) as a group health outcome –sick building syndrome. The study compared two conditions for each studied chemical: combined self-reported symptoms to no symptoms. Therefore, only one form 3 was completed.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1938385

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Residents of a housing estate of 3000 homes were invited to a community meeting to explain the purpose of the study and volunteers were invited to participate. It was not reported whether these volunteers were different from the overall eligible population.
	Metric 2:	Attrition	Low	Of the 70 families that agreed to participate, questionnaires were provided by 59. Reasons of uncompleted questionnaires were not fully provided, and there was no comparison between those who participated and those who did not.
	Metric 3:	Comparison Group	Low	The overall description of the analysis sample indicated a wide range of ages and lengths of stay at the current residence. Thus it is hard to know that subjects in all exposure groups were similar. In addition, the methods of selecting participants in all exposure groups were not fully reported. The numbers of male and female smokers were reported, respectively, but the smoking status and age were not controlled in the statistical analysis.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure concentrations for each home were obtained by diffusion sampling over 24 hrs in the bedroom, kitchen, and outdoors; temperature, the vertical height of samplers, and ventilation (hours windows left open) were reported. Samples were analyzed by GC/MS. The number of samples per home is unclear. The frequency of measurements for each house was not reported.
	Metric 5:	Exposure Levels	Low	The frequency of detection was not reported, so it is difficult to ascertain the actual exposure range. In addition, the reported exposure levels were median, geometric mean, and 95% CI, so they are inadequate to develop an exposure-response estimate.
	Metric 6:	Temporality	Uninformative	For 1,2-dichloroethane, the study evaluated self-reported symptoms in the past (”since they moved into their flats”) and their association with sampling conducted during the study; thus, exposure was measured after the outcome.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Low	Participants provided self-reported symptoms using a questionnaire. Study authors cited a previous study, Kamijima et al., 2005 (in Japanese, HERO ID 1598645) for further details on the questionnaire. It was not clear whether the questionnaire was validated.

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Study Citation:	Guo, P., Yokoyama, K., Piao, F., Sakai, K., Khalequzzaman, M., Kamijima, M., Nakajima, T., Kitamura, F. (2013). Sick building syndrome by indoor air pollution in Dalian, China. International Journal of Environmental Research and Public Health 10(4):1489-1504.
Health Outcome(s):	sick building syndrome
Reported Health Effect(s):	The statistical analysis considers all subjective self-reported symptoms together (not segregated by health outcome) as a group health outcome –sick building syndrome. The study compared two conditions for each studied chemical: combined self-reported symptoms to no symptoms. Therefore, only one form 3 was completed.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1938385

Domain	Metric		Rating	Comments
	Metric 8:	Reporting Bias	Low	The study only mentioned subjective symptoms in the abstract or methods. The abstract and method sections did not report the specific symptoms included in the questionnaire or whether the questionnaire was open-ended for symptoms. The questionnaire was cited to Kamijima et al. 2005 (in Japanese).
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	Comparisons were made separately by sex. The distribution of age and time spent living in residence differed greatly between those reporting symptoms and those not reporting symptoms. Smoking was indicated but not controlled for in the analysis. In short, the statistical analysis did not consider these three potential confounders, age, time spent living in residence, and smoking.
	Metric 10:	Covariate Characterization	Low	Covariates were presumably evaluated via a questionnaire that was cited to Kamijima et al. 2005 (in Japanese).
	Metric 11:	Co-exposure Counfounding	Low	The analysis did not account for other exposures. A number of other VOCs, HCHO, and NO2 were measured in the homes. The concentrations of several other VOCs and HCHO were much higher (5-30x) than 1,2-dichloroethane and may also be associated with these symptoms.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Low	The study design is best characterized as cross-sectional. Only one analysis to compare exposure concentrations between those with and without symptoms was adjusted for a confounder, sex, via stratification. Other potential confounders were not adjusted for. Study authors combine responses for symptoms reported before and during the sampling period in one statistical analysis, which may not reflect the relationship between symptoms and contaminants' exposure at each period.
	Metric 13:	Statistical Power	Medium	Statistical power was not reported. The number of participants was sufficient to detect a difference in median concentration between those with and without symptoms.
	Metric 14:	Reproducibility of Analyses	Medium	Study presents sufficient description of analysis (statistical methods) to be conceptually reproducible with access to the raw data.
	Metric 15:	Statistical Analysis	Low	Study uses a Wilcoxon's rank sum test to compare exposure concentrations in persons with and without symptoms; test for equal variance is not reported.

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Study Citation:	Guo, P., Yokoyama, K., Piao, F., Sakai, K., Khalequzzaman, M., Kamijima, M., Nakajima, T., Kitamura, F. (2013). Sick building syndrome by indoor air pollution in Dalian, China. International Journal of Environmental Research and Public Health 10(4):1489-1504.
Health Outcome(s):	sick building syndrome
Reported Health Effect(s):	The statistical analysis considers all subjective self-reported symptoms together (not segregated by health outcome) as a group health outcome –sick building syndrome. The study compared two conditions for each studied chemical: combined self-reported symptoms to no symptoms. Therefore, only one form 3 was completed.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1938385

Domain	Metric	Rating	Comments
Additional Comments:	Concentrations of VOCs (including 1,2-dichloroethane), HCHO, and NO2 were measured in the 59 homes of families that agreed to participate after being informed of the nature of the study. Participants completed questionnaires asking about symptoms since they moved into the homes and the concentrations of selected compounds were compared among men and women reporting any symptoms vs no symptoms. Concentrations of 1,2-dichloroethane in homes of people with symptoms were higher than in homes without. p-Dichlorobenzene was measured in the homes as well, but median concentration was <DL and no further analysis was made. Unacceptable due to selection bias, lack of confounding control, inadequate outcome characterization, and lack of temporality.		

Overall Quality Determination — Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Kernan, G.J., Ji, B.T., Dosemeci, M., Silverman, D.T., Balbus, J., Zahm, S.H. (1999). Occupational risk factors for pancreatic cancer: A case-control study based on death certificates from 24 U.S. states. American Journal of Industrial Medicine 36(2):260-270.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Death from pancreatic cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	194820

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	The National Cancer Institute, National Institute of Occupational Safety and Health, and the National Center for Health Statistics reviewed death certificates from 24 states to select cases from those that had died from pancreatic cancer and matched controls. Controls with cause of death related to the outcome of interest (i.e. pancreatic diseases) were excluded from the study. All key elements of the study design were reported.
	Metric 2:	Attrition	Medium	There was no direct evidence of subject loss or exclusion of subgroups from analyses. The authors provide the total number of cases and controls in the analysis. Case and control data were taken from a registry. It can be assumed that the data are complete for each subject.
	Metric 3:	Comparison Group	High	Controls were selected from the same pool of death certificates from 24 states that cases were selected from. Controls with cause of death related to the outcome of interest were eliminated. Differences in baseline characteristics were controlled for via matching, stratification, and adjustment.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure was assessed via occupation and industry data on death certificates. A job matrix was further applied to assess the likely levels of exposure. Probability and intensity of exposure were estimated across four levels for each occupation. Only employment captured on the death certificate could be considered. The exposure assessment needs exposure information before the job listed on the death certificates.
	Metric 5:	Exposure Levels	Medium	The study offers 4 levels of estimated probability and intensity of exposure (referent, low, medium, high).
	Metric 6:	Temporality	Medium	Exposure was determined by occupational and industry codes on death certificates and indicate that exposure would precede disease, however, the timing and latency period is less clear.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Causes of mortality were determined from death certificates for both cases and controls. Death certificates were drawn from death registries of participating states (n=24). Causes of death were coded using ICD-9 codes, and pancreatic cancer was identified as ICD 157.
	Metric 8:	Reporting Bias	Medium	Measured outcomes, effect estimates and confidence intervals are reported. Number of exposed cases is reported for each analysis, however the number of controls (exposed and unexposed) are not reported for analyses.

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Study Citation:	Kernan, G.J., Ji, B.T., Dosemeci, M., Silverman, D.T., Balbus, J., Zahm, S.H. (1999). Occupational risk factors for pancreatic cancer: A case-control study based on death certificates from 24 U.S. states. American Journal of Industrial Medicine 36(2):260-270.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Death from pancreatic cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	194820

Domain	Metric		Rating	Comments
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Potential confounders were accounted for in the following ways: matching (five year age group, state, race, and gender); adjustment in models (age, marital status, metropolitan, and residential status); and stratification (race and gender). Smoking was not included as a confounder.
	Metric 10:	Covariate Characterization	Medium	Data used to assess potential confounders was derived from death certificates, an adequate measure. However, no information about cigarette smoking and other lifestyle factors were available for adjustment in the analysis.
	Metric 11:	Co-exposure Counfounding	Medium	The variety of industries considered in the analysis diminishes concerns about co-exposures.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The case-control study design and statistical analysis methods were appropriate to assess the exposures/outcome of interest.
	Metric 13:	Statistical Power	Medium	This study had an adequate sample size to detect an effect (n for cases = 63,097; n for controls = 252,386).
	Metric 14:	Reproducibility of Analyses	Medium	The description of analysis was sufficient and would be reproducible.
	Metric 15:	Statistical Analysis	High	The model to calculate risk estimates was transparent.

Additional Comments: This case-control study examined the risk of death from pancreatic cancer in different occupational settings. Exposure was solely assessed using occupation/industry at time of death (reported on death certificate) and the application of a job matrix assessing likely levels of exposure for different positions. This means of estimating exposure may not fully represent a participant's exposure history. Additionally, the number of impacted participants (exposed cases) was inadequate to perform quality analyses for some exposure levels.

Overall Quality Determination High

* No biomarkers were identified for this evaluation.

Study Citation:	Kernan, G.J., Ji, B.T., Dosemeci, M., Silverman, D.T., Balbus, J., Zahm, S.H. (1999). Occupational risk factors for pancreatic cancer: A case-control study based on death certificates from 24 U.S. states. American Journal of Industrial Medicine 36(2):260-270.
Health Outcome(s):	Endocrine
Reported Health Effect(s):	Death from pancreatic cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	194820

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	The National Cancer Institute, National Institute of Occupational Safety and Health, and the National Center for Health Statistics reviewed death certificates from 24 states to select cases from those that had died from pancreatic cancer and matched controls. Controls with cause of death related to the outcome of interest (i.e. pancreatic diseases) were excluded from the study. All key elements of the study design were reported.
	Metric 2:	Attrition	Medium	There was no direct evidence of subject loss or exclusion of subgroups from analyses. The authors provide the total number of cases and controls in the analysis. Case and control data were taken from a registry. It can be assumed that the data are complete for each subject.
	Metric 3:	Comparison Group	High	Controls were selected from the same pool of death certificates from 24 states that cases were selected from. Controls with cause of death related to the outcome of interest were eliminated. Differences in baseline characteristics were controlled for via matching, stratification, and adjustment.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure was assessed via occupation and industry data on death certificates. A job matrix was further applied to assess the likely levels of exposure. Probability and intensity of exposure were estimated across four levels for each occupation. Only employment captured on the death certificate could be considered. The exposure assessment needs exposure information before the job listed on the death certificates.
	Metric 5:	Exposure Levels	Medium	The study offers 4 levels of estimated probability and intensity of exposure (referent, low, medium, high).
	Metric 6:	Temporality	Medium	Exposure was determined by occupational and industry codes on death certificates and indicate that exposure would precede disease, however, the timing and latency period is less clear.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Causes of mortality were determined from death certificates for both cases and controls. Death certificates were drawn from death registries of participating states (n=24). Causes of death were coded using ICD-9 codes, and pancreatic cancer was identified as ICD 157.
	Metric 8:	Reporting Bias	Medium	Measured outcomes, effect estimates and confidence intervals are reported. Number of exposed cases is reported for each analysis, however the number of controls (exposed and unexposed) are not reported for analyses.
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Kernan, G.J., Ji, B.T., Dosemeci, M., Silverman, D.T., Balbus, J., Zahm, S.H. (1999). Occupational risk factors for pancreatic cancer: A case-control study based on death certificates from 24 U.S. states. American Journal of Industrial Medicine 36(2):260-270.
Health Outcome(s):	Endocrine
Reported Health Effect(s):	Death from pancreatic cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	194820

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Medium	Potential confounders were accounted for in the following ways: matching (five year age group, state, race, and gender); adjustment in models (age, marital status, metropolitan, and residential status); and stratification (race and gender). Smoking was not included as a confounder.
	Metric 10:	Covariate Characterization	Medium	Data used to assess potential confounders was derived from death certificates, an adequate measure. However, no information about cigarette smoking and other lifestyle factors were available for adjustment in the analysis.
	Metric 11:	Co-exposure Counfounding	Medium	The variety of industries considered in the analysis diminishes concerns about co-exposures.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The case-control study design and statistical analysis methods were appropriate to assess the exposures/outcome of interest.
	Metric 13:	Statistical Power	Medium	This study had an adequate sample size to detect an effect (n for cases = 63,097; n for controls = 252,386).
	Metric 14:	Reproducibility of Analyses	Medium	The description of analysis was sufficient and would be reproducible.
	Metric 15:	Statistical Analysis	High	The model to calculate risk estimates was transparent.

Additional Comments: This case-control study examined the risk of death from pancreatic cancer in different occupational settings. Exposure was solely assessed using occupation/industry at time of death (reported on death certificate) and the application of a job matrix assessing likely levels of exposure for different positions. This means of estimating exposure may not fully represent a participant's exposure history. Additionally, the number of impacted participants (exposed cases) was inadequate to perform quality analyses for some exposure levels.

Overall Quality Determination High

* No biomarkers were identified for this evaluation.

Study Citation:	Niehoff, N.M., Gammon, M.D., Keil, A.P., Nichols, H.B., Engel, L.S., Sandler, D.P., White, A.J. (2019). Airborne mammary carcinogens and breast cancer risk in the Sister Study. Environment International 130:104897.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Breast cancer diagnosis (overall), tumor characteristics, and estrogen receptor positive (ER+) invasive breast cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5440630

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	Data from the Sister Study were used. The Sister Study is "a prospective cohort of 50,884 women from across the US who were ages 35–74 at enrollment (Sandler et al., 2017). Participants were recruited from 2003 to 2009 using a national advertising campaign in English and Spanish. Women were eligible for the Sister Study if they had a sister who had been diagnosed with breast cancer, but no prior breast cancer themselves."Exclusions from the study occurred for the following reasons:-breast cancer diagnosed before enrollment was complete, or did not have follow-up information (n = 163)-Residential address couldn't be geocoded (n = 1003, < 2%) - This is a small perecentage, but all of those who were excluded for this reason were from Puerto Rico, West Virginia, Missouri, or Oklahoma.Key elements of the study design are reported. There is some potential for selection bias, but based on the small percentage of those eligible who were excluded, participation was not likely to be substantially biased.
	Metric 2:	Attrition	High	Response rates in the overall Sister study remained over 91% over follow-up. Reasons for non-response were not reported, and characteristics of those lost to follow up were not reported or compared with those included, but 9% loss to follow-up is minimal.
	Metric 3:	Comparison Group	High	Differences in baseline characteristics of groups were considered as potential confounding variables.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	The EPA NATA database of census-tract level modeled air toxics data was used. The study authors note the potential for exposure misclassification: "Concentrations at the census tract level do not fully account for variation in an individual's daily activities that could lead to higher or lower exposure, and all women within a census tract are assigned the same concentration."
	Metric 5:	Exposure Levels	Medium	There were five quintiles of exposure, so there was a sufficient range and distribution of exposure.
	Metric 6:	Temporality	Medium	This is a prospective cohort study.Exposure data from 2005 were chosen because they represented the middle of the enrollment period (2003-2009).The study reported that "94% of women enrolled in 2005 or later, and thus the exposure assessment primarily predated enrollment for the majority of Sister Study participants."The six percent of women who had the potential to have the outcome before exposure was measured in 2005 are a concern. But sensitivity analyses were used to assess whether the associations changed when restricted to those who enrolled in 2005 or later.The authors note that the study is making assumptions about the relevant exposure windows - therefore the exposure window is not certain.

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Study Citation:	Niehoff, N.M., Gammon, M.D., Keil, A.P., Nichols, H.B., Engel, L.S., Sandler, D.P., White, A.J. (2019). Airborne mammary carcinogens and breast cancer risk in the Sister Study. Environment International 130:104897.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Breast cancer diagnosis (overall), tumor characteristics, and estrogen receptor positive (ER+) invasive breast cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5440630

Domain	Metric		Rating	Comments
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Women who reported a breast cancer diagnosis on the annual health updates or follow-up questionnaires were asked to provide additional diagnosis information, and to grant permission for the study to obtain medical records and pathology reports. Medical records were obtained for 81% of breast cancer diagnoses. Agreement between self-reported breast cancers and medical records was high (positive predictive value > 99%) (Sandler et al., 2017), so self-report was used when medical records were not available. Tumor characteristics (stage; histology; and estrogen receptor (ER) status) were abstracted from medical records, or self-reported.
	Metric 8:	Reporting Bias	High	A description of measured outcomes is reported. Effect estimates are reported with confidence intervals.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Covariates considered included age, race, BMI, residence type, education, and smoking status. Potential confounders were identified using DAGs and literature review. Appropriate considerations were made for potential confounders.
	Metric 10:	Covariate Characterization	Medium	”Most covariates were assessed by self-report at the baseline interview.””At baseline, women completed a computer-assisted telephone interview and written questionnaires.”Previous publications might describe whether the questionnaires were validated, but validation was not specified in this publication.
	Metric 11:	Co-exposure Counfounding	Medium	Co-exposures to other air pollutants were assessed, but at the census tract level.Multipollutant classification trees were used, which might provide useful qualitative information.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design (large prospective cohort) and analysis method (Cox proportional hazard single and multi-pollutant models accounting for potential confounders) were appropriate to assess the association between exposure and disease.
	Metric 13:	Statistical Power	Medium	The study had an adequate sample size (1975 cancer cases) and follow-up time (mean=8.4 years).
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to be conceptually reproducible.

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Study Citation:	Niehoff, N.M., Gammon, M.D., Keil, A.P., Nichols, H.B., Engel, L.S., Sandler, D.P., White, A.J. (2019). Airborne mammary carcinogens and breast cancer risk in the Sister Study. Environment International 130:104897.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Breast cancer diagnosis (overall), tumor characteristics, and estrogen receptor positive (ER+) invasive breast cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5440630

Domain	Metric	Rating	Comments
	Metric 15: Statistical Analysis	High	Hazard ratios and 95% confidence intervals (CIs) are reported "comparing index categories of exposure to exposures below the first quintile using Cox proportional hazards regression, with age as the time scale." The method of calculating the hazard ratios is transparent. The authors reported that "the proportional hazards assumption was evaluated by conducting a Wald test for an interaction between the continuous form of the air toxic measure and time." Censoring times and times at-risk are described.

Additional Comments: This was a well-conducted study of a large prospective cohort, but the measurement of exposure at the census-tract rather than the individual level is a limitation.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Sobel, W., Bond, G.G., Skowronski, B.J., Brownson, P.J., Cook, R.R. (1987). A soft tissue sarcoma case control study in a large multi-chemical manufacturing facility. Chemosphere 16(8-9):2095-2099.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	soft-tissue sarcoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1357737

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	From a pool of > 37,000 subjects who worked at least 1 year at chemical company between January 1940-December 1979, the study identified 14 people who died due to soft-cell sarcoma (via death certificate, medical records, or histopathology report). Referents were matched 9:1 with cases (126 matched controls).
	Metric 2:	Attrition	High	There was minimal subject exclusion from the analysis sample; one case could not be matched to controls and was excluded from analysis.
	Metric 3:	Comparison Group	High	Cases and controls were recruited from the same eligible population within the same time frame and matched on sex, race, year of birth and year of hire. Both cases and controls had to have worked ≥1 yr at the plant during the study period.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Work histories for cases and referents were coded to determine an individual's potential exposure to chemical of interest and reviewed by an industrial hygienist blinded to case status.
	Metric 5:	Exposure Levels	Low	Exposure was considered dichotomous, ever exposed or never exposed. There is no quantitative information on exposure levels or range of exposures.
	Metric 6:	Temporality	Low	Temporality of exposure and outcome is established. It is unclear if the interval between exposure and outcome is sufficient for soft tissue sarcoma outcomes.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	The soft-tissue sarcoma outcome was assessed by information provided by death certificates, medical records, and histopathology reports, but study authors did not report the proportions determined by each method.
	Metric 8:	Reporting Bias	High	All outcomes outlined were reported. Authors reported the number of cases and controls in the table. Maximum likelihood estimate ORs with respective 95 % confidence intervals were reported.
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Sobel, W., Bond, G.G., Skowronski, B.J., Brownson, P.J., Cook, R.R. (1987). A soft tissue sarcoma case control study in a large multi-chemical manufacturing facility. Chemosphere 16(8-9):2095-2099.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	soft-tissue sarcoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1357737

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Low	Controls were matched with cases on age, sex, year of hire and survival information. There is indirect evidence that the considerations were made to identify potential confounders through evaluation of medical records of cases and controls (various heritable syndromes, family history of cancer, history of lymphedema, steroids, throrotrast, foreign body implants, chronic extensive scarring, radiation therapy, and immunological defects). Identified confounders between cases and controls were not reported and it is unclear if adjustments for these confounders were included in the final analyses.
	Metric 10:	Covariate Characterization	High	Potential covariates were assessed through evaluation of work histories and medical records.
	Metric 11:	Co-exposure Counfounding	Low	The study documented 13 chemicals, known to be associated with soft-tissue sarcoma (according to NTP, 1983) that were used at the manufacturing facility at some point since 1940. The authors note that some individuals were exposed to multiple chemicals during their employment history and were counted multiple times in the analysis for different chemical exposures. Co-exposures to chemicals to not appear to be adjusted for in analysis.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Low	The study design was adequate to assess the association between exposure and the outcome of interest (soft-tissue sarcoma). The study authors noted they used programs developed by Rothman and Boice to calculate odds ratios with CI intervals; the statistical methods are not further described. The page containing the Rothman and Boice reference appears to be missing from the PDF (or the citation is missing).
	Metric 13:	Statistical Power	Low	Statistical power was not calculated. For 1,2-dichloroethane, there was one case and 6 controls included in the analysis, which was not adequate to detect and effect.
	Metric 14:	Reproducibility of Analyses	Low	The study calculated odd ratios, and 95% CIs were calculated using point estimates and chi from hypothesis testing. The study authors noted they used programs developed by Rothman and Boice to calculate odds ratios with 95% CIs; the statistical methods are not further described and there was no reference for the programs cited.
	Metric 15:	Statistical Analysis	Low	A description of analyses/assumptions was not reported.

Additional Comments: A case-control study of workers at a chemical production facility who worked at least 1 year between January 1940-December 1979 (n=37,000) investigated the incidence of deaths due to soft-tissue sarcoma. The study identified 14 people who died due to soft-tissue sarcoma (through death certificate, medical records, or histopathology reports). Cases were matched to controls based on sex, race, year of birth and year of hire. 13 chemicals, including 1,2-dichloroethane, associated with soft-tissue sarcoma were used at the facility; it does not appear that co-exposures were adjusted for in the analysis. Odds ratios and corresponding CIs were calculated. No significant association was found between exposure to 1,2-DCE and soft-tissue sarcoma.

Overall Quality Determination Medium

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Study Citation:	Sobel, W., Bond, G.G., Skowronski, B.J., Brownson, P.J., Cook, R.R. (1987). A soft tissue sarcoma case control study in a large multi-chemical manufacturing facility. Chemosphere 16(8-9):2095-2099.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	soft-tissue sarcoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1357737

Domain	Metric	Rating	Comments

* No biomarkers were identified for this evaluation.

Study Citation:	Sobel, W., Bond, G.G., Skowronski, B.J., Brownson, P.J., Cook, R.R. (1987). A soft tissue sarcoma case control study in a large multi-chemical manufacturing facility. Chemosphere 16(8-9):2095-2099.
Health Outcome(s):	Skin and Connective Tissue
Reported Health Effect(s):	soft-tissue sarcoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1357737

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	From a pool of > 37,000 subjects who worked at least 1 year at chemical company between January 1940-December 1979, the study identified 14 people who died due to soft-cell sarcoma (via death certificate, medical records, or histopathology report). Referents were matched 9:1 with cases (126 matched controls).
	Metric 2:	Attrition	High	There was minimal subject exclusion from the analysis sample; one case could not be matched to controls and was excluded from analysis.
	Metric 3:	Comparison Group	High	Cases and controls were recruited from the same eligible population within the same time frame and matched on sex, race, year of birth and year of hire. Both cases and controls had to have worked ≥1 yr at the plant during the study period.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Work histories for cases and referents were coded to determine an individual's potential exposure to chemical of interest and reviewed by an industrial hygienist blinded to case status.
	Metric 5:	Exposure Levels	Low	Exposure was considered dichotomous, ever exposed or never exposed. There is no quantitative information on exposure levels or range of exposures.
	Metric 6:	Temporality	Low	Temporality of exposure and outcome is established. It is unclear if the interval between exposure and outcome is sufficient for soft tissue sarcoma outcomes.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	The soft-tissue sarcoma outcome was assessed by information provided by death certificates, medical records, and histopathology reports, but study authors did not report the proportions determined by each method.
	Metric 8:	Reporting Bias	High	All outcomes outlined were reported. Authors reported the number of cases and controls in the table. Maximum likelihood estimate ORs with respective confidence intervals were reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	Controls were matched with cases on age, sex, year of hire and survival information. There is indirect evidence that that considerations were made to identify potential confounders through evaluation of medical records of cases and controls (various heritable syndromes, family history of cancer, history of lymphedema, steroids, throrotrast, foreign body implants, chronic extensive scarring, radiation therapy, and immunological defects). Identified confounders between cases and controls were not reported and it is unclear if adjustments for these confounders were included in the final analyses.

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Study Citation:	Sobel, W., Bond, G.G., Skowronski, B.J., Brownson, P.J., Cook, R.R. (1987). A soft tissue sarcoma case control study in a large multi-chemical manufacturing facility. Chemosphere 16(8-9):2095-2099.
Health Outcome(s):	Skin and Connective Tissue
Reported Health Effect(s):	soft-tissue sarcoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1357737

Domain	Metric		Rating	Comments
	Metric 10:	Covariate Characterization	High	Potential covariates were assessed through evaluation of work histories and medical records.
	Metric 11:	Co-exposure Counfounding	Low	The study documented 13 chemicals, known to be associated with soft-tissue sarcoma (according to NTP, 1983) that were used at the manufacturing facility at some point since 1940. The authors note that some individuals were exposed to multiple chemicals during their employment history and were counted multiple times in the analysis for different chemical exposures. Co-exposures to chemicals to not appear to be adjusted for in analysis.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Low	The study design was adequate to assess the association between exposure and the outcome of interest (soft-tissue sarcoma). The study authors noted they used programs developed by Rothman and Boice to calculate odds ratios with (95% CIs; the statistical methods are not further described. The page containing the Rothman and Boice reference appears to be missing from the PDF (or the citation is missing).
	Metric 13:	Statistical Power	Low	Statistical power was not calculated. For 1,2-dichloroethane, there was one case and 6 controls included in the analysis, which was not adequate to detect and effect.
	Metric 14:	Reproducibility of Analyses	Low	The study calculated odd ratios, and 95% CIs were calculated using point estimates and chi from hypothesis testing. The study authors noted they used programs developed by Rothman and Boice to calculate odds ratios with CI intervals; the statistical methods are not further described and there was no reference for the programs cited.
	Metric 15:	Statistical Analysis	Low	A description of analyses/assumptions was not reported.

Additional Comments: A case-control study of workers at a chemical production facility who worked at least 1 year between January 1940-December 1979 (n=37,000) investigated the incidence of deaths due to soft-tissue sarcoma. The study identified 14 people who died due to soft-tissue sarcoma (through death certificate, medical records, or histopathology reports). Cases were matched to controls based on sex, race, year of birth and year of hire. 13 chemicals, including 1,2-dichloroethane, associated with soft-tissue sarcoma were used at the facility; it does not appear that co-exposures were adjusted for in the analysis. Odds ratios and corresponding CIs were calculated. No significant association was found between exposure to 1,2-DCE and soft-tissue sarcoma.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Teta, M. J., Ott, M. G., Schnatter, A. R. (1991). An update of mortality due to brain neoplasms and other causes among employees of a petrochemical facility. Journal of Occupational Medicine 33(1):45-51.
Health Outcome(s):	Mortality
Reported Health Effect(s):	all cause mortality, gastrointestinal cancer mortality, respiratory system cancer mortality, kidney and other urinary organ cancer mortality, skin cancer mortality, brain cancer mortality, lymphatic and hematopoietic tissue cancer mortality, benign neoplasm mortality, heart disease mortality, and liver cirrhosis mortality.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200633, 1629047
HERO ID:	200633

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	The facility was described in some detail. All male employees working for one day or more between 1941 and 1983 were included. There may be some healthy worker effect in this population.
	Metric 2:	Attrition	High	Study authors reported that vital status was complete for 99% of the population, and death certificates were obtained for 99% of decedents.
	Metric 3:	Comparison Group	High	SMRs were calculated using age-, race-, and calendar year-specific mortality rates of males in the United States. All included employees were male.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	All employees were treated as exposed. Table 4 indicates that relatively few employees were employed in areas designated as 1,2-DCA work areas. There is potential for substantial exposure misclassification.
	Metric 5:	Exposure Levels	Low	All employed individuals were categorized as exposed, and the reference population was described as unexposed. This represents two levels of exposure. The distribution of exposure within the employed population is unclear.
	Metric 6:	Temporality	Medium	Employees were followed from 1950 (or date of first hire) through 1983. The relevant timing of exposure is not entirely clear; however, this represents a sufficiently long period of follow-up.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Mortality was tracked using company records, Social Security Administration records, and the National Death Index. Specific ICD codes and use of a nosologist were not described, but there was no evidence to suggest the method had poor validity.
	Metric 8:	Reporting Bias	High	SMRs were provided with confidence intervals in addition to observed and expected cases. The authors state they did not carry out regional specific SMRs due to the higher prevalence of neoplasms in the surrounding area.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	SMRs were restricted to males. Rates were age-, race-, and calendar period-specific. No consideration was made for smoking.
	Metric 10:	Covariate Characterization	Medium	Demographic information was obtained from employment records. This was not a validated method, but there was no evidence to suggest it was an invalid method.

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Study Citation:	Teta, M. J., Ott, M. G., Schnatter, A. R. (1991). An update of mortality due to brain neoplasms and other causes among employees of a petrochemical facility. Journal of Occupational Medicine 33(1):45-51.
Health Outcome(s):	Mortality
Reported Health Effect(s):	all cause mortality, gastrointestinal cancer mortality, respiratory system cancer mortality, kidney and other urinary organ cancer mortality, skin cancer mortality, brain cancer mortality, lymphatic and hematopoietic tissue cancer mortality, benign neoplasm mortality, heart disease mortality, and liver cirrhosis mortality.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200633, 1629047
HERO ID:	200633

Domain	Metric		Rating	Comments
	Metric 11:	Co-exposure Counfounding	Low	Several other occupational exposures linked to cancer mortality were present, including vinyl chloride, butanol, and other petrochemicals.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	This study design was appropriate for the research question. Authors utilized retrospective occupational cohort data to determine standardized mortality rates for cancer-specific mortalities.
	Metric 13:	Statistical Power	Medium	While power was not calculated, there were over 1350 deaths from 7849 employees which was adequate to detect robust effect estimates.
	Metric 14:	Reproducibility of Analyses	Low	Most details were provided; however, ICD codes used to determine and group cancer mortality diagnoses were not provided.
	Metric 15:	Statistical Analysis	High	No issues identified.

Additional Comments: This study utilized an occupational cohort to retrospectively evaluate elevated rates of cancer mortality among petrochemical plant workers. There were numerous potentially hazardous chemicals mentioned in the plant description which may lead to co-exposure. Additionally, it appears that only a moderate portion of workers may have been exposed to 1,2-DCA or worked in 1,2-DCA areas which may lead to some exposure misclassification and limit the study's ability to inform hazard on 1,2-DCA.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Cases in this case-control study were former Union Carbide Corporation (UCC) chemical plant employees in Texas City, Texas. Cases were identified through death certificate searches and tumor registries, and may have included individuals formerly employed at UCC whose cause of death was unknown to the company. Additionally, control deaths were stated to be pulled from corporate employee benefits department and through locally published obituary notices routinely screened by the medical department - it is possible to assume that cases were identified in a similar manner. The study identified cases of brain tumors by searching death certificates primarily, although tumor registries throughout the state of Texas were also searched. The study clarifies that it is possible that some cases were not found if they survived or died due to another cause - while this is likely to have impacted selection, there is no evidence that this would be differential by exposure status. Overall, there is limited information on the source population of workers from which cases were identified.
	Metric 2:	Attrition	Medium	Attrition is not discussed in the study, and outcome data appear to be complete. There was a large proportion of missing exposure data (roughly 50%) due to workers being employed in roles such as maintenance, where exposure to any chemical is possible but unknown. Analyses were run separately where these ”unknown” individuals were a) treated as exposed, b) treated as unexposed, or c) treated as unknown and thus excluded. The study only presents results for when these individuals were excluded but specifies that the first scenario resulted in increased exposure estimates for controls relative to cases.

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Study Citation:	Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
	Metric 3:	Comparison Group	Medium	The study identifies two series of control groups, selected from all former Union Carbide Corporation (UCC) employees. However, the total number of employees is not stated. Only those who were deceased were used as controls since they had known causes of death and could thus be verified as non-brain tumors. One group of controls excluded employees whose cause of death was due to any malignant neoplasm to allow for the possibility that a general chemical carcinogen may have been associated with cancers of other sites. The other group of controls included deaths from all causes; this included malignant neoplasms other than brain tumors. Both control groups had 80 male employees randomly selected from 450 deceased employees known to the company in June 1979. Control deaths were stated to be pulled from corporate employee benefits department and through locally published obituary notices routinely screened by the medical department - it is possible to assume that cases were identified in a similar manner. The study reports that cases were slightly more likely to have been employed for less than 10 years than controls - the study attributes this in part to the fact that employees whose deaths were known to the company were more likely to have worked for longer - regardless the mean number of years employed was similar between cases and controls. However, cases were more likely to have been terminated from their job for reasons other than death, disability, or retirement (quitting, being fired, etc.), were generally younger at hire, and were less likely to survive to their 70th birthday. None of these factors are controlled for in statistical analyses - however, since controls and cases were pulled from the same population, there is indirect evidence that the groups were similar.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was determined based on official employment records. Records included job title and department assignment codes for each employment from date of hire to date of termination. For each unique department code, UCC and NIOSH industrial hygienists identified principal chemicals used or produced at any time in the history of the plant and correlated those with individual departments. This assessment was not performed on a year-by-year basis due to concerns for recall bias for longer-term employees where less detailed records were kept. An employee was categorized as ”exposed” to 1,2-dichloroethane if they ever worked in a department associated with that chemical. An ”unknown” exposure group was also created to account for employees who had only worked in departments for which no specific chemical could be identified.
	Metric 5:	Exposure Levels	Low	The study does not report any quantitative information and only splits exposure into ”exposed”, ”unexposed”, and ”unknown”.
	Metric 6:	Temporality	High	In this study exposure is confirmed to occur before the outcome is measured. The study reports latency periods, with subjects dichotomized into less than 15 years of latency or more than 15 years of latency. The majority of cases and controls had a latency of greater than 15 years, which is sufficiently long for brain tumors.

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Study Citation:	Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Cases were identified through death certificate searches and partially through tumor registries in the state of Texas. Case validation was performed by NIOSH, and 5 different levels of confirmation were reported: 1) tissue specimen interpreted by the Armed Forces Institute of Pathology; 2) autopsy report; 3) histopathology report; 4) clinical diagnosis from hospital record; 5) dearth certificate diagnosis. Codes 1-3 were considered to be ”confirmed” cases of brain tumors, while 4-5 were considered unconfirmed. 5/21 cases were only evaluated using ”unconfirmed methods”, meaning there is likely a high amount of accuracy in roughly 75% of cases. While no case validation is reported for controls, the study specifies that only controls who had died and thus could be confirmed to be non-brain tumors were included.
	Metric 8:	Reporting Bias	Medium	All primary and secondary outcomes that are outlined in the methods are reported in the results. However, the only statistical outcome of their analysis were unadjusted p-values that were not reported and were just described qualitatively.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	The only statistical analysis performed were Mantel-Haenszel chi-squared tests, which did not allow for confounder adjustment. The study does not present a distribution of potential confounders by exposure status but by case/control status. Several variables, such as reason for termination, age at hire, and age at death were significantly different between cases and controls and were not accounted for in statistical modeling. The study explains that these differences are not likely to have any epidemiologic significance and appear to be relatively small differences.
	Metric 10:	Covariate Characterization	Medium	While the study does not explain where they obtained covariate information, it is reasonable to assume that they gathered the information from company records.
	Metric 11:	Co-exposure Counfounding	Low	The study assesses a wide range of other potential occupational co-exposures. While these co-exposures are not adjusted for in any statistical models, effect estimates are presented separately for benzene, diethyl sulfate, ethylene oxide, and vinyl chloride. The distribution of co-exposures across cases and controls is demonstrated to be mostly balanced by comparing proportions of exposed/unexposed between cases and controls. The only notable instance of imbalance is for benzene, where 11.1% of cases were exposed whereas 37.9% of all controls and 19.2% of non-neoplasm related controls were exposed.
Domain 5: Analysis				

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Study Citation:	Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	The study chose a case-control design, which was appropriate to study the rare disease of brain tumors and its association with occupational exposures. The only statistical analysis conducted is a Mantzel-Haenszel chi-squared test, but there is no reason to suggest that this would be inappropriate.
	Metric 13:	Statistical Power	Medium	The study does not calculate statistical power, but the number of cases (n=21) and controls (n=80 in each analysis) is likely sufficient to detect an effect.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to understand what was done and could be reproduced given access to the analytic data.
	Metric 15:	Statistical Analysis	High	The only statistical analysis conducted is a Mantel-Haenszel chi-squared test, and all assumptions were met. The statistical process is transparent.

Additional Comments: This case-control study pulled deceased former employees of the Union Carbide Corporation in Texas City, Texas. The study examined dichotomous exposure to a wide range of occupational exposures, including 1,2-dichloroethane, in relation to brain tumor cases. There is no quantitative estimate of exposure. The only statistical analysis in the study is a Mantel-Haenszel chi-squared test statistic and no statistically significant differences in exposure between cases and controls were observed. The fact that there are no effect estimates, no adjustment for confounders, and no quantitative exposure estimates limits the usefulness of this paper.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Cases in this case-control study were former Union Carbide Corporation (UCC) chemical plant employees in Texas City, Texas. Cases were identified through death certificate searches and tumor registries, and may have included individuals formerly employed at UCC whose cause of death was unknown to the company. Additionally, control deaths were stated to be pulled from corporate employee benefits department and through locally published obituary notices routinely screened by the medical department - it is possible to assume that cases were identified in a similar manner. The study identified cases of brain tumors by searching death certificates primarily, although tumor registries throughout the state of Texas were also searched. The study clarifies that it is possible that some cases were not found if they survived or died due to another cause - while this is likely to have impacted selection, there is no evidence that this would be differential by exposure status. Overall, there is limited information on the source population of workers from which cases were identified.
	Metric 2:	Attrition	Medium	Attrition is not discussed in the study, and outcome data appear to be complete. There was a large proportion of missing exposure data (roughly 50%) due to workers being employed in roles such as maintenance, where exposure to any chemical is possible but unknown. Analyses were run separately where these ”unknown” individuals were a) treated as exposed, b) treated as unexposed, or c) treated as unknown and thus excluded. The study only presents results for when these individuals were excluded but specifies that the first scenario resulted in increased exposure estimates for controls relative to cases.

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Study Citation:	Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
	Metric 3:	Comparison Group	Medium	The study identifies two series of control groups, selected from all former Union Carbide Corporation (UCC) employees. However, the total number of employees is not stated. Only those who were deceased were used as controls since they had known causes of death and could thus be verified as non-brain tumors. One group of controls excluded employees whose cause of death was due to any malignant neoplasm to allow for the possibility that a general chemical carcinogen may have been associated with cancers of other sites. The other group of controls included deaths from all causes; this included malignant neoplasms other than brain tumors. Both control groups had 80 male employees randomly selected from 450 deceased employees known to the company in June 1979. Control deaths were stated to be pulled from corporate employee benefits department and through locally published obituary notices routinely screened by the medical department - it is possible to assume that cases were identified in a similar manner. The study reports that cases were slightly more likely to have been employed for less than 10 years than controls - the study attributes this in part to the fact that employees whose deaths were known to the company were more likely to have worked for longer - regardless the mean number of years employed was similar between cases and controls. However, cases were more likely to have been terminated from their job for reasons other than death, disability, or retirement (quitting, being fired, etc.), were generally younger at hire, and were less likely to survive to their 70th birthday. None of these factors are controlled for in statistical analyses - however, since controls and cases were pulled from the same population, there is indirect evidence that the groups were similar.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was determined based on official employment records. Records included job title and department assignment codes for each employment from date of hire to date of termination. For each unique department code, UCC and NIOSH industrial hygienists identified principal chemicals used or produced at any time in the history of the plant and correlated those with individual departments. This assessment was not performed on a year-by-year basis due to concerns for recall bias for longer-term employees where less detailed records were kept. An employee was categorized as ”exposed” to 1,2-dichloroethane if they ever worked in a department associated with that chemical. An ”unknown” exposure group was also created to account for employees who had only worked in departments for which no specific chemical could be identified.
	Metric 5:	Exposure Levels	Low	The study does not report any quantitative information and only splits exposure into ”exposed”, ”unexposed”, and ”unknown”.
	Metric 6:	Temporality	High	In this study exposure is confirmed to occur before the outcome is measured. The study reports latency periods, with subjects dichotomized into less than 15 years of latency or more than 15 years of latency. The majority of cases and controls had a latency of greater than 15 years, which is sufficiently long for brain tumors.

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Study Citation:	Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Cases were identified through death certificate searches and partially through tumor registries in the state of Texas. Case validation was performed by NIOSH, and 5 different levels of confirmation were reported: 1) tissue specimen interpreted by the Armed Forces Institute of Pathology; 2) autopsy report; 3) histopathology report; 4) clinical diagnosis from hospital record; 5) dearth certificate diagnosis. Codes 1-3 were considered to be ”confirmed” cases of brain tumors, while 4-5 were considered unconfirmed. 5/21 cases were only evaluated using ”unconfirmed methods”, meaning there is likely a high amount of accuracy in roughly 75% of cases. While no case validation is reported for controls, the study specifies that only controls who had died and thus could be confirmed to be non-brain tumors were included.
	Metric 8:	Reporting Bias	Medium	All primary and secondary outcomes that are outlined in the methods are reported in the results. However, the only statistical outcome of their analysis were unadjusted p-values that were not reported and were just described qualitatively.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	The only statistical analysis performed were Mantel-Haenszel chi-squared tests, which did not allow for confounder adjustment. The study does not present a distribution of potential confounders by exposure status but by case/control status. Several variables, such as reason for termination, age at hire, and age at death were significantly different between cases and controls and were not accounted for in statistical modeling. The study explains that these differences are not likely to have any epidemiologic significance and appear to be relatively small differences.
	Metric 10:	Covariate Characterization	Medium	While the study does not explain where they obtained covariate information, it is reasonable to assume that they gathered the information from company records.
	Metric 11:	Co-exposure Counfounding	Low	The study assesses a wide range of other potential occupational co-exposures. While these co-exposures are not adjusted for in any statistical models, effect estimates are presented separately for benzene, diethyl sulfate, ethylene oxide, and vinyl chloride. The distribution of co-exposures across cases and controls is demonstrated to be mostly balanced by comparing proportions of exposed/unexposed between cases and controls. The only notable instance of imbalance is for benzene, where 11.1% of cases were exposed whereas 37.9% of all controls and 19.2% of non-neoplasm related controls were exposed.
Domain 5: Analysis				

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Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	The study chose a case-control design, which was appropriate to study the rare disease of brain tumors and its association with occupational exposures. The only statistical analysis conducted is a Mantzel-Haenszel chi-squared test, but there is no reason to suggest that this would be inappropriate.
	Metric 13:	Statistical Power	Medium	The study does not calculate statistical power, but the number of cases (n=21) and controls (n=80 in each analysis) is likely sufficient to detect an effect.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to understand what was done and could be reproduced given access to the analytic data.
	Metric 15:	Statistical Analysis	High	The only statistical analysis conducted is a Mantel-Haenszel chi-squared test, and all assumptions were met. The statistical process is transparent.

Additional Comments: This case-control study pulled deceased former employees of the Union Carbide Corporation in Texas City, Texas. The study examined dichotomous exposure to a wide range of occupational exposures, including 1,2-dichloroethane, in relation to brain tumor cases. There is no quantitative estimate of exposure. The only statistical analysis in the study is a Mantel-Haenszel chi-squared test statistic and no statistically significant differences in exposure between cases and controls were observed. The fact that there are no effect estimates, no adjustment for confounders, and no quantitative exposure estimates limits the usefulness of this paper.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	Urinary system cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	Urinary system cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	Urinary system cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Immune/Hematological
Reported Health Effect(s):	Lymphatic and hematopoietic tissue cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Health Outcome(s):	Immune/Hematological
Reported Health Effect(s):	Lymphatic and hematopoietic tissue cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Health Outcome(s):	Immune/Hematological
Reported Health Effect(s):	Lymphatic and hematopoietic tissue cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Other cancers (not specified)
Reported Health Effect(s):	Other cancers (not specified)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Health Outcome(s):	Other cancers (not specified)
Reported Health Effect(s):	Other cancers (not specified)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Other cancers (not specified)
Reported Health Effect(s):	Other cancers (not specified)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Mortality
Reported Health Effect(s):	All-cause mortality
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Vital status was tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Medium	Death rates among unit employees were compared to death rates in the U.S. population adjusted for age and gender. Demographics of the exposed workers are not provided; therefore, it is not clear whether additional adjustment for race may have been appropriate. No justification is provided for the choice of the entire U.S. population as the comparison group. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis. Additional analyses are conducted limiting workers to those with the greatest likelihood of exposure (i.e., those working in jobs with high likelihood of contact with chemicals for more than a year, those working for the full year of 1979 during which chemical exposures were most frequently reported); these smaller groups are also compared to the unexposed general population.
	Metric 6:	Temporality	High	Temporality was established due to the longitudinal design and the use of mortality as the outcome. Exposures occurred between 1979 and 1987 and follow-up for vital status was conducted through 2003.
Domain 3: Outcome Assessment				

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Mortality
Reported Health Effect(s):	All-cause mortality
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Medium	The study did not provide information on how mortality was assessed either in the exposed population or in the comparison population; use of death certificates is implied but not stated.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected deaths are reported, but SIRs and 95% confidence intervals are not provided.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Comparisons of observed versus expected deaths were adjusted for age and gender. Demographics of the exposed workers are not provided; therefore, it is not clear whether additional adjustment for race may have been appropriate.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records or death records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed deaths among a population of exposed workers compared to expected deaths among the U.S. population, adjusted for age and gender.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected deaths; no SIR was provided. Expected death rates were adjusted for age and gender.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Mortality
Reported Health Effect(s):	All-cause mortality
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	All cancer (excluding non-melanoma skin cancer), digestive system cancer, colorectal cancer, respiratory cancer, prostate cancer, urinary system cancer, lymphatic and hematopoietic tissue cancer, other cancers (not specified)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	All cancer (excluding non-melanoma skin cancer), digestive system cancer, colorectal cancer, respiratory cancer, prostate cancer, urinary system cancer, lymphatic and hematopoietic tissue cancer, other cancers (not specified)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	All cancer (excluding non-melanoma skin cancer), digestive system cancer, colorectal cancer, respiratory cancer, prostate cancer, urinary system cancer, lymphatic and hematopoietic tissue cancer, other cancers (not specified)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Gastrointestinal
Reported Health Effect(s):	Digestive system cancer, colorectal cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Gastrointestinal
Reported Health Effect(s):	Digestive system cancer, colorectal cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Health Outcome(s):	Gastrointestinal
Reported Health Effect(s):	Digestive system cancer, colorectal cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Lung/Respiratory
Reported Health Effect(s):	Respiratory cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Health Outcome(s):	Lung/Respiratory
Reported Health Effect(s):	Respiratory cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Lung/Respiratory
Reported Health Effect(s):	Respiratory cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Prostate cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Prostate cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Prostate cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Male workers who had ever been assigned to the chlorohydrin unit between 1 January 1940 and 31 December 1967 at Union Carbide's South Charleston plant were enrolled and matched to the US National Death Index. Status on 5 workers could not be identified. Information on how workers were matched to death index was not specified.
	Metric 2:	Attrition	Medium	Rate of inclusion/participation was very high, as records were able to be matched for 98% of participants. Medium rating given because information on how participants whose vital status was not known was not specified.
	Metric 3:	Comparison Group	Uninformative	Unacceptable rating given because SMRs were calculated based on expected deaths from a reference population matched on sex, but not age.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Exposure was assessed based on duration of work in the plant. No information is provided on exposure levels, and a JEM was not used.
	Metric 5:	Exposure Levels	Uninformative	No information provided on levels of exposure.
	Metric 6:	Temporality	High	Temporality is well established; person-years stopped accumulating in 1967 and outcome was assessed beginning at that time.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar period, and interval since assignments, but distribution of these covariates was not reported.
	Metric 10:	Covariate Characterization	Medium	Information on covariate characterization not provided, but the selected covariates (age, calendar period, and interval since assignments) were likely extracted from employee records and unlikely to be largely problematic
	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.

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Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Study design was appropriate for the research method. Statistical methods were also appropriate.
	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.
	Metric 14:	Reproducibility of Analyses	Medium	Methods are well-enough described that study could be adequately reproduced.
	Metric 15:	Statistical Analysis	High	SMRs calculated based on US general population mortality for white males through 1988. RRs were ”evaluated over levels of duration of assignment to the chlorohydrin unit, stratified by age, calendar year, and interval since first assignment to the chlorohydrin unit”.

Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

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	Metric 3:	Comparison Group	Uninformative	Unacceptable rating given because SMRs were calculated based on expected deaths from a reference population matched on sex, but not age.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Exposure was assessed based on duration of work in the plant. No information is provided on exposure levels, and a JEM was not used.
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	Metric 6:	Temporality	High	Temporality is well established; person-years stopped accumulating in 1967 and outcome was assessed beginning at that time.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar period, and interval since assignments, but distribution of these covariates was not reported.
	Metric 10:	Covariate Characterization	Medium	Information on covariate characterization not provided, but the selected covariates (age, calendar period, and interval since assignments) were likely extracted from employee records and unlikely to be largely problematic
	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.
Domain 5: Analysis				

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	Metric 14:	Reproducibility of Analyses	Medium	Methods are well-enough described that study could be adequately reproduced.
	Metric 15:	Statistical Analysis	High	SMRs calculated based on US general population mortality for white males through 1988. RRs were ”evaluated over levels of duration of assignment to the chlorohydrin unit, stratified by age, calendar year, and interval since first assignment to the chlorohydrin unit”.

Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

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	Metric 3:	Comparison Group	Uninformative	Unacceptable rating given because SMRs were calculated based on expected deaths from a reference population matched on sex, but not age.
Domain 2: Exposure Characterization				
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Domain 3: Outcome Assessment				
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	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar period, and interval since assignments, but distribution of these covariates was not reported.
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	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.
Domain 5: Analysis				

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Additional Comments: None

Overall Quality Determination Uninformative

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Domain 4: Potential Confounding / Variability Control				
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Domain 5: Analysis				

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Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

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Domain 5: Analysis				

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Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

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Additional Comments: None

Overall Quality Determination Uninformative

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Additional Comments: None

Overall Quality Determination Uninformative

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	Metric 6:	Temporality	High	Temporality is well established; person-years stopped accumulating in 1967 and outcome was assessed beginning at that time.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar period, and interval since assignments, but distribution of these covariates was not reported.
	Metric 10:	Covariate Characterization	Medium	Information on covariate characterization not provided, but the selected covariates (age, calendar period, and interval since assignments) were likely extracted from employee records and unlikely to be largely problematic
	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.
Domain 5: Analysis				

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Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Study design was appropriate for the research method. Statistical methods were also appropriate.
	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.
	Metric 14:	Reproducibility of Analyses	Medium	Methods are well-enough described that study could be adequately reproduced.
	Metric 15:	Statistical Analysis	High	SMRs calculated based on US general population mortality for white males through 1988. RRs were ”evaluated over levels of duration of assignment to the chlorohydrin unit, stratified by age, calendar year, and interval since first assignment to the chlorohydrin unit”.

Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Bove, F. J. (1996). Public drinking water contamination and birthweight, prematurity, fetal deaths, and birth defects. Toxicology and Industrial Health 12(2):255-266.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	200239

Domain	Metric	Rating	Comments
Domain 1: Study Participation			
Metric 1:	Participant Selection	Medium	This cross-sectional study (n=80,938) included all registered singleton live births and fetal deaths (>20 weeks' gestation) in 1985-88 in 75 New Jersey towns located in 4 counties with "some" water supplies contaminated with substances of interest and where: (i) residents were "mostly" served by public water systems; and (ii) births occurred "mostly" in state. Estimated proportions of residents served by public water systems, and of pregnancies/births captured, were not described. However, the inclusion of all eligible registered births, fetal deaths, and birth defects, as well as the selection of towns without knowledge of birth outcome prevalence, limited the likelihood of selection bias.
Metric 2:	Attrition	Medium	All registered births and fetal deaths were included. Attrition due to missing values for multiple variables was not quantified and is therefore uncertain. However, attrition was likely modest as the proportion of missing values for individual variables was relatively low: (i) ~6% of subjects were excluded from analyses of outcomes such as preterm birth due to invalid or missing gestational ages; and (ii) other covariates evaluated as confounders had up to 4.9% missing values.
Metric 3:	Comparison Group	High	After excluding plural pregnancies and chromosomal abnormalities, all registered live births during the study period in the areas included without the outcomes of interest were included in the comparison group. This comprehensive approach limited the potential for bias. Chromosomal abnormalities were not included as outcomes as they were not hypothesized to be associated with the exposures under study but were appropriately excluded given their uncertain etiology.
Domain 2: Exposure Characterization			

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Study Citation:	Bove, F. J. (1996). Public drinking water contamination and birthweight, prematurity, fetal deaths, and birth defects. Toxicology and Industrial Health 12(2):255-266.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	200239

Domain	Metric		Rating	Comments
	Metric 4:	Measurement of Exposure	Medium	Along with several other contaminants, residential drinking water exposure to 1,2-dichloroethane (as well as 1,1,1-trichloroethane and 'total dichloroethylenes') – was assigned based on maternal town of residence at birth. Exposure estimates were calculated using the average of water company sampling reports during the first trimester (for birth defects and fetal death) or the duration of pregnancy (for other outcomes). Detection limits and data availability were not specified in detail but were described as below 1 ppb, with reporting compliance >85%. A minimum of 1 sample per 6-month interval was required; variability in the number of measures available across water systems and towns was not described. Additional sources of measurement error included: changes in residence during pregnancy; water from alternate sources (ex. private wells, bottles, workplaces); variability in residential contaminant levels vs measured samples; unknown levels of tap water intake; and errors in estimated dermal and inhalation exposure while bathing or showering. While the extent of exposure misclassification is uncertain, there is no evidence to suggest it was differential rather than random.
	Metric 5:	Exposure Levels	Medium	Due to the high proportion of measures below detection limits, analyses relating exposure to health outcomes used only 2 categories for each of the chlorinated solvents of interest: cutoffs close to detection limits were used to define elevated exposure. Proportions defined as having elevated exposure was low (1.8% had 1,1-dichloroethylene ≥1 ppb). An important concern is that relatively low levels of exposure to these contaminants from sources other than residential drinking water, for which data were not available, could potentially have resulted in considerable misclassification.
	Metric 6:	Temporality	High	Exposure levels were assigned based on contaminant exposures estimated during: (i) the first trimester for analyses of birth defects and fetal deaths; and (ii) the duration of pregnancy for other pregnancy outcomes.

Domain 3: Outcome Assessment

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Study Citation:	Bove, F. J. (1996). Public drinking water contamination and birthweight, prematurity, fetal deaths, and birth defects. Toxicology and Industrial Health 12(2):255-266.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	200239

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcomes included measures of birthweight (continuous among term births, low term birthweight, very low birthweight), prematurity, fetal death, and congenital anomalies in live births or fetal deaths. The anomalies analyzed included defects of the central nervous system, neural tube, oral cleft, total cardiac, major cardiac, ventricular septum, and any surveillance defect excluding chromosomal defects. All outcomes were identified using birth certificates, fetal death certificates (>20 weeks' gestation), and the NJ congenital birth defect registry (ICD codes provided). These registry data are likely to be sufficiently valid for late pregnancy outcomes. However, their limited ability to capture early pregnancy losses is a weakness. The sample included only 594 fetal deaths (less than 1% of the >80,0000 sample). Typical estimates are that 10-20%, of recognized pregnancies ending in losses. Moreover, developmental defects contributing to early pregnancy losses were also not captured. A further limitation is that that potentially etiologically heterogeneous preterm birth types were analyzed together, as these data did not distinguish premature rupture of membranes vs idiopathic prematurity.
	Metric 8:	Reporting Bias	Medium	Models were constructed only for contaminants with associations > 1.0, and tables included only associations with odds ratios ≥1.5. No clear rationale was provided. Several positive odds ratios below the 1.5 cutoff were described in the results text (without confidence intervals), but no null/negative odds ratios were presented or described.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Potential confounding by maternal race, education, parity, and prior pregnancy loss, along with infant sex (for birth outcomes) and adequacy of prenatal care, was examined. Gestational age was addressed by analyzing birthweight among full term births, term low birth weight, and small size for gestational age. Only fully adjusted models were presented. In a companion case-control study (with low participation rates), adjustment for other variables not available on birth certificates (ex. maternal smoking, occupational exposures, medical history, and gestational weight gain) did not influence associations with other studied contaminants. This separate study reduces concerns for important confounding bias, but confounding cannot be ruled out.
	Metric 10:	Covariate Characterization	Medium	Data on covariates came from registry data: birth certificates, fetal death certificates, and the NJ congenital birth defects registry.
	Metric 11:	Co-exposure Counfounding	Medium	Co-exposure confounding by drinking water trihalomethane concentrations was evaluated. There was no evidence to suggest substantial confounding by this or other co-exposures.
Domain 5: Analysis				

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Study Citation:	Bove, F. J. (1996). Public drinking water contamination and birthweight, prematurity, fetal deaths, and birth defects. Toxicology and Industrial Health 12(2):255-266.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	200239

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Methods were appropriate. The study used logistic regression models to estimate odds ratios and confidence intervals for dichotomous outcomes, and linear regression for analysis of continuous birth weight.
	Metric 13:	Statistical Power	Medium	Statistical power was likely to have been limited as a consequence of the small proportion of the sample defined as having "elevated" residential water concentrations of the chemicals of interest. The range of exposure examined was limited, as cutoffs for elevated levels were close to the detection limits of 1 ppb. In addition, for most birth defect outcomes, fewer than 10 cases had elevated exposure.
	Metric 14:	Reproducibility of Analyses	Medium	The authors clearly described steps used to estimate exposure-outcome associations, including exposure category cutoffs and criteria for confounding. However, many results were not shown as tables included odds ratios ≥1.5.
	Metric 15:	Statistical Analysis	High	The authors estimated coefficients, odds ratios and 95% confidence intervals using adequate methods. Confounding was based on 15% change-in-estimate comparing nested models. Effect modification (ex by infant sex) was not evaluated as there was no a priori evidence to suggest such analyses at that time.

Additional Comments: This study analyzed the association between estimated residential drinking water concentrations of several chlorinated solvents including 1,2-dichloroethane (as well as 1,1,1-trichloroethane; ∑[trans-1,2-dichloroethylene and 1,1-dichloroethylene]) and pregnancy outcomes (size at birth, prematurity, fetal deaths, and congenital birth defects). The sample included more than 80,000 births during 1985-88 for residents of 75 towns in NJ using public water system records to estimate exposure during gestation, and registry data (birth certificate, fetal death certificates for pregnancies >20 weeks, state birth defect registry) to characterize outcomes. Strengths included the large sample size and inclusion of all eligible registered births and fetal deaths in the study period. A critical concern is the inability to capture early fetal deaths and any related malformations (1% of the sample had fetal deaths vs typical estimates of >10%). An important limitation was the low percentage of the sample with detectable (> 1ppb) concentrations of these contaminants (<1% to 6.2%). Small numbers for birth defect outcomes also limited power. Exposure misclassification (ex. drinking water from wells/ work/ bottles, changes in residence, exposure from other sources) is also a concern. However, such misclassification was likely non-differential, and thus more likely to under- vs. to over-estimate associations.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Bove, F. J., Fulcomer, M. C., Klotz, J. B., Esmart, J., Dufficy, E. M., Savrin, J. E. (1995). Public drinking water contamination and birth outcomes. American Journal of Epidemiology 141(9):850-862.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	194932

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	This semi-ecological study (n=80,938) included all registered singleton live births and fetal deaths (>20 weeks) in 1985-88 in 75 New Jersey towns located in 4 counties with "some" water supplies contaminated with substances of interest and where: (i) residents were "mostly" served by public water systems; and (ii) births occurred "mostly" in state. Estimated proportions of residents served by public water systems, and of pregnancies/births captured, were not described. However, the inclusion of all eligible registered births, fetal deaths, and birth defects, as well as the selection of towns without knowledge of birth outcome prevalence, limited the likelihood of selection bias.
	Metric 2:	Attrition	Medium	All registered births and fetal deaths were included. Attrition due to missing values for multiple variables was not quantified and is therefore uncertain. However, attrition was likely modest as the proportion of missing values for individual variables was relatively low: (i) ~6% of subjects were excluded from analyses of outcomes such as preterm birth due to invalid or missing gestational ages; and (ii) other covariates evaluated as confounders had up to 4.9% missing values.
	Metric 3:	Comparison Group	High	After excluding plural pregnancies and chromosomal abnormalities, all registered live births during the study period in the areas included without the outcomes of interest were included in the comparison group. This comprehensive approach limited the potential for bias. Chromosomal abnormalities were not included as outcomes as they were not hypothesized to be associated with the exposures under study but were appropriately excluded given their uncertain etiology.
Domain 2: Exposure Characterization				

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Study Citation:	Bove, F. J., Fulcomer, M. C., Klotz, J. B., Esmart, J., Dufficy, E. M., Savrin, J. E. (1995). Public drinking water contamination and birth outcomes. American Journal of Epidemiology 141(9):850-862.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	194932

Domain	Metric		Rating	Comments
	Metric 4:	Measurement of Exposure	Medium	Along with several other contaminants, residential drinking water exposure to 1,2-dichloroethane (as well as 1,1,1-trichloroethane and 'total dichloroethylenes') was assigned based on maternal town of residence at birth. Exposure estimates were calculated using the average of water company sampling reports during the first trimester (for birth defects and fetal death) or the duration of pregnancy (for other outcomes). Detection limits and data availability were not specified in detail but were described as below 1 ppb, with reporting compliance >85%. A minimum of 1 sample per 6-month interval was required; variability in the number of measures available across water systems and towns was not described. Additional sources of measurement error included: changes in residence during pregnancy; water from alternate sources (ex. private wells, bottles, workplaces); variability in residential contaminant levels vs measured samples; unknown levels of tap water intake; and errors in estimated dermal and inhalation exposure while bathing or showering. While the extent of exposure misclassification is uncertain, there is no evidence to suggest it was differential rather than random.
	Metric 5:	Exposure Levels	Low	Due to the high proportion of measures below detection limits, analyses relating exposure to health outcomes used only 2 categories for each of the three chemicals of interest: cutoffs close to detection limits were used to define elevated exposure. Proportions defined as having elevated exposure were low (1.8% had 1,1-dichloroethylene ≥1 ppb). An important concern is that relatively low levels of exposure to this contaminant from sources other than residential drinking water, for which data were not available, could potentially have resulted in considerable misclassification.
	Metric 6:	Temporality	High	Exposure levels were assigned based on contaminant exposures estimated during: (i) the first trimester for analyses of birth defects and fetal deaths; and (ii) the duration of pregnancy for other pregnancy outcomes.

Domain 3: Outcome Assessment

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Study Citation:	Bove, F. J., Fulcomer, M. C., Klotz, J. B., Esmart, J., Dufficy, E. M., Savrin, J. E. (1995). Public drinking water contamination and birth outcomes. American Journal of Epidemiology 141(9):850-862.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	194932

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcomes included measures of birthweight (continuous among term births, low term birthweight, very low birthweight), prematurity, fetal death, and congenital anomalies in live births or fetal deaths. The anomalies analyzed included defects of the central nervous system, neural tube, oral cleft, total cardiac, major cardiac, ventricular septum, and any surveillance defect excluding chromosomal defects. All outcomes were identified using birth certificates, fetal death certificates (>20 weeks' gestation), and the NJ congenital birth defect registry (ICD codes provided). These registry data are likely to be sufficiently valid for late pregnancy outcomes. However, their limited ability to capture early pregnancy losses is a weakness. The sample included only 594 fetal deaths (less than 1% of the >80,0000 sample). Typical estimates are that 10-20%, of recognized pregnancies ending in losses. Moreover, developmental defects contributing to early pregnancy losses were also not captured. A further limitation is that that potentially etiologically heterogeneous preterm birth types were analyzed together, as these data did not distinguish premature rupture of membranes vs idiopathic prematurity.
	Metric 8:	Reporting Bias	Low	Models were constructed only for contaminants with associations > 1.0, and tables included only associations with odds ratios ≥1.5. No clear rationale was provided. Several positive odds ratios below the 1.5 cutoff were described in the results text (without confidence intervals), but no null/negative odds ratios were presented or described.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Potential confounding by maternal race, education, parity, and prior pregnancy loss, along with infant sex (for birth outcomes) and adequacy of prenatal care, was examined. Gestational age was addressed by analyzing birthweight among full term births, term low birth weight, and small size for gestational age. Only fully adjusted models were presented. In a companion case-control study (with low participation rates), adjustment for other variables not available on birth certificates (ex. maternal smoking, occupational exposures, medical history, and gestational weight gain) did not influence associations with other studied contaminants. This separate study reduces concerns for important confounding bias, but confounding cannot be ruled out.
	Metric 10:	Covariate Characterization	Medium	Data on covariates came from registry data: birth certificates, fetal death certificates, and the NJ congenital birth defects registry.
	Metric 11:	Co-exposure Counfounding	Medium	Co-exposure confounding by drinking water trihalomethane concentrations was evaluated. There was no evidence to suggest substantial confounding by this or other co-exposures.
Domain 5: Analysis				

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Study Citation:	Bove, F. J., Fulcomer, M. C., Klotz, J. B., Esmart, J., Dufficy, E. M., Savrin, J. E. (1995). Public drinking water contamination and birth outcomes. American Journal of Epidemiology 141(9):850-862.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	194932

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Methods were appropriate. The study used logistic regression models to estimate odds ratios and confidence intervals for dichotomous outcomes, and linear regression for analysis of continuous birth weight.
	Metric 13:	Statistical Power	Low	Statistical power was likely to have been limited as a consequence of the small proportion of the sample defined as having "elevated" residential water concentrations of the chemicals of interest. The range of exposure examined was limited, as cutoffs for elevated levels were close to the detection limits of 1 ppb. In addition, for most birth defect outcomes, fewer than 10 cases had elevated exposure. However, the authors emphasized the magnitude of associations rather than statistical significance and presented multiple confidence intervals to aid interpretation of the precision of estimates (50%, 90% and 99%).
	Metric 14:	Reproducibility of Analyses	Medium	The authors clearly described steps used to estimate exposure-outcome associations, including exposure category cutoffs and criteria for confounding. However, many results were not shown as tables included odds ratios ≥1.5.
	Metric 15:	Statistical Analysis	High	The authors estimated coefficients, odds ratios and confidence intervals using adequate methods. Confounding was based on 15% change-in-estimate comparing nested models. Effect modification (ex by infant sex) was not evaluated as there was no a priori evidence to suggest such analyses at that time.

Additional Comments: This study analyzed the association between estimated residential drinking water concentrations of several chlorinated solvents including 1,2-dichloroethane (as well as 1,1,1-trichloroethane and the ∑[trans-1,2-dichloroethylene & 1,1-dichloroethylene]) and pregnancy outcomes (size at birth, prematurity, fetal deaths, and congenital birth defects). The sample included more than 80,000 births during 1985-88 for residents of 75 towns in NJ using public water system records to estimate exposure during gestation, and registry data (birth certificate, fetal death certificates for pregnancies >20 weeks' gestation, state birth defect registry) to characterize outcomes. Strengths included the large sample size and inclusion of all eligible registered births and fetal deaths in the study period. A critical concern is the inability to capture early fetal deaths and any related malformations (1% of the sample had fetal deaths vs typical estimates of >10%). An important limitation was the low percentage of the sample with detectable (> 1ppb) concentrations of this solvent (<2%), which likely limited power. Small numbers for birth defect outcomes also limited power. Exposure misclassification (ex. drinking water from wells/ work/ bottles, changes in residence, exposure from other sources) is also a concern. However, such misclassification was likely non-differential, and thus more likely to under- vs. to over-estimate associations.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Bowler, R.M., Gysens, S., Hartney, C. (2003). Neuropsychological effects of ethylene dichloride exposure. NeuroToxicology 24(4-5):553-562.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Wechsler Adult Intelligence Scale III (WAIS-III), Wechsler Memory Scale III (WMS-III), Boston Naming Test (BNT), Trail Making Test (TMT), Stroop Color-Word Test, Grooved Pegboard, Dynamometer, Wide Range Achievement Test (WRAT), Finger tapping, Beck Anxiety Index, Beck Depression Index, Symptom Checklist-90 (SCL-90).
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	200241

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Uninformative	221 workers that had been exposed to 1,2-DCE in the Southern United States were initially included. Exclusion criteria were provided, including the number of individuals excluded for each reason. The study authors note that those initially included in the analysis sample were referred by physicians after neurological complaints were documented. Detailed criteria for referral were not provided. Referral-based recruitment of neurological cases will likely result in an analysis sample with an exposure-outcome distribution that is not representative of the eligible population (i.e., contamination site clean-up workers).
	Metric 2:	Attrition	Medium	There was moderate subject loss. Reasons for exclusion from the analysis sample are provided, and only those with complete information were included in the analysis.
	Metric 3:	Comparison Group	Low	Impairment scores were compared to normative data from manuals and/or a "demographically similar control group" cited to Bowler et al. (2001). The controls from this study appeared similar (albeit somewhat older) than 1,2-DCE-exposed workers and reported no prior chemical exposure.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	A job-exposure matrix was not considered plausible; variables considered as surrogates of exposure were obtained from interviews. This method is expected to have poor validity because it relies on workers' recall of subjective events and their frequency (e.g., contact with water); workers (who are taking part in a lawsuit) may overestimate their exposure.
	Metric 5:	Exposure Levels	Low	Two levels of exposure (exposed and not exposed) were used to evaluate neurophysiological effects.
	Metric 6:	Temporality	Medium	Exposures primarily occurred between 1993 and 1995 and neurophysiological effects were evaluated in 2000. Temporality is established, but it is unclear whether exposures fall within relevant exposure windows for the outcome of interest.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Neurophysiological effects were evaluated using a number of standardized tests, including (but not limited to) the Wechsler Adult Intelligence Scale (WAIS-III), the Wechsler Memory Scale (WMS-III), and the Symptom Checklist 90-Revised (SCL90-R). There was no information whether tests were performed using the same methods for exposed and referent groups (e.g., timing and order of tests).

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Study Citation:	Bowler, R.M., Gysens, S., Hartney, C. (2003). Neuropsychological effects of ethylene dichloride exposure. NeuroToxicology 24(4-5):553-562.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Wechsler Adult Intelligence Scale III (WAIS-III), Wechsler Memory Scale III (WMS-III), Boston Naming Test (BNT), Trail Making Test (TMT), Stroop Color-Word Test, Grooved Pegboard, Dynamometer, Wide Range Achievement Test (WRAT), Finger tapping, Beck Anxiety Index, Beck Depression Index, Symptom Checklist-90 (SCL-90).
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	200241

Domain	Metric		Rating	Comments
	Metric 8:	Reporting Bias	Low	Neurobehavioral outcomes mentioned in the methods were reported for 1,2-DCE-exposed workers (as mean score, standard deviation, and percentage impaired); results for controls/normative data were not shown and/or p-values from t-tests were not provided. Control data were used to define impairment (based on z-score) but these values were not reported. Data pertaining to specific exposure variables were reported in the text only; no data were shown in a table.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Normative data permitted adjustments based on age, education, and gender. The control group was ”socio-demographically” similar but specific parameters used to define similarity were not indicated. Separate ANCOVA analyses on workers only were stratified by race (citation provided), and adjusted for ethnicity, age, and education. The methods for identifying and including potential confounders in the analytic approach was not described.
	Metric 10:	Covariate Characterization	Low	No description of the covariate collection method was provided. It was not clear whether the method used was valid or not.
	Metric 11:	Co-exposure Counfounding	Low	A number of workers (18%) reported current exposure to chemicals in their work environment. These potential co-exposures were not were not appropriately adjusted for in the analytical approach used.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Low	The study design was appropriate to evaluate the neurophysiological status of 1,2-DCE-exposed workers; however, statistical methods were not comprehensive.
	Metric 13:	Statistical Power	Medium	The report indicates ”significant impairments” were observed on various neurophysiological tests using t-tests, and significant exposure relationships were reported based on test scores and specific exposure variables (used as surrogates of exposure). Therefore, the number of participants was sufficient to detect an effect.
	Metric 14:	Reproducibility of Analyses	Low	Tests were scored according to relevant manuals; the calculation of z-scores, used in all impairment comparisons and analyses of exposure relationships, was not explained in adequate detail. The methods used to determine relationships between specific exposure variables and test scores (i.e., ANCOVA analyses) were not fully described.
	Metric 15:	Statistical Analysis	Low	Description of the ANCOVA analysis was largely not present. It is not clear whether model assumptions were met.

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Study Citation:	Bowler, R.M., Gysens, S., Hartney, C. (2003). Neuropsychological effects of ethylene dichloride exposure. NeuroToxicology 24(4-5):553-562.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Wechsler Adult Intelligence Scale III (WAIS-III), Wechsler Memory Scale III (WMS-III), Boston Naming Test (BNT), Trail Making Test (TMT), Stroop Color-Word Test, Grooved Pegboard, Dynamometer, Wide Range Achievement Test (WRAT), Finger tapping, Beck Anxiety Index, Beck Depression Index, Symptom Checklist-90 (SCL-90).
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	200241

Domain	Metric	Rating	Comments
Additional Comments:	The study evaluated the neurobehavioral status of a group of workers with known exposure to 1,2-DCE at a clean-up site. Impairments related to processing speed, attention, cognitive flexibility, motor coordination and speed, verbal memory/fluency, vision and visual-spatial abilities, and mood were reported in exposed workers. Serious and consequential flaws are associated with the study including methods of participant selection and retention, and exposure characterization among others.		

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Brender, J.D., Shinde, M.U., Zhan, F.B., Gong, X., Langlois, P.H. (2014). Maternal residential proximity to chlorinated solvent emissions and birth defects in offspring: A case-control study. Environmental Health: A Global Access Science Source 13(1):96.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	birth defects (neural tube defects, limbs deficiencies, oral cleft defects, heart defects, spina bifida, anencephaly)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	2799700

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Participants were drawn from the Texas Birth Defects Registry (TBDR) for years 1996-2008. Controls were frequency matched from the same registry. Study authors state that neural tube cases were more likely to not be successfully geocoded which may introduce selection bias, however, the authors note that both cases and controls with addresses that could not be geocoded were similar. In spite of that, the inclusion criteria, methods of participant selection, and frequency match were reported.
	Metric 2:	Attrition	Medium	13.3% case mother addresses and 12.8% control mother addresses were unable to be geocoded, however this most likely only lowered the precision of the study and most likely does not vary based on exposure level.
	Metric 3:	Comparison Group	Medium	Controls were matched to cases and pulled from the same eligible population by year of delivery and public health service region. Other demographic factors, e.g., race was not matched in population selection. However, statistical analyses were adjusted for year of delivery, maternal age, race/ethnicity, education, and public health region of residence.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Used Emission Weighted Proximity Model to estimate exposure at a given address based on proximity to emission sources and the specific amount or type of pollutant emitted. There may be some exposure misclassification due to mothers moving away from geocoded addresses. Previous studies indicate ~67% of mothers do not move between conception and delivery.
	Metric 5:	Exposure Levels	Medium	Reports exposure as ”exposure risk value” and groups the risk values into quartiles, with exposure risk values < 0 being the referent group
	Metric 6:	Temporality	Medium	The study authors estimated exposure based on residence during pregnancy and evaluated birth outcomes. Temporality is established. Previous studies indicate ~67% mothers don’t move between trimester and delivery. For mothers who moved during the pregnancy, the temporality is unknown.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Outcomes determined by Texas Birth Defect Registry, checking for birth defect diagnosis. Birth certificates came from Center for Health Statistics at Texas Department of State Health Services
	Metric 8:	Reporting Bias	High	Outcome data measured and reported clearly, stratified by specific type of birth defect
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Brender, J.D., Shinde, M.U., Zhan, F.B., Gong, X., Langlois, P.H. (2014). Maternal residential proximity to chlorinated solvent emissions and birth defects in offspring: A case-control study. Environmental Health: A Global Access Science Source 13(1):96.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	birth defects (neural tube defects, limbs deficiencies, oral cleft defects, heart defects, spina bifida, anencephaly)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	2799700

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	High	Cases were frequency matched by year of delivery and public health service region. Final models were adjusted for year of delivery, public health region, maternal age (<20, 20-24, 25-29, 30-34, 35-39, >39 years), education (<12 years, 12 years, >12 years), and race/ethnicity (Whit non-Hispanic, Black non-Hispanic, Hispanic, other non-Hispanic).
	Metric 10:	Covariate Characterization	High	Used birth and death certificates for demographic information
	Metric 11:	Co-exposure Counfounding	Medium	other co-exposures were not described
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	study used logistic regression to measure association between exposure and birth defects
	Metric 13:	Statistical Power	Medium	Overall adequate number of cases and controls - some effects have low cell counts, but at least one health effect has sufficient statistical power.
	Metric 14:	Reproducibility of Analyses	Medium	Methods sufficiently detailed for reproducibility
	Metric 15:	Statistical Analysis	High	No logistic regression model assumption violations were identified.

Additional Comments: This study examined the association between proximity to several point sources of chlorinated solvents and birth defects. Exposure was assessed using EPA's Toxic Release Inventory, and birth defects were assessed using Texas birth registries. The geocoded address of mothers on day of delivery and the amount of solvent was plugged into the Emission Weighted Probability model to assign each mother an exposure risk value. Limitations include limited evidence of temporality. Additionally, elective terminations lacked a vital record, which meant only 69% of mothers with neural tube defects were geocoded. Mothers highly exposed to 1,2-dichloroethane were 1.85 times more likely to have the spina bifida birth defect than mothers who were not significantly exposed.

Overall Quality Determination High

* No biomarkers were identified for this evaluation.

Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Nested case-control design; cases selected from deaths in cohort study was described by Rinsky et al (1988; HERO 597923) (29,139 workers in Union Carbide facilities in West Virginia followed from 1940 to 1978). Vital status complete for 95% of cohort members.
	Metric 2:	Attrition	High	There was minimal exclusion of subjects/missing data, because vital status follow-up was complete for 96% of the 29,139 men in the cohort study.
	Metric 3:	Comparison Group	Medium	Controls were randomly selected in a 5:1 ratio to cases from the total employee cohort such that they were first employed in the same decade and survived to the same five-year survival period as cases. Controls survived at least to the beginning of the five-year interval in which cases died. Controls were independently selected for each of the individual disease subcategories. However, the demographic information between cases and controls were not compared in the paper.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was partially described: (1) Potential employee contact with a specific substance was determined by tracing each employee's work assignments and linking these assignment records to a separate computer file that contained a history of departmental usage for each substance; (2) Potential exposure to each chemical group was assumed on the basis of assignment o a production unit with a history of usage of any member of that chemical group. However, exposure level either based on work assignment in departments such as job exposure matrix or on the chemical levels were not presented.
	Metric 5:	Exposure Levels	Low	The range of exposure is limited. For example, exposure was presented by the duration of work in two categories: <5 years and 5+ years.
	Metric 6:	Temporality	Medium	Temporality is established, but it is unclear whether the exposures fall within the relevant exposure window. Authors used a lag time of 5 years; since controls were selected for 5 yr intervals, the effective lag time ranged from 5-9 years with an average of 7.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Case definition was based on death certificate diagnosis; but no method validation was conducted against this well-established methods.
	Metric 8:	Reporting Bias	Medium	All outcomes reported, but ORs for many analyses presented without CIs (some CIs reported in text).
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Low	There is indirect evidence that considerations were not made for potential confounders (ORs not adjusted, controls not age- or race-matched). Even though authors note that "Age-adjusted stratified analyses, which were also conducted, did not materially modify the odds ratio estimates". Also stratified examination of odds ratios were conducted to assess duration of exposure effects. However, other key confounders e.g., smoking status and race were not accounted for.
	Metric 10:	Covariate Characterization	Medium	The only potential confounder considered was age; this was presumably evaluated based on employment records (no discussion presented). Age-adjusted stratified analyses were conducted.
	Metric 11:	Co-exposure Counfounding	Low	Co-exposures were present and were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Nested case-control study design is appropriate for research question. Initial data analysis included crude odds ratio and then stratified examination of odds ratios was conducted to ass duration of exposure effect. Also, age-adjusted stratified analysis was conducted.
	Metric 13:	Statistical Power	Low	Statistical power calculations were not reported. Case numbers for each disease were low. The number of subjects was not sufficient to detect an effect of 1,2-dichloroethylene exposure.
	Metric 14:	Reproducibility of Analyses	Medium	Description was sufficient to be conceptually reproducible.
	Metric 15:	Statistical Analysis	Low	Statistical model to calculate odds ratio was not described.

Additional Comments: This nested case-control study within a cohort study is a good study design to answer the research question regarding the association between multiple chemical exposures and four cancer sites. Cases and controls are selected appropriate. However, there are several limitations in this study: (1) confounders were not all considered and adjusted for, except that age-adjusted odds ratios were conducted; (2) it is not described if co-exposures were adjusted for; (3) numbers of cancer cases for each cancer type were small, so the statistical power is limited; (4) statistical models for calculating odds ratios were not described.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Nested case-control design; cases selected from deaths in cohort study was described by Rinsky et al (1988; HERO 597923) (29,139 workers in Union Carbide facilities in West Virginia followed from 1940 to 1978). Vital status complete for 95% of cohort members.
	Metric 2:	Attrition	High	There was minimal exclusion of subjects/missing data, because vital status follow-up was complete for 96% of the 29,139 men in the cohort study.
	Metric 3:	Comparison Group	Medium	Controls were randomly selected in a 5:1 ratio to cases from the total employee cohort such that they were first employed in the same decade and survived to the same five-year survival period as cases. Controls survived at least to the beginning of the five-year interval in which cases died. Controls were independently selected for each of the individual disease subcategories. However, the demographic information between cases and controls were not compared in the paper.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was partially described: (1) Potential employee contact with a specific substance was determined by tracing each employee's work assignments and linking these assignment records to a separate computer file that contained a history of departmental usage for each substance; (2) Potential exposure to each chemical group was assumed on the basis of assignment o a production unit with a history of usage of any member of that chemical group. However, exposure level either based on work assignment in departments such as job exposure matrix or on the chemical levels were not presented.
	Metric 5:	Exposure Levels	Low	The range of exposure is limited. For example, exposure was presented by the duration of work in two categories: <5 years and 5+ years.
	Metric 6:	Temporality	Medium	Temporality is established, but it is unclear whether the exposures fall within the relevant exposure window. Authors used a lag time of 5 years; since controls were selected for 5 yr intervals, the effective lag time ranged from 5-9 years with an average of 7.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Case definition was based on death certificate diagnosis; but no method validation was conducted against this well-established methods.
	Metric 8:	Reporting Bias	Medium	All outcomes reported, but ORs for many analyses presented without CIs (some CIs reported in text).
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Low	There is indirect evidence that considerations were not made for potential confounders (ORs not adjusted, controls not age- or race-matched). Even though authors note that "Age-adjusted stratified analyses, which were also conducted, did not materially modify the odds ratio estimates". Also stratified examination of odds ratios were conducted to assess duration of exposure effects. However, other key confounders e.g., smoking status and race were not accounted for.
	Metric 10:	Covariate Characterization	Medium	The only potential confounder considered was age; this was presumably evaluated based on employment records (no discussion presented). Age-adjusted stratified analyses were conducted.
	Metric 11:	Co-exposure Counfounding	Low	Co-exposures were present and were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Nested case-control study design is appropriate for research question. Initial data analysis included crude odds ratio and then stratified examination of odds ratios was conducted to ass duration of exposure effect. Also, age-adjusted stratified analysis was conducted.
	Metric 13:	Statistical Power	Low	Statistical power calculations were not reported. Case numbers for each disease were low. The number of subjects was not sufficient to detect an effect of 1,2-dichloroethylene exposure.
	Metric 14:	Reproducibility of Analyses	Medium	Description was sufficient to be conceptually reproducible.
	Metric 15:	Statistical Analysis	Low	Statistical model to calculate odds ratio was not described.

Additional Comments: This nested case-control study within a cohort study is a good study design to answer the research question regarding the association between multiple chemical exposures and four cancer sites. Cases and controls are selected appropriate. However, there are several limitations in this study: (1) confounders were not all considered and adjusted for, except that age-adjusted odds ratios were conducted; (2) it is not described if co-exposures were adjusted for; (3) numbers of cancer cases for each cancer type were small, so the statistical power is limited; (4) statistical models for calculating odds ratios were not described.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Nested case-control design; cases selected from deaths in cohort study was described by Rinsky et al (1988; HERO 597923) (29,139 workers in Union Carbide facilities in West Virginia followed from 1940 to 1978). Vital status complete for 95% of cohort members.
	Metric 2:	Attrition	High	There was minimal exclusion of subjects/missing data, because vital status follow-up was complete for 96% of the 29,139 men in the cohort study.
	Metric 3:	Comparison Group	Medium	Controls were randomly selected in a 5:1 ratio to cases from the total employee cohort such that they were first employed in the same decade and survived to the same five-year survival period as cases. Controls survived at least to the beginning of the five-year interval in which cases died. Controls were independently selected for each of the individual disease subcategories. However, the demographic information between cases and controls were not compared in the paper.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was partially described: (1) Potential employee contact with a specific substance was determined by tracing each employee's work assignments and linking these assignment records to a separate computer file that contained a history of departmental usage for each substance; (2) Potential exposure to each chemical group was assumed on the basis of assignment o a production unit with a history of usage of any member of that chemical group. However, exposure level either based on work assignment in departments such as job exposure matrix or on the chemical levels were not presented.
	Metric 5:	Exposure Levels	Low	The range of exposure is limited. For example, exposure was presented by the duration of work in two categories: <5 years and 5+ years.
	Metric 6:	Temporality	Medium	Temporality is established, but it is unclear whether the exposures fall within the relevant exposure window. Authors used a lag time of 5 years; since controls were selected for 5 yr intervals, the effective lag time ranged from 5-9 years with an average of 7.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Case definition was based on death certificate diagnosis; but no method validation was conducted against this well-established methods.
	Metric 8:	Reporting Bias	Medium	All outcomes reported, but ORs for many analyses presented without CIs (some CIs reported in text).
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Low	There is indirect evidence that considerations were not made for potential confounders (ORs not adjusted, controls not age- or race-matched). Even though authors note that "Age-adjusted stratified analyses, which were also conducted, did not materially modify the odds ratio estimates". Also stratified examination of odds ratios were conducted to assess duration of exposure effects. However, other key confounders e.g., smoking status and race were not accounted for.
	Metric 10:	Covariate Characterization	Medium	The only potential confounder considered was age; this was presumably evaluated based on employment records (no discussion presented). Age-adjusted stratified analyses were conducted.
	Metric 11:	Co-exposure Counfounding	Low	Co-exposures were present and were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Nested case-control study design is appropriate for research question. Initial data analysis included crude odds ratio and then stratified examination of odds ratios was conducted to ass duration of exposure effect. Also, age-adjusted stratified analysis was conducted.
	Metric 13:	Statistical Power	Low	Statistical power calculations were not reported. Case numbers for each disease were low. The number of subjects was not sufficient to detect an effect of 1,2-dichloroethylene exposure.
	Metric 14:	Reproducibility of Analyses	Medium	Description was sufficient to be conceptually reproducible.
	Metric 15:	Statistical Analysis	Low	Statistical model to calculate odds ratio was not described.

Additional Comments: This nested case-control study within a cohort study is a good study design to answer the research question regarding the association between multiple chemical exposures and four cancer sites. Cases and controls are selected appropriate. However, there are several limitations in this study: (1) confounders were not all considered and adjusted for, except that age-adjusted odds ratios were conducted; (2) it is not described if co-exposures were adjusted for; (3) numbers of cancer cases for each cancer type were small, so the statistical power is limited; (4) statistical models for calculating odds ratios were not described.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Nested case-control design; cases selected from deaths in cohort study was described by Rinsky et al (1988; HERO 597923) (29,139 workers in Union Carbide facilities in West Virginia followed from 1940 to 1978). Vital status complete for 95% of cohort members.
	Metric 2:	Attrition	High	There was minimal exclusion of subjects/missing data, because vital status follow-up was complete for 96% of the 29,139 men in the cohort study.
	Metric 3:	Comparison Group	Medium	Controls were randomly selected in a 5:1 ratio to cases from the total employee cohort such that they were first employed in the same decade and survived to the same five-year survival period as cases. Controls survived at least to the beginning of the five-year interval in which cases died. Controls were independently selected for each of the individual disease subcategories. However, the demographic information between cases and controls were not compared in the paper.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was partially described: (1) Potential employee contact with a specific substance was determined by tracing each employee's work assignments and linking these assignment records to a separate computer file that contained a history of departmental usage for each substance; (2) Potential exposure to each chemical group was assumed on the basis of assignment o a production unit with a history of usage of any member of that chemical group. However, exposure level either based on work assignment in departments such as job exposure matrix or on the chemical levels were not presented.
	Metric 5:	Exposure Levels	Low	The range of exposure is limited. For example, exposure was presented by the duration of work in two categories: <5 years and 5+ years.
	Metric 6:	Temporality	Medium	Temporality is established, but it is unclear whether the exposures fall within the relevant exposure window. Authors used a lag time of 5 years; since controls were selected for 5 yr intervals, the effective lag time ranged from 5-9 years with an average of 7.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Case definition was based on death certificate diagnosis; but no method validation was conducted against this well-established methods.
	Metric 8:	Reporting Bias	Medium	All outcomes reported, but ORs for many analyses presented without CIs (some CIs reported in text).
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Low	There is indirect evidence that considerations were not made for potential confounders (ORs not adjusted, controls not age- or race-matched). Even though authors note that "Age-adjusted stratified analyses, which were also conducted, did not materially modify the odds ratio estimates". Also stratified examination of odds ratios were conducted to assess duration of exposure effects. However, other key confounders e.g., smoking status and race were not accounted for.
	Metric 10:	Covariate Characterization	Medium	The only potential confounder considered was age; this was presumably evaluated based on employment records (no discussion presented). Age-adjusted stratified analyses were conducted.
	Metric 11:	Co-exposure Counfounding	Low	Co-exposures were present and were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Nested case-control study design is appropriate for research question. Initial data analysis included crude odds ratio and then stratified examination of odds ratios was conducted to ass duration of exposure effect. Also, age-adjusted stratified analysis was conducted.
	Metric 13:	Statistical Power	Low	Statistical power calculations were not reported. Case numbers for each disease were low. The number of subjects was not sufficient to detect an effect of 1,2-dichloroethylene exposure.
	Metric 14:	Reproducibility of Analyses	Medium	Description was sufficient to be conceptually reproducible.
	Metric 15:	Statistical Analysis	Low	Statistical model to calculate odds ratio was not described.

Additional Comments: This nested case-control study within a cohort study is a good study design to answer the research question regarding the association between multiple chemical exposures and four cancer sites. Cases and controls are selected appropriate. However, there are several limitations in this study: (1) confounders were not all considered and adjusted for, except that age-adjusted odds ratios were conducted; (2) it is not described if co-exposures were adjusted for; (3) numbers of cancer cases for each cancer type were small, so the statistical power is limited; (4) statistical models for calculating odds ratios were not described.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Cheng, T.J., Huang, M.L., You, N.C., Du, C.L., Chau, T.T. (1999). Abnormal liver function in workers exposed to low levels of ethylene dichloride and vinyl chloride monomer. Journal of Occupational and Environmental Medicine 41(12):1128-1133.
Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	AST, ALT, GGT, Hepatitis B virus surface antigen (HBsAg), and anti-hepatitis C virus antibody (anti-HCV).
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	200266

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	A total of 251 male workers were included from 4 vinyl chloride monomer manufacturing plants. Other details on recruitment strategy, eligibility criteria, year of enrollment, and participation rates were not provided.
	Metric 2:	Attrition	Low	There was no indication of attrition and details on the number of eligible participants throughout the study was limited. Attrition could not be adequately assessed due to a lack of information regarding recruitment and selection.
	Metric 3:	Comparison Group	Medium	The low-EDC-low-VCM group (187 participants) was used as the comparison group, and there is indirect evidence groups are similar. Limited details were provided for setting, inclusion and exclusion criteria, and methods of participant selection.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	NIOSH recommended methods 1003 and 1007 were used for personal and area sampling, respectively. Air samples were collected, stored at 4 deg. C, and analyzed within 2 weeks of the sampling event. However, historical job changes, changes in exposure levels over time, and timing (year or days during work week) or duration of area or personal sampling were not reported.
	Metric 5:	Exposure Levels	Medium	EDC and VCM levels were reported for the different categories of jobs, which were classified into low-EDC-low-VCM, mod-EDC-low-VCM, and low-EDC-mod-VCM groups.
	Metric 6:	Temporality	High	The age of participants (mean age 33.7-40.1 years) and employment duration (mean 7.5-14.3 years) were reported, and the temporality between the exposure and outcome appears to be appropriate.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	AST, ALT, and GGT "were analyzed with a Hitachi 7050 autoanalyzer". A basis for the cutoff values used in Table 4 to determine "abnormal" AST, ALT, and GGT levels was not provided.
	Metric 8:	Reporting Bias	High	Odds ratios for abnormal liver function were provided with 95% confidence intervals, the number per exposure level, and significance when applicable.
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Cheng, T.J., Huang, M.L., You, N.C., Du, C.L., Chau, T.T. (1999). Abnormal liver function in workers exposed to low levels of ethylene dichloride and vinyl chloride monomer. Journal of Occupational and Environmental Medicine 41(12):1128-1133.
Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	AST, ALT, GGT, Hepatitis B virus surface antigen (HBsAg), and anti-hepatitis C virus antibody (anti-HCV).
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	200266

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Medium	The study reports information on potential confounders (age, hepatitis, BMI, alcohol use, and employment duration), and controls for hepatitis, BMI and alcohol consumption in the multiple logistic regression analyses. There is indirect evidence that appropriate adjustments were made.
	Metric 10:	Covariate Characterization	Medium	An interviewer administered the questionnaires to collect information about potential confounders and occupational history.
	Metric 11:	Co-exposure Counfounding	Low	Exposure to ethylene dichloride was evaluated in a vinyl chloride monomer (VCM) manufacturing facility, and VCM was also subsequently analyzed using personal and area sampling. Results for VCM exposure concentrations were provided. VCM is also suspected to cause liver damage.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design (cohort) was appropriate to assess the outcome of interest (”markers of liver damage”). Chi-squared (X2) test and multiple logistic regression were used for statistical analyses.
	Metric 13:	Statistical Power	Medium	The number of participants was adequate to detect an effect in the exposed populations, although power calculations were not provided. There were >20 participants in each group.
	Metric 14:	Reproducibility of Analyses	Low	A description of the logistic regression analysis was provided, however, study authors do not provide information on categorization of abnormal liver function.
	Metric 15:	Statistical Analysis	High	There were no identifiable logistic regression model assumption violations.
Domain 6: Other (if applicable) Considerations for Biomarker Selection and Measurement (Lakind et al. 2014)				
	Metric 16:	Use of Biomarker of Exposure	N/A	Biomarker of exposures were not assessed.
	Metric 17:	Effect Biomarker	High	This study uses aspartate aminotransferase, alanine aminotransferase, and y-glutamyltransferase as biomarkers of effect. While these no works cited to explain their connection to liver function, all three are well-known marker of liver function. Similarly, Hepatitis B virus surface antigen and antihepatitis C virus anitbody are also well-known measures of liver function and health.
	Metric 18:	Method Sensitivity	Low	No limit of detection information is provided for any of the effect biomarkers.
	Metric 19:	Biomarker Stability	Medium	While the study does not provide a lot of information regarding biomarker storage or stability, the authors do mention that venous blood used to detect biomarkers was stored at 4 degrees C.
	Metric 20:	Sample Contamination	Medium	No specific information regarding potential sample contamination was provided.
	Metric 21:	Method Requirements	Medium	Aspartate aminotransferase, alanine aminotransferase, and y-glutamyltransferase were analyzed using a Hitachi 7050 autoanalyzer. Hepatitis B virus surface antibody and antihepatitis C virus antibody were assessed with radioimmunoassay and enzyme-linked immunosorbent assay.

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Study Citation:	Cheng, T.J., Huang, M.L., You, N.C., Du, C.L., Chau, T.T. (1999). Abnormal liver function in workers exposed to low levels of ethylene dichloride and vinyl chloride monomer. Journal of Occupational and Environmental Medicine 41(12):1128-1133.
Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	AST, ALT, GGT, Hepatitis B virus surface antigen (HBsAg), and anti-hepatitis C virus antibody (anti-HCV).
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	200266

Domain	Metric	Rating	Comments
	Metric 22: Matrix Adjustment	N/A	No information on matrix adjustment was provided/available.

Additional Comments: A group of 251 male workers from 4 vinyl chloride monomer (VCM) manufacturing plants were included in this assessment to examine if occupational exposure to VCM and ethylene dichloride (EDC) "resulted in increased risk of liver damage" by examining AST, ALT, and GGT levels in the blood. Increased ORs for abnormal AST (>37 IU/L) and ALT (>41 IU/L) in the mod-EDC-low-VCM group (0.17-333.7 ppm EDC, 0.18-0.34 ppm VCM), compared with the low-EDC-low-VCM group, was reported. Exposure levels were measured using area and personal sampling, but the timing and duration of the sampling events were not reported.

Overall Quality Determination Medium

Study Citation:	Dosemeci, M., Cocco, P., Chow, W.H. (1999). Gender differences in risk of renal cell carcinoma and occupational exposures to chlorinated aliphatic hydrocarbons. American Journal of Industrial Medicine 36(1):54-59.
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	renal cell carcinoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	4697224

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	The details of the study design were reported elsewhere (Chow et al. 1994, HERO ID 701514). Brief details about the setting, date, number of eligible participants, and control matching were reported. Reasons for exclusions/non-participation were described with details by Chow et al. (1994).
	Metric 2:	Attrition	High	For the details of the study design and attrition of study subjects, the study authors referred to another publication by Chow et al., 1994. Chow et al. (1994) mentioned that at the end of the personal interview, the respondents were given a self-administered food-frequency questionnaire. Of the subjects interviewed for the study, 632 patients (79% of 796 eligible patients) and 653 control subjects (79% of 707 eligible control subjects) returned the diet questionnaire. A number of subjects, whose responses were considered unreliable, were excluded from the analysis, including 48 patients and three control subjects who had seven or more skipped food items or had questionable data and 50 patients whose next-of-kin respondent was not a spouse. Also excluded were two patients with unknown smoking status, since smoking is a risk factor.
	Metric 3:	Comparison Group	Medium	The cases were pulled from the Minnesota Cancer Surveillance System. Controls were selected from the general population of Minnesota; controls age 20-64 years were selected through random digital dialing and controls age 65-85 years were collected from files through the Health Care Financing Administration. Controls were age- and gender-stratified and were of the same race. Characteristics of cases and controls were not provided in the text or a table.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	High	Occupational histories including the most recent and usual occupation and industry, job activities, started-year and ended-year, and part-time/full-time status were collected. Occupations and industries were coded according to the standard occupational classification (SOC) and standard industrial classification (SIC) schemes. The National Cancer Institute developed job exposure matrices (JEM) for nine individual chlorinated aliphatic hydrocarbons (CAHCs), all CAHCs-combined, and all organic solvents-combined. These JEMs were merged with assigned SOC and SIC to determine the exposure status to these chemicals for each study subject. Application of the JEM was described elsewhere (Dosemeci et al. 1994, HERO ID 632334; Gomez et al. 1994, HERO ID 702154).
	Metric 5:	Exposure Levels	Medium	Details of the application of the JEM were described elsewhere (Dosemeci et al. 1994, HERO ID 632334; Gomez et al. 1994, HERO ID 702154). Dosemeci et al. (1994) described more details about that this study assigned three levels of probability (low, medium, high) to industries and occupations for chemical exposure levels.

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Study Citation:	Dosemeci, M., Cocco, P., Chow, W.H. (1999). Gender differences in risk of renal cell carcinoma and occupational exposures to chlorinated aliphatic hydrocarbons. American Journal of Industrial Medicine 36(1):54-59.
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	renal cell carcinoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	4697224

Domain	Metric		Rating	Comments
	Metric 6:	Temporality	Medium	Occupational questionnaires identified prior exposures based on reported recent and usual occupations as well as duration of employment. Outcome status was determined from registry data. The authors note that some occupational history was incomplete which may result in some uncertainty in regard to temporality.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Cases were identified as newly diagnosed and histologically confirmed renal cell carcinoma through the Minnesota Cancer Surveillance System and information about each participant was collected using a questionnaire. Validation was not specified.
	Metric 8:	Reporting Bias	Medium	A description of measured outcomes is reported and ORs were stratified by sex. Effect estimates are reported with a confidence interval. One table showed the total numbers of men and women respectively for each chemical, but numbers of cases/controls were not reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Appropriate adjustments were made in the final analysis, including age, gender, smoking, hypertension and the use of diuretics and/or anti-hypertension drugs, and BMI. Results were stratified by sex.
	Metric 10:	Covariate Characterization	Medium	Information about participants was collected using a questionnaire, and it includes potential confounders, e.g., smoking habits. Validation was not specified.
	Metric 11:	Co-exposure Counfounding	Medium	Co-exposures were identified through the job exposure matrices. Chemicals were evaluated individually and as a group.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen (case-control) was appropriate for the research question (renal cell carcinoma risk from occupational organic solvent exposure). Logistic regression models were used to estimate the relative risk and 95% CI.
	Metric 13:	Statistical Power	Low	Statistical power calculations were not provided. No significant effects were observed with 1,2-dichloroethane. The number of participated women to calculate odds ratio was inadequate to detect an effect in the participants for other chemicals or the combined risk, because it was very low.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis was brief, but is sufficient to understand precisely what has been done and to be conceptually reproducible with access to the analytic data.
	Metric 15:	Statistical Analysis	High	Model assumptions for logistic regression were met. The odds ratios were adjusted for age, smoking, hypertension status and/or use of diuretic and/or anti-hypertension drugs, and body mass index for men and women separately.

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Study Citation:	Dosemeci, M., Cocco, P., Chow, W.H. (1999). Gender differences in risk of renal cell carcinoma and occupational exposures to chlorinated aliphatic hydrocarbons. American Journal of Industrial Medicine 36(1):54-59.
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	renal cell carcinoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	4697224

Domain	Metric	Rating	Comments
Additional Comments:	A group of 438 cases (273 men and 165 women) were selected from the Minnesota Cancer Surveillance System that had been newly diagnosed with renal cell carcinoma. Controls included 687 participants (462 men and 225 women) age- and gender- stratified that were selected from either the general population of Minnesota (age 20-64 years) or from the Health Care Financing Administration files (age 65-85). No significant increase in the risk of renal cell carcinoma was observed with exposure to 1,2-dichloroethane among men or women separately, or for all participants exposed.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Dosemeci, M., Cocco, P., Chow, W.H. (1999). Gender differences in risk of renal cell carcinoma and occupational exposures to chlorinated aliphatic hydrocarbons. American Journal of Industrial Medicine 36(1):54-59.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	renal cell carcinoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	4697224

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	The details of the study design were reported elsewhere (Chow et al. 1994, HERO ID 701514). Brief details about the setting, date, number of eligible participants, and control matching were reported. Reasons for exclusions/non-participation were described with details by Chow et al. (1994).
	Metric 2:	Attrition	Medium	For the details of the study design and attrition of study subjects, the study authors referred to another publication by Chow et al., 1994. Chow et al. (1994) mentioned that at the end of the personal interview, the respondents were given a self-administered food-frequency questionnaire. Of the subjects interviewed for the study, 632 patients (79% of 796 eligible patients) and 653 control subjects (79% of 707 eligible control subjects) returned the diet questionnaire. A number of subjects, whose responses were considered unreliable, were excluded from the analysis, including 48 patients and three control subjects who had seven or more skipped food items or had questionable data and 50 patients whose next-of-kin respondent was not a spouse. Also excluded were two patients with unknown smoking status, since smoking is a risk factor.
	Metric 3:	Comparison Group	Medium	The cases were pulled from the Minnesota Cancer Surveillance System. Controls were selected from the general population of Minnesota; controls age 20-64 years were selected through random digital dialing and controls age 65-85 years were collected from files through the Health Care Financing Administration. Controls were age- and gender-stratified and were of the same race. Characteristics of cases and controls were not provided in the text or a table.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	High	Occupational histories including the most recent and usual occupation and industry, job activities, started-year and ended-year, and part-time/full-time status were collected. Occupations and industries were coded according to the standard occupational classification (SOC) and standard industrial classification (SIC) schemes. The National Cancer Institute developed job exposure matrices (JEM) for nine individual chlorinated aliphatic hydrocarbons (CAHCs), all CAHCs-combined, and all organic solvents-combined. These JEMs were merged with assigned SOC and SIC to determine the exposure status to these chemicals for each study subject. Application of the JEM was described elsewhere (Dosemeci et al. 1994, HERO ID 632334; Gomez et al. 1994, HERO ID 702154).
	Metric 5:	Exposure Levels	Medium	Details of the application of the JEM were described elsewhere (Dosemeci et al. 1994, HERO ID 632334; Gomez et al. 1994, HERO ID 702154). Dosemeci et al. (1994) described more details about that this study assigned three levels of probability (low, medium, high) to industries and occupations for chemical exposure levels.

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Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	renal cell carcinoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	4697224

Domain	Metric		Rating	Comments
	Metric 6:	Temporality	Medium	Occupational questionnaires identified prior exposures based on reported recent and usual occupations as well as duration of employment. Outcome status was determined from registry data. The authors note that some occupational history was incomplete which may result in some uncertainty in regard to temporality.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Cases were identified as newly diagnosed and histologically confirmed renal cell carcinoma through the Minnesota Cancer Surveillance System and information about each participant was collected using a questionnaire. Validation was not specified.
	Metric 8:	Reporting Bias	Medium	A description of measured outcomes is reported and ORs were stratified by sex. Effect estimates are reported with a confidence interval. One table showed the total numbers of men and women respectively for each chemical, but numbers of cases/controls were not reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Appropriate adjustments were made in the final analysis, including age, gender, smoking, hypertension and the use of diuretics and/or anti-hypertension drugs, and BMI. Results were stratified by sex.
	Metric 10:	Covariate Characterization	Medium	Information about participants was collected using a questionnaire, and it includes potential confounders, e.g., smoking habits. Validation was not specified.
	Metric 11:	Co-exposure Counfounding	Medium	Co-exposures were identified through the job exposure matrices. Chemicals were evaluated individually and as a group.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen (case-control) was appropriate for the research question (renal cell carcinoma risk from occupational organic solvent exposure). Logistic regression models were used to estimate the relative risk and 95% CI.
	Metric 13:	Statistical Power	Low	Statistical power calculations were not provided. No significant effects were observed with 1,2-dichloroethane. The number of participated women to calculate odds ratio was inadequate to detect an effect in the participants for other chemicals or the combined risk, because it was very low.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis was brief, but is sufficient to understand precisely what has been done and to be conceptually reproducible with access to the analytic data.
	Metric 15:	Statistical Analysis	High	Model assumptions for logistic regression were met. The odds ratios were adjusted for age, smoking, hypertension status and/or use of diuretic and/or anti-hypertension drugs, and body mass index for men and women separately.

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Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	renal cell carcinoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	4697224

Domain	Metric	Rating	Comments
Additional Comments:	A group of 438 cases (273 men and 165 women) were selected from the Minnesota Cancer Surveillance System that had been newly diagnosed with renal cell carcinoma. Controls included 687 participants (462 men and 225 women) age- and gender- stratified that were selected from either the general population of Minnesota (age 20-64 years) or from the Health Care Financing Administration files (age 65-85). No significant increase in the risk of renal cell carcinoma was observed with exposure to 1,2-dichloroethane among men or women separately, or for all participants exposed.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Garcia, E., Hurley, S., Nelson, D.O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health: A Global Access Science Source 14(1):14.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	breast cancer in females
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	3014082

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	A total of 112,378 women were included in this study out of 133,479 eligible female participants from the California Teacher Study cohort. A full description of the cohort is provided in Bernstein et al. 2002 (HERO ID 808446). Reasons for exclusion were provided. The reported information indicates that participant selection in or out of the study and participation was not likely to be biased.
	Metric 2:	Attrition	High	112,378/133,479 participants were included in the study. Exclusions were for the purpose of the study and analysis. Exclusion criteria were documented. Included participants had completed questionnaires. The California Cancer Registry is estimated to be 99% complete.
	Metric 3:	Comparison Group	Medium	There is only indirect evidence that groups are similar. Participants were recruited from the same eligible population with the same method of ascertainment. Comparisons were provided for participants with and without breast cancer. Characteristics between these two groups were generally similar. 5 Quintiles of exposure were used, and Q2-5 were compared with Q1.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	High	The Assessment System for Population Exposure Nationwide and the Human Exposure Model are used as part of the National-Scale Air Toxics Assessment produced by the EPA and was used to estimate ambient HAP concentrations for geographic locations. Methods are described online through the US EPA Assessment Methods.
	Metric 5:	Exposure Levels	Medium	The distribution of the NATA annual ambient concentration for each compound was plotted in Figure 1 using a box plot, and 5 Quintiles were used in the analyses.
	Metric 6:	Temporality	Medium	The follow-up period was from 1995-2011, and the NATA estimates were made in 2002 because it was approximately half way between the start and end of the follow-up period. However, it is unclear whether exposures fall within relevant exposure windows for the outcome of interest.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Annual linkage between the CTS cohort and the California Cancer Registry (CCR) was used to identify cases of invasive breast cancer. The CCR is estimated to be 99% complete. The case of invasive breast cancer was defined by ICD codes.

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Study Citation:	Garcia, E., Hurley, S., Nelson, D.O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health: A Global Access Science Source 14(1):14.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	breast cancer in females
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	3014082

Domain	Metric		Rating	Comments
	Metric 8:	Reporting Bias	Medium	A description of measured outcome is reported for adjustments by age and race, and effect estimates are reported with a 95% confidence interval. The measured outcomes using multiple comparisons were generally described in the text, but non-significant results were excluded from Table 3.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	The models were stratified by age and race. Additionally, adjustments were made for multiple comparisons among subsets of the participants (significant results reported in Table 3). Socioeconomic status (SES) of each participant was not evaluated, however, cohort SES characteristics were thought to be similar by study authors.
	Metric 10:	Covariate Characterization	Medium	Information about baseline characteristics for each participant was collected through a questionnaire. It is unknown if the questionnaire was validated.
	Metric 11:	Co-exposure Counfounding	Medium	A total of 37 compounds were identified as mammary gland carcinogens, but 13 were not included in this analysis. Thirteen compounds were excluded from the analysis due to insufficient variability (nine because they had the same value for all census tracts in the state of California; and four because they had less than 25% non-zero values). Ethylene dichloride (1,2-dichloroethane) was among the 24 compounds evaluated in this assessment, and evaluations for breast cancer were conducted for each of these 24 individual compounds.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen (prospective cohort) was appropriate for the research question (incidence of breast cancer). Cox proportional hazard models and SAS 9.3 were used in this assessment. Data analysis was described.
	Metric 13:	Statistical Power	Medium	Statistical power calculations were not provided. No significant effects were observed with ethylene dichloride (1,2-dichloroethane), however, this study utilized a large cohort, approximately 112,000 individuals. Distributions of chemicals of interest suggest there were sufficient numbers of participants in exposure subgroups.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to understand precisely what has been done and to be conceptually reproducible with access to the analytic data.
	Metric 15:	Statistical Analysis	High	The statistical models that were used were identified and described. ”No apparent violation of the underlying assumption of proportional hazards was detected”.

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Study Citation:	Garcia, E., Hurley, S., Nelson, D.O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health: A Global Access Science Source 14(1):14.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	breast cancer in females
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	3014082

Domain	Metric	Rating	Comments
Additional Comments:	A group of 112,378 female participants from the California Teacher Study cohort were assessed for their estimated exposure to ambient air pollutants, including ethylene dichloride (1,2-dichloroethane), and the incidence of invasive breast cancer. Air contaminant concentrations were estimated using the US EPA NATA and the ASPEN and HEM models. The approximate median concentration of 1,2-dichloroethane is between 1E-4 and 1E-2 (estimated from Figure 1). Exposures were categorized into 5 Quintiles, and compared against Quintile 1. No significant increase in the estimated hazard rate ratio for invasive breast cancer was observed with Quintile 2-5 exposure estimates for 1,2-dichloroethane, adjusted for age and race, when compared against Quintile 1, or when further adjusted using multiple comparisons.		

Overall Quality Determination High

* No biomarkers were identified for this evaluation.

Study Citation:	Garcia, E., Hurley, S., Nelson, D.O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health: A Global Access Science Source 14(1):14.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	breast cancer in females
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	3014082

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	A total of 112,378 women were included in this study out of 133,479 eligible female participants from the California Teacher Study cohort. A full description of the cohort is provided in Bernstein et al. 2002 (HERO ID 808446). Reasons for exclusion were provided. The reported information indicates that participant selection in or out of the study and participation was not likely to be biased.
	Metric 2:	Attrition	High	112,378/133,479 participants were included in the study. Exclusions were for the purpose of the study and analysis. Exclusion criteria were documented. Included participants had completed questionnaires. The California Cancer Registry is estimated to be 99% complete.
	Metric 3:	Comparison Group	Medium	There is only indirect evidence that groups are similar. Participants were recruited from the same eligible population with the same method of ascertainment. Comparisons were provided for participants with and without breast cancer. Characteristics between these two groups were generally similar. 5 Quintiles of exposure were used, and Q2-5 were compared with Q1.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	High	The Assessment System for Population Exposure Nationwide and the Human Exposure Model are used as part of the National-Scale Air Toxics Assessment produced by the EPA and was used to estimate ambient HAP concentrations for geographic locations. Methods are described online through the US EPA Assessment Methods.
	Metric 5:	Exposure Levels	Medium	The distribution of the NATA annual ambient concentration for each compound was plotted in Figure 1 using a box plot, and 5 Quintiles were used in the analyses.
	Metric 6:	Temporality	Medium	The follow-up period was from 1995-2011, and the NATA estimates were made in 2002 because it was approximately half way between the start and end of the follow-up period. However, it is unclear whether exposures fall within relevant exposure windows for the outcome of interest.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Annual linkage between the CTS cohort and the California Cancer Registry (CCR) was used to identify cases of invasive breast cancer. The CCR is estimated to be 99% complete. The case of invasive breast cancer was defined by ICD codes.
	Metric 8:	Reporting Bias	Medium	A description of measured outcome is reported for adjustments by age and race, and effect estimates are reported with a 95% confidence interval. The measured outcomes using multiple comparisons were generally described in the text, but non-significant results were excluded from Table 3.

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Study Citation:	Garcia, E., Hurley, S., Nelson, D.O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health: A Global Access Science Source 14(1):14.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	breast cancer in females
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	3014082

Domain	Metric		Rating	Comments
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	The models were stratified by age and race. Additionally, adjustments were made for multiple comparisons among subsets of the participants (significant results reported in Table 3). Socioeconomic status (SES) of each participant was not evaluated, however, cohort SES characteristics were thought to be similar by study authors.
	Metric 10:	Covariate Characterization	Medium	Information about baseline characteristics for each participant was collected through a questionnaire. It is unknown if the questionnaire was validated.
	Metric 11:	Co-exposure Counfounding	Medium	A total of 37 compounds were identified as mammary gland carcinogens, but 13 were not included in this analysis. Thirteen compounds were excluded from the analysis due to insufficient variability (nine because they had the same value for all census tracts in the state of California; and four because they had less than 25% non-zero values). Ethylene dichloride (1,2-dichloroethane) was among the 24 compounds evaluated in this assessment, and evaluations for breast cancer were conducted for each of these 24 individual compounds.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen (prospective cohort) was appropriate for the research question (incidence of breast cancer). Cox proportional hazard models and SAS 9.3 were used in this assessment. Data analysis was described.
	Metric 13:	Statistical Power	Medium	Statistical power calculations were not provided. No significant effects were observed with ethylene dichloride (1,2-dichloroethane), however, this study utilized a large cohort, approximately 112,000 individuals. Distributions of chemicals of interest suggest there were sufficient numbers of participants in exposure subgroups.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to understand precisely what has been done and to be conceptually reproducible with access to the analytic data.
	Metric 15:	Statistical Analysis	High	The statistical models that were used were identified and described. ”No apparent violation of the underlying assumption of proportional hazards was detected”.

Additional Comments: A group of 112,378 female participants from the California Teacher Study cohort were assessed for their estimated exposure to ambient air pollutants, including ethylene dichloride (1,2-dichloroethane), and the incidence of invasive breast cancer. Air contaminant concentrations were estimated using the US EPA NATA and the ASPEN and HEM models. The approximate median concentration of 1,2-dichloroethane is between 1E-4 and 1E-2 (estimated from Figure 1). Exposures were categorized into 5 Quintiles, and compared against Quintile 1. No significant increase in the estimated hazard rate ratio for invasive breast cancer was observed with Quintile 2-5 exposure estimates for 1,2-dichloroethane, adjusted for age and race, when compared against Quintile 1, or when further adjusted using multiple comparisons.

Overall Quality Determination High

* No biomarkers were identified for this evaluation.

Study Citation:	Guo, P., Yokoyama, K., Piao, F., Sakai, K., Khalequzzaman, M., Kamijima, M., Nakajima, T., Kitamura, F. (2013). Sick building syndrome by indoor air pollution in Dalian, China. International Journal of Environmental Research and Public Health 10(4):1489-1504.
Health Outcome(s):	sick building syndrome
Reported Health Effect(s):	The statistical analysis considers all subjective self-reported symptoms together (not segregated by health outcome) as a group health outcome –sick building syndrome. The study compared two conditions for each studied chemical: combined self-reported symptoms to no symptoms. Therefore, only one form 3 was completed.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1938385

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Residents of a housing estate of 3000 homes were invited to a community meeting to explain the purpose of the study and volunteers were invited to participate. It was not reported whether these volunteers were different from the overall eligible population.
	Metric 2:	Attrition	Low	Of the 70 families that agreed to participate, questionnaires were provided by 59. Reasons of uncompleted questionnaires were not fully provided, and there was no comparison between those who participated and those who did not.
	Metric 3:	Comparison Group	Low	The overall description of the analysis sample indicated a wide range of ages and lengths of stay at the current residence. Thus it is hard to know that subjects in all exposure groups were similar. In addition, the methods of selecting participants in all exposure groups were not fully reported. The numbers of male and female smokers were reported, respectively, but the smoking status and age were not controlled in the statistical analysis.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure concentrations for each home were obtained by diffusion sampling over 24 hrs in the bedroom, kitchen, and outdoors; temperature, the vertical height of samplers, and ventilation (hours windows left open) were reported. Samples were analyzed by GC/MS. The number of samples per home is unclear. The frequency of measurements for each house was not reported.
	Metric 5:	Exposure Levels	Low	The frequency of detection was not reported, so it is difficult to ascertain the actual exposure range. In addition, the reported exposure levels were median, geometric mean, and 95% CI, so they are inadequate to develop an exposure-response estimate.
	Metric 6:	Temporality	Uninformative	For 1,2-dichloroethane, the study evaluated self-reported symptoms in the past (”since they moved into their flats”) and their association with sampling conducted during the study; thus, exposure was measured after the outcome.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Low	Participants provided self-reported symptoms using a questionnaire. Study authors cited a previous study, Kamijima et al., 2005 (in Japanese, HERO ID 1598645) for further details on the questionnaire. It was not clear whether the questionnaire was validated.

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Study Citation: Guo, P., Yokoyama, K., Piao, F., Sakai, K., Khalequzzaman, M., Kamijima, M., Nakajima, T., Kitamura, F. (2013). Sick building syndrome by indoor air pollution in Dalian, China. International Journal of Environmental Research and Public Health 10(4):1489-1504.

Health Outcome(s): sick building syndrome

Reported Health Effect(s): The statistical analysis considers all subjective self-reported symptoms together (not segregated by health outcome) as a group health outcome –sick building syndrome. The study compared two conditions for each studied chemical: combined self-reported symptoms to no symptoms. Therefore, only one form 3 was completed.

Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

Linked HERO ID(s): No linked references.

HERO ID: 1938385

Domain	Metric		Rating	Comments
	Metric 8:	Reporting Bias	Low	The study only mentioned subjective symptoms in the abstract or methods. The abstract and method sections did not report the specific symptoms included in the questionnaire or whether the questionnaire was open-ended for symptoms. The questionnaire was cited to Kamijima et al. 2005 (in Japanese).
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	Comparisons were made separately by sex. The distribution of age and time spent living in residence differed greatly between those reporting symptoms and those not reporting symptoms. Smoking was indicated but not controlled for in the analysis. In short, the statistical analysis did not consider these three potential confounders, age, time spent living in residence, and smoking.
	Metric 10:	Covariate Characterization	Low	Covariates were presumably evaluated via a questionnaire that was cited to Kamijima et al. 2005 (in Japanese).
	Metric 11:	Co-exposure Counfounding	Low	The analysis did not account for other exposures. A number of other VOCs, HCHO, and NO2 were measured in the homes. The concentrations of several other VOCs and HCHO were much higher (5-30x) than 1,2-dichloroethane and may also be associated with these symptoms.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Low	The study design is best characterized as cross-sectional. Only one analysis to compare exposure concentrations between those with and without symptoms was adjusted for a confounder, sex, via stratification. Other potential confounders were not adjusted for. Study authors combine responses for symptoms reported before and during the sampling period in one statistical analysis, which may not reflect the relationship between symptoms and contaminants' exposure at each period.
	Metric 13:	Statistical Power	Medium	Statistical power was not reported. The number of participants was sufficient to detect a difference in median concentration between those with and without symptoms.
	Metric 14:	Reproducibility of Analyses	Medium	Study presents sufficient description of analysis (statistical methods) to be conceptually reproducible with access to the raw data.
	Metric 15:	Statistical Analysis	Low	Study uses a Wilcoxon's rank sum test to compare exposure concentrations in persons with and without symptoms; test for equal variance is not reported.

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Study Citation:	Guo, P., Yokoyama, K., Piao, F., Sakai, K., Khalequzzaman, M., Kamijima, M., Nakajima, T., Kitamura, F. (2013). Sick building syndrome by indoor air pollution in Dalian, China. International Journal of Environmental Research and Public Health 10(4):1489-1504.
Health Outcome(s):	sick building syndrome
Reported Health Effect(s):	The statistical analysis considers all subjective self-reported symptoms together (not segregated by health outcome) as a group health outcome –sick building syndrome. The study compared two conditions for each studied chemical: combined self-reported symptoms to no symptoms. Therefore, only one form 3 was completed.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1938385

Domain	Metric	Rating	Comments
Additional Comments:	Concentrations of VOCs (including 1,2-dichloroethane), HCHO, and NO2 were measured in the 59 homes of families that agreed to participate after being informed of the nature of the study. Participants completed questionnaires asking about symptoms since they moved into the homes and the concentrations of selected compounds were compared among men and women reporting any symptoms vs no symptoms. Concentrations of 1,2-dichloroethane in homes of people with symptoms were higher than in homes without. p-Dichlorobenzene was measured in the homes as well, but median concentration was <DL and no further analysis was made. Unacceptable due to selection bias, lack of confounding control, inadequate outcome characterization, and lack of temporality.		

Overall Quality Determination — Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Kernan, G.J., Ji, B.T., Dosemeci, M., Silverman, D.T., Balbus, J., Zahm, S.H. (1999). Occupational risk factors for pancreatic cancer: A case-control study based on death certificates from 24 U.S. states. American Journal of Industrial Medicine 36(2):260-270.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Death from pancreatic cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	194820

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	The National Cancer Institute, National Institute of Occupational Safety and Health, and the National Center for Health Statistics reviewed death certificates from 24 states to select cases from those that had died from pancreatic cancer and matched controls. Controls with cause of death related to the outcome of interest (i.e. pancreatic diseases) were excluded from the study. All key elements of the study design were reported.
	Metric 2:	Attrition	Medium	There was no direct evidence of subject loss or exclusion of subgroups from analyses. The authors provide the total number of cases and controls in the analysis. Case and control data were taken from a registry. It can be assumed that the data are complete for each subject.
	Metric 3:	Comparison Group	High	Controls were selected from the same pool of death certificates from 24 states that cases were selected from. Controls with cause of death related to the outcome of interest were eliminated. Differences in baseline characteristics were controlled for via matching, stratification, and adjustment.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure was assessed via occupation and industry data on death certificates. A job matrix was further applied to assess the likely levels of exposure. Probability and intensity of exposure were estimated across four levels for each occupation. Only employment captured on the death certificate could be considered. The exposure assessment needs exposure information before the job listed on the death certificates.
	Metric 5:	Exposure Levels	Medium	The study offers 4 levels of estimated probability and intensity of exposure (referent, low, medium, high).
	Metric 6:	Temporality	Medium	Exposure was determined by occupational and industry codes on death certificates and indicate that exposure would precede disease, however, the timing and latency period is less clear.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Causes of mortality were determined from death certificates for both cases and controls. Death certificates were drawn from death registries of participating states (n=24). Causes of death were coded using ICD-9 codes, and pancreatic cancer was identified as ICD 157.
	Metric 8:	Reporting Bias	Medium	Measured outcomes, effect estimates and confidence intervals are reported. Number of exposed cases is reported for each analysis, however the number of controls (exposed and unexposed) are not reported for analyses.

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Study Citation:	Kernan, G.J., Ji, B.T., Dosemeci, M., Silverman, D.T., Balbus, J., Zahm, S.H. (1999). Occupational risk factors for pancreatic cancer: A case-control study based on death certificates from 24 U.S. states. American Journal of Industrial Medicine 36(2):260-270.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Death from pancreatic cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	194820

Domain	Metric		Rating	Comments
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Potential confounders were accounted for in the following ways: matching (five year age group, state, race, and gender); adjustment in models (age, marital status, metropolitan, and residential status); and stratification (race and gender). Smoking was not included as a confounder.
	Metric 10:	Covariate Characterization	Medium	Data used to assess potential confounders was derived from death certificates, an adequate measure. However, no information about cigarette smoking and other lifestyle factors were available for adjustment in the analysis.
	Metric 11:	Co-exposure Counfounding	Medium	The variety of industries considered in the analysis diminishes concerns about co-exposures.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The case-control study design and statistical analysis methods were appropriate to assess the exposures/outcome of interest.
	Metric 13:	Statistical Power	Medium	This study had an adequate sample size to detect an effect (n for cases = 63,097; n for controls = 252,386).
	Metric 14:	Reproducibility of Analyses	Medium	The description of analysis was sufficient and would be reproducible.
	Metric 15:	Statistical Analysis	High	The model to calculate risk estimates was transparent.

Additional Comments: This case-control study examined the risk of death from pancreatic cancer in different occupational settings. Exposure was solely assessed using occupation/industry at time of death (reported on death certificate) and the application of a job matrix assessing likely levels of exposure for different positions. This means of estimating exposure may not fully represent a participant's exposure history. Additionally, the number of impacted participants (exposed cases) was inadequate to perform quality analyses for some exposure levels.

Overall Quality Determination High

* No biomarkers were identified for this evaluation.

Study Citation:	Kernan, G.J., Ji, B.T., Dosemeci, M., Silverman, D.T., Balbus, J., Zahm, S.H. (1999). Occupational risk factors for pancreatic cancer: A case-control study based on death certificates from 24 U.S. states. American Journal of Industrial Medicine 36(2):260-270.
Health Outcome(s):	Endocrine
Reported Health Effect(s):	Death from pancreatic cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	194820

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	The National Cancer Institute, National Institute of Occupational Safety and Health, and the National Center for Health Statistics reviewed death certificates from 24 states to select cases from those that had died from pancreatic cancer and matched controls. Controls with cause of death related to the outcome of interest (i.e. pancreatic diseases) were excluded from the study. All key elements of the study design were reported.
	Metric 2:	Attrition	Medium	There was no direct evidence of subject loss or exclusion of subgroups from analyses. The authors provide the total number of cases and controls in the analysis. Case and control data were taken from a registry. It can be assumed that the data are complete for each subject.
	Metric 3:	Comparison Group	High	Controls were selected from the same pool of death certificates from 24 states that cases were selected from. Controls with cause of death related to the outcome of interest were eliminated. Differences in baseline characteristics were controlled for via matching, stratification, and adjustment.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure was assessed via occupation and industry data on death certificates. A job matrix was further applied to assess the likely levels of exposure. Probability and intensity of exposure were estimated across four levels for each occupation. Only employment captured on the death certificate could be considered. The exposure assessment needs exposure information before the job listed on the death certificates.
	Metric 5:	Exposure Levels	Medium	The study offers 4 levels of estimated probability and intensity of exposure (referent, low, medium, high).
	Metric 6:	Temporality	Medium	Exposure was determined by occupational and industry codes on death certificates and indicate that exposure would precede disease, however, the timing and latency period is less clear.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Causes of mortality were determined from death certificates for both cases and controls. Death certificates were drawn from death registries of participating states (n=24). Causes of death were coded using ICD-9 codes, and pancreatic cancer was identified as ICD 157.
	Metric 8:	Reporting Bias	Medium	Measured outcomes, effect estimates and confidence intervals are reported. Number of exposed cases is reported for each analysis, however the number of controls (exposed and unexposed) are not reported for analyses.
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Kernan, G.J., Ji, B.T., Dosemeci, M., Silverman, D.T., Balbus, J., Zahm, S.H. (1999). Occupational risk factors for pancreatic cancer: A case-control study based on death certificates from 24 U.S. states. American Journal of Industrial Medicine 36(2):260-270.
Health Outcome(s):	Endocrine
Reported Health Effect(s):	Death from pancreatic cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	194820

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Medium	Potential confounders were accounted for in the following ways: matching (five year age group, state, race, and gender); adjustment in models (age, marital status, metropolitan, and residential status); and stratification (race and gender). Smoking was not included as a confounder.
	Metric 10:	Covariate Characterization	Medium	Data used to assess potential confounders was derived from death certificates, an adequate measure. However, no information about cigarette smoking and other lifestyle factors were available for adjustment in the analysis.
	Metric 11:	Co-exposure Counfounding	Medium	The variety of industries considered in the analysis diminishes concerns about co-exposures.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The case-control study design and statistical analysis methods were appropriate to assess the exposures/outcome of interest.
	Metric 13:	Statistical Power	Medium	This study had an adequate sample size to detect an effect (n for cases = 63,097; n for controls = 252,386).
	Metric 14:	Reproducibility of Analyses	Medium	The description of analysis was sufficient and would be reproducible.
	Metric 15:	Statistical Analysis	High	The model to calculate risk estimates was transparent.

Additional Comments: This case-control study examined the risk of death from pancreatic cancer in different occupational settings. Exposure was solely assessed using occupation/industry at time of death (reported on death certificate) and the application of a job matrix assessing likely levels of exposure for different positions. This means of estimating exposure may not fully represent a participant's exposure history. Additionally, the number of impacted participants (exposed cases) was inadequate to perform quality analyses for some exposure levels.

Overall Quality Determination High

* No biomarkers were identified for this evaluation.

Study Citation:	Niehoff, N.M., Gammon, M.D., Keil, A.P., Nichols, H.B., Engel, L.S., Sandler, D.P., White, A.J. (2019). Airborne mammary carcinogens and breast cancer risk in the Sister Study. Environment International 130:104897.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Breast cancer diagnosis (overall), tumor characteristics, and estrogen receptor positive (ER+) invasive breast cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5440630

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	Data from the Sister Study were used. The Sister Study is "a prospective cohort of 50,884 women from across the US who were ages 35–74 at enrollment (Sandler et al., 2017). Participants were recruited from 2003 to 2009 using a national advertising campaign in English and Spanish. Women were eligible for the Sister Study if they had a sister who had been diagnosed with breast cancer, but no prior breast cancer themselves."Exclusions from the study occurred for the following reasons:-breast cancer diagnosed before enrollment was complete, or did not have follow-up information (n = 163)-Residential address couldn't be geocoded (n = 1003, < 2%) - This is a small perecentage, but all of those who were excluded for this reason were from Puerto Rico, West Virginia, Missouri, or Oklahoma.Key elements of the study design are reported. There is some potential for selection bias, but based on the small percentage of those eligible who were excluded, participation was not likely to be substantially biased.
	Metric 2:	Attrition	High	Response rates in the overall Sister study remained over 91% over follow-up. Reasons for non-response were not reported, and characteristics of those lost to follow up were not reported or compared with those included, but 9% loss to follow-up is minimal.
	Metric 3:	Comparison Group	High	Differences in baseline characteristics of groups were considered as potential confounding variables.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	The EPA NATA database of census-tract level modeled air toxics data was used. The study authors note the potential for exposure misclassification: "Concentrations at the census tract level do not fully account for variation in an individual's daily activities that could lead to higher or lower exposure, and all women within a census tract are assigned the same concentration."
	Metric 5:	Exposure Levels	Medium	There were five quintiles of exposure, so there was a sufficient range and distribution of exposure.
	Metric 6:	Temporality	Medium	This is a prospective cohort study.Exposure data from 2005 were chosen because they represented the middle of the enrollment period (2003-2009).The study reported that "94% of women enrolled in 2005 or later, and thus the exposure assessment primarily predated enrollment for the majority of Sister Study participants."The six percent of women who had the potential to have the outcome before exposure was measured in 2005 are a concern. But sensitivity analyses were used to assess whether the associations changed when restricted to those who enrolled in 2005 or later.The authors note that the study is making assumptions about the relevant exposure windows - therefore the exposure window is not certain.

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Study Citation:	Niehoff, N.M., Gammon, M.D., Keil, A.P., Nichols, H.B., Engel, L.S., Sandler, D.P., White, A.J. (2019). Airborne mammary carcinogens and breast cancer risk in the Sister Study. Environment International 130:104897.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Breast cancer diagnosis (overall), tumor characteristics, and estrogen receptor positive (ER+) invasive breast cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5440630

Domain	Metric		Rating	Comments
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Women who reported a breast cancer diagnosis on the annual health updates or follow-up questionnaires were asked to provide additional diagnosis information, and to grant permission for the study to obtain medical records and pathology reports. Medical records were obtained for 81% of breast cancer diagnoses. Agreement between self-reported breast cancers and medical records was high (positive predictive value > 99%) (Sandler et al., 2017), so self-report was used when medical records were not available. Tumor characteristics (stage; histology; and estrogen receptor (ER) status) were abstracted from medical records, or self-reported.
	Metric 8:	Reporting Bias	High	A description of measured outcomes is reported. Effect estimates are reported with confidence intervals.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Covariates considered included age, race, BMI, residence type, education, and smoking status. Potential confounders were identified using DAGs and literature review. Appropriate considerations were made for potential confounders.
	Metric 10:	Covariate Characterization	Medium	”Most covariates were assessed by self-report at the baseline interview.””At baseline, women completed a computer-assisted telephone interview and written questionnaires.”Previous publications might describe whether the questionnaires were validated, but validation was not specified in this publication.
	Metric 11:	Co-exposure Counfounding	Medium	Co-exposures to other air pollutants were assessed, but at the census tract level.Multipollutant classification trees were used, which might provide useful qualitative information.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design (large prospective cohort) and analysis method (Cox proportional hazard single and multi-pollutant models accounting for potential confounders) were appropriate to assess the association between exposure and disease.
	Metric 13:	Statistical Power	Medium	The study had an adequate sample size (1975 cancer cases) and follow-up time (mean=8.4 years).
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to be conceptually reproducible.

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Study Citation:	Niehoff, N.M., Gammon, M.D., Keil, A.P., Nichols, H.B., Engel, L.S., Sandler, D.P., White, A.J. (2019). Airborne mammary carcinogens and breast cancer risk in the Sister Study. Environment International 130:104897.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Breast cancer diagnosis (overall), tumor characteristics, and estrogen receptor positive (ER+) invasive breast cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5440630

Domain	Metric	Rating	Comments
	Metric 15: Statistical Analysis	High	Hazard ratios and 95% confidence intervals (CIs) are reported "comparing index categories of exposure to exposures below the first quintile using Cox proportional hazards regression, with age as the time scale." The method of calculating the hazard ratios is transparent. The authors reported that "the proportional hazards assumption was evaluated by conducting a Wald test for an interaction between the continuous form of the air toxic measure and time." Censoring times and times at-risk are described.

Additional Comments: This was a well-conducted study of a large prospective cohort, but the measurement of exposure at the census-tract rather than the individual level is a limitation.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Sobel, W., Bond, G.G., Skowronski, B.J., Brownson, P.J., Cook, R.R. (1987). A soft tissue sarcoma case control study in a large multi-chemical manufacturing facility. Chemosphere 16(8-9):2095-2099.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	soft-tissue sarcoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1357737

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	From a pool of > 37,000 subjects who worked at least 1 year at chemical company between January 1940-December 1979, the study identified 14 people who died due to soft-cell sarcoma (via death certificate, medical records, or histopathology report). Referents were matched 9:1 with cases (126 matched controls).
	Metric 2:	Attrition	High	There was minimal subject exclusion from the analysis sample; one case could not be matched to controls and was excluded from analysis.
	Metric 3:	Comparison Group	High	Cases and controls were recruited from the same eligible population within the same time frame and matched on sex, race, year of birth and year of hire. Both cases and controls had to have worked ≥1 yr at the plant during the study period.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Work histories for cases and referents were coded to determine an individual's potential exposure to chemical of interest and reviewed by an industrial hygienist blinded to case status.
	Metric 5:	Exposure Levels	Low	Exposure was considered dichotomous, ever exposed or never exposed. There is no quantitative information on exposure levels or range of exposures.
	Metric 6:	Temporality	Low	Temporality of exposure and outcome is established. It is unclear if the interval between exposure and outcome is sufficient for soft tissue sarcoma outcomes.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	The soft-tissue sarcoma outcome was assessed by information provided by death certificates, medical records, and histopathology reports, but study authors did not report the proportions determined by each method.
	Metric 8:	Reporting Bias	High	All outcomes outlined were reported. Authors reported the number of cases and controls in the table. Maximum likelihood estimate ORs with respective 95 % confidence intervals were reported.
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Sobel, W., Bond, G.G., Skowronski, B.J., Brownson, P.J., Cook, R.R. (1987). A soft tissue sarcoma case control study in a large multi-chemical manufacturing facility. Chemosphere 16(8-9):2095-2099.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	soft-tissue sarcoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1357737

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Low	Controls were matched with cases on age, sex, year of hire and survival information. There is indirect evidence that the considerations were made to identify potential confounders through evaluation of medical records of cases and controls (various heritable syndromes, family history of cancer, history of lymphedema, steroids, throrotrast, foreign body implants, chronic extensive scarring, radiation therapy, and immunological defects). Identified confounders between cases and controls were not reported and it is unclear if adjustments for these confounders were included in the final analyses.
	Metric 10:	Covariate Characterization	High	Potential covariates were assessed through evaluation of work histories and medical records.
	Metric 11:	Co-exposure Counfounding	Low	The study documented 13 chemicals, known to be associated with soft-tissue sarcoma (according to NTP, 1983) that were used at the manufacturing facility at some point since 1940. The authors note that some individuals were exposed to multiple chemicals during their employment history and were counted multiple times in the analysis for different chemical exposures. Co-exposures to chemicals to not appear to be adjusted for in analysis.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Low	The study design was adequate to assess the association between exposure and the outcome of interest (soft-tissue sarcoma). The study authors noted they used programs developed by Rothman and Boice to calculate odds ratios with CI intervals; the statistical methods are not further described. The page containing the Rothman and Boice reference appears to be missing from the PDF (or the citation is missing).
	Metric 13:	Statistical Power	Low	Statistical power was not calculated. For 1,2-dichloroethane, there was one case and 6 controls included in the analysis, which was not adequate to detect and effect.
	Metric 14:	Reproducibility of Analyses	Low	The study calculated odd ratios, and 95% CIs were calculated using point estimates and chi from hypothesis testing. The study authors noted they used programs developed by Rothman and Boice to calculate odds ratios with 95% CIs; the statistical methods are not further described and there was no reference for the programs cited.
	Metric 15:	Statistical Analysis	Low	A description of analyses/assumptions was not reported.

Additional Comments: A case-control study of workers at a chemical production facility who worked at least 1 year between January 1940-December 1979 (n=37,000) investigated the incidence of deaths due to soft-tissue sarcoma. The study identified 14 people who died due to soft-tissue sarcoma (through death certificate, medical records, or histopathology reports). Cases were matched to controls based on sex, race, year of birth and year of hire. 13 chemicals, including 1,2-dichloroethane, associated with soft-tissue sarcoma were used at the facility; it does not appear that co-exposures were adjusted for in the analysis. Odds ratios and corresponding CIs were calculated. No significant association was found between exposure to 1,2-DCE and soft-tissue sarcoma.

Overall Quality Determination Medium

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Study Citation:	Sobel, W., Bond, G.G., Skowronski, B.J., Brownson, P.J., Cook, R.R. (1987). A soft tissue sarcoma case control study in a large multi-chemical manufacturing facility. Chemosphere 16(8-9):2095-2099.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	soft-tissue sarcoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1357737

Domain	Metric	Rating	Comments

* No biomarkers were identified for this evaluation.

Study Citation:	Sobel, W., Bond, G.G., Skowronski, B.J., Brownson, P.J., Cook, R.R. (1987). A soft tissue sarcoma case control study in a large multi-chemical manufacturing facility. Chemosphere 16(8-9):2095-2099.
Health Outcome(s):	Skin and Connective Tissue
Reported Health Effect(s):	soft-tissue sarcoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1357737

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	From a pool of > 37,000 subjects who worked at least 1 year at chemical company between January 1940-December 1979, the study identified 14 people who died due to soft-cell sarcoma (via death certificate, medical records, or histopathology report). Referents were matched 9:1 with cases (126 matched controls).
	Metric 2:	Attrition	High	There was minimal subject exclusion from the analysis sample; one case could not be matched to controls and was excluded from analysis.
	Metric 3:	Comparison Group	High	Cases and controls were recruited from the same eligible population within the same time frame and matched on sex, race, year of birth and year of hire. Both cases and controls had to have worked ≥1 yr at the plant during the study period.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Work histories for cases and referents were coded to determine an individual's potential exposure to chemical of interest and reviewed by an industrial hygienist blinded to case status.
	Metric 5:	Exposure Levels	Low	Exposure was considered dichotomous, ever exposed or never exposed. There is no quantitative information on exposure levels or range of exposures.
	Metric 6:	Temporality	Low	Temporality of exposure and outcome is established. It is unclear if the interval between exposure and outcome is sufficient for soft tissue sarcoma outcomes.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	The soft-tissue sarcoma outcome was assessed by information provided by death certificates, medical records, and histopathology reports, but study authors did not report the proportions determined by each method.
	Metric 8:	Reporting Bias	High	All outcomes outlined were reported. Authors reported the number of cases and controls in the table. Maximum likelihood estimate ORs with respective confidence intervals were reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	Controls were matched with cases on age, sex, year of hire and survival information. There is indirect evidence that that considerations were made to identify potential confounders through evaluation of medical records of cases and controls (various heritable syndromes, family history of cancer, history of lymphedema, steroids, throrotrast, foreign body implants, chronic extensive scarring, radiation therapy, and immunological defects). Identified confounders between cases and controls were not reported and it is unclear if adjustments for these confounders were included in the final analyses.

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Study Citation:	Sobel, W., Bond, G.G., Skowronski, B.J., Brownson, P.J., Cook, R.R. (1987). A soft tissue sarcoma case control study in a large multi-chemical manufacturing facility. Chemosphere 16(8-9):2095-2099.
Health Outcome(s):	Skin and Connective Tissue
Reported Health Effect(s):	soft-tissue sarcoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1357737

Domain	Metric		Rating	Comments
	Metric 10:	Covariate Characterization	High	Potential covariates were assessed through evaluation of work histories and medical records.
	Metric 11:	Co-exposure Counfounding	Low	The study documented 13 chemicals, known to be associated with soft-tissue sarcoma (according to NTP, 1983) that were used at the manufacturing facility at some point since 1940. The authors note that some individuals were exposed to multiple chemicals during their employment history and were counted multiple times in the analysis for different chemical exposures. Co-exposures to chemicals to not appear to be adjusted for in analysis.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Low	The study design was adequate to assess the association between exposure and the outcome of interest (soft-tissue sarcoma). The study authors noted they used programs developed by Rothman and Boice to calculate odds ratios with (95% CIs; the statistical methods are not further described. The page containing the Rothman and Boice reference appears to be missing from the PDF (or the citation is missing).
	Metric 13:	Statistical Power	Low	Statistical power was not calculated. For 1,2-dichloroethane, there was one case and 6 controls included in the analysis, which was not adequate to detect and effect.
	Metric 14:	Reproducibility of Analyses	Low	The study calculated odd ratios, and 95% CIs were calculated using point estimates and chi from hypothesis testing. The study authors noted they used programs developed by Rothman and Boice to calculate odds ratios with CI intervals; the statistical methods are not further described and there was no reference for the programs cited.
	Metric 15:	Statistical Analysis	Low	A description of analyses/assumptions was not reported.

Additional Comments: A case-control study of workers at a chemical production facility who worked at least 1 year between January 1940-December 1979 (n=37,000) investigated the incidence of deaths due to soft-tissue sarcoma. The study identified 14 people who died due to soft-tissue sarcoma (through death certificate, medical records, or histopathology reports). Cases were matched to controls based on sex, race, year of birth and year of hire. 13 chemicals, including 1,2-dichloroethane, associated with soft-tissue sarcoma were used at the facility; it does not appear that co-exposures were adjusted for in the analysis. Odds ratios and corresponding CIs were calculated. No significant association was found between exposure to 1,2-DCE and soft-tissue sarcoma.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Teta, M. J., Ott, M. G., Schnatter, A. R. (1991). An update of mortality due to brain neoplasms and other causes among employees of a petrochemical facility. Journal of Occupational Medicine 33(1):45-51.
Health Outcome(s):	Mortality
Reported Health Effect(s):	all cause mortality, gastrointestinal cancer mortality, respiratory system cancer mortality, kidney and other urinary organ cancer mortality, skin cancer mortality, brain cancer mortality, lymphatic and hematopoietic tissue cancer mortality, benign neoplasm mortality, heart disease mortality, and liver cirrhosis mortality.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200633, 1629047
HERO ID:	200633

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	The facility was described in some detail. All male employees working for one day or more between 1941 and 1983 were included. There may be some healthy worker effect in this population.
	Metric 2:	Attrition	High	Study authors reported that vital status was complete for 99% of the population, and death certificates were obtained for 99% of decedents.
	Metric 3:	Comparison Group	High	SMRs were calculated using age-, race-, and calendar year-specific mortality rates of males in the United States. All included employees were male.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	All employees were treated as exposed. Table 4 indicates that relatively few employees were employed in areas designated as 1,2-DCA work areas. There is potential for substantial exposure misclassification.
	Metric 5:	Exposure Levels	Low	All employed individuals were categorized as exposed, and the reference population was described as unexposed. This represents two levels of exposure. The distribution of exposure within the employed population is unclear.
	Metric 6:	Temporality	Medium	Employees were followed from 1950 (or date of first hire) through 1983. The relevant timing of exposure is not entirely clear; however, this represents a sufficiently long period of follow-up.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Mortality was tracked using company records, Social Security Administration records, and the National Death Index. Specific ICD codes and use of a nosologist were not described, but there was no evidence to suggest the method had poor validity.
	Metric 8:	Reporting Bias	High	SMRs were provided with confidence intervals in addition to observed and expected cases. The authors state they did not carry out regional specific SMRs due to the higher prevalence of neoplasms in the surrounding area.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	SMRs were restricted to males. Rates were age-, race-, and calendar period-specific. No consideration was made for smoking.
	Metric 10:	Covariate Characterization	Medium	Demographic information was obtained from employment records. This was not a validated method, but there was no evidence to suggest it was an invalid method.

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Study Citation:	Teta, M. J., Ott, M. G., Schnatter, A. R. (1991). An update of mortality due to brain neoplasms and other causes among employees of a petrochemical facility. Journal of Occupational Medicine 33(1):45-51.
Health Outcome(s):	Mortality
Reported Health Effect(s):	all cause mortality, gastrointestinal cancer mortality, respiratory system cancer mortality, kidney and other urinary organ cancer mortality, skin cancer mortality, brain cancer mortality, lymphatic and hematopoietic tissue cancer mortality, benign neoplasm mortality, heart disease mortality, and liver cirrhosis mortality.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200633, 1629047
HERO ID:	200633

Domain	Metric		Rating	Comments
	Metric 11:	Co-exposure Counfounding	Low	Several other occupational exposures linked to cancer mortality were present, including vinyl chloride, butanol, and other petrochemicals.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	This study design was appropriate for the research question. Authors utilized retrospective occupational cohort data to determine standardized mortality rates for cancer-specific mortalities.
	Metric 13:	Statistical Power	Medium	While power was not calculated, there were over 1350 deaths from 7849 employees which was adequate to detect robust effect estimates.
	Metric 14:	Reproducibility of Analyses	Low	Most details were provided; however, ICD codes used to determine and group cancer mortality diagnoses were not provided.
	Metric 15:	Statistical Analysis	High	No issues identified.

Additional Comments: This study utilized an occupational cohort to retrospectively evaluate elevated rates of cancer mortality among petrochemical plant workers. There were numerous potentially hazardous chemicals mentioned in the plant description which may lead to co-exposure. Additionally, it appears that only a moderate portion of workers may have been exposed to 1,2-DCA or worked in 1,2-DCA areas which may lead to some exposure misclassification and limit the study's ability to inform hazard on 1,2-DCA.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Cases in this case-control study were former Union Carbide Corporation (UCC) chemical plant employees in Texas City, Texas. Cases were identified through death certificate searches and tumor registries, and may have included individuals formerly employed at UCC whose cause of death was unknown to the company. Additionally, control deaths were stated to be pulled from corporate employee benefits department and through locally published obituary notices routinely screened by the medical department - it is possible to assume that cases were identified in a similar manner. The study identified cases of brain tumors by searching death certificates primarily, although tumor registries throughout the state of Texas were also searched. The study clarifies that it is possible that some cases were not found if they survived or died due to another cause - while this is likely to have impacted selection, there is no evidence that this would be differential by exposure status. Overall, there is limited information on the source population of workers from which cases were identified.
	Metric 2:	Attrition	Medium	Attrition is not discussed in the study, and outcome data appear to be complete. There was a large proportion of missing exposure data (roughly 50%) due to workers being employed in roles such as maintenance, where exposure to any chemical is possible but unknown. Analyses were run separately where these ”unknown” individuals were a) treated as exposed, b) treated as unexposed, or c) treated as unknown and thus excluded. The study only presents results for when these individuals were excluded but specifies that the first scenario resulted in increased exposure estimates for controls relative to cases.

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Study Citation:	Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
	Metric 3:	Comparison Group	Medium	The study identifies two series of control groups, selected from all former Union Carbide Corporation (UCC) employees. However, the total number of employees is not stated. Only those who were deceased were used as controls since they had known causes of death and could thus be verified as non-brain tumors. One group of controls excluded employees whose cause of death was due to any malignant neoplasm to allow for the possibility that a general chemical carcinogen may have been associated with cancers of other sites. The other group of controls included deaths from all causes; this included malignant neoplasms other than brain tumors. Both control groups had 80 male employees randomly selected from 450 deceased employees known to the company in June 1979. Control deaths were stated to be pulled from corporate employee benefits department and through locally published obituary notices routinely screened by the medical department - it is possible to assume that cases were identified in a similar manner. The study reports that cases were slightly more likely to have been employed for less than 10 years than controls - the study attributes this in part to the fact that employees whose deaths were known to the company were more likely to have worked for longer - regardless the mean number of years employed was similar between cases and controls. However, cases were more likely to have been terminated from their job for reasons other than death, disability, or retirement (quitting, being fired, etc.), were generally younger at hire, and were less likely to survive to their 70th birthday. None of these factors are controlled for in statistical analyses - however, since controls and cases were pulled from the same population, there is indirect evidence that the groups were similar.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was determined based on official employment records. Records included job title and department assignment codes for each employment from date of hire to date of termination. For each unique department code, UCC and NIOSH industrial hygienists identified principal chemicals used or produced at any time in the history of the plant and correlated those with individual departments. This assessment was not performed on a year-by-year basis due to concerns for recall bias for longer-term employees where less detailed records were kept. An employee was categorized as ”exposed” to 1,2-dichloroethane if they ever worked in a department associated with that chemical. An ”unknown” exposure group was also created to account for employees who had only worked in departments for which no specific chemical could be identified.
	Metric 5:	Exposure Levels	Low	The study does not report any quantitative information and only splits exposure into ”exposed”, ”unexposed”, and ”unknown”.
	Metric 6:	Temporality	High	In this study exposure is confirmed to occur before the outcome is measured. The study reports latency periods, with subjects dichotomized into less than 15 years of latency or more than 15 years of latency. The majority of cases and controls had a latency of greater than 15 years, which is sufficiently long for brain tumors.

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Study Citation:	Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Cases were identified through death certificate searches and partially through tumor registries in the state of Texas. Case validation was performed by NIOSH, and 5 different levels of confirmation were reported: 1) tissue specimen interpreted by the Armed Forces Institute of Pathology; 2) autopsy report; 3) histopathology report; 4) clinical diagnosis from hospital record; 5) dearth certificate diagnosis. Codes 1-3 were considered to be ”confirmed” cases of brain tumors, while 4-5 were considered unconfirmed. 5/21 cases were only evaluated using ”unconfirmed methods”, meaning there is likely a high amount of accuracy in roughly 75% of cases. While no case validation is reported for controls, the study specifies that only controls who had died and thus could be confirmed to be non-brain tumors were included.
	Metric 8:	Reporting Bias	Medium	All primary and secondary outcomes that are outlined in the methods are reported in the results. However, the only statistical outcome of their analysis were unadjusted p-values that were not reported and were just described qualitatively.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	The only statistical analysis performed were Mantel-Haenszel chi-squared tests, which did not allow for confounder adjustment. The study does not present a distribution of potential confounders by exposure status but by case/control status. Several variables, such as reason for termination, age at hire, and age at death were significantly different between cases and controls and were not accounted for in statistical modeling. The study explains that these differences are not likely to have any epidemiologic significance and appear to be relatively small differences.
	Metric 10:	Covariate Characterization	Medium	While the study does not explain where they obtained covariate information, it is reasonable to assume that they gathered the information from company records.
	Metric 11:	Co-exposure Counfounding	Low	The study assesses a wide range of other potential occupational co-exposures. While these co-exposures are not adjusted for in any statistical models, effect estimates are presented separately for benzene, diethyl sulfate, ethylene oxide, and vinyl chloride. The distribution of co-exposures across cases and controls is demonstrated to be mostly balanced by comparing proportions of exposed/unexposed between cases and controls. The only notable instance of imbalance is for benzene, where 11.1% of cases were exposed whereas 37.9% of all controls and 19.2% of non-neoplasm related controls were exposed.
Domain 5: Analysis				

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Study Citation:	Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	The study chose a case-control design, which was appropriate to study the rare disease of brain tumors and its association with occupational exposures. The only statistical analysis conducted is a Mantzel-Haenszel chi-squared test, but there is no reason to suggest that this would be inappropriate.
	Metric 13:	Statistical Power	Medium	The study does not calculate statistical power, but the number of cases (n=21) and controls (n=80 in each analysis) is likely sufficient to detect an effect.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to understand what was done and could be reproduced given access to the analytic data.
	Metric 15:	Statistical Analysis	High	The only statistical analysis conducted is a Mantel-Haenszel chi-squared test, and all assumptions were met. The statistical process is transparent.

Additional Comments: This case-control study pulled deceased former employees of the Union Carbide Corporation in Texas City, Texas. The study examined dichotomous exposure to a wide range of occupational exposures, including 1,2-dichloroethane, in relation to brain tumor cases. There is no quantitative estimate of exposure. The only statistical analysis in the study is a Mantel-Haenszel chi-squared test statistic and no statistically significant differences in exposure between cases and controls were observed. The fact that there are no effect estimates, no adjustment for confounders, and no quantitative exposure estimates limits the usefulness of this paper.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Cases in this case-control study were former Union Carbide Corporation (UCC) chemical plant employees in Texas City, Texas. Cases were identified through death certificate searches and tumor registries, and may have included individuals formerly employed at UCC whose cause of death was unknown to the company. Additionally, control deaths were stated to be pulled from corporate employee benefits department and through locally published obituary notices routinely screened by the medical department - it is possible to assume that cases were identified in a similar manner. The study identified cases of brain tumors by searching death certificates primarily, although tumor registries throughout the state of Texas were also searched. The study clarifies that it is possible that some cases were not found if they survived or died due to another cause - while this is likely to have impacted selection, there is no evidence that this would be differential by exposure status. Overall, there is limited information on the source population of workers from which cases were identified.
	Metric 2:	Attrition	Medium	Attrition is not discussed in the study, and outcome data appear to be complete. There was a large proportion of missing exposure data (roughly 50%) due to workers being employed in roles such as maintenance, where exposure to any chemical is possible but unknown. Analyses were run separately where these ”unknown” individuals were a) treated as exposed, b) treated as unexposed, or c) treated as unknown and thus excluded. The study only presents results for when these individuals were excluded but specifies that the first scenario resulted in increased exposure estimates for controls relative to cases.

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Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
	Metric 3:	Comparison Group	Medium	The study identifies two series of control groups, selected from all former Union Carbide Corporation (UCC) employees. However, the total number of employees is not stated. Only those who were deceased were used as controls since they had known causes of death and could thus be verified as non-brain tumors. One group of controls excluded employees whose cause of death was due to any malignant neoplasm to allow for the possibility that a general chemical carcinogen may have been associated with cancers of other sites. The other group of controls included deaths from all causes; this included malignant neoplasms other than brain tumors. Both control groups had 80 male employees randomly selected from 450 deceased employees known to the company in June 1979. Control deaths were stated to be pulled from corporate employee benefits department and through locally published obituary notices routinely screened by the medical department - it is possible to assume that cases were identified in a similar manner. The study reports that cases were slightly more likely to have been employed for less than 10 years than controls - the study attributes this in part to the fact that employees whose deaths were known to the company were more likely to have worked for longer - regardless the mean number of years employed was similar between cases and controls. However, cases were more likely to have been terminated from their job for reasons other than death, disability, or retirement (quitting, being fired, etc.), were generally younger at hire, and were less likely to survive to their 70th birthday. None of these factors are controlled for in statistical analyses - however, since controls and cases were pulled from the same population, there is indirect evidence that the groups were similar.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was determined based on official employment records. Records included job title and department assignment codes for each employment from date of hire to date of termination. For each unique department code, UCC and NIOSH industrial hygienists identified principal chemicals used or produced at any time in the history of the plant and correlated those with individual departments. This assessment was not performed on a year-by-year basis due to concerns for recall bias for longer-term employees where less detailed records were kept. An employee was categorized as ”exposed” to 1,2-dichloroethane if they ever worked in a department associated with that chemical. An ”unknown” exposure group was also created to account for employees who had only worked in departments for which no specific chemical could be identified.
	Metric 5:	Exposure Levels	Low	The study does not report any quantitative information and only splits exposure into ”exposed”, ”unexposed”, and ”unknown”.
	Metric 6:	Temporality	High	In this study exposure is confirmed to occur before the outcome is measured. The study reports latency periods, with subjects dichotomized into less than 15 years of latency or more than 15 years of latency. The majority of cases and controls had a latency of greater than 15 years, which is sufficiently long for brain tumors.

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Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Cases were identified through death certificate searches and partially through tumor registries in the state of Texas. Case validation was performed by NIOSH, and 5 different levels of confirmation were reported: 1) tissue specimen interpreted by the Armed Forces Institute of Pathology; 2) autopsy report; 3) histopathology report; 4) clinical diagnosis from hospital record; 5) dearth certificate diagnosis. Codes 1-3 were considered to be ”confirmed” cases of brain tumors, while 4-5 were considered unconfirmed. 5/21 cases were only evaluated using ”unconfirmed methods”, meaning there is likely a high amount of accuracy in roughly 75% of cases. While no case validation is reported for controls, the study specifies that only controls who had died and thus could be confirmed to be non-brain tumors were included.
	Metric 8:	Reporting Bias	Medium	All primary and secondary outcomes that are outlined in the methods are reported in the results. However, the only statistical outcome of their analysis were unadjusted p-values that were not reported and were just described qualitatively.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	The only statistical analysis performed were Mantel-Haenszel chi-squared tests, which did not allow for confounder adjustment. The study does not present a distribution of potential confounders by exposure status but by case/control status. Several variables, such as reason for termination, age at hire, and age at death were significantly different between cases and controls and were not accounted for in statistical modeling. The study explains that these differences are not likely to have any epidemiologic significance and appear to be relatively small differences.
	Metric 10:	Covariate Characterization	Medium	While the study does not explain where they obtained covariate information, it is reasonable to assume that they gathered the information from company records.
	Metric 11:	Co-exposure Counfounding	Low	The study assesses a wide range of other potential occupational co-exposures. While these co-exposures are not adjusted for in any statistical models, effect estimates are presented separately for benzene, diethyl sulfate, ethylene oxide, and vinyl chloride. The distribution of co-exposures across cases and controls is demonstrated to be mostly balanced by comparing proportions of exposed/unexposed between cases and controls. The only notable instance of imbalance is for benzene, where 11.1% of cases were exposed whereas 37.9% of all controls and 19.2% of non-neoplasm related controls were exposed.
Domain 5: Analysis				

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Study Citation:	Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	The study chose a case-control design, which was appropriate to study the rare disease of brain tumors and its association with occupational exposures. The only statistical analysis conducted is a Mantzel-Haenszel chi-squared test, but there is no reason to suggest that this would be inappropriate.
	Metric 13:	Statistical Power	Medium	The study does not calculate statistical power, but the number of cases (n=21) and controls (n=80 in each analysis) is likely sufficient to detect an effect.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to understand what was done and could be reproduced given access to the analytic data.
	Metric 15:	Statistical Analysis	High	The only statistical analysis conducted is a Mantel-Haenszel chi-squared test, and all assumptions were met. The statistical process is transparent.

Additional Comments: This case-control study pulled deceased former employees of the Union Carbide Corporation in Texas City, Texas. The study examined dichotomous exposure to a wide range of occupational exposures, including 1,2-dichloroethane, in relation to brain tumor cases. There is no quantitative estimate of exposure. The only statistical analysis in the study is a Mantel-Haenszel chi-squared test statistic and no statistically significant differences in exposure between cases and controls were observed. The fact that there are no effect estimates, no adjustment for confounders, and no quantitative exposure estimates limits the usefulness of this paper.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	Urinary system cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	Urinary system cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	Urinary system cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Immune/Hematological
Reported Health Effect(s):	Lymphatic and hematopoietic tissue cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Immune/Hematological
Reported Health Effect(s):	Lymphatic and hematopoietic tissue cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Immune/Hematological
Reported Health Effect(s):	Lymphatic and hematopoietic tissue cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Other cancers (not specified)
Reported Health Effect(s):	Other cancers (not specified)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Other cancers (not specified)
Reported Health Effect(s):	Other cancers (not specified)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Other cancers (not specified)
Reported Health Effect(s):	Other cancers (not specified)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Mortality
Reported Health Effect(s):	All-cause mortality
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Vital status was tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Medium	Death rates among unit employees were compared to death rates in the U.S. population adjusted for age and gender. Demographics of the exposed workers are not provided; therefore, it is not clear whether additional adjustment for race may have been appropriate. No justification is provided for the choice of the entire U.S. population as the comparison group. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis. Additional analyses are conducted limiting workers to those with the greatest likelihood of exposure (i.e., those working in jobs with high likelihood of contact with chemicals for more than a year, those working for the full year of 1979 during which chemical exposures were most frequently reported); these smaller groups are also compared to the unexposed general population.
	Metric 6:	Temporality	High	Temporality was established due to the longitudinal design and the use of mortality as the outcome. Exposures occurred between 1979 and 1987 and follow-up for vital status was conducted through 2003.
Domain 3: Outcome Assessment				

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Mortality
Reported Health Effect(s):	All-cause mortality
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Medium	The study did not provide information on how mortality was assessed either in the exposed population or in the comparison population; use of death certificates is implied but not stated.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected deaths are reported, but SIRs and 95% confidence intervals are not provided.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Comparisons of observed versus expected deaths were adjusted for age and gender. Demographics of the exposed workers are not provided; therefore, it is not clear whether additional adjustment for race may have been appropriate.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records or death records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed deaths among a population of exposed workers compared to expected deaths among the U.S. population, adjusted for age and gender.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected deaths; no SIR was provided. Expected death rates were adjusted for age and gender.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Mortality
Reported Health Effect(s):	All-cause mortality
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	All cancer (excluding non-melanoma skin cancer), digestive system cancer, colorectal cancer, respiratory cancer, prostate cancer, urinary system cancer, lymphatic and hematopoietic tissue cancer, other cancers (not specified)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	All cancer (excluding non-melanoma skin cancer), digestive system cancer, colorectal cancer, respiratory cancer, prostate cancer, urinary system cancer, lymphatic and hematopoietic tissue cancer, other cancers (not specified)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	All cancer (excluding non-melanoma skin cancer), digestive system cancer, colorectal cancer, respiratory cancer, prostate cancer, urinary system cancer, lymphatic and hematopoietic tissue cancer, other cancers (not specified)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Gastrointestinal
Reported Health Effect(s):	Digestive system cancer, colorectal cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Gastrointestinal
Reported Health Effect(s):	Digestive system cancer, colorectal cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Gastrointestinal
Reported Health Effect(s):	Digestive system cancer, colorectal cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Lung/Respiratory
Reported Health Effect(s):	Respiratory cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Lung/Respiratory
Reported Health Effect(s):	Respiratory cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Lung/Respiratory
Reported Health Effect(s):	Respiratory cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Prostate cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Study Citation: BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s): Reproductive/Developmental
Reported Health Effect(s): Prostate cancer
Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s): 6570017, 6570014
HERO ID: 6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Prostate cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Male workers who had ever been assigned to the chlorohydrin unit between 1 January 1940 and 31 December 1967 at Union Carbide's South Charleston plant were enrolled and matched to the US National Death Index. Status on 5 workers could not be identified. Information on how workers were matched to death index was not specified.
	Metric 2:	Attrition	Medium	Rate of inclusion/participation was very high, as records were able to be matched for 98% of participants. Medium rating given because information on how participants whose vital status was not known was not specified.
	Metric 3:	Comparison Group	Uninformative	Unacceptable rating given because SMRs were calculated based on expected deaths from a reference population matched on sex, but not age.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Exposure was assessed based on duration of work in the plant. No information is provided on exposure levels, and a JEM was not used.
	Metric 5:	Exposure Levels	Uninformative	No information provided on levels of exposure.
	Metric 6:	Temporality	High	Temporality is well established; person-years stopped accumulating in 1967 and outcome was assessed beginning at that time.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar period, and interval since assignments, but distribution of these covariates was not reported.
	Metric 10:	Covariate Characterization	Medium	Information on covariate characterization not provided, but the selected covariates (age, calendar period, and interval since assignments) were likely extracted from employee records and unlikely to be largely problematic
	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.

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Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Study design was appropriate for the research method. Statistical methods were also appropriate.
	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.
	Metric 14:	Reproducibility of Analyses	Medium	Methods are well-enough described that study could be adequately reproduced.
	Metric 15:	Statistical Analysis	High	SMRs calculated based on US general population mortality for white males through 1988. RRs were ”evaluated over levels of duration of assignment to the chlorohydrin unit, stratified by age, calendar year, and interval since first assignment to the chlorohydrin unit”.

Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Male workers who had ever been assigned to the chlorohydrin unit between 1 January 1940 and 31 December 1967 at Union Carbide's South Charleston plant were enrolled and matched to the US National Death Index. Status on 5 workers could not be identified. Information on how workers were matched to death index was not specified.
	Metric 2:	Attrition	Medium	Rate of inclusion/participation was very high, as records were able to be matched for 98% of participants. Medium rating given because information on how participants whose vital status was not known was not specified.
	Metric 3:	Comparison Group	Uninformative	Unacceptable rating given because SMRs were calculated based on expected deaths from a reference population matched on sex, but not age.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Exposure was assessed based on duration of work in the plant. No information is provided on exposure levels, and a JEM was not used.
	Metric 5:	Exposure Levels	Uninformative	No information provided on levels of exposure.
	Metric 6:	Temporality	High	Temporality is well established; person-years stopped accumulating in 1967 and outcome was assessed beginning at that time.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar period, and interval since assignments, but distribution of these covariates was not reported.
	Metric 10:	Covariate Characterization	Medium	Information on covariate characterization not provided, but the selected covariates (age, calendar period, and interval since assignments) were likely extracted from employee records and unlikely to be largely problematic
	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.
Domain 5: Analysis				

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Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Study design was appropriate for the research method. Statistical methods were also appropriate.
	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.
	Metric 14:	Reproducibility of Analyses	Medium	Methods are well-enough described that study could be adequately reproduced.
	Metric 15:	Statistical Analysis	High	SMRs calculated based on US general population mortality for white males through 1988. RRs were ”evaluated over levels of duration of assignment to the chlorohydrin unit, stratified by age, calendar year, and interval since first assignment to the chlorohydrin unit”.

Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Male workers who had ever been assigned to the chlorohydrin unit between 1 January 1940 and 31 December 1967 at Union Carbide's South Charleston plant were enrolled and matched to the US National Death Index. Status on 5 workers could not be identified. Information on how workers were matched to death index was not specified.
	Metric 2:	Attrition	Medium	Rate of inclusion/participation was very high, as records were able to be matched for 98% of participants. Medium rating given because information on how participants whose vital status was not known was not specified.
	Metric 3:	Comparison Group	Uninformative	Unacceptable rating given because SMRs were calculated based on expected deaths from a reference population matched on sex, but not age.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Exposure was assessed based on duration of work in the plant. No information is provided on exposure levels, and a JEM was not used.
	Metric 5:	Exposure Levels	Uninformative	No information provided on levels of exposure.
	Metric 6:	Temporality	High	Temporality is well established; person-years stopped accumulating in 1967 and outcome was assessed beginning at that time.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar period, and interval since assignments, but distribution of these covariates was not reported.
	Metric 10:	Covariate Characterization	Medium	Information on covariate characterization not provided, but the selected covariates (age, calendar period, and interval since assignments) were likely extracted from employee records and unlikely to be largely problematic
	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.
Domain 5: Analysis				

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Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Study design was appropriate for the research method. Statistical methods were also appropriate.
	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.
	Metric 14:	Reproducibility of Analyses	Medium	Methods are well-enough described that study could be adequately reproduced.
	Metric 15:	Statistical Analysis	High	SMRs calculated based on US general population mortality for white males through 1988. RRs were ”evaluated over levels of duration of assignment to the chlorohydrin unit, stratified by age, calendar year, and interval since first assignment to the chlorohydrin unit”.

Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

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	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar period, and interval since assignments, but distribution of these covariates was not reported.
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	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.
Domain 5: Analysis				

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	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.
	Metric 14:	Reproducibility of Analyses	Medium	Methods are well-enough described that study could be adequately reproduced.
	Metric 15:	Statistical Analysis	High	SMRs calculated based on US general population mortality for white males through 1988. RRs were ”evaluated over levels of duration of assignment to the chlorohydrin unit, stratified by age, calendar year, and interval since first assignment to the chlorohydrin unit”.

Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

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Domain 5: Analysis				

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Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

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Domain 5: Analysis				

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Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

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Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar period, and interval since assignments, but distribution of these covariates was not reported.
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Domain 5: Analysis				

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Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Study design was appropriate for the research method. Statistical methods were also appropriate.
	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.
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Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

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Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Male workers who had ever been assigned to the chlorohydrin unit between 1 January 1940 and 31 December 1967 at Union Carbide's South Charleston plant were enrolled and matched to the US National Death Index. Status on 5 workers could not be identified. Information on how workers were matched to death index was not specified.
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Domain 2: Exposure Characterization				
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	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar period, and interval since assignments, but distribution of these covariates was not reported.
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Domain 5: Analysis				

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Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Study design was appropriate for the research method. Statistical methods were also appropriate.
	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.
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Additional Comments: None

Overall Quality Determination **Uninformative**

* No biomarkers were identified for this evaluation.

Study Citation:	Bove, F. J. (1996). Public drinking water contamination and birthweight, prematurity, fetal deaths, and birth defects. Toxicology and Industrial Health 12(2):255-266.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	200239

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	This cross-sectional study (n=80,938) included all registered singleton live births and fetal deaths (>20 weeks' gestation) in 1985-88 in 75 New Jersey towns located in 4 counties with "some" water supplies contaminated with substances of interest and where: (i) residents were "mostly" served by public water systems; and (ii) births occurred "mostly" in state. Estimated proportions of residents served by public water systems, and of pregnancies/births captured, were not described. However, the inclusion of all eligible registered births, fetal deaths, and birth defects, as well as the selection of towns without knowledge of birth outcome prevalence, limited the likelihood of selection bias.
	Metric 2:	Attrition	Medium	All registered births and fetal deaths were included. Attrition due to missing values for multiple variables was not quantified and is therefore uncertain. However, attrition was likely modest as the proportion of missing values for individual variables was relatively low: (i) ~6% of subjects were excluded from analyses of outcomes such as preterm birth due to invalid or missing gestational ages; and (ii) other covariates evaluated as confounders had up to 4.9% missing values.
	Metric 3:	Comparison Group	High	After excluding plural pregnancies and chromosomal abnormalities, all registered live births during the study period in the areas included without the outcomes of interest were included in the comparison group. This comprehensive approach limited the potential for bias. Chromosomal abnormalities were not included as outcomes as they were not hypothesized to be associated with the exposures under study but were appropriately excluded given their uncertain etiology.
Domain 2: Exposure Characterization				

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Linked HERO ID(s):	194932, 200239
HERO ID:	200239

Domain	Metric		Rating	Comments
	Metric 4:	Measurement of Exposure	Medium	Along with several other contaminants, residential drinking water exposure to 1,2-dichloroethane (as well as 1,1,1-trichloroethane and 'total dichloroethylenes') – was assigned based on maternal town of residence at birth. Exposure estimates were calculated using the average of water company sampling reports during the first trimester (for birth defects and fetal death) or the duration of pregnancy (for other outcomes). Detection limits and data availability were not specified in detail but were described as below 1 ppb, with reporting compliance >85%. A minimum of 1 sample per 6-month interval was required; variability in the number of measures available across water systems and towns was not described. Additional sources of measurement error included: changes in residence during pregnancy; water from alternate sources (ex. private wells, bottles, workplaces); variability in residential contaminant levels vs measured samples; unknown levels of tap water intake; and errors in estimated dermal and inhalation exposure while bathing or showering. While the extent of exposure misclassification is uncertain, there is no evidence to suggest it was differential rather than random.
	Metric 5:	Exposure Levels	Medium	Due to the high proportion of measures below detection limits, analyses relating exposure to health outcomes used only 2 categories for each of the chlorinated solvents of interest: cutoffs close to detection limits were used to define elevated exposure. Proportions defined as having elevated exposure was low (1.8% had 1,1-dichloroethylene ≥1 ppb). An important concern is that relatively low levels of exposure to these contaminants from sources other than residential drinking water, for which data were not available, could potentially have resulted in considerable misclassification.
	Metric 6:	Temporality	High	Exposure levels were assigned based on contaminant exposures estimated during: (i) the first trimester for analyses of birth defects and fetal deaths; and (ii) the duration of pregnancy for other pregnancy outcomes.

Domain 3: Outcome Assessment

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Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	200239

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcomes included measures of birthweight (continuous among term births, low term birthweight, very low birthweight), prematurity, fetal death, and congenital anomalies in live births or fetal deaths. The anomalies analyzed included defects of the central nervous system, neural tube, oral cleft, total cardiac, major cardiac, ventricular septum, and any surveillance defect excluding chromosomal defects. All outcomes were identified using birth certificates, fetal death certificates (>20 weeks' gestation), and the NJ congenital birth defect registry (ICD codes provided). These registry data are likely to be sufficiently valid for late pregnancy outcomes. However, their limited ability to capture early pregnancy losses is a weakness. The sample included only 594 fetal deaths (less than 1% of the >80,0000 sample). Typical estimates are that 10-20%, of recognized pregnancies ending in losses. Moreover, developmental defects contributing to early pregnancy losses were also not captured. A further limitation is that that potentially etiologically heterogeneous preterm birth types were analyzed together, as these data did not distinguish premature rupture of membranes vs idiopathic prematurity.
	Metric 8:	Reporting Bias	Medium	Models were constructed only for contaminants with associations > 1.0, and tables included only associations with odds ratios ≥1.5. No clear rationale was provided. Several positive odds ratios below the 1.5 cutoff were described in the results text (without confidence intervals), but no null/negative odds ratios were presented or described.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Potential confounding by maternal race, education, parity, and prior pregnancy loss, along with infant sex (for birth outcomes) and adequacy of prenatal care, was examined. Gestational age was addressed by analyzing birthweight among full term births, term low birth weight, and small size for gestational age. Only fully adjusted models were presented. In a companion case-control study (with low participation rates), adjustment for other variables not available on birth certificates (ex. maternal smoking, occupational exposures, medical history, and gestational weight gain) did not influence associations with other studied contaminants. This separate study reduces concerns for important confounding bias, but confounding cannot be ruled out.
	Metric 10:	Covariate Characterization	Medium	Data on covariates came from registry data: birth certificates, fetal death certificates, and the NJ congenital birth defects registry.
	Metric 11:	Co-exposure Counfounding	Medium	Co-exposure confounding by drinking water trihalomethane concentrations was evaluated. There was no evidence to suggest substantial confounding by this or other co-exposures.
Domain 5: Analysis				

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Study Citation:	Bove, F. J. (1996). Public drinking water contamination and birthweight, prematurity, fetal deaths, and birth defects. Toxicology and Industrial Health 12(2):255-266.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	200239

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Methods were appropriate. The study used logistic regression models to estimate odds ratios and confidence intervals for dichotomous outcomes, and linear regression for analysis of continuous birth weight.
	Metric 13:	Statistical Power	Medium	Statistical power was likely to have been limited as a consequence of the small proportion of the sample defined as having "elevated" residential water concentrations of the chemicals of interest. The range of exposure examined was limited, as cutoffs for elevated levels were close to the detection limits of 1 ppb. In addition, for most birth defect outcomes, fewer than 10 cases had elevated exposure.
	Metric 14:	Reproducibility of Analyses	Medium	The authors clearly described steps used to estimate exposure-outcome associations, including exposure category cutoffs and criteria for confounding. However, many results were not shown as tables included odds ratios ≥1.5.
	Metric 15:	Statistical Analysis	High	The authors estimated coefficients, odds ratios and 95% confidence intervals using adequate methods. Confounding was based on 15% change-in-estimate comparing nested models. Effect modification (ex by infant sex) was not evaluated as there was no a priori evidence to suggest such analyses at that time.

Additional Comments: This study analyzed the association between estimated residential drinking water concentrations of several chlorinated solvents including 1,2-dichloroethane (as well as 1,1,1-trichloroethane; ∑[trans-1,2-dichloroethylene and 1,1-dichloroethylene]) and pregnancy outcomes (size at birth, prematurity, fetal deaths, and congenital birth defects). The sample included more than 80,000 births during 1985-88 for residents of 75 towns in NJ using public water system records to estimate exposure during gestation, and registry data (birth certificate, fetal death certificates for pregnancies >20 weeks, state birth defect registry) to characterize outcomes. Strengths included the large sample size and inclusion of all eligible registered births and fetal deaths in the study period. A critical concern is the inability to capture early fetal deaths and any related malformations (1% of the sample had fetal deaths vs typical estimates of >10%). An important limitation was the low percentage of the sample with detectable (> 1ppb) concentrations of these contaminants (<1% to 6.2%). Small numbers for birth defect outcomes also limited power. Exposure misclassification (ex. drinking water from wells/ work/ bottles, changes in residence, exposure from other sources) is also a concern. However, such misclassification was likely non-differential, and thus more likely to under- vs. to over-estimate associations.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Bove, F. J., Fulcomer, M. C., Klotz, J. B., Esmart, J., Dufficy, E. M., Savrin, J. E. (1995). Public drinking water contamination and birth outcomes. American Journal of Epidemiology 141(9):850-862.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	194932

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	This semi-ecological study (n=80,938) included all registered singleton live births and fetal deaths (>20 weeks) in 1985-88 in 75 New Jersey towns located in 4 counties with "some" water supplies contaminated with substances of interest and where: (i) residents were "mostly" served by public water systems; and (ii) births occurred "mostly" in state. Estimated proportions of residents served by public water systems, and of pregnancies/births captured, were not described. However, the inclusion of all eligible registered births, fetal deaths, and birth defects, as well as the selection of towns without knowledge of birth outcome prevalence, limited the likelihood of selection bias.
	Metric 2:	Attrition	Medium	All registered births and fetal deaths were included. Attrition due to missing values for multiple variables was not quantified and is therefore uncertain. However, attrition was likely modest as the proportion of missing values for individual variables was relatively low: (i) ~6% of subjects were excluded from analyses of outcomes such as preterm birth due to invalid or missing gestational ages; and (ii) other covariates evaluated as confounders had up to 4.9% missing values.
	Metric 3:	Comparison Group	High	After excluding plural pregnancies and chromosomal abnormalities, all registered live births during the study period in the areas included without the outcomes of interest were included in the comparison group. This comprehensive approach limited the potential for bias. Chromosomal abnormalities were not included as outcomes as they were not hypothesized to be associated with the exposures under study but were appropriately excluded given their uncertain etiology.
Domain 2: Exposure Characterization				

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Study Citation:	Bove, F. J., Fulcomer, M. C., Klotz, J. B., Esmart, J., Dufficy, E. M., Savrin, J. E. (1995). Public drinking water contamination and birth outcomes. American Journal of Epidemiology 141(9):850-862.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	194932

Domain	Metric		Rating	Comments
	Metric 4:	Measurement of Exposure	Medium	Along with several other contaminants, residential drinking water exposure to 1,2-dichloroethane (as well as 1,1,1-trichloroethane and 'total dichloroethylenes') was assigned based on maternal town of residence at birth. Exposure estimates were calculated using the average of water company sampling reports during the first trimester (for birth defects and fetal death) or the duration of pregnancy (for other outcomes). Detection limits and data availability were not specified in detail but were described as below 1 ppb, with reporting compliance >85%. A minimum of 1 sample per 6-month interval was required; variability in the number of measures available across water systems and towns was not described. Additional sources of measurement error included: changes in residence during pregnancy; water from alternate sources (ex. private wells, bottles, workplaces); variability in residential contaminant levels vs measured samples; unknown levels of tap water intake; and errors in estimated dermal and inhalation exposure while bathing or showering. While the extent of exposure misclassification is uncertain, there is no evidence to suggest it was differential rather than random.
	Metric 5:	Exposure Levels	Low	Due to the high proportion of measures below detection limits, analyses relating exposure to health outcomes used only 2 categories for each of the three chemicals of interest: cutoffs close to detection limits were used to define elevated exposure. Proportions defined as having elevated exposure were low (1.8% had 1,1-dichloroethylene ≥1 ppb). An important concern is that relatively low levels of exposure to this contaminant from sources other than residential drinking water, for which data were not available, could potentially have resulted in considerable misclassification.
	Metric 6:	Temporality	High	Exposure levels were assigned based on contaminant exposures estimated during: (i) the first trimester for analyses of birth defects and fetal deaths; and (ii) the duration of pregnancy for other pregnancy outcomes.

Domain 3: Outcome Assessment

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Study Citation:	Bove, F. J., Fulcomer, M. C., Klotz, J. B., Esmart, J., Dufficy, E. M., Savrin, J. E. (1995). Public drinking water contamination and birth outcomes. American Journal of Epidemiology 141(9):850-862.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	194932

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcomes included measures of birthweight (continuous among term births, low term birthweight, very low birthweight), prematurity, fetal death, and congenital anomalies in live births or fetal deaths. The anomalies analyzed included defects of the central nervous system, neural tube, oral cleft, total cardiac, major cardiac, ventricular septum, and any surveillance defect excluding chromosomal defects. All outcomes were identified using birth certificates, fetal death certificates (>20 weeks' gestation), and the NJ congenital birth defect registry (ICD codes provided). These registry data are likely to be sufficiently valid for late pregnancy outcomes. However, their limited ability to capture early pregnancy losses is a weakness. The sample included only 594 fetal deaths (less than 1% of the >80,0000 sample). Typical estimates are that 10-20%, of recognized pregnancies ending in losses. Moreover, developmental defects contributing to early pregnancy losses were also not captured. A further limitation is that that potentially etiologically heterogeneous preterm birth types were analyzed together, as these data did not distinguish premature rupture of membranes vs idiopathic prematurity.
	Metric 8:	Reporting Bias	Low	Models were constructed only for contaminants with associations > 1.0, and tables included only associations with odds ratios ≥1.5. No clear rationale was provided. Several positive odds ratios below the 1.5 cutoff were described in the results text (without confidence intervals), but no null/negative odds ratios were presented or described.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Potential confounding by maternal race, education, parity, and prior pregnancy loss, along with infant sex (for birth outcomes) and adequacy of prenatal care, was examined. Gestational age was addressed by analyzing birthweight among full term births, term low birth weight, and small size for gestational age. Only fully adjusted models were presented. In a companion case-control study (with low participation rates), adjustment for other variables not available on birth certificates (ex. maternal smoking, occupational exposures, medical history, and gestational weight gain) did not influence associations with other studied contaminants. This separate study reduces concerns for important confounding bias, but confounding cannot be ruled out.
	Metric 10:	Covariate Characterization	Medium	Data on covariates came from registry data: birth certificates, fetal death certificates, and the NJ congenital birth defects registry.
	Metric 11:	Co-exposure Counfounding	Medium	Co-exposure confounding by drinking water trihalomethane concentrations was evaluated. There was no evidence to suggest substantial confounding by this or other co-exposures.
Domain 5: Analysis				

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Study Citation:	Bove, F. J., Fulcomer, M. C., Klotz, J. B., Esmart, J., Dufficy, E. M., Savrin, J. E. (1995). Public drinking water contamination and birth outcomes. American Journal of Epidemiology 141(9):850-862.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	194932

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Methods were appropriate. The study used logistic regression models to estimate odds ratios and confidence intervals for dichotomous outcomes, and linear regression for analysis of continuous birth weight.
	Metric 13:	Statistical Power	Low	Statistical power was likely to have been limited as a consequence of the small proportion of the sample defined as having "elevated" residential water concentrations of the chemicals of interest. The range of exposure examined was limited, as cutoffs for elevated levels were close to the detection limits of 1 ppb. In addition, for most birth defect outcomes, fewer than 10 cases had elevated exposure. However, the authors emphasized the magnitude of associations rather than statistical significance and presented multiple confidence intervals to aid interpretation of the precision of estimates (50%, 90% and 99%).
	Metric 14:	Reproducibility of Analyses	Medium	The authors clearly described steps used to estimate exposure-outcome associations, including exposure category cutoffs and criteria for confounding. However, many results were not shown as tables included odds ratios ≥1.5.
	Metric 15:	Statistical Analysis	High	The authors estimated coefficients, odds ratios and confidence intervals using adequate methods. Confounding was based on 15% change-in-estimate comparing nested models. Effect modification (ex by infant sex) was not evaluated as there was no a priori evidence to suggest such analyses at that time.

Additional Comments: This study analyzed the association between estimated residential drinking water concentrations of several chlorinated solvents including 1,2-dichloroethane (as well as 1,1,1-trichloroethane and the ∑[trans-1,2-dichloroethylene & 1,1-dichloroethylene]) and pregnancy outcomes (size at birth, prematurity, fetal deaths, and congenital birth defects). The sample included more than 80,000 births during 1985-88 for residents of 75 towns in NJ using public water system records to estimate exposure during gestation, and registry data (birth certificate, fetal death certificates for pregnancies >20 weeks' gestation, state birth defect registry) to characterize outcomes. Strengths included the large sample size and inclusion of all eligible registered births and fetal deaths in the study period. A critical concern is the inability to capture early fetal deaths and any related malformations (1% of the sample had fetal deaths vs typical estimates of >10%). An important limitation was the low percentage of the sample with detectable (> 1ppb) concentrations of this solvent (<2%), which likely limited power. Small numbers for birth defect outcomes also limited power. Exposure misclassification (ex. drinking water from wells/ work/ bottles, changes in residence, exposure from other sources) is also a concern. However, such misclassification was likely non-differential, and thus more likely to under- vs. to over-estimate associations.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Bowler, R.M., Gysens, S., Hartney, C. (2003). Neuropsychological effects of ethylene dichloride exposure. NeuroToxicology 24(4-5):553-562.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Wechsler Adult Intelligence Scale III (WAIS-III), Wechsler Memory Scale III (WMS-III), Boston Naming Test (BNT), Trail Making Test (TMT), Stroop Color-Word Test, Grooved Pegboard, Dynamometer, Wide Range Achievement Test (WRAT), Finger tapping, Beck Anxiety Index, Beck Depression Index, Symptom Checklist-90 (SCL-90).
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	200241

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Uninformative	221 workers that had been exposed to 1,2-DCE in the Southern United States were initially included. Exclusion criteria were provided, including the number of individuals excluded for each reason. The study authors note that those initially included in the analysis sample were referred by physicians after neurological complaints were documented. Detailed criteria for referral were not provided. Referral-based recruitment of neurological cases will likely result in an analysis sample with an exposure-outcome distribution that is not representative of the eligible population (i.e., contamination site clean-up workers).
	Metric 2:	Attrition	Medium	There was moderate subject loss. Reasons for exclusion from the analysis sample are provided, and only those with complete information were included in the analysis.
	Metric 3:	Comparison Group	Low	Impairment scores were compared to normative data from manuals and/or a "demographically similar control group" cited to Bowler et al. (2001). The controls from this study appeared similar (albeit somewhat older) than 1,2-DCE-exposed workers and reported no prior chemical exposure.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	A job-exposure matrix was not considered plausible; variables considered as surrogates of exposure were obtained from interviews. This method is expected to have poor validity because it relies on workers' recall of subjective events and their frequency (e.g., contact with water); workers (who are taking part in a lawsuit) may overestimate their exposure.
	Metric 5:	Exposure Levels	Low	Two levels of exposure (exposed and not exposed) were used to evaluate neurophysiological effects.
	Metric 6:	Temporality	Medium	Exposures primarily occurred between 1993 and 1995 and neurophysiological effects were evaluated in 2000. Temporality is established, but it is unclear whether exposures fall within relevant exposure windows for the outcome of interest.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Neurophysiological effects were evaluated using a number of standardized tests, including (but not limited to) the Wechsler Adult Intelligence Scale (WAIS-III), the Wechsler Memory Scale (WMS-III), and the Symptom Checklist 90-Revised (SCL90-R). There was no information whether tests were performed using the same methods for exposed and referent groups (e.g., timing and order of tests).

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Study Citation:	Bowler, R.M., Gysens, S., Hartney, C. (2003). Neuropsychological effects of ethylene dichloride exposure. NeuroToxicology 24(4-5):553-562.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Wechsler Adult Intelligence Scale III (WAIS-III), Wechsler Memory Scale III (WMS-III), Boston Naming Test (BNT), Trail Making Test (TMT), Stroop Color-Word Test, Grooved Pegboard, Dynamometer, Wide Range Achievement Test (WRAT), Finger tapping, Beck Anxiety Index, Beck Depression Index, Symptom Checklist-90 (SCL-90).
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	200241

Domain	Metric		Rating	Comments
	Metric 8:	Reporting Bias	Low	Neurobehavioral outcomes mentioned in the methods were reported for 1,2-DCE-exposed workers (as mean score, standard deviation, and percentage impaired); results for controls/normative data were not shown and/or p-values from t-tests were not provided. Control data were used to define impairment (based on z-score) but these values were not reported. Data pertaining to specific exposure variables were reported in the text only; no data were shown in a table.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Normative data permitted adjustments based on age, education, and gender. The control group was "socio-demographically" similar but specific parameters used to define similarity were not indicated. Separate ANCOVA analyses on workers only were stratified by race (citation provided), and adjusted for ethnicity, age, and education. The methods for identifying and including potential confounders in the analytic approach was not described.
	Metric 10:	Covariate Characterization	Low	No description of the covariate collection method was provided. It was not clear whether the method used was valid or not.
	Metric 11:	Co-exposure Counfounding	Low	A number of workers (18%) reported current exposure to chemicals in their work environment. These potential co-exposures were not were not appropriately adjusted for in the analytical approach used.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Low	The study design was appropriate to evaluate the neurophysiological status of 1,2-DCE-exposed workers; however, statistical methods were not comprehensive.
	Metric 13:	Statistical Power	Medium	The report indicates "significant impairments" were observed on various neurophysiological tests using t-tests, and significant exposure relationships were reported based on test scores and specific exposure variables (used as surrogates of exposure). Therefore, the number of participants was sufficient to detect an effect.
	Metric 14:	Reproducibility of Analyses	Low	Tests were scored according to relevant manuals; the calculation of z-scores, used in all impairment comparisons and analyses of exposure relationships, was not explained in adequate detail. The methods used to determine relationships between specific exposure variables and test scores (i.e., ANCOVA analyses) were not fully described.
	Metric 15:	Statistical Analysis	Low	Description of the ANCOVA analysis was largely not present. It is not clear whether model assumptions were met.

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Study Citation:	Bowler, R.M., Gysens, S., Hartney, C. (2003). Neuropsychological effects of ethylene dichloride exposure. NeuroToxicology 24(4-5):553-562.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Wechsler Adult Intelligence Scale III (WAIS-III), Wechsler Memory Scale III (WMS-III), Boston Naming Test (BNT), Trail Making Test (TMT), Stroop Color-Word Test, Grooved Pegboard, Dynamometer, Wide Range Achievement Test (WRAT), Finger tapping, Beck Anxiety Index, Beck Depression Index, Symptom Checklist-90 (SCL-90).
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	200241

Domain	Metric	Rating	Comments
Additional Comments:	The study evaluated the neurobehavioral status of a group of workers with known exposure to 1,2-DCE at a clean-up site. Impairments related to processing speed, attention, cognitive flexibility, motor coordination and speed, verbal memory/fluency, vision and visual-spatial abilities, and mood were reported in exposed workers. Serious and consequential flaws are associated with the study including methods of participant selection and retention, and exposure characterization among others.		

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Brender, J.D., Shinde, M.U., Zhan, F.B., Gong, X., Langlois, P.H. (2014). Maternal residential proximity to chlorinated solvent emissions and birth defects in offspring: A case-control study. Environmental Health: A Global Access Science Source 13(1):96.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	birth defects (neural tube defects, limbs deficiencies, oral cleft defects, heart defects, spina bifida, anencephaly)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	2799700

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Participants were drawn from the Texas Birth Defects Registry (TBDR) for years 1996-2008. Controls were frequency matched from the same registry. Study authors state that neural tube cases were more likely to not be successfully geocoded which may introduce selection bias, however, the authors note that both cases and controls with addresses that could not be geocoded were similar. In spite of that, the inclusion criteria, methods of participant selection, and frequency match were reported.
	Metric 2:	Attrition	Medium	13.3% case mother addresses and 12.8% control mother addresses were unable to be geocoded, however this most likely only lowered the precision of the study and most likely does not vary based on exposure level.
	Metric 3:	Comparison Group	Medium	Controls were matched to cases and pulled from the same eligible population by year of delivery and public health service region. Other demographic factors, e.g., race was not matched in population selection. However, statistical analyses were adjusted for year of delivery, maternal age, race/ethnicity, education, and public health region of residence.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Used Emission Weighted Proximity Model to estimate exposure at a given address based on proximity to emission sources and the specific amount or type of pollutant emitted. There may be some exposure misclassification due to mothers moving away from geocoded addresses. Previous studies indicate ~67% of mothers do not move between conception and delivery.
	Metric 5:	Exposure Levels	Medium	Reports exposure as "exposure risk value" and groups the risk values into quartiles, with exposure risk values < 0 being the referent group
	Metric 6:	Temporality	Medium	The study authors estimated exposure based on residence during pregnancy and evaluated birth outcomes. Temporality is established. Previous studies indicate ~67% mothers don't move between trimester and delivery. For mothers who moved during the pregnancy, the temporality is unknown.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Outcomes determined by Texas Birth Defect Registry, checking for birth defect diagnosis. Birth certificates came from Center for Health Statistics at Texas Department of State Health Services
	Metric 8:	Reporting Bias	High	Outcome data measured and reported clearly, stratified by specific type of birth defect
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Brender, J.D., Shinde, M.U., Zhan, F.B., Gong, X., Langlois, P.H. (2014). Maternal residential proximity to chlorinated solvent emissions and birth defects in offspring: A case-control study. Environmental Health: A Global Access Science Source 13(1):96.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	birth defects (neural tube defects, limbs deficiencies, oral cleft defects, heart defects, spina bifida, anencephaly)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	2799700

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	High	Cases were frequency matched by year of delivery and public health service region. Final models were adjusted for year of delivery, public health region, maternal age (<20, 20-24, 25-29, 30-34, 35-39, >39 years), education (<12 years, 12 years, >12 years), and race/ethnicity (Whit non-Hispanic, Black non-Hispanic, Hispanic, other non-Hispanic).
	Metric 10:	Covariate Characterization	High	Used birth and death certificates for demographic information
	Metric 11:	Co-exposure Counfounding	Medium	other co-exposures were not described
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	study used logistic regression to measure association between exposure and birth defects
	Metric 13:	Statistical Power	Medium	Overall adequate number of cases and controls - some effects have low cell counts, but at least one health effect has sufficient statistical power.
	Metric 14:	Reproducibility of Analyses	Medium	Methods sufficiently detailed for reproducibility
	Metric 15:	Statistical Analysis	High	No logistic regression model assumption violations were identified.

Additional Comments: This study examined the association between proximity to several point sources of chlorinated solvents and birth defects. Exposure was assessed using EPA's Toxic Release Inventory, and birth defects were assessed using Texas birth registries. The geocoded address of mothers on day of delivery and the amount of solvent was plugged into the Emission Weighted Probability model to assign each mother an exposure risk value. Limitations include limited evidence of temporality. Additionally, elective terminations lacked a vital record, which meant only 69% of mothers with neural tube defects were geocoded. Mothers highly exposed to 1,2-dichloroethane were 1.85 times more likely to have the spina bifida birth defect than mothers who were not significantly exposed.

Overall Quality Determination High

* No biomarkers were identified for this evaluation.

Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Nested case-control design; cases selected from deaths in cohort study was described by Rinsky et al (1988; HERO 597923) (29,139 workers in Union Carbide facilities in West Virginia followed from 1940 to 1978). Vital status complete for 95% of cohort members.
	Metric 2:	Attrition	High	There was minimal exclusion of subjects/missing data, because vital status follow-up was complete for 96% of the 29,139 men in the cohort study.
	Metric 3:	Comparison Group	Medium	Controls were randomly selected in a 5:1 ratio to cases from the total employee cohort such that they were first employed in the same decade and survived to the same five-year survival period as cases. Controls survived at least to the beginning of the five-year interval in which cases died. Controls were independently selected for each of the individual disease subcategories. However, the demographic information between cases and controls were not compared in the paper.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was partially described: (1) Potential employee contact with a specific substance was determined by tracing each employee's work assignments and linking these assignment records to a separate computer file that contained a history of departmental usage for each substance; (2) Potential exposure to each chemical group was assumed on the basis of assignment o a production unit with a history of usage of any member of that chemical group. However, exposure level either based on work assignment in departments such as job exposure matrix or on the chemical levels were not presented.
	Metric 5:	Exposure Levels	Low	The range of exposure is limited. For example, exposure was presented by the duration of work in two categories: <5 years and 5+ years.
	Metric 6:	Temporality	Medium	Temporality is established, but it is unclear whether the exposures fall within the relevant exposure window. Authors used a lag time of 5 years; since controls were selected for 5 yr intervals, the effective lag time ranged from 5-9 years with an average of 7.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Case definition was based on death certificate diagnosis; but no method validation was conducted against this well-established methods.
	Metric 8:	Reporting Bias	Medium	All outcomes reported, but ORs for many analyses presented without CIs (some CIs reported in text).
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Low	There is indirect evidence that considerations were not made for potential confounders (ORs not adjusted, controls not age- or race-matched). Even though authors note that "Age-adjusted stratified analyses, which were also conducted, did not materially modify the odds ratio estimates". Also stratified examination of odds ratios were conducted to assess duration of exposure effects. However, other key confounders e.g., smoking status and race were not accounted for.
	Metric 10:	Covariate Characterization	Medium	The only potential confounder considered was age; this was presumably evaluated based on employment records (no discussion presented). Age-adjusted stratified analyses were conducted.
	Metric 11:	Co-exposure Counfounding	Low	Co-exposures were present and were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Nested case-control study design is appropriate for research question. Initial data analysis included crude odds ratio and then stratified examination of odds ratios was conducted to ass duration of exposure effect. Also, age-adjusted stratified analysis was conducted.
	Metric 13:	Statistical Power	Low	Statistical power calculations were not reported. Case numbers for each disease were low. The number of subjects was not sufficient to detect an effect of 1,2-dichloroethylene exposure.
	Metric 14:	Reproducibility of Analyses	Medium	Description was sufficient to be conceptually reproducible.
	Metric 15:	Statistical Analysis	Low	Statistical model to calculate odds ratio was not described.

Additional Comments: This nested case-control study within a cohort study is a good study design to answer the research question regarding the association between multiple chemical exposures and four cancer sites. Cases and controls are selected appropriate. However, there are several limitations in this study: (1) confounders were not all considered and adjusted for, except that age-adjusted odds ratios were conducted; (2) it is not described if co-exposures were adjusted for; (3) numbers of cancer cases for each cancer type were small, so the statistical power is limited; (4) statistical models for calculating odds ratios were not described.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
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Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Nested case-control design; cases selected from deaths in cohort study was described by Rinsky et al (1988; HERO 597923) (29,139 workers in Union Carbide facilities in West Virginia followed from 1940 to 1978). Vital status complete for 95% of cohort members.
	Metric 2:	Attrition	High	There was minimal exclusion of subjects/missing data, because vital status follow-up was complete for 96% of the 29,139 men in the cohort study.
	Metric 3:	Comparison Group	Medium	Controls were randomly selected in a 5:1 ratio to cases from the total employee cohort such that they were first employed in the same decade and survived to the same five-year survival period as cases. Controls survived at least to the beginning of the five-year interval in which cases died. Controls were independently selected for each of the individual disease subcategories. However, the demographic information between cases and controls were not compared in the paper.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was partially described: (1) Potential employee contact with a specific substance was determined by tracing each employee's work assignments and linking these assignment records to a separate computer file that contained a history of departmental usage for each substance; (2) Potential exposure to each chemical group was assumed on the basis of assignment o a production unit with a history of usage of any member of that chemical group. However, exposure level either based on work assignment in departments such as job exposure matrix or on the chemical levels were not presented.
	Metric 5:	Exposure Levels	Low	The range of exposure is limited. For example, exposure was presented by the duration of work in two categories: <5 years and 5+ years.
	Metric 6:	Temporality	Medium	Temporality is established, but it is unclear whether the exposures fall within the relevant exposure window. Authors used a lag time of 5 years; since controls were selected for 5 yr intervals, the effective lag time ranged from 5-9 years with an average of 7.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Case definition was based on death certificate diagnosis; but no method validation was conducted against this well-established methods.
	Metric 8:	Reporting Bias	Medium	All outcomes reported, but ORs for many analyses presented without CIs (some CIs reported in text).
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Low	There is indirect evidence that considerations were not made for potential confounders (ORs not adjusted, controls not age- or race-matched). Even though authors note that "Age-adjusted stratified analyses, which were also conducted, did not materially modify the odds ratio estimates". Also stratified examination of odds ratios were conducted to assess duration of exposure effects. However, other key confounders e.g., smoking status and race were not accounted for.
	Metric 10:	Covariate Characterization	Medium	The only potential confounder considered was age; this was presumably evaluated based on employment records (no discussion presented). Age-adjusted stratified analyses were conducted.
	Metric 11:	Co-exposure Counfounding	Low	Co-exposures were present and were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Nested case-control study design is appropriate for research question. Initial data analysis included crude odds ratio and then stratified examination of odds ratios was conducted to ass duration of exposure effect. Also, age-adjusted stratified analysis was conducted.
	Metric 13:	Statistical Power	Low	Statistical power calculations were not reported. Case numbers for each disease were low. The number of subjects was not sufficient to detect an effect of 1,2-dichloroethylene exposure.
	Metric 14:	Reproducibility of Analyses	Medium	Description was sufficient to be conceptually reproducible.
	Metric 15:	Statistical Analysis	Low	Statistical model to calculate odds ratio was not described.

Additional Comments: This nested case-control study within a cohort study is a good study design to answer the research question regarding the association between multiple chemical exposures and four cancer sites. Cases and controls are selected appropriate. However, there are several limitations in this study: (1) confounders were not all considered and adjusted for, except that age-adjusted odds ratios were conducted; (2) it is not described if co-exposures were adjusted for; (3) numbers of cancer cases for each cancer type were small, so the statistical power is limited; (4) statistical models for calculating odds ratios were not described.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
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Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Nested case-control design; cases selected from deaths in cohort study was described by Rinsky et al (1988; HERO 597923) (29,139 workers in Union Carbide facilities in West Virginia followed from 1940 to 1978). Vital status complete for 95% of cohort members.
	Metric 2:	Attrition	High	There was minimal exclusion of subjects/missing data, because vital status follow-up was complete for 96% of the 29,139 men in the cohort study.
	Metric 3:	Comparison Group	Medium	Controls were randomly selected in a 5:1 ratio to cases from the total employee cohort such that they were first employed in the same decade and survived to the same five-year survival period as cases. Controls survived at least to the beginning of the five-year interval in which cases died. Controls were independently selected for each of the individual disease subcategories. However, the demographic information between cases and controls were not compared in the paper.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was partially described: (1) Potential employee contact with a specific substance was determined by tracing each employee's work assignments and linking these assignment records to a separate computer file that contained a history of departmental usage for each substance; (2) Potential exposure to each chemical group was assumed on the basis of assignment o a production unit with a history of usage of any member of that chemical group. However, exposure level either based on work assignment in departments such as job exposure matrix or on the chemical levels were not presented.
	Metric 5:	Exposure Levels	Low	The range of exposure is limited. For example, exposure was presented by the duration of work in two categories: <5 years and 5+ years.
	Metric 6:	Temporality	Medium	Temporality is established, but it is unclear whether the exposures fall within the relevant exposure window. Authors used a lag time of 5 years; since controls were selected for 5 yr intervals, the effective lag time ranged from 5-9 years with an average of 7.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Case definition was based on death certificate diagnosis; but no method validation was conducted against this well-established methods.
	Metric 8:	Reporting Bias	Medium	All outcomes reported, but ORs for many analyses presented without CIs (some CIs reported in text).
Domain 4: Potential Confounding / Variability Control				

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Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Low	There is indirect evidence that considerations were not made for potential confounders (ORs not adjusted, controls not age- or race-matched). Even though authors note that "Age-adjusted stratified analyses, which were also conducted, did not materially modify the odds ratio estimates". Also stratified examination of odds ratios were conducted to assess duration of exposure effects. However, other key confounders e.g., smoking status and race were not accounted for.
	Metric 10:	Covariate Characterization	Medium	The only potential confounder considered was age; this was presumably evaluated based on employment records (no discussion presented). Age-adjusted stratified analyses were conducted.
	Metric 11:	Co-exposure Counfounding	Low	Co-exposures were present and were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Nested case-control study design is appropriate for research question. Initial data analysis included crude odds ratio and then stratified examination of odds ratios was conducted to ass duration of exposure effect. Also, age-adjusted stratified analysis was conducted.
	Metric 13:	Statistical Power	Low	Statistical power calculations were not reported. Case numbers for each disease were low. The number of subjects was not sufficient to detect an effect of 1,2-dichloroethylene exposure.
	Metric 14:	Reproducibility of Analyses	Medium	Description was sufficient to be conceptually reproducible.
	Metric 15:	Statistical Analysis	Low	Statistical model to calculate odds ratio was not described.

Additional Comments: This nested case-control study within a cohort study is a good study design to answer the research question regarding the association between multiple chemical exposures and four cancer sites. Cases and controls are selected appropriate. However, there are several limitations in this study: (1) confounders were not all considered and adjusted for, except that age-adjusted odds ratios were conducted; (2) it is not described if co-exposures were adjusted for; (3) numbers of cancer cases for each cancer type were small, so the statistical power is limited; (4) statistical models for calculating odds ratios were not described.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Nested case-control design; cases selected from deaths in cohort study was described by Rinsky et al (1988; HERO 597923) (29,139 workers in Union Carbide facilities in West Virginia followed from 1940 to 1978). Vital status complete for 95% of cohort members.
	Metric 2:	Attrition	High	There was minimal exclusion of subjects/missing data, because vital status follow-up was complete for 96% of the 29,139 men in the cohort study.
	Metric 3:	Comparison Group	Medium	Controls were randomly selected in a 5:1 ratio to cases from the total employee cohort such that they were first employed in the same decade and survived to the same five-year survival period as cases. Controls survived at least to the beginning of the five-year interval in which cases died. Controls were independently selected for each of the individual disease subcategories. However, the demographic information between cases and controls were not compared in the paper.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was partially described: (1) Potential employee contact with a specific substance was determined by tracing each employee's work assignments and linking these assignment records to a separate computer file that contained a history of departmental usage for each substance; (2) Potential exposure to each chemical group was assumed on the basis of assignment o a production unit with a history of usage of any member of that chemical group. However, exposure level either based on work assignment in departments such as job exposure matrix or on the chemical levels were not presented.
	Metric 5:	Exposure Levels	Low	The range of exposure is limited. For example, exposure was presented by the duration of work in two categories: <5 years and 5+ years.
	Metric 6:	Temporality	Medium	Temporality is established, but it is unclear whether the exposures fall within the relevant exposure window. Authors used a lag time of 5 years; since controls were selected for 5 yr intervals, the effective lag time ranged from 5-9 years with an average of 7.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Case definition was based on death certificate diagnosis; but no method validation was conducted against this well-established methods.
	Metric 8:	Reporting Bias	Medium	All outcomes reported, but ORs for many analyses presented without CIs (some CIs reported in text).
Domain 4: Potential Confounding / Variability Control				

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Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Low	There is indirect evidence that considerations were not made for potential confounders (ORs not adjusted, controls not age- or race-matched). Even though authors note that "Age-adjusted stratified analyses, which were also conducted, did not materially modify the odds ratio estimates". Also stratified examination of odds ratios were conducted to assess duration of exposure effects. However, other key confounders e.g., smoking status and race were not accounted for.
	Metric 10:	Covariate Characterization	Medium	The only potential confounder considered was age; this was presumably evaluated based on employment records (no discussion presented). Age-adjusted stratified analyses were conducted.
	Metric 11:	Co-exposure Counfounding	Low	Co-exposures were present and were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Nested case-control study design is appropriate for research question. Initial data analysis included crude odds ratio and then stratified examination of odds ratios was conducted to ass duration of exposure effect. Also, age-adjusted stratified analysis was conducted.
	Metric 13:	Statistical Power	Low	Statistical power calculations were not reported. Case numbers for each disease were low. The number of subjects was not sufficient to detect an effect of 1,2-dichloroethylene exposure.
	Metric 14:	Reproducibility of Analyses	Medium	Description was sufficient to be conceptually reproducible.
	Metric 15:	Statistical Analysis	Low	Statistical model to calculate odds ratio was not described.

Additional Comments: This nested case-control study within a cohort study is a good study design to answer the research question regarding the association between multiple chemical exposures and four cancer sites. Cases and controls are selected appropriate. However, there are several limitations in this study: (1) confounders were not all considered and adjusted for, except that age-adjusted odds ratios were conducted; (2) it is not described if co-exposures were adjusted for; (3) numbers of cancer cases for each cancer type were small, so the statistical power is limited; (4) statistical models for calculating odds ratios were not described.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Cheng, T.J., Huang, M.L., You, N.C., Du, C.L., Chau, T.T. (1999). Abnormal liver function in workers exposed to low levels of ethylene dichloride and vinyl chloride monomer. Journal of Occupational and Environmental Medicine 41(12):1128-1133.
Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	AST, ALT, GGT, Hepatitis B virus surface antigen (HBsAg), and anti-hepatitis C virus antibody (anti-HCV).
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	200266

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	A total of 251 male workers were included from 4 vinyl chloride monomer manufacturing plants. Other details on recruitment strategy, eligibility criteria, year of enrollment, and participation rates were not provided.
	Metric 2:	Attrition	Low	There was no indication of attrition and details on the number of eligible participants throughout the study was limited. Attrition could not be adequately assessed due to a lack of information regarding recruitment and selection.
	Metric 3:	Comparison Group	Medium	The low-EDC-low-VCM group (187 participants) was used as the comparison group, and there is indirect evidence groups are similar. Limited details were provided for setting, inclusion and exclusion criteria, and methods of participant selection.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	NIOSH recommended methods 1003 and 1007 were used for personal and area sampling, respectively. Air samples were collected, stored at 4 deg. C, and analyzed within 2 weeks of the sampling event. However, historical job changes, changes in exposure levels over time, and timing (year or days during work week) or duration of area or personal sampling were not reported.
	Metric 5:	Exposure Levels	Medium	EDC and VCM levels were reported for the different categories of jobs, which were classified into low-EDC-low-VCM, mod-EDC-low-VCM, and low-EDC-mod-VCM groups.
	Metric 6:	Temporality	High	The age of participants (mean age 33.7-40.1 years) and employment duration (mean 7.5-14.3 years) were reported, and the temporality between the exposure and outcome appears to be appropriate.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	AST, ALT, and GGT "were analyzed with a Hitachi 7050 autoanalyzer". A basis for the cutoff values used in Table 4 to determine "abnormal" AST, ALT, and GGT levels was not provided.
	Metric 8:	Reporting Bias	High	Odds ratios for abnormal liver function were provided with 95% confidence intervals, the number per exposure level, and significance when applicable.
Domain 4: Potential Confounding / Variability Control				

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Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	AST, ALT, GGT, Hepatitis B virus surface antigen (HBsAg), and anti-hepatitis C virus antibody (anti-HCV).
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	200266

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Medium	The study reports information on potential confounders (age, hepatitis, BMI, alcohol use, and employment duration), and controls for hepatitis, BMI and alcohol consumption in the multiple logistic regression analyses. There is indirect evidence that appropriate adjustments were made.
	Metric 10:	Covariate Characterization	Medium	An interviewer administered the questionnaires to collect information about potential confounders and occupational history.
	Metric 11:	Co-exposure Counfounding	Low	Exposure to ethylene dichloride was evaluated in a vinyl chloride monomer (VCM) manufacturing facility, and VCM was also subsequently analyzed using personal and area sampling. Results for VCM exposure concentrations were provided. VCM is also suspected to cause liver damage.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design (cohort) was appropriate to assess the outcome of interest (”markers of liver damage”). Chi-squared (X2) test and multiple logistic regression were used for statistical analyses.
	Metric 13:	Statistical Power	Medium	The number of participants was adequate to detect an effect in the exposed populations, although power calculations were not provided. There were >20 participants in each group.
	Metric 14:	Reproducibility of Analyses	Low	A description of the logistic regression analysis was provided, however, study authors do not provide information on categorization of abnormal liver function.
	Metric 15:	Statistical Analysis	High	There were no identifiable logistic regression model assumption violations.
Domain 6: Other (if applicable) Considerations for Biomarker Selection and Measurement (Lakind et al. 2014)				
	Metric 16:	Use of Biomarker of Exposure	N/A	Biomarker of exposures were not assessed.
	Metric 17:	Effect Biomarker	High	This study uses aspartate aminotransferase, alanine aminotransferase, and y-glutamyltransferase as biomarkers of effect. While these no works cited to explain their connection to liver function, all three are well-known marker of liver function. Similarly, Hepatitis B virus surface antigen and antihepatitis C virus anitbody are also well-known measures of liver function and health.
	Metric 18:	Method Sensitivity	Low	No limit of detection information is provided for any of the effect biomarkers.
	Metric 19:	Biomarker Stability	Medium	While the study does not provide a lot of information regarding biomarker storage or stability, the authors do mention that venous blood used to detect biomarkers was stored at 4 degrees C.
	Metric 20:	Sample Contamination	Medium	No specific information regarding potential sample contamination was provided.
	Metric 21:	Method Requirements	Medium	Aspartate aminotransferase, alanine aminotransferase, and y-glutamyltransferase were analyzed using a Hitachi 7050 autoanalyzer. Hepatitis B virus surface antibody and antihepatitis C virus antibody were assessed with radioimmunoassay and enzyme-linked immunosorbent assay.

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Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	AST, ALT, GGT, Hepatitis B virus surface antigen (HBsAg), and anti-hepatitis C virus antibody (anti-HCV).
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	200266

Domain	Metric	Rating	Comments
	Metric 22: Matrix Adjustment	N/A	No information on matrix adjustment was provided/available.

Additional Comments: A group of 251 male workers from 4 vinyl chloride monomer (VCM) manufacturing plants were included in this assessment to examine if occupational exposure to VCM and ethylene dichloride (EDC) "resulted in increased risk of liver damage" by examining AST, ALT, and GGT levels in the blood. Increased ORs for abnormal AST (>37 IU/L) and ALT (>41 IU/L) in the mod-EDC-low-VCM group (0.17-333.7 ppm EDC, 0.18-0.34 ppm VCM), compared with the low-EDC-low-VCM group, was reported. Exposure levels were measured using area and personal sampling, but the timing and duration of the sampling events were not reported.

Overall Quality Determination Medium

Study Citation:	Dosemeci, M., Cocco, P., Chow, W.H. (1999). Gender differences in risk of renal cell carcinoma and occupational exposures to chlorinated aliphatic hydrocarbons. American Journal of Industrial Medicine 36(1):54-59.
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	renal cell carcinoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	4697224

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	The details of the study design were reported elsewhere (Chow et al. 1994, HERO ID 701514). Brief details about the setting, date, number of eligible participants, and control matching were reported. Reasons for exclusions/non-participation were described with details by Chow et al. (1994).
	Metric 2:	Attrition	High	For the details of the study design and attrition of study subjects, the study authors referred to another publication by Chow et al., 1994. Chow et al. (1994) mentioned that at the end of the personal interview, the respondents were given a self-administered food-frequency questionnaire. Of the subjects interviewed for the study, 632 patients (79% of 796 eligible patients) and 653 control subjects (79% of 707 eligible control subjects) returned the diet questionnaire. A number of subjects, whose responses were considered unreliable, were excluded from the analysis, including 48 patients and three control subjects who had seven or more skipped food items or had questionable data and 50 patients whose next-of-kin respondent was not a spouse. Also excluded were two patients with unknown smoking status, since smoking is a risk factor.
	Metric 3:	Comparison Group	Medium	The cases were pulled from the Minnesota Cancer Surveillance System. Controls were selected from the general population of Minnesota; controls age 20-64 years were selected through random digital dialing and controls age 65-85 years were collected from files through the Health Care Financing Administration. Controls were age- and gender-stratified and were of the same race. Characteristics of cases and controls were not provided in the text or a table.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	High	Occupational histories including the most recent and usual occupation and industry, job activities, started-year and ended-year, and part-time/full-time status were collected. Occupations and industries were coded according to the standard occupational classification (SOC) and standard industrial classification (SIC) schemes. The National Cancer Institute developed job exposure matrices (JEM) for nine individual chlorinated aliphatic hydrocarbons (CAHCs), all CAHCs-combined, and all organic solvents-combined. These JEMs were merged with assigned SOC and SIC to determine the exposure status to these chemicals for each study subject. Application of the JEM was described elsewhere (Dosemeci et al. 1994, HERO ID 632334; Gomez et al. 1994, HERO ID 702154).
	Metric 5:	Exposure Levels	Medium	Details of the application of the JEM were described elsewhere (Dosemeci et al. 1994, HERO ID 632334; Gomez et al. 1994, HERO ID 702154). Dosemeci et al. (1994) described more details about that this study assigned three levels of probability (low, medium, high) to industries and occupations for chemical exposure levels.

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Study Citation:	Dosemeci, M., Cocco, P., Chow, W.H. (1999). Gender differences in risk of renal cell carcinoma and occupational exposures to chlorinated aliphatic hydrocarbons. American Journal of Industrial Medicine 36(1):54-59.
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	renal cell carcinoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	4697224

Domain	Metric		Rating	Comments
	Metric 6:	Temporality	Medium	Occupational questionnaires identified prior exposures based on reported recent and usual occupations as well as duration of employment. Outcome status was determined from registry data. The authors note that some occupational history was incomplete which may result in some uncertainty in regard to temporality.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Cases were identified as newly diagnosed and histologically confirmed renal cell carcinoma through the Minnesota Cancer Surveillance System and information about each participant was collected using a questionnaire. Validation was not specified.
	Metric 8:	Reporting Bias	Medium	A description of measured outcomes is reported and ORs were stratified by sex. Effect estimates are reported with a confidence interval. One table showed the total numbers of men and women respectively for each chemical, but numbers of cases/controls were not reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Appropriate adjustments were made in the final analysis, including age, gender, smoking, hypertension and the use of diuretics and/or anti-hypertension drugs, and BMI. Results were stratified by sex.
	Metric 10:	Covariate Characterization	Medium	Information about participants was collected using a questionnaire, and it includes potential confounders, e.g., smoking habits. Validation was not specified.
	Metric 11:	Co-exposure Counfounding	Medium	Co-exposures were identified through the job exposure matrices. Chemicals were evaluated individually and as a group.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen (case-control) was appropriate for the research question (renal cell carcinoma risk from occupational organic solvent exposure). Logistic regression models were used to estimate the relative risk and 95% CI.
	Metric 13:	Statistical Power	Low	Statistical power calculations were not provided. No significant effects were observed with 1,2-dichloroethane. The number of participated women to calculate odds ratio was inadequate to detect an effect in the participants for other chemicals or the combined risk, because it was very low.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis was brief, but is sufficient to understand precisely what has been done and to be conceptually reproducible with access to the analytic data.
	Metric 15:	Statistical Analysis	High	Model assumptions for logistic regression were met. The odds ratios were adjusted for age, smoking, hypertension status and/or use of diuretic and/or anti-hypertension drugs, and body mass index for men and women separately.

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Study Citation:	Dosemeci, M., Cocco, P., Chow, W.H. (1999). Gender differences in risk of renal cell carcinoma and occupational exposures to chlorinated aliphatic hydrocarbons. American Journal of Industrial Medicine 36(1):54-59.
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	renal cell carcinoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	4697224

Domain	Metric	Rating	Comments
Additional Comments:	A group of 438 cases (273 men and 165 women) were selected from the Minnesota Cancer Surveillance System that had been newly diagnosed with renal cell carcinoma. Controls included 687 participants (462 men and 225 women) age- and gender- stratified that were selected from either the general population of Minnesota (age 20-64 years) or from the Health Care Financing Administration files (age 65-85). No significant increase in the risk of renal cell carcinoma was observed with exposure to 1,2-dichloroethane among men or women separately, or for all participants exposed.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Dosemeci, M., Cocco, P., Chow, W.H. (1999). Gender differences in risk of renal cell carcinoma and occupational exposures to chlorinated aliphatic hydrocarbons. American Journal of Industrial Medicine 36(1):54-59.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	renal cell carcinoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	4697224

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	The details of the study design were reported elsewhere (Chow et al. 1994, HERO ID 701514). Brief details about the setting, date, number of eligible participants, and control matching were reported. Reasons for exclusions/non-participation were described with details by Chow et al. (1994).
	Metric 2:	Attrition	Medium	For the details of the study design and attrition of study subjects, the study authors referred to another publication by Chow et al., 1994. Chow et al. (1994) mentioned that at the end of the personal interview, the respondents were given a self-administered food-frequency questionnaire. Of the subjects interviewed for the study, 632 patients (79% of 796 eligible patients) and 653 control subjects (79% of 707 eligible control subjects) returned the diet questionnaire. A number of subjects, whose responses were considered unreliable, were excluded from the analysis, including 48 patients and three control subjects who had seven or more skipped food items or had questionable data and 50 patients whose next-of-kin respondent was not a spouse. Also excluded were two patients with unknown smoking status, since smoking is a risk factor.
	Metric 3:	Comparison Group	Medium	The cases were pulled from the Minnesota Cancer Surveillance System. Controls were selected from the general population of Minnesota; controls age 20-64 years were selected through random digital dialing and controls age 65-85 years were collected from files through the Health Care Financing Administration. Controls were age- and gender-stratified and were of the same race. Characteristics of cases and controls were not provided in the text or a table.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	High	Occupational histories including the most recent and usual occupation and industry, job activities, started-year and ended-year, and part-time/full-time status were collected. Occupations and industries were coded according to the standard occupational classification (SOC) and standard industrial classification (SIC) schemes. The National Cancer Institute developed job exposure matrices (JEM) for nine individual chlorinated aliphatic hydrocarbons (CAHCs), all CAHCs-combined, and all organic solvents-combined. These JEMs were merged with assigned SOC and SIC to determine the exposure status to these chemicals for each study subject. Application of the JEM was described elsewhere (Dosemeci et al. 1994, HERO ID 632334; Gomez et al. 1994, HERO ID 702154).
	Metric 5:	Exposure Levels	Medium	Details of the application of the JEM were described elsewhere (Dosemeci et al. 1994, HERO ID 632334; Gomez et al. 1994, HERO ID 702154). Dosemeci et al. (1994) described more details about that this study assigned three levels of probability (low, medium, high) to industries and occupations for chemical exposure levels.

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Study Citation:	Dosemeci, M., Cocco, P., Chow, W.H. (1999). Gender differences in risk of renal cell carcinoma and occupational exposures to chlorinated aliphatic hydrocarbons. American Journal of Industrial Medicine 36(1):54-59.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	renal cell carcinoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	4697224

Domain	Metric		Rating	Comments
	Metric 6:	Temporality	Medium	Occupational questionnaires identified prior exposures based on reported recent and usual occupations as well as duration of employment. Outcome status was determined from registry data. The authors note that some occupational history was incomplete which may result in some uncertainty in regard to temporality.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Cases were identified as newly diagnosed and histologically confirmed renal cell carcinoma through the Minnesota Cancer Surveillance System and information about each participant was collected using a questionnaire. Validation was not specified.
	Metric 8:	Reporting Bias	Medium	A description of measured outcomes is reported and ORs were stratified by sex. Effect estimates are reported with a confidence interval. One table showed the total numbers of men and women respectively for each chemical, but numbers of cases/controls were not reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Appropriate adjustments were made in the final analysis, including age, gender, smoking, hypertension and the use of diuretics and/or anti-hypertension drugs, and BMI. Results were stratified by sex.
	Metric 10:	Covariate Characterization	Medium	Information about participants was collected using a questionnaire, and it includes potential confounders, e.g., smoking habits. Validation was not specified.
	Metric 11:	Co-exposure Counfounding	Medium	Co-exposures were identified through the job exposure matrices. Chemicals were evaluated individually and as a group.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen (case-control) was appropriate for the research question (renal cell carcinoma risk from occupational organic solvent exposure). Logistic regression models were used to estimate the relative risk and 95% CI.
	Metric 13:	Statistical Power	Low	Statistical power calculations were not provided. No significant effects were observed with 1,2-dichloroethane. The number of participated women to calculate odds ratio was inadequate to detect an effect in the participants for other chemicals or the combined risk, because it was very low.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis was brief, but is sufficient to understand precisely what has been done and to be conceptually reproducible with access to the analytic data.
	Metric 15:	Statistical Analysis	High	Model assumptions for logistic regression were met. The odds ratios were adjusted for age, smoking, hypertension status and/or use of diuretic and/or anti-hypertension drugs, and body mass index for men and women separately.

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Study Citation:	Dosemeci, M., Cocco, P., Chow, W.H. (1999). Gender differences in risk of renal cell carcinoma and occupational exposures to chlorinated aliphatic hydrocarbons. American Journal of Industrial Medicine 36(1):54-59.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	renal cell carcinoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	4697224

Domain	Metric	Rating	Comments
Additional Comments:	A group of 438 cases (273 men and 165 women) were selected from the Minnesota Cancer Surveillance System that had been newly diagnosed with renal cell carcinoma. Controls included 687 participants (462 men and 225 women) age- and gender- stratified that were selected from either the general population of Minnesota (age 20-64 years) or from the Health Care Financing Administration files (age 65-85). No significant increase in the risk of renal cell carcinoma was observed with exposure to 1,2-dichloroethane among men or women separately, or for all participants exposed.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Garcia, E., Hurley, S., Nelson, D.O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health: A Global Access Science Source 14(1):14.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	breast cancer in females
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	3014082

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	A total of 112,378 women were included in this study out of 133,479 eligible female participants from the California Teacher Study cohort. A full description of the cohort is provided in Bernstein et al. 2002 (HERO ID 808446). Reasons for exclusion were provided. The reported information indicates that participant selection in or out of the study and participation was not likely to be biased.
	Metric 2:	Attrition	High	112,378/133,479 participants were included in the study. Exclusions were for the purpose of the study and analysis. Exclusion criteria were documented. Included participants had completed questionnaires. The California Cancer Registry is estimated to be 99% complete.
	Metric 3:	Comparison Group	Medium	There is only indirect evidence that groups are similar. Participants were recruited from the same eligible population with the same method of ascertainment. Comparisons were provided for participants with and without breast cancer. Characteristics between these two groups were generally similar. 5 Quintiles of exposure were used, and Q2-5 were compared with Q1.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	High	The Assessment System for Population Exposure Nationwide and the Human Exposure Model are used as part of the National-Scale Air Toxics Assessment produced by the EPA and was used to estimate ambient HAP concentrations for geographic locations. Methods are described online through the US EPA Assessment Methods.
	Metric 5:	Exposure Levels	Medium	The distribution of the NATA annual ambient concentration for each compound was plotted in Figure 1 using a box plot, and 5 Quintiles were used in the analyses.
	Metric 6:	Temporality	Medium	The follow-up period was from 1995-2011, and the NATA estimates were made in 2002 because it was approximately half way between the start and end of the follow-up period. However, it is unclear whether exposures fall within relevant exposure windows for the outcome of interest.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Annual linkage between the CTS cohort and the California Cancer Registry (CCR) was used to identify cases of invasive breast cancer. The CCR is estimated to be 99% complete. The case of invasive breast cancer was defined by ICD codes.

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Study Citation:	Garcia, E., Hurley, S., Nelson, D.O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health: A Global Access Science Source 14(1):14.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	breast cancer in females
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	3014082

Domain	Metric		Rating	Comments
	Metric 8:	Reporting Bias	Medium	A description of measured outcome is reported for adjustments by age and race, and effect estimates are reported with a 95% confidence interval. The measured outcomes using multiple comparisons were generally described in the text, but non-significant results were excluded from Table 3.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	The models were stratified by age and race. Additionally, adjustments were made for multiple comparisons among subsets of the participants (significant results reported in Table 3). Socioeconomic status (SES) of each participant was not evaluated, however, cohort SES characteristics were thought to be similar by study authors.
	Metric 10:	Covariate Characterization	Medium	Information about baseline characteristics for each participant was collected through a questionnaire. It is unknown if the questionnaire was validated.
	Metric 11:	Co-exposure Counfounding	Medium	A total of 37 compounds were identified as mammary gland carcinogens, but 13 were not included in this analysis. Thirteen compounds were excluded from the analysis due to insufficient variability (nine because they had the same value for all census tracts in the state of California; and four because they had less than 25% non-zero values). Ethylene dichloride (1,2-dichloroethane) was among the 24 compounds evaluated in this assessment, and evaluations for breast cancer were conducted for each of these 24 individual compounds.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen (prospective cohort) was appropriate for the research question (incidence of breast cancer). Cox proportional hazard models and SAS 9.3 were used in this assessment. Data analysis was described.
	Metric 13:	Statistical Power	Medium	Statistical power calculations were not provided. No significant effects were observed with ethylene dichloride (1,2-dichloroethane), however, this study utilized a large cohort, approximately 112,000 individuals. Distributions of chemicals of interest suggest there were sufficient numbers of participants in exposure subgroups.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to understand precisely what has been done and to be conceptually reproducible with access to the analytic data.
	Metric 15:	Statistical Analysis	High	The statistical models that were used were identified and described. ”No apparent violation of the underlying assumption of proportional hazards was detected”.

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Study Citation:	Garcia, E., Hurley, S., Nelson, D.O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health: A Global Access Science Source 14(1):14.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	breast cancer in females
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	3014082

Domain	Metric	Rating	Comments
Additional Comments:	A group of 112,378 female participants from the California Teacher Study cohort were assessed for their estimated exposure to ambient air pollutants, including ethylene dichloride (1,2-dichloroethane), and the incidence of invasive breast cancer. Air contaminant concentrations were estimated using the US EPA NATA and the ASPEN and HEM models. The approximate median concentration of 1,2-dichloroethane is between 1E-4 and 1E-2 (estimated from Figure 1). Exposures were categorized into 5 Quintiles, and compared against Quintile 1. No significant increase in the estimated hazard rate ratio for invasive breast cancer was observed with Quintile 2-5 exposure estimates for 1,2-dichloroethane, adjusted for age and race, when compared against Quintile 1, or when further adjusted using multiple comparisons.		

Overall Quality Determination High

* No biomarkers were identified for this evaluation.

Study Citation:	Garcia, E., Hurley, S., Nelson, D.O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health: A Global Access Science Source 14(1):14.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	breast cancer in females
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	3014082

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	A total of 112,378 women were included in this study out of 133,479 eligible female participants from the California Teacher Study cohort. A full description of the cohort is provided in Bernstein et al. 2002 (HERO ID 808446). Reasons for exclusion were provided. The reported information indicates that participant selection in or out of the study and participation was not likely to be biased.
	Metric 2:	Attrition	High	112,378/133,479 participants were included in the study. Exclusions were for the purpose of the study and analysis. Exclusion criteria were documented. Included participants had completed questionnaires. The California Cancer Registry is estimated to be 99% complete.
	Metric 3:	Comparison Group	Medium	There is only indirect evidence that groups are similar. Participants were recruited from the same eligible population with the same method of ascertainment. Comparisons were provided for participants with and without breast cancer. Characteristics between these two groups were generally similar. 5 Quintiles of exposure were used, and Q2-5 were compared with Q1.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	High	The Assessment System for Population Exposure Nationwide and the Human Exposure Model are used as part of the National-Scale Air Toxics Assessment produced by the EPA and was used to estimate ambient HAP concentrations for geographic locations. Methods are described online through the US EPA Assessment Methods.
	Metric 5:	Exposure Levels	Medium	The distribution of the NATA annual ambient concentration for each compound was plotted in Figure 1 using a box plot, and 5 Quintiles were used in the analyses.
	Metric 6:	Temporality	Medium	The follow-up period was from 1995-2011, and the NATA estimates were made in 2002 because it was approximately half way between the start and end of the follow-up period. However, it is unclear whether exposures fall within relevant exposure windows for the outcome of interest.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Annual linkage between the CTS cohort and the California Cancer Registry (CCR) was used to identify cases of invasive breast cancer. The CCR is estimated to be 99% complete. The case of invasive breast cancer was defined by ICD codes.
	Metric 8:	Reporting Bias	Medium	A description of measured outcome is reported for adjustments by age and race, and effect estimates are reported with a 95% confidence interval. The measured outcomes using multiple comparisons were generally described in the text, but non-significant results were excluded from Table 3.

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Study Citation:	Garcia, E., Hurley, S., Nelson, D.O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health: A Global Access Science Source 14(1):14.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	breast cancer in females
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	3014082

Domain	Metric		Rating	Comments
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	The models were stratified by age and race. Additionally, adjustments were made for multiple comparisons among subsets of the participants (significant results reported in Table 3). Socioeconomic status (SES) of each participant was not evaluated, however, cohort SES characteristics were thought to be similar by study authors.
	Metric 10:	Covariate Characterization	Medium	Information about baseline characteristics for each participant was collected through a questionnaire. It is unknown if the questionnaire was validated.
	Metric 11:	Co-exposure Counfounding	Medium	A total of 37 compounds were identified as mammary gland carcinogens, but 13 were not included in this analysis. Thirteen compounds were excluded from the analysis due to insufficient variability (nine because they had the same value for all census tracts in the state of California; and four because they had less than 25% non-zero values). Ethylene dichloride (1,2-dichloroethane) was among the 24 compounds evaluated in this assessment, and evaluations for breast cancer were conducted for each of these 24 individual compounds.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen (prospective cohort) was appropriate for the research question (incidence of breast cancer). Cox proportional hazard models and SAS 9.3 were used in this assessment. Data analysis was described.
	Metric 13:	Statistical Power	Medium	Statistical power calculations were not provided. No significant effects were observed with ethylene dichloride (1,2-dichloroethane), however, this study utilized a large cohort, approximately 112,000 individuals. Distributions of chemicals of interest suggest there were sufficient numbers of participants in exposure subgroups.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to understand precisely what has been done and to be conceptually reproducible with access to the analytic data.
	Metric 15:	Statistical Analysis	High	The statistical models that were used were identified and described. ”No apparent violation of the underlying assumption of proportional hazards was detected”.

Additional Comments: A group of 112,378 female participants from the California Teacher Study cohort were assessed for their estimated exposure to ambient air pollutants, including ethylene dichloride (1,2-dichloroethane), and the incidence of invasive breast cancer. Air contaminant concentrations were estimated using the US EPA NATA and the ASPEN and HEM models. The approximate median concentration of 1,2-dichloroethane is between 1E-4 and 1E-2 (estimated from Figure 1). Exposures were categorized into 5 Quintiles, and compared against Quintile 1. No significant increase in the estimated hazard rate ratio for invasive breast cancer was observed with Quintile 2-5 exposure estimates for 1,2-dichloroethane, adjusted for age and race, when compared against Quintile 1, or when further adjusted using multiple comparisons.

Overall Quality Determination High

* No biomarkers were identified for this evaluation.

Study Citation:	Guo, P., Yokoyama, K., Piao, F., Sakai, K., Khalequzzaman, M., Kamijima, M., Nakajima, T., Kitamura, F. (2013). Sick building syndrome by indoor air pollution in Dalian, China. International Journal of Environmental Research and Public Health 10(4):1489-1504.
Health Outcome(s):	sick building syndrome
Reported Health Effect(s):	The statistical analysis considers all subjective self-reported symptoms together (not segregated by health outcome) as a group health outcome –sick building syndrome. The study compared two conditions for each studied chemical: combined self-reported symptoms to no symptoms. Therefore, only one form 3 was completed.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1938385

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Residents of a housing estate of 3000 homes were invited to a community meeting to explain the purpose of the study and volunteers were invited to participate. It was not reported whether these volunteers were different from the overall eligible population.
	Metric 2:	Attrition	Low	Of the 70 families that agreed to participate, questionnaires were provided by 59. Reasons of uncompleted questionnaires were not fully provided, and there was no comparison between those who participated and those who did not.
	Metric 3:	Comparison Group	Low	The overall description of the analysis sample indicated a wide range of ages and lengths of stay at the current residence. Thus it is hard to know that subjects in all exposure groups were similar. In addition, the methods of selecting participants in all exposure groups were not fully reported. The numbers of male and female smokers were reported, respectively, but the smoking status and age were not controlled in the statistical analysis.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure concentrations for each home were obtained by diffusion sampling over 24 hrs in the bedroom, kitchen, and outdoors; temperature, the vertical height of samplers, and ventilation (hours windows left open) were reported. Samples were analyzed by GC/MS. The number of samples per home is unclear. The frequency of measurements for each house was not reported.
	Metric 5:	Exposure Levels	Low	The frequency of detection was not reported, so it is difficult to ascertain the actual exposure range. In addition, the reported exposure levels were median, geometric mean, and 95% CI, so they are inadequate to develop an exposure-response estimate.
	Metric 6:	Temporality	Uninformative	For 1,2-dichloroethane, the study evaluated self-reported symptoms in the past (”since they moved into their flats”) and their association with sampling conducted during the study; thus, exposure was measured after the outcome.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Low	Participants provided self-reported symptoms using a questionnaire. Study authors cited a previous study, Kamijima et al., 2005 (in Japanese, HERO ID 1598645) for further details on the questionnaire. It was not clear whether the questionnaire was validated.

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Study Citation: Guo, P., Yokoyama, K., Piao, F., Sakai, K., Khalequzzaman, M., Kamijima, M., Nakajima, T., Kitamura, F. (2013). Sick building syndrome by indoor air pollution in Dalian, China. International Journal of Environmental Research and Public Health 10(4):1489-1504.

Health Outcome(s): sick building syndrome

Reported Health Effect(s): The statistical analysis considers all subjective self-reported symptoms together (not segregated by health outcome) as a group health outcome –sick building syndrome. The study compared two conditions for each studied chemical: combined self-reported symptoms to no symptoms. Therefore, only one form 3 was completed.

Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

Linked HERO ID(s): No linked references.

HERO ID: 1938385

Domain	Metric		Rating	Comments
	Metric 8:	Reporting Bias	Low	The study only mentioned subjective symptoms in the abstract or methods. The abstract and method sections did not report the specific symptoms included in the questionnaire or whether the questionnaire was open-ended for symptoms. The questionnaire was cited to Kamijima et al. 2005 (in Japanese).
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	Comparisons were made separately by sex. The distribution of age and time spent living in residence differed greatly between those reporting symptoms and those not reporting symptoms. Smoking was indicated but not controlled for in the analysis. In short, the statistical analysis did not consider these three potential confounders, age, time spent living in residence, and smoking.
	Metric 10:	Covariate Characterization	Low	Covariates were presumably evaluated via a questionnaire that was cited to Kamijima et al. 2005 (in Japanese).
	Metric 11:	Co-exposure Counfounding	Low	The analysis did not account for other exposures. A number of other VOCs, HCHO, and NO2 were measured in the homes. The concentrations of several other VOCs and HCHO were much higher (5-30x) than 1,2-dichloroethane and may also be associated with these symptoms.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Low	The study design is best characterized as cross-sectional. Only one analysis to compare exposure concentrations between those with and without symptoms was adjusted for a confounder, sex, via stratification. Other potential confounders were not adjusted for. Study authors combine responses for symptoms reported before and during the sampling period in one statistical analysis, which may not reflect the relationship between symptoms and contaminants' exposure at each period.
	Metric 13:	Statistical Power	Medium	Statistical power was not reported. The number of participants was sufficient to detect a difference in median concentration between those with and without symptoms.
	Metric 14:	Reproducibility of Analyses	Medium	Study presents sufficient description of analysis (statistical methods) to be conceptually reproducible with access to the raw data.
	Metric 15:	Statistical Analysis	Low	Study uses a Wilcoxon's rank sum test to compare exposure concentrations in persons with and without symptoms; test for equal variance is not reported.

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Study Citation:	Guo, P., Yokoyama, K., Piao, F., Sakai, K., Khalequzzaman, M., Kamijima, M., Nakajima, T., Kitamura, F. (2013). Sick building syndrome by indoor air pollution in Dalian, China. International Journal of Environmental Research and Public Health 10(4):1489-1504.
Health Outcome(s):	sick building syndrome
Reported Health Effect(s):	The statistical analysis considers all subjective self-reported symptoms together (not segregated by health outcome) as a group health outcome –sick building syndrome. The study compared two conditions for each studied chemical: combined self-reported symptoms to no symptoms. Therefore, only one form 3 was completed.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1938385

Domain	Metric	Rating	Comments
Additional Comments:	Concentrations of VOCs (including 1,2-dichloroethane), HCHO, and NO2 were measured in the 59 homes of families that agreed to participate after being informed of the nature of the study. Participants completed questionnaires asking about symptoms since they moved into the homes and the concentrations of selected compounds were compared among men and women reporting any symptoms vs no symptoms. Concentrations of 1,2-dichloroethane in homes of people with symptoms were higher than in homes without. p-Dichlorobenzene was measured in the homes as well, but median concentration was <DL and no further analysis was made. Unacceptable due to selection bias, lack of confounding control, inadequate outcome characterization, and lack of temporality.		

Overall Quality Determination — Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Kernan, G.J., Ji, B.T., Dosemeci, M., Silverman, D.T., Balbus, J., Zahm, S.H. (1999). Occupational risk factors for pancreatic cancer: A case-control study based on death certificates from 24 U.S. states. American Journal of Industrial Medicine 36(2):260-270.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Death from pancreatic cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	194820

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	The National Cancer Institute, National Institute of Occupational Safety and Health, and the National Center for Health Statistics reviewed death certificates from 24 states to select cases from those that had died from pancreatic cancer and matched controls. Controls with cause of death related to the outcome of interest (i.e. pancreatic diseases) were excluded from the study. All key elements of the study design were reported.
	Metric 2:	Attrition	Medium	There was no direct evidence of subject loss or exclusion of subgroups from analyses. The authors provide the total number of cases and controls in the analysis. Case and control data were taken from a registry. It can be assumed that the data are complete for each subject.
	Metric 3:	Comparison Group	High	Controls were selected from the same pool of death certificates from 24 states that cases were selected from. Controls with cause of death related to the outcome of interest were eliminated. Differences in baseline characteristics were controlled for via matching, stratification, and adjustment.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure was assessed via occupation and industry data on death certificates. A job matrix was further applied to assess the likely levels of exposure. Probability and intensity of exposure were estimated across four levels for each occupation. Only employment captured on the death certificate could be considered. The exposure assessment needs exposure information before the job listed on the death certificates.
	Metric 5:	Exposure Levels	Medium	The study offers 4 levels of estimated probability and intensity of exposure (referent, low, medium, high).
	Metric 6:	Temporality	Medium	Exposure was determined by occupational and industry codes on death certificates and indicate that exposure would precede disease, however, the timing and latency period is less clear.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Causes of mortality were determined from death certificates for both cases and controls. Death certificates were drawn from death registries of participating states (n=24). Causes of death were coded using ICD-9 codes, and pancreatic cancer was identified as ICD 157.
	Metric 8:	Reporting Bias	Medium	Measured outcomes, effect estimates and confidence intervals are reported. Number of exposed cases is reported for each analysis, however the number of controls (exposed and unexposed) are not reported for analyses.

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Study Citation:	Kernan, G.J., Ji, B.T., Dosemeci, M., Silverman, D.T., Balbus, J., Zahm, S.H. (1999). Occupational risk factors for pancreatic cancer: A case-control study based on death certificates from 24 U.S. states. American Journal of Industrial Medicine 36(2):260-270.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Death from pancreatic cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	194820

Domain	Metric		Rating	Comments
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Potential confounders were accounted for in the following ways: matching (five year age group, state, race, and gender); adjustment in models (age, marital status, metropolitan, and residential status); and stratification (race and gender). Smoking was not included as a confounder.
	Metric 10:	Covariate Characterization	Medium	Data used to assess potential confounders was derived from death certificates, an adequate measure. However, no information about cigarette smoking and other lifestyle factors were available for adjustment in the analysis.
	Metric 11:	Co-exposure Counfounding	Medium	The variety of industries considered in the analysis diminishes concerns about co-exposures.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The case-control study design and statistical analysis methods were appropriate to assess the exposures/outcome of interest.
	Metric 13:	Statistical Power	Medium	This study had an adequate sample size to detect an effect (n for cases = 63,097; n for controls = 252,386).
	Metric 14:	Reproducibility of Analyses	Medium	The description of analysis was sufficient and would be reproducible.
	Metric 15:	Statistical Analysis	High	The model to calculate risk estimates was transparent.

Additional Comments: This case-control study examined the risk of death from pancreatic cancer in different occupational settings. Exposure was solely assessed using occupation/industry at time of death (reported on death certificate) and the application of a job matrix assessing likely levels of exposure for different positions. This means of estimating exposure may not fully represent a participant's exposure history. Additionally, the number of impacted participants (exposed cases) was inadequate to perform quality analyses for some exposure levels.

Overall Quality Determination High

* No biomarkers were identified for this evaluation.

Study Citation:	Kernan, G.J., Ji, B.T., Dosemeci, M., Silverman, D.T., Balbus, J., Zahm, S.H. (1999). Occupational risk factors for pancreatic cancer: A case-control study based on death certificates from 24 U.S. states. American Journal of Industrial Medicine 36(2):260-270.
Health Outcome(s):	Endocrine
Reported Health Effect(s):	Death from pancreatic cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	194820

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	The National Cancer Institute, National Institute of Occupational Safety and Health, and the National Center for Health Statistics reviewed death certificates from 24 states to select cases from those that had died from pancreatic cancer and matched controls. Controls with cause of death related to the outcome of interest (i.e. pancreatic diseases) were excluded from the study. All key elements of the study design were reported.
	Metric 2:	Attrition	Medium	There was no direct evidence of subject loss or exclusion of subgroups from analyses. The authors provide the total number of cases and controls in the analysis. Case and control data were taken from a registry. It can be assumed that the data are complete for each subject.
	Metric 3:	Comparison Group	High	Controls were selected from the same pool of death certificates from 24 states that cases were selected from. Controls with cause of death related to the outcome of interest were eliminated. Differences in baseline characteristics were controlled for via matching, stratification, and adjustment.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure was assessed via occupation and industry data on death certificates. A job matrix was further applied to assess the likely levels of exposure. Probability and intensity of exposure were estimated across four levels for each occupation. Only employment captured on the death certificate could be considered. The exposure assessment needs exposure information before the job listed on the death certificates.
	Metric 5:	Exposure Levels	Medium	The study offers 4 levels of estimated probability and intensity of exposure (referent, low, medium, high).
	Metric 6:	Temporality	Medium	Exposure was determined by occupational and industry codes on death certificates and indicate that exposure would precede disease, however, the timing and latency period is less clear.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Causes of mortality were determined from death certificates for both cases and controls. Death certificates were drawn from death registries of participating states (n=24). Causes of death were coded using ICD-9 codes, and pancreatic cancer was identified as ICD 157.
	Metric 8:	Reporting Bias	Medium	Measured outcomes, effect estimates and confidence intervals are reported. Number of exposed cases is reported for each analysis, however the number of controls (exposed and unexposed) are not reported for analyses.
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Kernan, G.J., Ji, B.T., Dosemeci, M., Silverman, D.T., Balbus, J., Zahm, S.H. (1999). Occupational risk factors for pancreatic cancer: A case-control study based on death certificates from 24 U.S. states. American Journal of Industrial Medicine 36(2):260-270.
Health Outcome(s):	Endocrine
Reported Health Effect(s):	Death from pancreatic cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	194820

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Medium	Potential confounders were accounted for in the following ways: matching (five year age group, state, race, and gender); adjustment in models (age, marital status, metropolitan, and residential status); and stratification (race and gender). Smoking was not included as a confounder.
	Metric 10:	Covariate Characterization	Medium	Data used to assess potential confounders was derived from death certificates, an adequate measure. However, no information about cigarette smoking and other lifestyle factors were available for adjustment in the analysis.
	Metric 11:	Co-exposure Counfounding	Medium	The variety of industries considered in the analysis diminishes concerns about co-exposures.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The case-control study design and statistical analysis methods were appropriate to assess the exposures/outcome of interest.
	Metric 13:	Statistical Power	Medium	This study had an adequate sample size to detect an effect (n for cases = 63,097; n for controls = 252,386).
	Metric 14:	Reproducibility of Analyses	Medium	The description of analysis was sufficient and would be reproducible.
	Metric 15:	Statistical Analysis	High	The model to calculate risk estimates was transparent.

Additional Comments: This case-control study examined the risk of death from pancreatic cancer in different occupational settings. Exposure was solely assessed using occupation/industry at time of death (reported on death certificate) and the application of a job matrix assessing likely levels of exposure for different positions. This means of estimating exposure may not fully represent a participant's exposure history. Additionally, the number of impacted participants (exposed cases) was inadequate to perform quality analyses for some exposure levels.

Overall Quality Determination High

* No biomarkers were identified for this evaluation.

Study Citation:	Niehoff, N.M., Gammon, M.D., Keil, A.P., Nichols, H.B., Engel, L.S., Sandler, D.P., White, A.J. (2019). Airborne mammary carcinogens and breast cancer risk in the Sister Study. Environment International 130:104897.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Breast cancer diagnosis (overall), tumor characteristics, and estrogen receptor positive (ER+) invasive breast cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5440630

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	Data from the Sister Study were used. The Sister Study is "a prospective cohort of 50,884 women from across the US who were ages 35–74 at enrollment (Sandler et al., 2017). Participants were recruited from 2003 to 2009 using a national advertising campaign in English and Spanish. Women were eligible for the Sister Study if they had a sister who had been diagnosed with breast cancer, but no prior breast cancer themselves."Exclusions from the study occurred for the following reasons:-breast cancer diagnosed before enrollment was complete, or did not have follow-up information (n = 163)-Residential address couldn't be geocoded (n = 1003, < 2%) - This is a small perecentage, but all of those who were excluded for this reason were from Puerto Rico, West Virginia, Missouri, or Oklahoma.Key elements of the study design are reported. There is some potential for selection bias, but based on the small percentage of those eligible who were excluded, participation was not likely to be substantially biased.
	Metric 2:	Attrition	High	Response rates in the overall Sister study remained over 91% over follow-up. Reasons for non-response were not reported, and characteristics of those lost to follow up were not reported or compared with those included, but 9% loss to follow-up is minimal.
	Metric 3:	Comparison Group	High	Differences in baseline characteristics of groups were considered as potential confounding variables.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	The EPA NATA database of census-tract level modeled air toxics data was used. The study authors note the potential for exposure misclassification: "Concentrations at the census tract level do not fully account for variation in an individual's daily activities that could lead to higher or lower exposure, and all women within a census tract are assigned the same concentration."
	Metric 5:	Exposure Levels	Medium	There were five quintiles of exposure, so there was a sufficient range and distribution of exposure.
	Metric 6:	Temporality	Medium	This is a prospective cohort study.Exposure data from 2005 were chosen because they represented the middle of the enrollment period (2003-2009).The study reported that "94% of women enrolled in 2005 or later, and thus the exposure assessment primarily predated enrollment for the majority of Sister Study participants."The six percent of women who had the potential to have the outcome before exposure was measured in 2005 are a concern. But sensitivity analyses were used to assess whether the associations changed when restricted to those who enrolled in 2005 or later.The authors note that the study is making assumptions about the relevant exposure windows - therefore the exposure window is not certain.

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Study Citation:	Niehoff, N.M., Gammon, M.D., Keil, A.P., Nichols, H.B., Engel, L.S., Sandler, D.P., White, A.J. (2019). Airborne mammary carcinogens and breast cancer risk in the Sister Study. Environment International 130:104897.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Breast cancer diagnosis (overall), tumor characteristics, and estrogen receptor positive (ER+) invasive breast cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5440630

Domain	Metric		Rating	Comments
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Women who reported a breast cancer diagnosis on the annual health updates or follow-up questionnaires were asked to provide additional diagnosis information, and to grant permission for the study to obtain medical records and pathology reports. Medical records were obtained for 81% of breast cancer diagnoses. Agreement between self-reported breast cancers and medical records was high (positive predictive value > 99%) (Sandler et al., 2017), so self-report was used when medical records were not available. Tumor characteristics (stage; histology; and estrogen receptor (ER) status) were abstracted from medical records, or self-reported.
	Metric 8:	Reporting Bias	High	A description of measured outcomes is reported. Effect estimates are reported with confidence intervals.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Covariates considered included age, race, BMI, residence type, education, and smoking status. Potential confounders were identified using DAGs and literature review. Appropriate considerations were made for potential confounders.
	Metric 10:	Covariate Characterization	Medium	”Most covariates were assessed by self-report at the baseline interview.””At baseline, women completed a computer-assisted telephone interview and written questionnaires.”Previous publications might describe whether the questionnaires were validated, but validation was not specified in this publication.
	Metric 11:	Co-exposure Counfounding	Medium	Co-exposures to other air pollutants were assessed, but at the census tract level.Multipollutant classification trees were used, which might provide useful qualitative information.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design (large prospective cohort) and analysis method (Cox proportional hazard single and multi-pollutant models accounting for potential confounders) were appropriate to assess the association between exposure and disease.
	Metric 13:	Statistical Power	Medium	The study had an adequate sample size (1975 cancer cases) and follow-up time (mean=8.4 years).
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to be conceptually reproducible.

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Study Citation:	Niehoff, N.M., Gammon, M.D., Keil, A.P., Nichols, H.B., Engel, L.S., Sandler, D.P., White, A.J. (2019). Airborne mammary carcinogens and breast cancer risk in the Sister Study. Environment International 130:104897.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Breast cancer diagnosis (overall), tumor characteristics, and estrogen receptor positive (ER+) invasive breast cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5440630

Domain	Metric	Rating	Comments
	Metric 15: Statistical Analysis	High	Hazard ratios and 95% confidence intervals (CIs) are reported "comparing index categories of exposure to exposures below the first quintile using Cox proportional hazards regression, with age as the time scale." The method of calculating the hazard ratios is transparent. The authors reported that "the proportional hazards assumption was evaluated by conducting a Wald test for an interaction between the continuous form of the air toxic measure and time." Censoring times and times at-risk are described.

Additional Comments: This was a well-conducted study of a large prospective cohort, but the measurement of exposure at the census-tract rather than the individual level is a limitation.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Sobel, W., Bond, G.G., Skowronski, B.J., Brownson, P.J., Cook, R.R. (1987). A soft tissue sarcoma case control study in a large multi-chemical manufacturing facility. Chemosphere 16(8-9):2095-2099.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	soft-tissue sarcoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1357737

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	From a pool of > 37,000 subjects who worked at least 1 year at chemical company between January 1940-December 1979, the study identified 14 people who died due to soft-cell sarcoma (via death certificate, medical records, or histopathology report). Referents were matched 9:1 with cases (126 matched controls).
	Metric 2:	Attrition	High	There was minimal subject exclusion from the analysis sample; one case could not be matched to controls and was excluded from analysis.
	Metric 3:	Comparison Group	High	Cases and controls were recruited from the same eligible population within the same time frame and matched on sex, race, year of birth and year of hire. Both cases and controls had to have worked ≥1 yr at the plant during the study period.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Work histories for cases and referents were coded to determine an individual's potential exposure to chemical of interest and reviewed by an industrial hygienist blinded to case status.
	Metric 5:	Exposure Levels	Low	Exposure was considered dichotomous, ever exposed or never exposed. There is no quantitative information on exposure levels or range of exposures.
	Metric 6:	Temporality	Low	Temporality of exposure and outcome is established. It is unclear if the interval between exposure and outcome is sufficient for soft tissue sarcoma outcomes.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	The soft-tissue sarcoma outcome was assessed by information provided by death certificates, medical records, and histopathology reports, but study authors did not report the proportions determined by each method.
	Metric 8:	Reporting Bias	High	All outcomes outlined were reported. Authors reported the number of cases and controls in the table. Maximum likelihood estimate ORs with respective 95 % confidence intervals were reported.
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Sobel, W., Bond, G.G., Skowronski, B.J., Brownson, P.J., Cook, R.R. (1987). A soft tissue sarcoma case control study in a large multi-chemical manufacturing facility. Chemosphere 16(8-9):2095-2099.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	soft-tissue sarcoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1357737

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Low	Controls were matched with cases on age, sex, year of hire and survival information. There is indirect evidence that the considerations were made to identify potential confounders through evaluation of medical records of cases and controls (various heritable syndromes, family history of cancer, history of lymphedema, steroids, throrotrast, foreign body implants, chronic extensive scarring, radiation therapy, and immunological defects). Identified confounders between cases and controls were not reported and it is unclear if adjustments for these confounders were included in the final analyses.
	Metric 10:	Covariate Characterization	High	Potential covariates were assessed through evaluation of work histories and medical records.
	Metric 11:	Co-exposure Counfounding	Low	The study documented 13 chemicals, known to be associated with soft-tissue sarcoma (according to NTP, 1983) that were used at the manufacturing facility at some point since 1940. The authors note that some individuals were exposed to multiple chemicals during their employment history and were counted multiple times in the analysis for different chemical exposures. Co-exposures to chemicals to not appear to be adjusted for in analysis.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Low	The study design was adequate to assess the association between exposure and the outcome of interest (soft-tissue sarcoma). The study authors noted they used programs developed by Rothman and Boice to calculate odds ratios with CI intervals; the statistical methods are not further described. The page containing the Rothman and Boice reference appears to be missing from the PDF (or the citation is missing).
	Metric 13:	Statistical Power	Low	Statistical power was not calculated. For 1,2-dichloroethane, there was one case and 6 controls included in the analysis, which was not adequate to detect and effect.
	Metric 14:	Reproducibility of Analyses	Low	The study calculated odd ratios, and 95% CIs were calculated using point estimates and chi from hypothesis testing. The study authors noted they used programs developed by Rothman and Boice to calculate odds ratios with 95% CIs; the statistical methods are not further described and there was no reference for the programs cited.
	Metric 15:	Statistical Analysis	Low	A description of analyses/assumptions was not reported.

Additional Comments: A case-control study of workers at a chemical production facility who worked at least 1 year between January 1940-December 1979 (n=37,000) investigated the incidence of deaths due to soft-tissue sarcoma. The study identified 14 people who died due to soft-tissue sarcoma (through death certificate, medical records, or histopathology reports). Cases were matched to controls based on sex, race, year of birth and year of hire. 13 chemicals, including 1,2-dichloroethane, associated with soft-tissue sarcoma were used at the facility; it does not appear that co-exposures were adjusted for in the analysis. Odds ratios and corresponding CIs were calculated. No significant association was found between exposure to 1,2-DCE and soft-tissue sarcoma.

Overall Quality Determination Medium

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Study Citation:	Sobel, W., Bond, G.G., Skowronski, B.J., Brownson, P.J., Cook, R.R. (1987). A soft tissue sarcoma case control study in a large multi-chemical manufacturing facility. Chemosphere 16(8-9):2095-2099.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	soft-tissue sarcoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1357737

Domain	Metric	Rating	Comments

* No biomarkers were identified for this evaluation.

Study Citation:	Sobel, W., Bond, G.G., Skowronski, B.J., Brownson, P.J., Cook, R.R. (1987). A soft tissue sarcoma case control study in a large multi-chemical manufacturing facility. Chemosphere 16(8-9):2095-2099.
Health Outcome(s):	Skin and Connective Tissue
Reported Health Effect(s):	soft-tissue sarcoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1357737

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	From a pool of > 37,000 subjects who worked at least 1 year at chemical company between January 1940-December 1979, the study identified 14 people who died due to soft-cell sarcoma (via death certificate, medical records, or histopathology report). Referents were matched 9:1 with cases (126 matched controls).
	Metric 2:	Attrition	High	There was minimal subject exclusion from the analysis sample; one case could not be matched to controls and was excluded from analysis.
	Metric 3:	Comparison Group	High	Cases and controls were recruited from the same eligible population within the same time frame and matched on sex, race, year of birth and year of hire. Both cases and controls had to have worked ≥1 yr at the plant during the study period.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Work histories for cases and referents were coded to determine an individual's potential exposure to chemical of interest and reviewed by an industrial hygienist blinded to case status.
	Metric 5:	Exposure Levels	Low	Exposure was considered dichotomous, ever exposed or never exposed. There is no quantitative information on exposure levels or range of exposures.
	Metric 6:	Temporality	Low	Temporality of exposure and outcome is established. It is unclear if the interval between exposure and outcome is sufficient for soft tissue sarcoma outcomes.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	The soft-tissue sarcoma outcome was assessed by information provided by death certificates, medical records, and histopathology reports, but study authors did not report the proportions determined by each method.
	Metric 8:	Reporting Bias	High	All outcomes outlined were reported. Authors reported the number of cases and controls in the table. Maximum likelihood estimate ORs with respective confidence intervals were reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	Controls were matched with cases on age, sex, year of hire and survival information. There is indirect evidence that that considerations were made to identify potential confounders through evaluation of medical records of cases and controls (various heritable syndromes, family history of cancer, history of lymphedema, steroids, throrotrast, foreign body implants, chronic extensive scarring, radiation therapy, and immunological defects). Identified confounders between cases and controls were not reported and it is unclear if adjustments for these confounders were included in the final analyses.

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Study Citation:	Sobel, W., Bond, G.G., Skowronski, B.J., Brownson, P.J., Cook, R.R. (1987). A soft tissue sarcoma case control study in a large multi-chemical manufacturing facility. Chemosphere 16(8-9):2095-2099.
Health Outcome(s):	Skin and Connective Tissue
Reported Health Effect(s):	soft-tissue sarcoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1357737

Domain	Metric		Rating	Comments
	Metric 10:	Covariate Characterization	High	Potential covariates were assessed through evaluation of work histories and medical records.
	Metric 11:	Co-exposure Counfounding	Low	The study documented 13 chemicals, known to be associated with soft-tissue sarcoma (according to NTP, 1983) that were used at the manufacturing facility at some point since 1940. The authors note that some individuals were exposed to multiple chemicals during their employment history and were counted multiple times in the analysis for different chemical exposures. Co-exposures to chemicals to not appear to be adjusted for in analysis.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Low	The study design was adequate to assess the association between exposure and the outcome of interest (soft-tissue sarcoma). The study authors noted they used programs developed by Rothman and Boice to calculate odds ratios with (95% CIs; the statistical methods are not further described. The page containing the Rothman and Boice reference appears to be missing from the PDF (or the citation is missing).
	Metric 13:	Statistical Power	Low	Statistical power was not calculated. For 1,2-dichloroethane, there was one case and 6 controls included in the analysis, which was not adequate to detect and effect.
	Metric 14:	Reproducibility of Analyses	Low	The study calculated odd ratios, and 95% CIs were calculated using point estimates and chi from hypothesis testing. The study authors noted they used programs developed by Rothman and Boice to calculate odds ratios with CI intervals; the statistical methods are not further described and there was no reference for the programs cited.
	Metric 15:	Statistical Analysis	Low	A description of analyses/assumptions was not reported.

Additional Comments: A case-control study of workers at a chemical production facility who worked at least 1 year between January 1940-December 1979 (n=37,000) investigated the incidence of deaths due to soft-tissue sarcoma. The study identified 14 people who died due to soft-tissue sarcoma (through death certificate, medical records, or histopathology reports). Cases were matched to controls based on sex, race, year of birth and year of hire. 13 chemicals, including 1,2-dichloroethane, associated with soft-tissue sarcoma were used at the facility; it does not appear that co-exposures were adjusted for in the analysis. Odds ratios and corresponding CIs were calculated. No significant association was found between exposure to 1,2-DCE and soft-tissue sarcoma.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Teta, M. J., Ott, M. G., Schnatter, A. R. (1991). An update of mortality due to brain neoplasms and other causes among employees of a petrochemical facility. Journal of Occupational Medicine 33(1):45-51.
Health Outcome(s):	Mortality
Reported Health Effect(s):	all cause mortality, gastrointestinal cancer mortality, respiratory system cancer mortality, kidney and other urinary organ cancer mortality, skin cancer mortality, brain cancer mortality, lymphatic and hematopoietic tissue cancer mortality, benign neoplasm mortality, heart disease mortality, and liver cirrhosis mortality.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200633, 1629047
HERO ID:	200633

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	The facility was described in some detail. All male employees working for one day or more between 1941 and 1983 were included. There may be some healthy worker effect in this population.
	Metric 2:	Attrition	High	Study authors reported that vital status was complete for 99% of the population, and death certificates were obtained for 99% of decedents.
	Metric 3:	Comparison Group	High	SMRs were calculated using age-, race-, and calendar year-specific mortality rates of males in the United States. All included employees were male.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	All employees were treated as exposed. Table 4 indicates that relatively few employees were employed in areas designated as 1,2-DCA work areas. There is potential for substantial exposure misclassification.
	Metric 5:	Exposure Levels	Low	All employed individuals were categorized as exposed, and the reference population was described as unexposed. This represents two levels of exposure. The distribution of exposure within the employed population is unclear.
	Metric 6:	Temporality	Medium	Employees were followed from 1950 (or date of first hire) through 1983. The relevant timing of exposure is not entirely clear; however, this represents a sufficiently long period of follow-up.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Mortality was tracked using company records, Social Security Administration records, and the National Death Index. Specific ICD codes and use of a nosologist were not described, but there was no evidence to suggest the method had poor validity.
	Metric 8:	Reporting Bias	High	SMRs were provided with confidence intervals in addition to observed and expected cases. The authors state they did not carry out regional specific SMRs due to the higher prevalence of neoplasms in the surrounding area.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	SMRs were restricted to males. Rates were age-, race-, and calendar period-specific. No consideration was made for smoking.
	Metric 10:	Covariate Characterization	Medium	Demographic information was obtained from employment records. This was not a validated method, but there was no evidence to suggest it was an invalid method.

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Study Citation:	Teta, M. J., Ott, M. G., Schnatter, A. R. (1991). An update of mortality due to brain neoplasms and other causes among employees of a petrochemical facility. Journal of Occupational Medicine 33(1):45-51.
Health Outcome(s):	Mortality
Reported Health Effect(s):	all cause mortality, gastrointestinal cancer mortality, respiratory system cancer mortality, kidney and other urinary organ cancer mortality, skin cancer mortality, brain cancer mortality, lymphatic and hematopoietic tissue cancer mortality, benign neoplasm mortality, heart disease mortality, and liver cirrhosis mortality.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200633, 1629047
HERO ID:	200633

Domain	Metric		Rating	Comments
	Metric 11:	Co-exposure Counfounding	Low	Several other occupational exposures linked to cancer mortality were present, including vinyl chloride, butanol, and other petrochemicals.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	This study design was appropriate for the research question. Authors utilized retrospective occupational cohort data to determine standardized mortality rates for cancer-specific mortalities.
	Metric 13:	Statistical Power	Medium	While power was not calculated, there were over 1350 deaths from 7849 employees which was adequate to detect robust effect estimates.
	Metric 14:	Reproducibility of Analyses	Low	Most details were provided; however, ICD codes used to determine and group cancer mortality diagnoses were not provided.
	Metric 15:	Statistical Analysis	High	No issues identified.

Additional Comments: This study utilized an occupational cohort to retrospectively evaluate elevated rates of cancer mortality among petrochemical plant workers. There were numerous potentially hazardous chemicals mentioned in the plant description which may lead to co-exposure. Additionally, it appears that only a moderate portion of workers may have been exposed to 1,2-DCA or worked in 1,2-DCA areas which may lead to some exposure misclassification and limit the study's ability to inform hazard on 1,2-DCA.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Cases in this case-control study were former Union Carbide Corporation (UCC) chemical plant employees in Texas City, Texas. Cases were identified through death certificate searches and tumor registries, and may have included individuals formerly employed at UCC whose cause of death was unknown to the company. Additionally, control deaths were stated to be pulled from corporate employee benefits department and through locally published obituary notices routinely screened by the medical department - it is possible to assume that cases were identified in a similar manner. The study identified cases of brain tumors by searching death certificates primarily, although tumor registries throughout the state of Texas were also searched. The study clarifies that it is possible that some cases were not found if they survived or died due to another cause - while this is likely to have impacted selection, there is no evidence that this would be differential by exposure status. Overall, there is limited information on the source population of workers from which cases were identified.
	Metric 2:	Attrition	Medium	Attrition is not discussed in the study, and outcome data appear to be complete. There was a large proportion of missing exposure data (roughly 50%) due to workers being employed in roles such as maintenance, where exposure to any chemical is possible but unknown. Analyses were run separately where these ”unknown” individuals were a) treated as exposed, b) treated as unexposed, or c) treated as unknown and thus excluded. The study only presents results for when these individuals were excluded but specifies that the first scenario resulted in increased exposure estimates for controls relative to cases.

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Study Citation:	Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
	Metric 3:	Comparison Group	Medium	The study identifies two series of control groups, selected from all former Union Carbide Corporation (UCC) employees. However, the total number of employees is not stated. Only those who were deceased were used as controls since they had known causes of death and could thus be verified as non-brain tumors. One group of controls excluded employees whose cause of death was due to any malignant neoplasm to allow for the possibility that a general chemical carcinogen may have been associated with cancers of other sites. The other group of controls included deaths from all causes; this included malignant neoplasms other than brain tumors. Both control groups had 80 male employees randomly selected from 450 deceased employees known to the company in June 1979. Control deaths were stated to be pulled from corporate employee benefits department and through locally published obituary notices routinely screened by the medical department - it is possible to assume that cases were identified in a similar manner. The study reports that cases were slightly more likely to have been employed for less than 10 years than controls - the study attributes this in part to the fact that employees whose deaths were known to the company were more likely to have worked for longer - regardless the mean number of years employed was similar between cases and controls. However, cases were more likely to have been terminated from their job for reasons other than death, disability, or retirement (quitting, being fired, etc.), were generally younger at hire, and were less likely to survive to their 70th birthday. None of these factors are controlled for in statistical analyses - however, since controls and cases were pulled from the same population, there is indirect evidence that the groups were similar.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was determined based on official employment records. Records included job title and department assignment codes for each employment from date of hire to date of termination. For each unique department code, UCC and NIOSH industrial hygienists identified principal chemicals used or produced at any time in the history of the plant and correlated those with individual departments. This assessment was not performed on a year-by-year basis due to concerns for recall bias for longer-term employees where less detailed records were kept. An employee was categorized as ”exposed” to 1,2-dichloroethane if they ever worked in a department associated with that chemical. An ”unknown” exposure group was also created to account for employees who had only worked in departments for which no specific chemical could be identified.
	Metric 5:	Exposure Levels	Low	The study does not report any quantitative information and only splits exposure into ”exposed”, ”unexposed”, and ”unknown”.
	Metric 6:	Temporality	High	In this study exposure is confirmed to occur before the outcome is measured. The study reports latency periods, with subjects dichotomized into less than 15 years of latency or more than 15 years of latency. The majority of cases and controls had a latency of greater than 15 years, which is sufficiently long for brain tumors.

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Study Citation:	Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Cases were identified through death certificate searches and partially through tumor registries in the state of Texas. Case validation was performed by NIOSH, and 5 different levels of confirmation were reported: 1) tissue specimen interpreted by the Armed Forces Institute of Pathology; 2) autopsy report; 3) histopathology report; 4) clinical diagnosis from hospital record; 5) dearth certificate diagnosis. Codes 1-3 were considered to be ”confirmed” cases of brain tumors, while 4-5 were considered unconfirmed. 5/21 cases were only evaluated using ”unconfirmed methods”, meaning there is likely a high amount of accuracy in roughly 75% of cases. While no case validation is reported for controls, the study specifies that only controls who had died and thus could be confirmed to be non-brain tumors were included.
	Metric 8:	Reporting Bias	Medium	All primary and secondary outcomes that are outlined in the methods are reported in the results. However, the only statistical outcome of their analysis were unadjusted p-values that were not reported and were just described qualitatively.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	The only statistical analysis performed were Mantel-Haenszel chi-squared tests, which did not allow for confounder adjustment. The study does not present a distribution of potential confounders by exposure status but by case/control status. Several variables, such as reason for termination, age at hire, and age at death were significantly different between cases and controls and were not accounted for in statistical modeling. The study explains that these differences are not likely to have any epidemiologic significance and appear to be relatively small differences.
	Metric 10:	Covariate Characterization	Medium	While the study does not explain where they obtained covariate information, it is reasonable to assume that they gathered the information from company records.
	Metric 11:	Co-exposure Counfounding	Low	The study assesses a wide range of other potential occupational co-exposures. While these co-exposures are not adjusted for in any statistical models, effect estimates are presented separately for benzene, diethyl sulfate, ethylene oxide, and vinyl chloride. The distribution of co-exposures across cases and controls is demonstrated to be mostly balanced by comparing proportions of exposed/unexposed between cases and controls. The only notable instance of imbalance is for benzene, where 11.1% of cases were exposed whereas 37.9% of all controls and 19.2% of non-neoplasm related controls were exposed.
Domain 5: Analysis				

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Study Citation:	Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	The study chose a case-control design, which was appropriate to study the rare disease of brain tumors and its association with occupational exposures. The only statistical analysis conducted is a Mantzel-Haenszel chi-squared test, but there is no reason to suggest that this would be inappropriate.
	Metric 13:	Statistical Power	Medium	The study does not calculate statistical power, but the number of cases (n=21) and controls (n=80 in each analysis) is likely sufficient to detect an effect.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to understand what was done and could be reproduced given access to the analytic data.
	Metric 15:	Statistical Analysis	High	The only statistical analysis conducted is a Mantel-Haenszel chi-squared test, and all assumptions were met. The statistical process is transparent.

Additional Comments: This case-control study pulled deceased former employees of the Union Carbide Corporation in Texas City, Texas. The study examined dichotomous exposure to a wide range of occupational exposures, including 1,2-dichloroethane, in relation to brain tumor cases. There is no quantitative estimate of exposure. The only statistical analysis in the study is a Mantel-Haenszel chi-squared test statistic and no statistically significant differences in exposure between cases and controls were observed. The fact that there are no effect estimates, no adjustment for confounders, and no quantitative exposure estimates limits the usefulness of this paper.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Cases in this case-control study were former Union Carbide Corporation (UCC) chemical plant employees in Texas City, Texas. Cases were identified through death certificate searches and tumor registries, and may have included individuals formerly employed at UCC whose cause of death was unknown to the company. Additionally, control deaths were stated to be pulled from corporate employee benefits department and through locally published obituary notices routinely screened by the medical department - it is possible to assume that cases were identified in a similar manner. The study identified cases of brain tumors by searching death certificates primarily, although tumor registries throughout the state of Texas were also searched. The study clarifies that it is possible that some cases were not found if they survived or died due to another cause - while this is likely to have impacted selection, there is no evidence that this would be differential by exposure status. Overall, there is limited information on the source population of workers from which cases were identified.
	Metric 2:	Attrition	Medium	Attrition is not discussed in the study, and outcome data appear to be complete. There was a large proportion of missing exposure data (roughly 50%) due to workers being employed in roles such as maintenance, where exposure to any chemical is possible but unknown. Analyses were run separately where these ”unknown” individuals were a) treated as exposed, b) treated as unexposed, or c) treated as unknown and thus excluded. The study only presents results for when these individuals were excluded but specifies that the first scenario resulted in increased exposure estimates for controls relative to cases.

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Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
	Metric 3:	Comparison Group	Medium	The study identifies two series of control groups, selected from all former Union Carbide Corporation (UCC) employees. However, the total number of employees is not stated. Only those who were deceased were used as controls since they had known causes of death and could thus be verified as non-brain tumors. One group of controls excluded employees whose cause of death was due to any malignant neoplasm to allow for the possibility that a general chemical carcinogen may have been associated with cancers of other sites. The other group of controls included deaths from all causes; this included malignant neoplasms other than brain tumors. Both control groups had 80 male employees randomly selected from 450 deceased employees known to the company in June 1979. Control deaths were stated to be pulled from corporate employee benefits department and through locally published obituary notices routinely screened by the medical department - it is possible to assume that cases were identified in a similar manner. The study reports that cases were slightly more likely to have been employed for less than 10 years than controls - the study attributes this in part to the fact that employees whose deaths were known to the company were more likely to have worked for longer - regardless the mean number of years employed was similar between cases and controls. However, cases were more likely to have been terminated from their job for reasons other than death, disability, or retirement (quitting, being fired, etc.), were generally younger at hire, and were less likely to survive to their 70th birthday. None of these factors are controlled for in statistical analyses - however, since controls and cases were pulled from the same population, there is indirect evidence that the groups were similar.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was determined based on official employment records. Records included job title and department assignment codes for each employment from date of hire to date of termination. For each unique department code, UCC and NIOSH industrial hygienists identified principal chemicals used or produced at any time in the history of the plant and correlated those with individual departments. This assessment was not performed on a year-by-year basis due to concerns for recall bias for longer-term employees where less detailed records were kept. An employee was categorized as ”exposed” to 1,2-dichloroethane if they ever worked in a department associated with that chemical. An ”unknown” exposure group was also created to account for employees who had only worked in departments for which no specific chemical could be identified.
	Metric 5:	Exposure Levels	Low	The study does not report any quantitative information and only splits exposure into ”exposed”, ”unexposed”, and ”unknown”.
	Metric 6:	Temporality	High	In this study exposure is confirmed to occur before the outcome is measured. The study reports latency periods, with subjects dichotomized into less than 15 years of latency or more than 15 years of latency. The majority of cases and controls had a latency of greater than 15 years, which is sufficiently long for brain tumors.

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Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Cases were identified through death certificate searches and partially through tumor registries in the state of Texas. Case validation was performed by NIOSH, and 5 different levels of confirmation were reported: 1) tissue specimen interpreted by the Armed Forces Institute of Pathology; 2) autopsy report; 3) histopathology report; 4) clinical diagnosis from hospital record; 5) dearth certificate diagnosis. Codes 1-3 were considered to be ”confirmed” cases of brain tumors, while 4-5 were considered unconfirmed. 5/21 cases were only evaluated using ”unconfirmed methods”, meaning there is likely a high amount of accuracy in roughly 75% of cases. While no case validation is reported for controls, the study specifies that only controls who had died and thus could be confirmed to be non-brain tumors were included.
	Metric 8:	Reporting Bias	Medium	All primary and secondary outcomes that are outlined in the methods are reported in the results. However, the only statistical outcome of their analysis were unadjusted p-values that were not reported and were just described qualitatively.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	The only statistical analysis performed were Mantel-Haenszel chi-squared tests, which did not allow for confounder adjustment. The study does not present a distribution of potential confounders by exposure status but by case/control status. Several variables, such as reason for termination, age at hire, and age at death were significantly different between cases and controls and were not accounted for in statistical modeling. The study explains that these differences are not likely to have any epidemiologic significance and appear to be relatively small differences.
	Metric 10:	Covariate Characterization	Medium	While the study does not explain where they obtained covariate information, it is reasonable to assume that they gathered the information from company records.
	Metric 11:	Co-exposure Counfounding	Low	The study assesses a wide range of other potential occupational co-exposures. While these co-exposures are not adjusted for in any statistical models, effect estimates are presented separately for benzene, diethyl sulfate, ethylene oxide, and vinyl chloride. The distribution of co-exposures across cases and controls is demonstrated to be mostly balanced by comparing proportions of exposed/unexposed between cases and controls. The only notable instance of imbalance is for benzene, where 11.1% of cases were exposed whereas 37.9% of all controls and 19.2% of non-neoplasm related controls were exposed.
Domain 5: Analysis				

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Study Citation:	Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	The study chose a case-control design, which was appropriate to study the rare disease of brain tumors and its association with occupational exposures. The only statistical analysis conducted is a Mantzel-Haenszel chi-squared test, but there is no reason to suggest that this would be inappropriate.
	Metric 13:	Statistical Power	Medium	The study does not calculate statistical power, but the number of cases (n=21) and controls (n=80 in each analysis) is likely sufficient to detect an effect.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to understand what was done and could be reproduced given access to the analytic data.
	Metric 15:	Statistical Analysis	High	The only statistical analysis conducted is a Mantel-Haenszel chi-squared test, and all assumptions were met. The statistical process is transparent.

Additional Comments: This case-control study pulled deceased former employees of the Union Carbide Corporation in Texas City, Texas. The study examined dichotomous exposure to a wide range of occupational exposures, including 1,2-dichloroethane, in relation to brain tumor cases. There is no quantitative estimate of exposure. The only statistical analysis in the study is a Mantel-Haenszel chi-squared test statistic and no statistically significant differences in exposure between cases and controls were observed. The fact that there are no effect estimates, no adjustment for confounders, and no quantitative exposure estimates limits the usefulness of this paper.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	Urinary system cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	Urinary system cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	Urinary system cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Immune/Hematological
Reported Health Effect(s):	Lymphatic and hematopoietic tissue cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Immune/Hematological
Reported Health Effect(s):	Lymphatic and hematopoietic tissue cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Immune/Hematological
Reported Health Effect(s):	Lymphatic and hematopoietic tissue cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Other cancers (not specified)
Reported Health Effect(s):	Other cancers (not specified)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Other cancers (not specified)
Reported Health Effect(s):	Other cancers (not specified)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Other cancers (not specified)
Reported Health Effect(s):	Other cancers (not specified)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Mortality
Reported Health Effect(s):	All-cause mortality
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Vital status was tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Medium	Death rates among unit employees were compared to death rates in the U.S. population adjusted for age and gender. Demographics of the exposed workers are not provided; therefore, it is not clear whether additional adjustment for race may have been appropriate. No justification is provided for the choice of the entire U.S. population as the comparison group. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis. Additional analyses are conducted limiting workers to those with the greatest likelihood of exposure (i.e., those working in jobs with high likelihood of contact with chemicals for more than a year, those working for the full year of 1979 during which chemical exposures were most frequently reported); these smaller groups are also compared to the unexposed general population.
	Metric 6:	Temporality	High	Temporality was established due to the longitudinal design and the use of mortality as the outcome. Exposures occurred between 1979 and 1987 and follow-up for vital status was conducted through 2003.
Domain 3: Outcome Assessment				

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Mortality
Reported Health Effect(s):	All-cause mortality
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Medium	The study did not provide information on how mortality was assessed either in the exposed population or in the comparison population; use of death certificates is implied but not stated.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected deaths are reported, but SIRs and 95% confidence intervals are not provided.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Comparisons of observed versus expected deaths were adjusted for age and gender. Demographics of the exposed workers are not provided; therefore, it is not clear whether additional adjustment for race may have been appropriate.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records or death records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed deaths among a population of exposed workers compared to expected deaths among the U.S. population, adjusted for age and gender.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected deaths; no SIR was provided. Expected death rates were adjusted for age and gender.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Mortality
Reported Health Effect(s):	All-cause mortality
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	All cancer (excluding non-melanoma skin cancer), digestive system cancer, colorectal cancer, respiratory cancer, prostate cancer, urinary system cancer, lymphatic and hematopoietic tissue cancer, other cancers (not specified)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	All cancer (excluding non-melanoma skin cancer), digestive system cancer, colorectal cancer, respiratory cancer, prostate cancer, urinary system cancer, lymphatic and hematopoietic tissue cancer, other cancers (not specified)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	All cancer (excluding non-melanoma skin cancer), digestive system cancer, colorectal cancer, respiratory cancer, prostate cancer, urinary system cancer, lymphatic and hematopoietic tissue cancer, other cancers (not specified)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Gastrointestinal
Reported Health Effect(s):	Digestive system cancer, colorectal cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Gastrointestinal
Reported Health Effect(s):	Digestive system cancer, colorectal cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Gastrointestinal
Reported Health Effect(s):	Digestive system cancer, colorectal cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Lung/Respiratory
Reported Health Effect(s):	Respiratory cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Lung/Respiratory
Reported Health Effect(s):	Respiratory cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Lung/Respiratory
Reported Health Effect(s):	Respiratory cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Prostate cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Prostate cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Prostate cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Male workers who had ever been assigned to the chlorohydrin unit between 1 January 1940 and 31 December 1967 at Union Carbide's South Charleston plant were enrolled and matched to the US National Death Index. Status on 5 workers could not be identified. Information on how workers were matched to death index was not specified.
	Metric 2:	Attrition	Medium	Rate of inclusion/participation was very high, as records were able to be matched for 98% of participants. Medium rating given because information on how participants whose vital status was not known was not specified.
	Metric 3:	Comparison Group	Uninformative	Unacceptable rating given because SMRs were calculated based on expected deaths from a reference population matched on sex, but not age.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Exposure was assessed based on duration of work in the plant. No information is provided on exposure levels, and a JEM was not used.
	Metric 5:	Exposure Levels	Uninformative	No information provided on levels of exposure.
	Metric 6:	Temporality	High	Temporality is well established; person-years stopped accumulating in 1967 and outcome was assessed beginning at that time.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar period, and interval since assignments, but distribution of these covariates was not reported.
	Metric 10:	Covariate Characterization	Medium	Information on covariate characterization not provided, but the selected covariates (age, calendar period, and interval since assignments) were likely extracted from employee records and unlikely to be largely problematic
	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.

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Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Study design was appropriate for the research method. Statistical methods were also appropriate.
	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.
	Metric 14:	Reproducibility of Analyses	Medium	Methods are well-enough described that study could be adequately reproduced.
	Metric 15:	Statistical Analysis	High	SMRs calculated based on US general population mortality for white males through 1988. RRs were ”evaluated over levels of duration of assignment to the chlorohydrin unit, stratified by age, calendar year, and interval since first assignment to the chlorohydrin unit”.

Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Male workers who had ever been assigned to the chlorohydrin unit between 1 January 1940 and 31 December 1967 at Union Carbide's South Charleston plant were enrolled and matched to the US National Death Index. Status on 5 workers could not be identified. Information on how workers were matched to death index was not specified.
	Metric 2:	Attrition	Medium	Rate of inclusion/participation was very high, as records were able to be matched for 98% of participants. Medium rating given because information on how participants whose vital status was not known was not specified.
	Metric 3:	Comparison Group	Uninformative	Unacceptable rating given because SMRs were calculated based on expected deaths from a reference population matched on sex, but not age.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Exposure was assessed based on duration of work in the plant. No information is provided on exposure levels, and a JEM was not used.
	Metric 5:	Exposure Levels	Uninformative	No information provided on levels of exposure.
	Metric 6:	Temporality	High	Temporality is well established; person-years stopped accumulating in 1967 and outcome was assessed beginning at that time.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar period, and interval since assignments, but distribution of these covariates was not reported.
	Metric 10:	Covariate Characterization	Medium	Information on covariate characterization not provided, but the selected covariates (age, calendar period, and interval since assignments) were likely extracted from employee records and unlikely to be largely problematic
	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.
Domain 5: Analysis				

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Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Study design was appropriate for the research method. Statistical methods were also appropriate.
	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.
	Metric 14:	Reproducibility of Analyses	Medium	Methods are well-enough described that study could be adequately reproduced.
	Metric 15:	Statistical Analysis	High	SMRs calculated based on US general population mortality for white males through 1988. RRs were ”evaluated over levels of duration of assignment to the chlorohydrin unit, stratified by age, calendar year, and interval since first assignment to the chlorohydrin unit”.

Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Male workers who had ever been assigned to the chlorohydrin unit between 1 January 1940 and 31 December 1967 at Union Carbide's South Charleston plant were enrolled and matched to the US National Death Index. Status on 5 workers could not be identified. Information on how workers were matched to death index was not specified.
	Metric 2:	Attrition	Medium	Rate of inclusion/participation was very high, as records were able to be matched for 98% of participants. Medium rating given because information on how participants whose vital status was not known was not specified.
	Metric 3:	Comparison Group	Uninformative	Unacceptable rating given because SMRs were calculated based on expected deaths from a reference population matched on sex, but not age.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Exposure was assessed based on duration of work in the plant. No information is provided on exposure levels, and a JEM was not used.
	Metric 5:	Exposure Levels	Uninformative	No information provided on levels of exposure.
	Metric 6:	Temporality	High	Temporality is well established; person-years stopped accumulating in 1967 and outcome was assessed beginning at that time.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar period, and interval since assignments, but distribution of these covariates was not reported.
	Metric 10:	Covariate Characterization	Medium	Information on covariate characterization not provided, but the selected covariates (age, calendar period, and interval since assignments) were likely extracted from employee records and unlikely to be largely problematic
	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.
Domain 5: Analysis				

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Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma
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Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Study design was appropriate for the research method. Statistical methods were also appropriate.
	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.
	Metric 14:	Reproducibility of Analyses	Medium	Methods are well-enough described that study could be adequately reproduced.
	Metric 15:	Statistical Analysis	High	SMRs calculated based on US general population mortality for white males through 1988. RRs were ”evaluated over levels of duration of assignment to the chlorohydrin unit, stratified by age, calendar year, and interval since first assignment to the chlorohydrin unit”.

Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
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Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
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Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Male workers who had ever been assigned to the chlorohydrin unit between 1 January 1940 and 31 December 1967 at Union Carbide's South Charleston plant were enrolled and matched to the US National Death Index. Status on 5 workers could not be identified. Information on how workers were matched to death index was not specified.
	Metric 2:	Attrition	Medium	Rate of inclusion/participation was very high, as records were able to be matched for 98% of participants. Medium rating given because information on how participants whose vital status was not known was not specified.
	Metric 3:	Comparison Group	Uninformative	Unacceptable rating given because SMRs were calculated based on expected deaths from a reference population matched on sex, but not age.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Exposure was assessed based on duration of work in the plant. No information is provided on exposure levels, and a JEM was not used.
	Metric 5:	Exposure Levels	Uninformative	No information provided on levels of exposure.
	Metric 6:	Temporality	High	Temporality is well established; person-years stopped accumulating in 1967 and outcome was assessed beginning at that time.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar period, and interval since assignments, but distribution of these covariates was not reported.
	Metric 10:	Covariate Characterization	Medium	Information on covariate characterization not provided, but the selected covariates (age, calendar period, and interval since assignments) were likely extracted from employee records and unlikely to be largely problematic
	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.
Domain 5: Analysis				

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Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Study design was appropriate for the research method. Statistical methods were also appropriate.
	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.
	Metric 14:	Reproducibility of Analyses	Medium	Methods are well-enough described that study could be adequately reproduced.
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Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
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Linked HERO ID(s):	200224, 5447107
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Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Male workers who had ever been assigned to the chlorohydrin unit between 1 January 1940 and 31 December 1967 at Union Carbide's South Charleston plant were enrolled and matched to the US National Death Index. Status on 5 workers could not be identified. Information on how workers were matched to death index was not specified.
	Metric 2:	Attrition	Medium	Rate of inclusion/participation was very high, as records were able to be matched for 98% of participants. Medium rating given because information on how participants whose vital status was not known was not specified.
	Metric 3:	Comparison Group	Uninformative	Unacceptable rating given because SMRs were calculated based on expected deaths from a reference population matched on sex, but not age.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Exposure was assessed based on duration of work in the plant. No information is provided on exposure levels, and a JEM was not used.
	Metric 5:	Exposure Levels	Uninformative	No information provided on levels of exposure.
	Metric 6:	Temporality	High	Temporality is well established; person-years stopped accumulating in 1967 and outcome was assessed beginning at that time.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar period, and interval since assignments, but distribution of these covariates was not reported.
	Metric 10:	Covariate Characterization	Medium	Information on covariate characterization not provided, but the selected covariates (age, calendar period, and interval since assignments) were likely extracted from employee records and unlikely to be largely problematic
	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.
Domain 5: Analysis				

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Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Study design was appropriate for the research method. Statistical methods were also appropriate.
	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.
	Metric 14:	Reproducibility of Analyses	Medium	Methods are well-enough described that study could be adequately reproduced.
	Metric 15:	Statistical Analysis	High	SMRs calculated based on US general population mortality for white males through 1988. RRs were ”evaluated over levels of duration of assignment to the chlorohydrin unit, stratified by age, calendar year, and interval since first assignment to the chlorohydrin unit”.

Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Male workers who had ever been assigned to the chlorohydrin unit between 1 January 1940 and 31 December 1967 at Union Carbide's South Charleston plant were enrolled and matched to the US National Death Index. Status on 5 workers could not be identified. Information on how workers were matched to death index was not specified.
	Metric 2:	Attrition	Medium	Rate of inclusion/participation was very high, as records were able to be matched for 98% of participants. Medium rating given because information on how participants whose vital status was not known was not specified.
	Metric 3:	Comparison Group	Uninformative	Unacceptable rating given because SMRs were calculated based on expected deaths from a reference population matched on sex, but not age.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Exposure was assessed based on duration of work in the plant. No information is provided on exposure levels, and a JEM was not used.
	Metric 5:	Exposure Levels	Uninformative	No information provided on levels of exposure.
	Metric 6:	Temporality	High	Temporality is well established; person-years stopped accumulating in 1967 and outcome was assessed beginning at that time.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar period, and interval since assignments, but distribution of these covariates was not reported.
	Metric 10:	Covariate Characterization	Medium	Information on covariate characterization not provided, but the selected covariates (age, calendar period, and interval since assignments) were likely extracted from employee records and unlikely to be largely problematic
	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.
Domain 5: Analysis				

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Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Study design was appropriate for the research method. Statistical methods were also appropriate.
	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.
	Metric 14:	Reproducibility of Analyses	Medium	Methods are well-enough described that study could be adequately reproduced.
	Metric 15:	Statistical Analysis	High	SMRs calculated based on US general population mortality for white males through 1988. RRs were ”evaluated over levels of duration of assignment to the chlorohydrin unit, stratified by age, calendar year, and interval since first assignment to the chlorohydrin unit”.

Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Male workers who had ever been assigned to the chlorohydrin unit between 1 January 1940 and 31 December 1967 at Union Carbide's South Charleston plant were enrolled and matched to the US National Death Index. Status on 5 workers could not be identified. Information on how workers were matched to death index was not specified.
	Metric 2:	Attrition	Medium	Rate of inclusion/participation was very high, as records were able to be matched for 98% of participants. Medium rating given because information on how participants whose vital status was not known was not specified.
	Metric 3:	Comparison Group	Uninformative	Unacceptable rating given because SMRs were calculated based on expected deaths from a reference population matched on sex, but not age.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Exposure was assessed based on duration of work in the plant. No information is provided on exposure levels, and a JEM was not used.
	Metric 5:	Exposure Levels	Uninformative	No information provided on levels of exposure.
	Metric 6:	Temporality	High	Temporality is well established; person-years stopped accumulating in 1967 and outcome was assessed beginning at that time.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar period, and interval since assignments, but distribution of these covariates was not reported.
	Metric 10:	Covariate Characterization	Medium	Information on covariate characterization not provided, but the selected covariates (age, calendar period, and interval since assignments) were likely extracted from employee records and unlikely to be largely problematic
	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.
Domain 5: Analysis				

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Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Study design was appropriate for the research method. Statistical methods were also appropriate.
	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.
	Metric 14:	Reproducibility of Analyses	Medium	Methods are well-enough described that study could be adequately reproduced.
	Metric 15:	Statistical Analysis	High	SMRs calculated based on US general population mortality for white males through 1988. RRs were ”evaluated over levels of duration of assignment to the chlorohydrin unit, stratified by age, calendar year, and interval since first assignment to the chlorohydrin unit”.

Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Male workers who had ever been assigned to the chlorohydrin unit between 1 January 1940 and 31 December 1967 at Union Carbide's South Charleston plant were enrolled and matched to the US National Death Index. Status on 5 workers could not be identified. Information on how workers were matched to death index was not specified.
	Metric 2:	Attrition	Medium	Rate of inclusion/participation was very high, as records were able to be matched for 98% of participants. Medium rating given because information on how participants whose vital status was not known was not specified.
	Metric 3:	Comparison Group	Uninformative	Unacceptable rating given because SMRs were calculated based on expected deaths from a reference population matched on sex, but not age.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Exposure was assessed based on duration of work in the plant. No information is provided on exposure levels, and a JEM was not used.
	Metric 5:	Exposure Levels	Uninformative	No information provided on levels of exposure.
	Metric 6:	Temporality	High	Temporality is well established; person-years stopped accumulating in 1967 and outcome was assessed beginning at that time.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar period, and interval since assignments, but distribution of these covariates was not reported.
	Metric 10:	Covariate Characterization	Medium	Information on covariate characterization not provided, but the selected covariates (age, calendar period, and interval since assignments) were likely extracted from employee records and unlikely to be largely problematic
	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.
Domain 5: Analysis				

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Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Study design was appropriate for the research method. Statistical methods were also appropriate.
	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.
	Metric 14:	Reproducibility of Analyses	Medium	Methods are well-enough described that study could be adequately reproduced.
	Metric 15:	Statistical Analysis	High	SMRs calculated based on US general population mortality for white males through 1988. RRs were ”evaluated over levels of duration of assignment to the chlorohydrin unit, stratified by age, calendar year, and interval since first assignment to the chlorohydrin unit”.

Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Bove, F. J. (1996). Public drinking water contamination and birthweight, prematurity, fetal deaths, and birth defects. Toxicology and Industrial Health 12(2):255-266.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	200239

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	This cross-sectional study (n=80,938) included all registered singleton live births and fetal deaths (>20 weeks' gestation) in 1985-88 in 75 New Jersey towns located in 4 counties with "some" water supplies contaminated with substances of interest and where: (i) residents were "mostly" served by public water systems; and (ii) births occurred "mostly" in state. Estimated proportions of residents served by public water systems, and of pregnancies/births captured, were not described. However, the inclusion of all eligible registered births, fetal deaths, and birth defects, as well as the selection of towns without knowledge of birth outcome prevalence, limited the likelihood of selection bias.
	Metric 2:	Attrition	Medium	All registered births and fetal deaths were included. Attrition due to missing values for multiple variables was not quantified and is therefore uncertain. However, attrition was likely modest as the proportion of missing values for individual variables was relatively low: (i) ~6% of subjects were excluded from analyses of outcomes such as preterm birth due to invalid or missing gestational ages; and (ii) other covariates evaluated as confounders had up to 4.9% missing values.
	Metric 3:	Comparison Group	High	After excluding plural pregnancies and chromosomal abnormalities, all registered live births during the study period in the areas included without the outcomes of interest were included in the comparison group. This comprehensive approach limited the potential for bias. Chromosomal abnormalities were not included as outcomes as they were not hypothesized to be associated with the exposures under study but were appropriately excluded given their uncertain etiology.
Domain 2: Exposure Characterization				

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Study Citation:	Bove, F. J. (1996). Public drinking water contamination and birthweight, prematurity, fetal deaths, and birth defects. Toxicology and Industrial Health 12(2):255-266.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	200239

Domain	Metric		Rating	Comments
	Metric 4:	Measurement of Exposure	Medium	Along with several other contaminants, residential drinking water exposure to 1,2-dichloroethane (as well as 1,1,1-trichloroethane and 'total dichloroethylenes') – was assigned based on maternal town of residence at birth. Exposure estimates were calculated using the average of water company sampling reports during the first trimester (for birth defects and fetal death) or the duration of pregnancy (for other outcomes). Detection limits and data availability were not specified in detail but were described as below 1 ppb, with reporting compliance >85%. A minimum of 1 sample per 6-month interval was required; variability in the number of measures available across water systems and towns was not described. Additional sources of measurement error included: changes in residence during pregnancy; water from alternate sources (ex. private wells, bottles, workplaces); variability in residential contaminant levels vs measured samples; unknown levels of tap water intake; and errors in estimated dermal and inhalation exposure while bathing or showering. While the extent of exposure misclassification is uncertain, there is no evidence to suggest it was differential rather than random.
	Metric 5:	Exposure Levels	Medium	Due to the high proportion of measures below detection limits, analyses relating exposure to health outcomes used only 2 categories for each of the chlorinated solvents of interest: cutoffs close to detection limits were used to define elevated exposure. Proportions defined as having elevated exposure was low (1.8% had 1,1-dichloroethylene ≥1 ppb). An important concern is that relatively low levels of exposure to these contaminants from sources other than residential drinking water, for which data were not available, could potentially have resulted in considerable misclassification.
	Metric 6:	Temporality	High	Exposure levels were assigned based on contaminant exposures estimated during: (i) the first trimester for analyses of birth defects and fetal deaths; and (ii) the duration of pregnancy for other pregnancy outcomes.

Domain 3: Outcome Assessment

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Study Citation:	Bove, F. J. (1996). Public drinking water contamination and birthweight, prematurity, fetal deaths, and birth defects. Toxicology and Industrial Health 12(2):255-266.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	200239

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcomes included measures of birthweight (continuous among term births, low term birthweight, very low birthweight), prematurity, fetal death, and congenital anomalies in live births or fetal deaths. The anomalies analyzed included defects of the central nervous system, neural tube, oral cleft, total cardiac, major cardiac, ventricular septum, and any surveillance defect excluding chromosomal defects. All outcomes were identified using birth certificates, fetal death certificates (>20 weeks' gestation), and the NJ congenital birth defect registry (ICD codes provided). These registry data are likely to be sufficiently valid for late pregnancy outcomes. However, their limited ability to capture early pregnancy losses is a weakness. The sample included only 594 fetal deaths (less than 1% of the >80,0000 sample). Typical estimates are that 10-20%, of recognized pregnancies ending in losses. Moreover, developmental defects contributing to early pregnancy losses were also not captured. A further limitation is that that potentially etiologically heterogeneous preterm birth types were analyzed together, as these data did not distinguish premature rupture of membranes vs idiopathic prematurity.
	Metric 8:	Reporting Bias	Medium	Models were constructed only for contaminants with associations > 1.0, and tables included only associations with odds ratios ≥1.5. No clear rationale was provided. Several positive odds ratios below the 1.5 cutoff were described in the results text (without confidence intervals), but no null/negative odds ratios were presented or described.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Potential confounding by maternal race, education, parity, and prior pregnancy loss, along with infant sex (for birth outcomes) and adequacy of prenatal care, was examined. Gestational age was addressed by analyzing birthweight among full term births, term low birth weight, and small size for gestational age. Only fully adjusted models were presented. In a companion case-control study (with low participation rates), adjustment for other variables not available on birth certificates (ex. maternal smoking, occupational exposures, medical history, and gestational weight gain) did not influence associations with other studied contaminants. This separate study reduces concerns for important confounding bias, but confounding cannot be ruled out.
	Metric 10:	Covariate Characterization	Medium	Data on covariates came from registry data: birth certificates, fetal death certificates, and the NJ congenital birth defects registry.
	Metric 11:	Co-exposure Counfounding	Medium	Co-exposure confounding by drinking water trihalomethane concentrations was evaluated. There was no evidence to suggest substantial confounding by this or other co-exposures.
Domain 5: Analysis				

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Study Citation:	Bove, F. J. (1996). Public drinking water contamination and birthweight, prematurity, fetal deaths, and birth defects. Toxicology and Industrial Health 12(2):255-266.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	200239

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Methods were appropriate. The study used logistic regression models to estimate odds ratios and confidence intervals for dichotomous outcomes, and linear regression for analysis of continuous birth weight.
	Metric 13:	Statistical Power	Medium	Statistical power was likely to have been limited as a consequence of the small proportion of the sample defined as having "elevated" residential water concentrations of the chemicals of interest. The range of exposure examined was limited, as cutoffs for elevated levels were close to the detection limits of 1 ppb. In addition, for most birth defect outcomes, fewer than 10 cases had elevated exposure.
	Metric 14:	Reproducibility of Analyses	Medium	The authors clearly described steps used to estimate exposure-outcome associations, including exposure category cutoffs and criteria for confounding. However, many results were not shown as tables included odds ratios ≥1.5.
	Metric 15:	Statistical Analysis	High	The authors estimated coefficients, odds ratios and 95% confidence intervals using adequate methods. Confounding was based on 15% change-in-estimate comparing nested models. Effect modification (ex by infant sex) was not evaluated as there was no a priori evidence to suggest such analyses at that time.

Additional Comments: This study analyzed the association between estimated residential drinking water concentrations of several chlorinated solvents including 1,2-dichloroethane (as well as 1,1,1-trichloroethane; ∑[trans-1,2-dichloroethylene and 1,1-dichloroethylene]) and pregnancy outcomes (size at birth, prematurity, fetal deaths, and congenital birth defects). The sample included more than 80,000 births during 1985-88 for residents of 75 towns in NJ using public water system records to estimate exposure during gestation, and registry data (birth certificate, fetal death certificates for pregnancies >20 weeks, state birth defect registry) to characterize outcomes. Strengths included the large sample size and inclusion of all eligible registered births and fetal deaths in the study period. A critical concern is the inability to capture early fetal deaths and any related malformations (1% of the sample had fetal deaths vs typical estimates of >10%). An important limitation was the low percentage of the sample with detectable (> 1ppb) concentrations of these contaminants (<1% to 6.2%). Small numbers for birth defect outcomes also limited power. Exposure misclassification (ex. drinking water from wells/ work/ bottles, changes in residence, exposure from other sources) is also a concern. However, such misclassification was likely non-differential, and thus more likely to under- vs. to over-estimate associations.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Bove, F. J., Fulcomer, M. C., Klotz, J. B., Esmart, J., Dufficy, E. M., Savrin, J. E. (1995). Public drinking water contamination and birth outcomes. American Journal of Epidemiology 141(9):850-862.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	194932

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	This semi-ecological study (n=80,938) included all registered singleton live births and fetal deaths (>20 weeks) in 1985-88 in 75 New Jersey towns located in 4 counties with "some" water supplies contaminated with substances of interest and where: (i) residents were "mostly" served by public water systems; and (ii) births occurred "mostly" in state. Estimated proportions of residents served by public water systems, and of pregnancies/births captured, were not described. However, the inclusion of all eligible registered births, fetal deaths, and birth defects, as well as the selection of towns without knowledge of birth outcome prevalence, limited the likelihood of selection bias.
	Metric 2:	Attrition	Medium	All registered births and fetal deaths were included. Attrition due to missing values for multiple variables was not quantified and is therefore uncertain. However, attrition was likely modest as the proportion of missing values for individual variables was relatively low: (i) ~6% of subjects were excluded from analyses of outcomes such as preterm birth due to invalid or missing gestational ages; and (ii) other covariates evaluated as confounders had up to 4.9% missing values.
	Metric 3:	Comparison Group	High	After excluding plural pregnancies and chromosomal abnormalities, all registered live births during the study period in the areas included without the outcomes of interest were included in the comparison group. This comprehensive approach limited the potential for bias. Chromosomal abnormalities were not included as outcomes as they were not hypothesized to be associated with the exposures under study but were appropriately excluded given their uncertain etiology.
Domain 2: Exposure Characterization				

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Study Citation:	Bove, F. J., Fulcomer, M. C., Klotz, J. B., Esmart, J., Dufficy, E. M., Savrin, J. E. (1995). Public drinking water contamination and birth outcomes. American Journal of Epidemiology 141(9):850-862.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	194932

Domain	Metric		Rating	Comments
	Metric 4:	Measurement of Exposure	Medium	Along with several other contaminants, residential drinking water exposure to 1,2-dichloroethane (as well as 1,1,1-trichloroethane and 'total dichloroethylenes') was assigned based on maternal town of residence at birth. Exposure estimates were calculated using the average of water company sampling reports during the first trimester (for birth defects and fetal death) or the duration of pregnancy (for other outcomes). Detection limits and data availability were not specified in detail but were described as below 1 ppb, with reporting compliance >85%. A minimum of 1 sample per 6-month interval was required; variability in the number of measures available across water systems and towns was not described. Additional sources of measurement error included: changes in residence during pregnancy; water from alternate sources (ex. private wells, bottles, workplaces); variability in residential contaminant levels vs measured samples; unknown levels of tap water intake; and errors in estimated dermal and inhalation exposure while bathing or showering. While the extent of exposure misclassification is uncertain, there is no evidence to suggest it was differential rather than random.
	Metric 5:	Exposure Levels	Low	Due to the high proportion of measures below detection limits, analyses relating exposure to health outcomes used only 2 categories for each of the three chemicals of interest: cutoffs close to detection limits were used to define elevated exposure. Proportions defined as having elevated exposure were low (1.8% had 1,1-dichloroethylene ≥1 ppb). An important concern is that relatively low levels of exposure to this contaminant from sources other than residential drinking water, for which data were not available, could potentially have resulted in considerable misclassification.
	Metric 6:	Temporality	High	Exposure levels were assigned based on contaminant exposures estimated during: (i) the first trimester for analyses of birth defects and fetal deaths; and (ii) the duration of pregnancy for other pregnancy outcomes.

Domain 3: Outcome Assessment

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Study Citation:	Bove, F. J., Fulcomer, M. C., Klotz, J. B., Esmart, J., Dufficy, E. M., Savrin, J. E. (1995). Public drinking water contamination and birth outcomes. American Journal of Epidemiology 141(9):850-862.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	194932

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcomes included measures of birthweight (continuous among term births, low term birthweight, very low birthweight), prematurity, fetal death, and congenital anomalies in live births or fetal deaths. The anomalies analyzed included defects of the central nervous system, neural tube, oral cleft, total cardiac, major cardiac, ventricular septum, and any surveillance defect excluding chromosomal defects. All outcomes were identified using birth certificates, fetal death certificates (>20 weeks' gestation), and the NJ congenital birth defect registry (ICD codes provided). These registry data are likely to be sufficiently valid for late pregnancy outcomes. However, their limited ability to capture early pregnancy losses is a weakness. The sample included only 594 fetal deaths (less than 1% of the >80,0000 sample). Typical estimates are that 10-20%, of recognized pregnancies ending in losses. Moreover, developmental defects contributing to early pregnancy losses were also not captured. A further limitation is that that potentially etiologically heterogeneous preterm birth types were analyzed together, as these data did not distinguish premature rupture of membranes vs idiopathic prematurity.
	Metric 8:	Reporting Bias	Low	Models were constructed only for contaminants with associations > 1.0, and tables included only associations with odds ratios ≥1.5. No clear rationale was provided. Several positive odds ratios below the 1.5 cutoff were described in the results text (without confidence intervals), but no null/negative odds ratios were presented or described.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Potential confounding by maternal race, education, parity, and prior pregnancy loss, along with infant sex (for birth outcomes) and adequacy of prenatal care, was examined. Gestational age was addressed by analyzing birthweight among full term births, term low birth weight, and small size for gestational age. Only fully adjusted models were presented. In a companion case-control study (with low participation rates), adjustment for other variables not available on birth certificates (ex. maternal smoking, occupational exposures, medical history, and gestational weight gain) did not influence associations with other studied contaminants. This separate study reduces concerns for important confounding bias, but confounding cannot be ruled out.
	Metric 10:	Covariate Characterization	Medium	Data on covariates came from registry data: birth certificates, fetal death certificates, and the NJ congenital birth defects registry.
	Metric 11:	Co-exposure Counfounding	Medium	Co-exposure confounding by drinking water trihalomethane concentrations was evaluated. There was no evidence to suggest substantial confounding by this or other co-exposures.
Domain 5: Analysis				

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Study Citation:	Bove, F. J., Fulcomer, M. C., Klotz, J. B., Esmart, J., Dufficy, E. M., Savrin, J. E. (1995). Public drinking water contamination and birth outcomes. American Journal of Epidemiology 141(9):850-862.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	194932

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Methods were appropriate. The study used logistic regression models to estimate odds ratios and confidence intervals for dichotomous outcomes, and linear regression for analysis of continuous birth weight.
	Metric 13:	Statistical Power	Low	Statistical power was likely to have been limited as a consequence of the small proportion of the sample defined as having "elevated" residential water concentrations of the chemicals of interest. The range of exposure examined was limited, as cutoffs for elevated levels were close to the detection limits of 1 ppb. In addition, for most birth defect outcomes, fewer than 10 cases had elevated exposure. However, the authors emphasized the magnitude of associations rather than statistical significance and presented multiple confidence intervals to aid interpretation of the precision of estimates (50%, 90% and 99%).
	Metric 14:	Reproducibility of Analyses	Medium	The authors clearly described steps used to estimate exposure-outcome associations, including exposure category cutoffs and criteria for confounding. However, many results were not shown as tables included odds ratios ≥1.5.
	Metric 15:	Statistical Analysis	High	The authors estimated coefficients, odds ratios and confidence intervals using adequate methods. Confounding was based on 15% change-in-estimate comparing nested models. Effect modification (ex by infant sex) was not evaluated as there was no a priori evidence to suggest such analyses at that time.

Additional Comments: This study analyzed the association between estimated residential drinking water concentrations of several chlorinated solvents including 1,2-dichloroethane (as well as 1,1,1-trichloroethane and the ∑[trans-1,2-dichloroethylene & 1,1-dichloroethylene]) and pregnancy outcomes (size at birth, prematurity, fetal deaths, and congenital birth defects). The sample included more than 80,000 births during 1985-88 for residents of 75 towns in NJ using public water system records to estimate exposure during gestation, and registry data (birth certificate, fetal death certificates for pregnancies >20 weeks' gestation, state birth defect registry) to characterize outcomes. Strengths included the large sample size and inclusion of all eligible registered births and fetal deaths in the study period. A critical concern is the inability to capture early fetal deaths and any related malformations (1% of the sample had fetal deaths vs typical estimates of >10%). An important limitation was the low percentage of the sample with detectable (> 1ppb) concentrations of this solvent (<2%), which likely limited power. Small numbers for birth defect outcomes also limited power. Exposure misclassification (ex. drinking water from wells/ work/ bottles, changes in residence, exposure from other sources) is also a concern. However, such misclassification was likely non-differential, and thus more likely to under- vs. to over-estimate associations.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Bowler, R.M., Gysens, S., Hartney, C. (2003). Neuropsychological effects of ethylene dichloride exposure. NeuroToxicology 24(4-5):553-562.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Wechsler Adult Intelligence Scale III (WAIS-III), Wechsler Memory Scale III (WMS-III), Boston Naming Test (BNT), Trail Making Test (TMT), Stroop Color-Word Test, Grooved Pegboard, Dynamometer, Wide Range Achievement Test (WRAT), Finger tapping, Beck Anxiety Index, Beck Depression Index, Symptom Checklist-90 (SCL-90).
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	200241

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Uninformative	221 workers that had been exposed to 1,2-DCE in the Southern United States were initially included. Exclusion criteria were provided, including the number of individuals excluded for each reason. The study authors note that those initially included in the analysis sample were referred by physicians after neurological complaints were documented. Detailed criteria for referral were not provided. Referral-based recruitment of neurological cases will likely result in an analysis sample with an exposure-outcome distribution that is not representative of the eligible population (i.e., contamination site clean-up workers).
	Metric 2:	Attrition	Medium	There was moderate subject loss. Reasons for exclusion from the analysis sample are provided, and only those with complete information were included in the analysis.
	Metric 3:	Comparison Group	Low	Impairment scores were compared to normative data from manuals and/or a "demographically similar control group" cited to Bowler et al. (2001). The controls from this study appeared similar (albeit somewhat older) than 1,2-DCE-exposed workers and reported no prior chemical exposure.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	A job-exposure matrix was not considered plausible; variables considered as surrogates of exposure were obtained from interviews. This method is expected to have poor validity because it relies on workers' recall of subjective events and their frequency (e.g., contact with water); workers (who are taking part in a lawsuit) may overestimate their exposure.
	Metric 5:	Exposure Levels	Low	Two levels of exposure (exposed and not exposed) were used to evaluate neurophysiological effects.
	Metric 6:	Temporality	Medium	Exposures primarily occurred between 1993 and 1995 and neurophysiological effects were evaluated in 2000. Temporality is established, but it is unclear whether exposures fall within relevant exposure windows for the outcome of interest.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Neurophysiological effects were evaluated using a number of standardized tests, including (but not limited to) the Wechsler Adult Intelligence Scale (WAIS-III), the Wechsler Memory Scale (WMS-III), and the Symptom Checklist 90-Revised (SCL90-R). There was no information whether tests were performed using the same methods for exposed and referent groups (e.g., timing and order of tests).

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Study Citation:	Bowler, R.M., Gysens, S., Hartney, C. (2003). Neuropsychological effects of ethylene dichloride exposure. NeuroToxicology 24(4-5):553-562.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Wechsler Adult Intelligence Scale III (WAIS-III), Wechsler Memory Scale III (WMS-III), Boston Naming Test (BNT), Trail Making Test (TMT), Stroop Color-Word Test, Grooved Pegboard, Dynamometer, Wide Range Achievement Test (WRAT), Finger tapping, Beck Anxiety Index, Beck Depression Index, Symptom Checklist-90 (SCL-90).
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	200241

Domain	Metric		Rating	Comments
	Metric 8:	Reporting Bias	Low	Neurobehavioral outcomes mentioned in the methods were reported for 1,2-DCE-exposed workers (as mean score, standard deviation, and percentage impaired); results for controls/normative data were not shown and/or p-values from t-tests were not provided. Control data were used to define impairment (based on z-score) but these values were not reported. Data pertaining to specific exposure variables were reported in the text only; no data were shown in a table.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Normative data permitted adjustments based on age, education, and gender. The control group was "socio-demographically" similar but specific parameters used to define similarity were not indicated. Separate ANCOVA analyses on workers only were stratified by race (citation provided), and adjusted for ethnicity, age, and education. The methods for identifying and including potential confounders in the analytic approach was not described.
	Metric 10:	Covariate Characterization	Low	No description of the covariate collection method was provided. It was not clear whether the method used was valid or not.
	Metric 11:	Co-exposure Counfounding	Low	A number of workers (18%) reported current exposure to chemicals in their work environment. These potential co-exposures were not were not appropriately adjusted for in the analytical approach used.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Low	The study design was appropriate to evaluate the neurophysiological status of 1,2-DCE-exposed workers; however, statistical methods were not comprehensive.
	Metric 13:	Statistical Power	Medium	The report indicates "significant impairments" were observed on various neurophysiological tests using t-tests, and significant exposure relationships were reported based on test scores and specific exposure variables (used as surrogates of exposure). Therefore, the number of participants was sufficient to detect an effect.
	Metric 14:	Reproducibility of Analyses	Low	Tests were scored according to relevant manuals; the calculation of z-scores, used in all impairment comparisons and analyses of exposure relationships, was not explained in adequate detail. The methods used to determine relationships between specific exposure variables and test scores (i.e., ANCOVA analyses) were not fully described.
	Metric 15:	Statistical Analysis	Low	Description of the ANCOVA analysis was largely not present. It is not clear whether model assumptions were met.

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Study Citation:	Bowler, R.M., Gysens, S., Hartney, C. (2003). Neuropsychological effects of ethylene dichloride exposure. NeuroToxicology 24(4-5):553-562.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Wechsler Adult Intelligence Scale III (WAIS-III), Wechsler Memory Scale III (WMS-III), Boston Naming Test (BNT), Trail Making Test (TMT), Stroop Color-Word Test, Grooved Pegboard, Dynamometer, Wide Range Achievement Test (WRAT), Finger tapping, Beck Anxiety Index, Beck Depression Index, Symptom Checklist-90 (SCL-90).
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	200241

Domain	Metric	Rating	Comments
Additional Comments:	The study evaluated the neurobehavioral status of a group of workers with known exposure to 1,2-DCE at a clean-up site. Impairments related to processing speed, attention, cognitive flexibility, motor coordination and speed, verbal memory/fluency, vision and visual-spatial abilities, and mood were reported in exposed workers. Serious and consequential flaws are associated with the study including methods of participant selection and retention, and exposure characterization among others.		

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Brender, J.D., Shinde, M.U., Zhan, F.B., Gong, X., Langlois, P.H. (2014). Maternal residential proximity to chlorinated solvent emissions and birth defects in offspring: A case-control study. Environmental Health: A Global Access Science Source 13(1):96.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	birth defects (neural tube defects, limbs deficiencies, oral cleft defects, heart defects, spina bifida, anencephaly)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	2799700

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Participants were drawn from the Texas Birth Defects Registry (TBDR) for years 1996-2008. Controls were frequency matched from the same registry. Study authors state that neural tube cases were more likely to not be successfully geocoded which may introduce selection bias, however, the authors note that both cases and controls with addresses that could not be geocoded were similar. In spite of that, the inclusion criteria, methods of participant selection, and frequency match were reported.
	Metric 2:	Attrition	Medium	13.3% case mother addresses and 12.8% control mother addresses were unable to be geocoded, however this most likely only lowered the precision of the study and most likely does not vary based on exposure level.
	Metric 3:	Comparison Group	Medium	Controls were matched to cases and pulled from the same eligible population by year of delivery and public health service region. Other demographic factors, e.g., race was not matched in population selection. However, statistical analyses were adjusted for year of delivery, maternal age, race/ethnicity, education, and public health region of residence.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Used Emission Weighted Proximity Model to estimate exposure at a given address based on proximity to emission sources and the specific amount or type of pollutant emitted. There may be some exposure misclassification due to mothers moving away from geocoded addresses. Previous studies indicate ~67% of mothers do not move between conception and delivery.
	Metric 5:	Exposure Levels	Medium	Reports exposure as "exposure risk value" and groups the risk values into quartiles, with exposure risk values < 0 being the referent group
	Metric 6:	Temporality	Medium	The study authors estimated exposure based on residence during pregnancy and evaluated birth outcomes. Temporality is established. Previous studies indicate ~67% mothers don't move between trimester and delivery. For mothers who moved during the pregnancy, the temporality is unknown.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Outcomes determined by Texas Birth Defect Registry, checking for birth defect diagnosis. Birth certificates came from Center for Health Statistics at Texas Department of State Health Services
	Metric 8:	Reporting Bias	High	Outcome data measured and reported clearly, stratified by specific type of birth defect
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Brender, J.D., Shinde, M.U., Zhan, F.B., Gong, X., Langlois, P.H. (2014). Maternal residential proximity to chlorinated solvent emissions and birth defects in offspring: A case-control study. Environmental Health: A Global Access Science Source 13(1):96.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	birth defects (neural tube defects, limbs deficiencies, oral cleft defects, heart defects, spina bifida, anencephaly)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	2799700

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	High	Cases were frequency matched by year of delivery and public health service region. Final models were adjusted for year of delivery, public health region, maternal age (<20, 20-24, 25-29, 30-34, 35-39, >39 years), education (<12 years, 12 years, >12 years), and race/ethnicity (Whit non-Hispanic, Black non-Hispanic, Hispanic, other non-Hispanic).
	Metric 10:	Covariate Characterization	High	Used birth and death certificates for demographic information
	Metric 11:	Co-exposure Counfounding	Medium	other co-exposures were not described
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	study used logistic regression to measure association between exposure and birth defects
	Metric 13:	Statistical Power	Medium	Overall adequate number of cases and controls - some effects have low cell counts, but at least one health effect has sufficient statistical power.
	Metric 14:	Reproducibility of Analyses	Medium	Methods sufficiently detailed for reproducibility
	Metric 15:	Statistical Analysis	High	No logistic regression model assumption violations were identified.

Additional Comments: This study examined the association between proximity to several point sources of chlorinated solvents and birth defects. Exposure was assessed using EPA's Toxic Release Inventory, and birth defects were assessed using Texas birth registries. The geocoded address of mothers on day of delivery and the amount of solvent was plugged into the Emission Weighted Probability model to assign each mother an exposure risk value. Limitations include limited evidence of temporality. Additionally, elective terminations lacked a vital record, which meant only 69% of mothers with neural tube defects were geocoded. Mothers highly exposed to 1,2-dichloroethane were 1.85 times more likely to have the spina bifida birth defect than mothers who were not significantly exposed.

Overall Quality Determination High

* No biomarkers were identified for this evaluation.

Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Nested case-control design; cases selected from deaths in cohort study was described by Rinsky et al (1988; HERO 597923) (29,139 workers in Union Carbide facilities in West Virginia followed from 1940 to 1978). Vital status complete for 95% of cohort members.
	Metric 2:	Attrition	High	There was minimal exclusion of subjects/missing data, because vital status follow-up was complete for 96% of the 29,139 men in the cohort study.
	Metric 3:	Comparison Group	Medium	Controls were randomly selected in a 5:1 ratio to cases from the total employee cohort such that they were first employed in the same decade and survived to the same five-year survival period as cases. Controls survived at least to the beginning of the five-year interval in which cases died. Controls were independently selected for each of the individual disease subcategories. However, the demographic information between cases and controls were not compared in the paper.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was partially described: (1) Potential employee contact with a specific substance was determined by tracing each employee's work assignments and linking these assignment records to a separate computer file that contained a history of departmental usage for each substance; (2) Potential exposure to each chemical group was assumed on the basis of assignment o a production unit with a history of usage of any member of that chemical group. However, exposure level either based on work assignment in departments such as job exposure matrix or on the chemical levels were not presented.
	Metric 5:	Exposure Levels	Low	The range of exposure is limited. For example, exposure was presented by the duration of work in two categories: <5 years and 5+ years.
	Metric 6:	Temporality	Medium	Temporality is established, but it is unclear whether the exposures fall within the relevant exposure window. Authors used a lag time of 5 years; since controls were selected for 5 yr intervals, the effective lag time ranged from 5-9 years with an average of 7.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Case definition was based on death certificate diagnosis; but no method validation was conducted against this well-established methods.
	Metric 8:	Reporting Bias	Medium	All outcomes reported, but ORs for many analyses presented without CIs (some CIs reported in text).
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Low	There is indirect evidence that considerations were not made for potential confounders (ORs not adjusted, controls not age- or race-matched). Even though authors note that "Age-adjusted stratified analyses, which were also conducted, did not materially modify the odds ratio estimates". Also stratified examination of odds ratios were conducted to assess duration of exposure effects. However, other key confounders e.g., smoking status and race were not accounted for.
	Metric 10:	Covariate Characterization	Medium	The only potential confounder considered was age; this was presumably evaluated based on employment records (no discussion presented). Age-adjusted stratified analyses were conducted.
	Metric 11:	Co-exposure Counfounding	Low	Co-exposures were present and were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Nested case-control study design is appropriate for research question. Initial data analysis included crude odds ratio and then stratified examination of odds ratios was conducted to ass duration of exposure effect. Also, age-adjusted stratified analysis was conducted.
	Metric 13:	Statistical Power	Low	Statistical power calculations were not reported. Case numbers for each disease were low. The number of subjects was not sufficient to detect an effect of 1,2-dichloroethylene exposure.
	Metric 14:	Reproducibility of Analyses	Medium	Description was sufficient to be conceptually reproducible.
	Metric 15:	Statistical Analysis	Low	Statistical model to calculate odds ratio was not described.

Additional Comments: This nested case-control study within a cohort study is a good study design to answer the research question regarding the association between multiple chemical exposures and four cancer sites. Cases and controls are selected appropriate. However, there are several limitations in this study: (1) confounders were not all considered and adjusted for, except that age-adjusted odds ratios were conducted; (2) it is not described if co-exposures were adjusted for; (3) numbers of cancer cases for each cancer type were small, so the statistical power is limited; (4) statistical models for calculating odds ratios were not described.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Nested case-control design; cases selected from deaths in cohort study was described by Rinsky et al (1988; HERO 597923) (29,139 workers in Union Carbide facilities in West Virginia followed from 1940 to 1978). Vital status complete for 95% of cohort members.
	Metric 2:	Attrition	High	There was minimal exclusion of subjects/missing data, because vital status follow-up was complete for 96% of the 29,139 men in the cohort study.
	Metric 3:	Comparison Group	Medium	Controls were randomly selected in a 5:1 ratio to cases from the total employee cohort such that they were first employed in the same decade and survived to the same five-year survival period as cases. Controls survived at least to the beginning of the five-year interval in which cases died. Controls were independently selected for each of the individual disease subcategories. However, the demographic information between cases and controls were not compared in the paper.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was partially described: (1) Potential employee contact with a specific substance was determined by tracing each employee's work assignments and linking these assignment records to a separate computer file that contained a history of departmental usage for each substance; (2) Potential exposure to each chemical group was assumed on the basis of assignment o a production unit with a history of usage of any member of that chemical group. However, exposure level either based on work assignment in departments such as job exposure matrix or on the chemical levels were not presented.
	Metric 5:	Exposure Levels	Low	The range of exposure is limited. For example, exposure was presented by the duration of work in two categories: <5 years and 5+ years.
	Metric 6:	Temporality	Medium	Temporality is established, but it is unclear whether the exposures fall within the relevant exposure window. Authors used a lag time of 5 years; since controls were selected for 5 yr intervals, the effective lag time ranged from 5-9 years with an average of 7.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Case definition was based on death certificate diagnosis; but no method validation was conducted against this well-established methods.
	Metric 8:	Reporting Bias	Medium	All outcomes reported, but ORs for many analyses presented without CIs (some CIs reported in text).
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Low	There is indirect evidence that considerations were not made for potential confounders (ORs not adjusted, controls not age- or race-matched). Even though authors note that "Age-adjusted stratified analyses, which were also conducted, did not materially modify the odds ratio estimates". Also stratified examination of odds ratios were conducted to assess duration of exposure effects. However, other key confounders e.g., smoking status and race were not accounted for.
	Metric 10:	Covariate Characterization	Medium	The only potential confounder considered was age; this was presumably evaluated based on employment records (no discussion presented). Age-adjusted stratified analyses were conducted.
	Metric 11:	Co-exposure Counfounding	Low	Co-exposures were present and were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Nested case-control study design is appropriate for research question. Initial data analysis included crude odds ratio and then stratified examination of odds ratios was conducted to ass duration of exposure effect. Also, age-adjusted stratified analysis was conducted.
	Metric 13:	Statistical Power	Low	Statistical power calculations were not reported. Case numbers for each disease were low. The number of subjects was not sufficient to detect an effect of 1,2-dichloroethylene exposure.
	Metric 14:	Reproducibility of Analyses	Medium	Description was sufficient to be conceptually reproducible.
	Metric 15:	Statistical Analysis	Low	Statistical model to calculate odds ratio was not described.

Additional Comments: This nested case-control study within a cohort study is a good study design to answer the research question regarding the association between multiple chemical exposures and four cancer sites. Cases and controls are selected appropriate. However, there are several limitations in this study: (1) confounders were not all considered and adjusted for, except that age-adjusted odds ratios were conducted; (2) it is not described if co-exposures were adjusted for; (3) numbers of cancer cases for each cancer type were small, so the statistical power is limited; (4) statistical models for calculating odds ratios were not described.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Nested case-control design; cases selected from deaths in cohort study was described by Rinsky et al (1988; HERO 597923) (29,139 workers in Union Carbide facilities in West Virginia followed from 1940 to 1978). Vital status complete for 95% of cohort members.
	Metric 2:	Attrition	High	There was minimal exclusion of subjects/missing data, because vital status follow-up was complete for 96% of the 29,139 men in the cohort study.
	Metric 3:	Comparison Group	Medium	Controls were randomly selected in a 5:1 ratio to cases from the total employee cohort such that they were first employed in the same decade and survived to the same five-year survival period as cases. Controls survived at least to the beginning of the five-year interval in which cases died. Controls were independently selected for each of the individual disease subcategories. However, the demographic information between cases and controls were not compared in the paper.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was partially described: (1) Potential employee contact with a specific substance was determined by tracing each employee's work assignments and linking these assignment records to a separate computer file that contained a history of departmental usage for each substance; (2) Potential exposure to each chemical group was assumed on the basis of assignment o a production unit with a history of usage of any member of that chemical group. However, exposure level either based on work assignment in departments such as job exposure matrix or on the chemical levels were not presented.
	Metric 5:	Exposure Levels	Low	The range of exposure is limited. For example, exposure was presented by the duration of work in two categories: <5 years and 5+ years.
	Metric 6:	Temporality	Medium	Temporality is established, but it is unclear whether the exposures fall within the relevant exposure window. Authors used a lag time of 5 years; since controls were selected for 5 yr intervals, the effective lag time ranged from 5-9 years with an average of 7.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Case definition was based on death certificate diagnosis; but no method validation was conducted against this well-established methods.
	Metric 8:	Reporting Bias	Medium	All outcomes reported, but ORs for many analyses presented without CIs (some CIs reported in text).
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Low	There is indirect evidence that considerations were not made for potential confounders (ORs not adjusted, controls not age- or race-matched). Even though authors note that "Age-adjusted stratified analyses, which were also conducted, did not materially modify the odds ratio estimates". Also stratified examination of odds ratios were conducted to assess duration of exposure effects. However, other key confounders e.g., smoking status and race were not accounted for.
	Metric 10:	Covariate Characterization	Medium	The only potential confounder considered was age; this was presumably evaluated based on employment records (no discussion presented). Age-adjusted stratified analyses were conducted.
	Metric 11:	Co-exposure Counfounding	Low	Co-exposures were present and were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Nested case-control study design is appropriate for research question. Initial data analysis included crude odds ratio and then stratified examination of odds ratios was conducted to ass duration of exposure effect. Also, age-adjusted stratified analysis was conducted.
	Metric 13:	Statistical Power	Low	Statistical power calculations were not reported. Case numbers for each disease were low. The number of subjects was not sufficient to detect an effect of 1,2-dichloroethylene exposure.
	Metric 14:	Reproducibility of Analyses	Medium	Description was sufficient to be conceptually reproducible.
	Metric 15:	Statistical Analysis	Low	Statistical model to calculate odds ratio was not described.

Additional Comments: This nested case-control study within a cohort study is a good study design to answer the research question regarding the association between multiple chemical exposures and four cancer sites. Cases and controls are selected appropriate. However, there are several limitations in this study: (1) confounders were not all considered and adjusted for, except that age-adjusted odds ratios were conducted; (2) it is not described if co-exposures were adjusted for; (3) numbers of cancer cases for each cancer type were small, so the statistical power is limited; (4) statistical models for calculating odds ratios were not described.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Nested case-control design; cases selected from deaths in cohort study was described by Rinsky et al (1988; HERO 597923) (29,139 workers in Union Carbide facilities in West Virginia followed from 1940 to 1978). Vital status complete for 95% of cohort members.
	Metric 2:	Attrition	High	There was minimal exclusion of subjects/missing data, because vital status follow-up was complete for 96% of the 29,139 men in the cohort study.
	Metric 3:	Comparison Group	Medium	Controls were randomly selected in a 5:1 ratio to cases from the total employee cohort such that they were first employed in the same decade and survived to the same five-year survival period as cases. Controls survived at least to the beginning of the five-year interval in which cases died. Controls were independently selected for each of the individual disease subcategories. However, the demographic information between cases and controls were not compared in the paper.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was partially described: (1) Potential employee contact with a specific substance was determined by tracing each employee's work assignments and linking these assignment records to a separate computer file that contained a history of departmental usage for each substance; (2) Potential exposure to each chemical group was assumed on the basis of assignment o a production unit with a history of usage of any member of that chemical group. However, exposure level either based on work assignment in departments such as job exposure matrix or on the chemical levels were not presented.
	Metric 5:	Exposure Levels	Low	The range of exposure is limited. For example, exposure was presented by the duration of work in two categories: <5 years and 5+ years.
	Metric 6:	Temporality	Medium	Temporality is established, but it is unclear whether the exposures fall within the relevant exposure window. Authors used a lag time of 5 years; since controls were selected for 5 yr intervals, the effective lag time ranged from 5-9 years with an average of 7.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Case definition was based on death certificate diagnosis; but no method validation was conducted against this well-established methods.
	Metric 8:	Reporting Bias	Medium	All outcomes reported, but ORs for many analyses presented without CIs (some CIs reported in text).
Domain 4: Potential Confounding / Variability Control				

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Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Low	There is indirect evidence that considerations were not made for potential confounders (ORs not adjusted, controls not age- or race-matched). Even though authors note that "Age-adjusted stratified analyses, which were also conducted, did not materially modify the odds ratio estimates". Also stratified examination of odds ratios were conducted to assess duration of exposure effects. However, other key confounders e.g., smoking status and race were not accounted for.
	Metric 10:	Covariate Characterization	Medium	The only potential confounder considered was age; this was presumably evaluated based on employment records (no discussion presented). Age-adjusted stratified analyses were conducted.
	Metric 11:	Co-exposure Counfounding	Low	Co-exposures were present and were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Nested case-control study design is appropriate for research question. Initial data analysis included crude odds ratio and then stratified examination of odds ratios was conducted to ass duration of exposure effect. Also, age-adjusted stratified analysis was conducted.
	Metric 13:	Statistical Power	Low	Statistical power calculations were not reported. Case numbers for each disease were low. The number of subjects was not sufficient to detect an effect of 1,2-dichloroethylene exposure.
	Metric 14:	Reproducibility of Analyses	Medium	Description was sufficient to be conceptually reproducible.
	Metric 15:	Statistical Analysis	Low	Statistical model to calculate odds ratio was not described.

Additional Comments: This nested case-control study within a cohort study is a good study design to answer the research question regarding the association between multiple chemical exposures and four cancer sites. Cases and controls are selected appropriate. However, there are several limitations in this study: (1) confounders were not all considered and adjusted for, except that age-adjusted odds ratios were conducted; (2) it is not described if co-exposures were adjusted for; (3) numbers of cancer cases for each cancer type were small, so the statistical power is limited; (4) statistical models for calculating odds ratios were not described.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Cheng, T.J., Huang, M.L., You, N.C., Du, C.L., Chau, T.T. (1999). Abnormal liver function in workers exposed to low levels of ethylene dichloride and vinyl chloride monomer. Journal of Occupational and Environmental Medicine 41(12):1128-1133.
Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	AST, ALT, GGT, Hepatitis B virus surface antigen (HBsAg), and anti-hepatitis C virus antibody (anti-HCV).
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	200266

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	A total of 251 male workers were included from 4 vinyl chloride monomer manufacturing plants. Other details on recruitment strategy, eligibility criteria, year of enrollment, and participation rates were not provided.
	Metric 2:	Attrition	Low	There was no indication of attrition and details on the number of eligible participants throughout the study was limited. Attrition could not be adequately assessed due to a lack of information regarding recruitment and selection.
	Metric 3:	Comparison Group	Medium	The low-EDC-low-VCM group (187 participants) was used as the comparison group, and there is indirect evidence groups are similar. Limited details were provided for setting, inclusion and exclusion criteria, and methods of participant selection.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	NIOSH recommended methods 1003 and 1007 were used for personal and area sampling, respectively. Air samples were collected, stored at 4 deg. C, and analyzed within 2 weeks of the sampling event. However, historical job changes, changes in exposure levels over time, and timing (year or days during work week) or duration of area or personal sampling were not reported.
	Metric 5:	Exposure Levels	Medium	EDC and VCM levels were reported for the different categories of jobs, which were classified into low-EDC-low-VCM, mod-EDC-low-VCM, and low-EDC-mod-VCM groups.
	Metric 6:	Temporality	High	The age of participants (mean age 33.7-40.1 years) and employment duration (mean 7.5-14.3 years) were reported, and the temporality between the exposure and outcome appears to be appropriate.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	AST, ALT, and GGT "were analyzed with a Hitachi 7050 autoanalyzer". A basis for the cutoff values used in Table 4 to determine "abnormal" AST, ALT, and GGT levels was not provided.
	Metric 8:	Reporting Bias	High	Odds ratios for abnormal liver function were provided with 95% confidence intervals, the number per exposure level, and significance when applicable.
Domain 4: Potential Confounding / Variability Control				

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Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	AST, ALT, GGT, Hepatitis B virus surface antigen (HBsAg), and anti-hepatitis C virus antibody (anti-HCV).
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	200266

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Medium	The study reports information on potential confounders (age, hepatitis, BMI, alcohol use, and employment duration), and controls for hepatitis, BMI and alcohol consumption in the multiple logistic regression analyses. There is indirect evidence that appropriate adjustments were made.
	Metric 10:	Covariate Characterization	Medium	An interviewer administered the questionnaires to collect information about potential confounders and occupational history.
	Metric 11:	Co-exposure Counfounding	Low	Exposure to ethylene dichloride was evaluated in a vinyl chloride monomer (VCM) manufacturing facility, and VCM was also subsequently analyzed using personal and area sampling. Results for VCM exposure concentrations were provided. VCM is also suspected to cause liver damage.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design (cohort) was appropriate to assess the outcome of interest (”markers of liver damage”). Chi-squared (X2) test and multiple logistic regression were used for statistical analyses.
	Metric 13:	Statistical Power	Medium	The number of participants was adequate to detect an effect in the exposed populations, although power calculations were not provided. There were >20 participants in each group.
	Metric 14:	Reproducibility of Analyses	Low	A description of the logistic regression analysis was provided, however, study authors do not provide information on categorization of abnormal liver function.
	Metric 15:	Statistical Analysis	High	There were no identifiable logistic regression model assumption violations.
Domain 6: Other (if applicable) Considerations for Biomarker Selection and Measurement (Lakind et al. 2014)				
	Metric 16:	Use of Biomarker of Exposure	N/A	Biomarker of exposures were not assessed.
	Metric 17:	Effect Biomarker	High	This study uses aspartate aminotransferase, alanine aminotransferase, and y-glutamyltransferase as biomarkers of effect. While these no works cited to explain their connection to liver function, all three are well-known marker of liver function. Similarly, Hepatitis B virus surface antigen and antihepatitis C virus anitbody are also well-known measures of liver function and health.
	Metric 18:	Method Sensitivity	Low	No limit of detection information is provided for any of the effect biomarkers.
	Metric 19:	Biomarker Stability	Medium	While the study does not provide a lot of information regarding biomarker storage or stability, the authors do mention that venous blood used to detect biomarkers was stored at 4 degrees C.
	Metric 20:	Sample Contamination	Medium	No specific information regarding potential sample contamination was provided.
	Metric 21:	Method Requirements	Medium	Aspartate aminotransferase, alanine aminotransferase, and y-glutamyltransferase were analyzed using a Hitachi 7050 autoanalyzer. Hepatitis B virus surface antibody and antihepatitis C virus antibody were assessed with radioimmunoassay and enzyme-linked immunosorbent assay.

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Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	AST, ALT, GGT, Hepatitis B virus surface antigen (HBsAg), and anti-hepatitis C virus antibody (anti-HCV).
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	200266

Domain	Metric	Rating	Comments
	Metric 22: Matrix Adjustment	N/A	No information on matrix adjustment was provided/available.

Additional Comments: A group of 251 male workers from 4 vinyl chloride monomer (VCM) manufacturing plants were included in this assessment to examine if occupational exposure to VCM and ethylene dichloride (EDC) ”resulted in increased risk of liver damage” by examining AST, ALT, and GGT levels in the blood. Increased ORs for abnormal AST (>37 IU/L) and ALT (>41 IU/L) in the mod-EDC-low-VCM group (0.17-333.7 ppm EDC, 0.18-0.34 ppm VCM), compared with the low-EDC-low-VCM group, was reported. Exposure levels were measured using area and personal sampling, but the timing and duration of the sampling events were not reported.

Overall Quality Determination Medium

Study Citation:	Dosemeci, M., Cocco, P., Chow, W.H. (1999). Gender differences in risk of renal cell carcinoma and occupational exposures to chlorinated aliphatic hydrocarbons. American Journal of Industrial Medicine 36(1):54-59.
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	renal cell carcinoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	4697224

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	The details of the study design were reported elsewhere (Chow et al. 1994, HERO ID 701514). Brief details about the setting, date, number of eligible participants, and control matching were reported. Reasons for exclusions/non-participation were described with details by Chow et al. (1994).
	Metric 2:	Attrition	High	For the details of the study design and attrition of study subjects, the study authors referred to another publication by Chow et al., 1994. Chow et al. (1994) mentioned that at the end of the personal interview, the respondents were given a self-administered food-frequency questionnaire. Of the subjects interviewed for the study, 632 patients (79% of 796 eligible patients) and 653 control subjects (79% of 707 eligible control subjects) returned the diet questionnaire. A number of subjects, whose responses were considered unreliable, were excluded from the analysis, including 48 patients and three control subjects who had seven or more skipped food items or had questionable data and 50 patients whose next-of-kin respondent was not a spouse. Also excluded were two patients with unknown smoking status, since smoking is a risk factor.
	Metric 3:	Comparison Group	Medium	The cases were pulled from the Minnesota Cancer Surveillance System. Controls were selected from the general population of Minnesota; controls age 20-64 years were selected through random digital dialing and controls age 65-85 years were collected from files through the Health Care Financing Administration. Controls were age- and gender-stratified and were of the same race. Characteristics of cases and controls were not provided in the text or a table.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	High	Occupational histories including the most recent and usual occupation and industry, job activities, started-year and ended-year, and part-time/full-time status were collected. Occupations and industries were coded according to the standard occupational classification (SOC) and standard industrial classification (SIC) schemes. The National Cancer Institute developed job exposure matrices (JEM) for nine individual chlorinated aliphatic hydrocarbons (CAHCs), all CAHCs-combined, and all organic solvents-combined. These JEMs were merged with assigned SOC and SIC to determine the exposure status to these chemicals for each study subject. Application of the JEM was described elsewhere (Dosemeci et al. 1994, HERO ID 632334; Gomez et al. 1994, HERO ID 702154).
	Metric 5:	Exposure Levels	Medium	Details of the application of the JEM were described elsewhere (Dosemeci et al. 1994, HERO ID 632334; Gomez et al. 1994, HERO ID 702154). Dosemeci et al. (1994) described more details about that this study assigned three levels of probability (low, medium, high) to industries and occupations for chemical exposure levels.

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Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	renal cell carcinoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	4697224

Domain	Metric		Rating	Comments
	Metric 6:	Temporality	Medium	Occupational questionnaires identified prior exposures based on reported recent and usual occupations as well as duration of employment. Outcome status was determined from registry data. The authors note that some occupational history was incomplete which may result in some uncertainty in regard to temporality.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Cases were identified as newly diagnosed and histologically confirmed renal cell carcinoma through the Minnesota Cancer Surveillance System and information about each participant was collected using a questionnaire. Validation was not specified.
	Metric 8:	Reporting Bias	Medium	A description of measured outcomes is reported and ORs were stratified by sex. Effect estimates are reported with a confidence interval. One table showed the total numbers of men and women respectively for each chemical, but numbers of cases/controls were not reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Appropriate adjustments were made in the final analysis, including age, gender, smoking, hypertension and the use of diuretics and/or anti-hypertension drugs, and BMI. Results were stratified by sex.
	Metric 10:	Covariate Characterization	Medium	Information about participants was collected using a questionnaire, and it includes potential confounders, e.g., smoking habits. Validation was not specified.
	Metric 11:	Co-exposure Counfounding	Medium	Co-exposures were identified through the job exposure matrices. Chemicals were evaluated individually and as a group.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen (case-control) was appropriate for the research question (renal cell carcinoma risk from occupational organic solvent exposure). Logistic regression models were used to estimate the relative risk and 95% CI.
	Metric 13:	Statistical Power	Low	Statistical power calculations were not provided. No significant effects were observed with 1,2-dichloroethane. The number of participated women to calculate odds ratio was inadequate to detect an effect in the participants for other chemicals or the combined risk, because it was very low.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis was brief, but is sufficient to understand precisely what has been done and to be conceptually reproducible with access to the analytic data.
	Metric 15:	Statistical Analysis	High	Model assumptions for logistic regression were met. The odds ratios were adjusted for age, smoking, hypertension status and/or use of diuretic and/or anti-hypertension drugs, and body mass index for men and women separately.

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Study Citation:	Dosemeci, M., Cocco, P., Chow, W.H. (1999). Gender differences in risk of renal cell carcinoma and occupational exposures to chlorinated aliphatic hydrocarbons. American Journal of Industrial Medicine 36(1):54-59.
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	renal cell carcinoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	4697224

Domain	Metric	Rating	Comments
Additional Comments:	A group of 438 cases (273 men and 165 women) were selected from the Minnesota Cancer Surveillance System that had been newly diagnosed with renal cell carcinoma. Controls included 687 participants (462 men and 225 women) age- and gender- stratified that were selected from either the general population of Minnesota (age 20-64 years) or from the Health Care Financing Administration files (age 65-85). No significant increase in the risk of renal cell carcinoma was observed with exposure to 1,2-dichloroethane among men or women separately, or for all participants exposed.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Dosemeci, M., Cocco, P., Chow, W.H. (1999). Gender differences in risk of renal cell carcinoma and occupational exposures to chlorinated aliphatic hydrocarbons. American Journal of Industrial Medicine 36(1):54-59.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	renal cell carcinoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	4697224

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	The details of the study design were reported elsewhere (Chow et al. 1994, HERO ID 701514). Brief details about the setting, date, number of eligible participants, and control matching were reported. Reasons for exclusions/non-participation were described with details by Chow et al. (1994).
	Metric 2:	Attrition	Medium	For the details of the study design and attrition of study subjects, the study authors referred to another publication by Chow et al., 1994. Chow et al. (1994) mentioned that at the end of the personal interview, the respondents were given a self-administered food-frequency questionnaire. Of the subjects interviewed for the study, 632 patients (79% of 796 eligible patients) and 653 control subjects (79% of 707 eligible control subjects) returned the diet questionnaire. A number of subjects, whose responses were considered unreliable, were excluded from the analysis, including 48 patients and three control subjects who had seven or more skipped food items or had questionable data and 50 patients whose next-of-kin respondent was not a spouse. Also excluded were two patients with unknown smoking status, since smoking is a risk factor.
	Metric 3:	Comparison Group	Medium	The cases were pulled from the Minnesota Cancer Surveillance System. Controls were selected from the general population of Minnesota; controls age 20-64 years were selected through random digital dialing and controls age 65-85 years were collected from files through the Health Care Financing Administration. Controls were age- and gender-stratified and were of the same race. Characteristics of cases and controls were not provided in the text or a table.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	High	Occupational histories including the most recent and usual occupation and industry, job activities, started-year and ended-year, and part-time/full-time status were collected. Occupations and industries were coded according to the standard occupational classification (SOC) and standard industrial classification (SIC) schemes. The National Cancer Institute developed job exposure matrices (JEM) for nine individual chlorinated aliphatic hydrocarbons (CAHCs), all CAHCs-combined, and all organic solvents-combined. These JEMs were merged with assigned SOC and SIC to determine the exposure status to these chemicals for each study subject. Application of the JEM was described elsewhere (Dosemeci et al. 1994, HERO ID 632334; Gomez et al. 1994, HERO ID 702154).
	Metric 5:	Exposure Levels	Medium	Details of the application of the JEM were described elsewhere (Dosemeci et al. 1994, HERO ID 632334; Gomez et al. 1994, HERO ID 702154). Dosemeci et al. (1994) described more details about that this study assigned three levels of probability (low, medium, high) to industries and occupations for chemical exposure levels.

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Linked HERO ID(s):	No linked references.
HERO ID:	4697224

Domain	Metric		Rating	Comments
	Metric 6:	Temporality	Medium	Occupational questionnaires identified prior exposures based on reported recent and usual occupations as well as duration of employment. Outcome status was determined from registry data. The authors note that some occupational history was incomplete which may result in some uncertainty in regard to temporality.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Cases were identified as newly diagnosed and histologically confirmed renal cell carcinoma through the Minnesota Cancer Surveillance System and information about each participant was collected using a questionnaire. Validation was not specified.
	Metric 8:	Reporting Bias	Medium	A description of measured outcomes is reported and ORs were stratified by sex. Effect estimates are reported with a confidence interval. One table showed the total numbers of men and women respectively for each chemical, but numbers of cases/controls were not reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Appropriate adjustments were made in the final analysis, including age, gender, smoking, hypertension and the use of diuretics and/or anti-hypertension drugs, and BMI. Results were stratified by sex.
	Metric 10:	Covariate Characterization	Medium	Information about participants was collected using a questionnaire, and it includes potential confounders, e.g., smoking habits. Validation was not specified.
	Metric 11:	Co-exposure Counfounding	Medium	Co-exposures were identified through the job exposure matrices. Chemicals were evaluated individually and as a group.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen (case-control) was appropriate for the research question (renal cell carcinoma risk from occupational organic solvent exposure). Logistic regression models were used to estimate the relative risk and 95% CI.
	Metric 13:	Statistical Power	Low	Statistical power calculations were not provided. No significant effects were observed with 1,2-dichloroethane. The number of participated women to calculate odds ratio was inadequate to detect an effect in the participants for other chemicals or the combined risk, because it was very low.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis was brief, but is sufficient to understand precisely what has been done and to be conceptually reproducible with access to the analytic data.
	Metric 15:	Statistical Analysis	High	Model assumptions for logistic regression were met. The odds ratios were adjusted for age, smoking, hypertension status and/or use of diuretic and/or anti-hypertension drugs, and body mass index for men and women separately.

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Domain	Metric	Rating	Comments
Additional Comments:	A group of 438 cases (273 men and 165 women) were selected from the Minnesota Cancer Surveillance System that had been newly diagnosed with renal cell carcinoma. Controls included 687 participants (462 men and 225 women) age- and gender- stratified that were selected from either the general population of Minnesota (age 20-64 years) or from the Health Care Financing Administration files (age 65-85). No significant increase in the risk of renal cell carcinoma was observed with exposure to 1,2-dichloroethane among men or women separately, or for all participants exposed.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Garcia, E., Hurley, S., Nelson, D.O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health: A Global Access Science Source 14(1):14.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	breast cancer in females
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	3014082

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	A total of 112,378 women were included in this study out of 133,479 eligible female participants from the California Teacher Study cohort. A full description of the cohort is provided in Bernstein et al. 2002 (HERO ID 808446). Reasons for exclusion were provided. The reported information indicates that participant selection in or out of the study and participation was not likely to be biased.
	Metric 2:	Attrition	High	112,378/133,479 participants were included in the study. Exclusions were for the purpose of the study and analysis. Exclusion criteria were documented. Included participants had completed questionnaires. The California Cancer Registry is estimated to be 99% complete.
	Metric 3:	Comparison Group	Medium	There is only indirect evidence that groups are similar. Participants were recruited from the same eligible population with the same method of ascertainment. Comparisons were provided for participants with and without breast cancer. Characteristics between these two groups were generally similar. 5 Quintiles of exposure were used, and Q2-5 were compared with Q1.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	High	The Assessment System for Population Exposure Nationwide and the Human Exposure Model are used as part of the National-Scale Air Toxics Assessment produced by the EPA and was used to estimate ambient HAP concentrations for geographic locations. Methods are described online through the US EPA Assessment Methods.
	Metric 5:	Exposure Levels	Medium	The distribution of the NATA annual ambient concentration for each compound was plotted in Figure 1 using a box plot, and 5 Quintiles were used in the analyses.
	Metric 6:	Temporality	Medium	The follow-up period was from 1995-2011, and the NATA estimates were made in 2002 because it was approximately half way between the start and end of the follow-up period. However, it is unclear whether exposures fall within relevant exposure windows for the outcome of interest.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Annual linkage between the CTS cohort and the California Cancer Registry (CCR) was used to identify cases of invasive breast cancer. The CCR is estimated to be 99% complete. The case of invasive breast cancer was defined by ICD codes.

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Study Citation:	Garcia, E., Hurley, S., Nelson, D.O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health: A Global Access Science Source 14(1):14.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	breast cancer in females
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	3014082

Domain	Metric		Rating	Comments
	Metric 8:	Reporting Bias	Medium	A description of measured outcome is reported for adjustments by age and race, and effect estimates are reported with a 95% confidence interval. The measured outcomes using multiple comparisons were generally described in the text, but non-significant results were excluded from Table 3.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	The models were stratified by age and race. Additionally, adjustments were made for multiple comparisons among subsets of the participants (significant results reported in Table 3). Socioeconomic status (SES) of each participant was not evaluated, however, cohort SES characteristics were thought to be similar by study authors.
	Metric 10:	Covariate Characterization	Medium	Information about baseline characteristics for each participant was collected through a questionnaire. It is unknown if the questionnaire was validated.
	Metric 11:	Co-exposure Counfounding	Medium	A total of 37 compounds were identified as mammary gland carcinogens, but 13 were not included in this analysis. Thirteen compounds were excluded from the analysis due to insufficient variability (nine because they had the same value for all census tracts in the state of California; and four because they had less than 25% non-zero values). Ethylene dichloride (1,2-dichloroethane) was among the 24 compounds evaluated in this assessment, and evaluations for breast cancer were conducted for each of these 24 individual compounds.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen (prospective cohort) was appropriate for the research question (incidence of breast cancer). Cox proportional hazard models and SAS 9.3 were used in this assessment. Data analysis was described.
	Metric 13:	Statistical Power	Medium	Statistical power calculations were not provided. No significant effects were observed with ethylene dichloride (1,2-dichloroethane), however, this study utilized a large cohort, approximately 112,000 individuals. Distributions of chemicals of interest suggest there were sufficient numbers of participants in exposure subgroups.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to understand precisely what has been done and to be conceptually reproducible with access to the analytic data.
	Metric 15:	Statistical Analysis	High	The statistical models that were used were identified and described. ”No apparent violation of the underlying assumption of proportional hazards was detected”.

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Study Citation:	Garcia, E., Hurley, S., Nelson, D.O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health: A Global Access Science Source 14(1):14.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	breast cancer in females
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	3014082

Domain	Metric	Rating	Comments
Additional Comments:	A group of 112,378 female participants from the California Teacher Study cohort were assessed for their estimated exposure to ambient air pollutants, including ethylene dichloride (1,2-dichloroethane), and the incidence of invasive breast cancer. Air contaminant concentrations were estimated using the US EPA NATA and the ASPEN and HEM models. The approximate median concentration of 1,2-dichloroethane is between 1E-4 and 1E-2 (estimated from Figure 1). Exposures were categorized into 5 Quintiles, and compared against Quintile 1. No significant increase in the estimated hazard rate ratio for invasive breast cancer was observed with Quintile 2-5 exposure estimates for 1,2-dichloroethane, adjusted for age and race, when compared against Quintile 1, or when further adjusted using multiple comparisons.		

Overall Quality Determination High

* No biomarkers were identified for this evaluation.

Study Citation:	Garcia, E., Hurley, S., Nelson, D.O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health: A Global Access Science Source 14(1):14.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	breast cancer in females
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	3014082

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	A total of 112,378 women were included in this study out of 133,479 eligible female participants from the California Teacher Study cohort. A full description of the cohort is provided in Bernstein et al. 2002 (HERO ID 808446). Reasons for exclusion were provided. The reported information indicates that participant selection in or out of the study and participation was not likely to be biased.
	Metric 2:	Attrition	High	112,378/133,479 participants were included in the study. Exclusions were for the purpose of the study and analysis. Exclusion criteria were documented. Included participants had completed questionnaires. The California Cancer Registry is estimated to be 99% complete.
	Metric 3:	Comparison Group	Medium	There is only indirect evidence that groups are similar. Participants were recruited from the same eligible population with the same method of ascertainment. Comparisons were provided for participants with and without breast cancer. Characteristics between these two groups were generally similar. 5 Quintiles of exposure were used, and Q2-5 were compared with Q1.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	High	The Assessment System for Population Exposure Nationwide and the Human Exposure Model are used as part of the National-Scale Air Toxics Assessment produced by the EPA and was used to estimate ambient HAP concentrations for geographic locations. Methods are described online through the US EPA Assessment Methods.
	Metric 5:	Exposure Levels	Medium	The distribution of the NATA annual ambient concentration for each compound was plotted in Figure 1 using a box plot, and 5 Quintiles were used in the analyses.
	Metric 6:	Temporality	Medium	The follow-up period was from 1995-2011, and the NATA estimates were made in 2002 because it was approximately half way between the start and end of the follow-up period. However, it is unclear whether exposures fall within relevant exposure windows for the outcome of interest.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Annual linkage between the CTS cohort and the California Cancer Registry (CCR) was used to identify cases of invasive breast cancer. The CCR is estimated to be 99% complete. The case of invasive breast cancer was defined by ICD codes.
	Metric 8:	Reporting Bias	Medium	A description of measured outcome is reported for adjustments by age and race, and effect estimates are reported with a 95% confidence interval. The measured outcomes using multiple comparisons were generally described in the text, but non-significant results were excluded from Table 3.

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Study Citation:	Garcia, E., Hurley, S., Nelson, D.O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health: A Global Access Science Source 14(1):14.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	breast cancer in females
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	3014082

Domain	Metric		Rating	Comments
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	The models were stratified by age and race. Additionally, adjustments were made for multiple comparisons among subsets of the participants (significant results reported in Table 3). Socioeconomic status (SES) of each participant was not evaluated, however, cohort SES characteristics were thought to be similar by study authors.
	Metric 10:	Covariate Characterization	Medium	Information about baseline characteristics for each participant was collected through a questionnaire. It is unknown if the questionnaire was validated.
	Metric 11:	Co-exposure Counfounding	Medium	A total of 37 compounds were identified as mammary gland carcinogens, but 13 were not included in this analysis. Thirteen compounds were excluded from the analysis due to insufficient variability (nine because they had the same value for all census tracts in the state of California; and four because they had less than 25% non-zero values). Ethylene dichloride (1,2-dichloroethane) was among the 24 compounds evaluated in this assessment, and evaluations for breast cancer were conducted for each of these 24 individual compounds.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen (prospective cohort) was appropriate for the research question (incidence of breast cancer). Cox proportional hazard models and SAS 9.3 were used in this assessment. Data analysis was described.
	Metric 13:	Statistical Power	Medium	Statistical power calculations were not provided. No significant effects were observed with ethylene dichloride (1,2-dichloroethane), however, this study utilized a large cohort, approximately 112,000 individuals. Distributions of chemicals of interest suggest there were sufficient numbers of participants in exposure subgroups.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to understand precisely what has been done and to be conceptually reproducible with access to the analytic data.
	Metric 15:	Statistical Analysis	High	The statistical models that were used were identified and described. ”No apparent violation of the underlying assumption of proportional hazards was detected”.

Additional Comments: A group of 112,378 female participants from the California Teacher Study cohort were assessed for their estimated exposure to ambient air pollutants, including ethylene dichloride (1,2-dichloroethane), and the incidence of invasive breast cancer. Air contaminant concentrations were estimated using the US EPA NATA and the ASPEN and HEM models. The approximate median concentration of 1,2-dichloroethane is between 1E-4 and 1E-2 (estimated from Figure 1). Exposures were categorized into 5 Quintiles, and compared against Quintile 1. No significant increase in the estimated hazard rate ratio for invasive breast cancer was observed with Quintile 2-5 exposure estimates for 1,2-dichloroethane, adjusted for age and race, when compared against Quintile 1, or when further adjusted using multiple comparisons.

Overall Quality Determination High

* No biomarkers were identified for this evaluation.

Study Citation:	Guo, P., Yokoyama, K., Piao, F., Sakai, K., Khalequzzaman, M., Kamijima, M., Nakajima, T., Kitamura, F. (2013). Sick building syndrome by indoor air pollution in Dalian, China. International Journal of Environmental Research and Public Health 10(4):1489-1504.
Health Outcome(s):	sick building syndrome
Reported Health Effect(s):	The statistical analysis considers all subjective self-reported symptoms together (not segregated by health outcome) as a group health outcome –sick building syndrome. The study compared two conditions for each studied chemical: combined self-reported symptoms to no symptoms. Therefore, only one form 3 was completed.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1938385

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Residents of a housing estate of 3000 homes were invited to a community meeting to explain the purpose of the study and volunteers were invited to participate. It was not reported whether these volunteers were different from the overall eligible population.
	Metric 2:	Attrition	Low	Of the 70 families that agreed to participate, questionnaires were provided by 59. Reasons of uncompleted questionnaires were not fully provided, and there was no comparison between those who participated and those who did not.
	Metric 3:	Comparison Group	Low	The overall description of the analysis sample indicated a wide range of ages and lengths of stay at the current residence. Thus it is hard to know that subjects in all exposure groups were similar. In addition, the methods of selecting participants in all exposure groups were not fully reported. The numbers of male and female smokers were reported, respectively, but the smoking status and age were not controlled in the statistical analysis.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure concentrations for each home were obtained by diffusion sampling over 24 hrs in the bedroom, kitchen, and outdoors; temperature, the vertical height of samplers, and ventilation (hours windows left open) were reported. Samples were analyzed by GC/MS. The number of samples per home is unclear. The frequency of measurements for each house was not reported.
	Metric 5:	Exposure Levels	Low	The frequency of detection was not reported, so it is difficult to ascertain the actual exposure range. In addition, the reported exposure levels were median, geometric mean, and 95% CI, so they are inadequate to develop an exposure-response estimate.
	Metric 6:	Temporality	Uninformative	For 1,2-dichloroethane, the study evaluated self-reported symptoms in the past (”since they moved into their flats”) and their association with sampling conducted during the study; thus, exposure was measured after the outcome.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Low	Participants provided self-reported symptoms using a questionnaire. Study authors cited a previous study, Kamijima et al., 2005 (in Japanese, HERO ID 1598645) for further details on the questionnaire. It was not clear whether the questionnaire was validated.

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Study Citation: Guo, P., Yokoyama, K., Piao, F., Sakai, K., Khalequzzaman, M., Kamijima, M., Nakajima, T., Kitamura, F. (2013). Sick building syndrome by indoor air pollution in Dalian, China. International Journal of Environmental Research and Public Health 10(4):1489-1504.

Health Outcome(s): sick building syndrome

Reported Health Effect(s): The statistical analysis considers all subjective self-reported symptoms together (not segregated by health outcome) as a group health outcome –sick building syndrome. The study compared two conditions for each studied chemical: combined self-reported symptoms to no symptoms. Therefore, only one form 3 was completed.

Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

Linked HERO ID(s): No linked references.

HERO ID: 1938385

Domain	Metric		Rating	Comments
	Metric 8:	Reporting Bias	Low	The study only mentioned subjective symptoms in the abstract or methods. The abstract and method sections did not report the specific symptoms included in the questionnaire or whether the questionnaire was open-ended for symptoms. The questionnaire was cited to Kamijima et al. 2005 (in Japanese).
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	Comparisons were made separately by sex. The distribution of age and time spent living in residence differed greatly between those reporting symptoms and those not reporting symptoms. Smoking was indicated but not controlled for in the analysis. In short, the statistical analysis did not consider these three potential confounders, age, time spent living in residence, and smoking.
	Metric 10:	Covariate Characterization	Low	Covariates were presumably evaluated via a questionnaire that was cited to Kamijima et al. 2005 (in Japanese).
	Metric 11:	Co-exposure Counfounding	Low	The analysis did not account for other exposures. A number of other VOCs, HCHO, and NO2 were measured in the homes. The concentrations of several other VOCs and HCHO were much higher (5-30x) than 1,2-dichloroethane and may also be associated with these symptoms.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Low	The study design is best characterized as cross-sectional. Only one analysis to compare exposure concentrations between those with and without symptoms was adjusted for a confounder, sex, via stratification. Other potential confounders were not adjusted for. Study authors combine responses for symptoms reported before and during the sampling period in one statistical analysis, which may not reflect the relationship between symptoms and contaminants' exposure at each period.
	Metric 13:	Statistical Power	Medium	Statistical power was not reported. The number of participants was sufficient to detect a difference in median concentration between those with and without symptoms.
	Metric 14:	Reproducibility of Analyses	Medium	Study presents sufficient description of analysis (statistical methods) to be conceptually reproducible with access to the raw data.
	Metric 15:	Statistical Analysis	Low	Study uses a Wilcoxon's rank sum test to compare exposure concentrations in persons with and without symptoms; test for equal variance is not reported.

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Study Citation:	Guo, P., Yokoyama, K., Piao, F., Sakai, K., Khalequzzaman, M., Kamijima, M., Nakajima, T., Kitamura, F. (2013). Sick building syndrome by indoor air pollution in Dalian, China. International Journal of Environmental Research and Public Health 10(4):1489-1504.
Health Outcome(s):	sick building syndrome
Reported Health Effect(s):	The statistical analysis considers all subjective self-reported symptoms together (not segregated by health outcome) as a group health outcome –sick building syndrome. The study compared two conditions for each studied chemical: combined self-reported symptoms to no symptoms. Therefore, only one form 3 was completed.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1938385

Domain	Metric	Rating	Comments
Additional Comments:	Concentrations of VOCs (including 1,2-dichloroethane), HCHO, and NO2 were measured in the 59 homes of families that agreed to participate after being informed of the nature of the study. Participants completed questionnaires asking about symptoms since they moved into the homes and the concentrations of selected compounds were compared among men and women reporting any symptoms vs no symptoms. Concentrations of 1,2-dichloroethane in homes of people with symptoms were higher than in homes without. p-Dichlorobenzene was measured in the homes as well, but median concentration was <DL and no further analysis was made. Unacceptable due to selection bias, lack of confounding control, inadequate outcome characterization, and lack of temporality.		

Overall Quality Determination — Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Kernan, G.J., Ji, B.T., Dosemeci, M., Silverman, D.T., Balbus, J., Zahm, S.H. (1999). Occupational risk factors for pancreatic cancer: A case-control study based on death certificates from 24 U.S. states. American Journal of Industrial Medicine 36(2):260-270.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Death from pancreatic cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	194820

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	The National Cancer Institute, National Institute of Occupational Safety and Health, and the National Center for Health Statistics reviewed death certificates from 24 states to select cases from those that had died from pancreatic cancer and matched controls. Controls with cause of death related to the outcome of interest (i.e. pancreatic diseases) were excluded from the study. All key elements of the study design were reported.
	Metric 2:	Attrition	Medium	There was no direct evidence of subject loss or exclusion of subgroups from analyses. The authors provide the total number of cases and controls in the analysis. Case and control data were taken from a registry. It can be assumed that the data are complete for each subject.
	Metric 3:	Comparison Group	High	Controls were selected from the same pool of death certificates from 24 states that cases were selected from. Controls with cause of death related to the outcome of interest were eliminated. Differences in baseline characteristics were controlled for via matching, stratification, and adjustment.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure was assessed via occupation and industry data on death certificates. A job matrix was further applied to assess the likely levels of exposure. Probability and intensity of exposure were estimated across four levels for each occupation. Only employment captured on the death certificate could be considered. The exposure assessment needs exposure information before the job listed on the death certificates.
	Metric 5:	Exposure Levels	Medium	The study offers 4 levels of estimated probability and intensity of exposure (referent, low, medium, high).
	Metric 6:	Temporality	Medium	Exposure was determined by occupational and industry codes on death certificates and indicate that exposure would precede disease, however, the timing and latency period is less clear.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Causes of mortality were determined from death certificates for both cases and controls. Death certificates were drawn from death registries of participating states (n=24). Causes of death were coded using ICD-9 codes, and pancreatic cancer was identified as ICD 157.
	Metric 8:	Reporting Bias	Medium	Measured outcomes, effect estimates and confidence intervals are reported. Number of exposed cases is reported for each analysis, however the number of controls (exposed and unexposed) are not reported for analyses.

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Study Citation:	Kernan, G.J., Ji, B.T., Dosemeci, M., Silverman, D.T., Balbus, J., Zahm, S.H. (1999). Occupational risk factors for pancreatic cancer: A case-control study based on death certificates from 24 U.S. states. American Journal of Industrial Medicine 36(2):260-270.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Death from pancreatic cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	194820

Domain	Metric		Rating	Comments
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Potential confounders were accounted for in the following ways: matching (five year age group, state, race, and gender); adjustment in models (age, marital status, metropolitan, and residential status); and stratification (race and gender). Smoking was not included as a confounder.
	Metric 10:	Covariate Characterization	Medium	Data used to assess potential confounders was derived from death certificates, an adequate measure. However, no information about cigarette smoking and other lifestyle factors were available for adjustment in the analysis.
	Metric 11:	Co-exposure Counfounding	Medium	The variety of industries considered in the analysis diminishes concerns about co-exposures.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The case-control study design and statistical analysis methods were appropriate to assess the exposures/outcome of interest.
	Metric 13:	Statistical Power	Medium	This study had an adequate sample size to detect an effect (n for cases = 63,097; n for controls = 252,386).
	Metric 14:	Reproducibility of Analyses	Medium	The description of analysis was sufficient and would be reproducible.
	Metric 15:	Statistical Analysis	High	The model to calculate risk estimates was transparent.

Additional Comments: This case-control study examined the risk of death from pancreatic cancer in different occupational settings. Exposure was solely assessed using occupation/industry at time of death (reported on death certificate) and the application of a job matrix assessing likely levels of exposure for different positions. This means of estimating exposure may not fully represent a participant's exposure history. Additionally, the number of impacted participants (exposed cases) was inadequate to perform quality analyses for some exposure levels.

Overall Quality Determination High

* No biomarkers were identified for this evaluation.

Study Citation:	Kernan, G.J., Ji, B.T., Dosemeci, M., Silverman, D.T., Balbus, J., Zahm, S.H. (1999). Occupational risk factors for pancreatic cancer: A case-control study based on death certificates from 24 U.S. states. American Journal of Industrial Medicine 36(2):260-270.
Health Outcome(s):	Endocrine
Reported Health Effect(s):	Death from pancreatic cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	194820

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	The National Cancer Institute, National Institute of Occupational Safety and Health, and the National Center for Health Statistics reviewed death certificates from 24 states to select cases from those that had died from pancreatic cancer and matched controls. Controls with cause of death related to the outcome of interest (i.e. pancreatic diseases) were excluded from the study. All key elements of the study design were reported.
	Metric 2:	Attrition	Medium	There was no direct evidence of subject loss or exclusion of subgroups from analyses. The authors provide the total number of cases and controls in the analysis. Case and control data were taken from a registry. It can be assumed that the data are complete for each subject.
	Metric 3:	Comparison Group	High	Controls were selected from the same pool of death certificates from 24 states that cases were selected from. Controls with cause of death related to the outcome of interest were eliminated. Differences in baseline characteristics were controlled for via matching, stratification, and adjustment.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure was assessed via occupation and industry data on death certificates. A job matrix was further applied to assess the likely levels of exposure. Probability and intensity of exposure were estimated across four levels for each occupation. Only employment captured on the death certificate could be considered. The exposure assessment needs exposure information before the job listed on the death certificates.
	Metric 5:	Exposure Levels	Medium	The study offers 4 levels of estimated probability and intensity of exposure (referent, low, medium, high).
	Metric 6:	Temporality	Medium	Exposure was determined by occupational and industry codes on death certificates and indicate that exposure would precede disease, however, the timing and latency period is less clear.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Causes of mortality were determined from death certificates for both cases and controls. Death certificates were drawn from death registries of participating states (n=24). Causes of death were coded using ICD-9 codes, and pancreatic cancer was identified as ICD 157.
	Metric 8:	Reporting Bias	Medium	Measured outcomes, effect estimates and confidence intervals are reported. Number of exposed cases is reported for each analysis, however the number of controls (exposed and unexposed) are not reported for analyses.
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Kernan, G.J., Ji, B.T., Dosemeci, M., Silverman, D.T., Balbus, J., Zahm, S.H. (1999). Occupational risk factors for pancreatic cancer: A case-control study based on death certificates from 24 U.S. states. American Journal of Industrial Medicine 36(2):260-270.
Health Outcome(s):	Endocrine
Reported Health Effect(s):	Death from pancreatic cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	194820

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Medium	Potential confounders were accounted for in the following ways: matching (five year age group, state, race, and gender); adjustment in models (age, marital status, metropolitan, and residential status); and stratification (race and gender). Smoking was not included as a confounder.
	Metric 10:	Covariate Characterization	Medium	Data used to assess potential confounders was derived from death certificates, an adequate measure. However, no information about cigarette smoking and other lifestyle factors were available for adjustment in the analysis.
	Metric 11:	Co-exposure Counfounding	Medium	The variety of industries considered in the analysis diminishes concerns about co-exposures.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The case-control study design and statistical analysis methods were appropriate to assess the exposures/outcome of interest.
	Metric 13:	Statistical Power	Medium	This study had an adequate sample size to detect an effect (n for cases = 63,097; n for controls = 252,386).
	Metric 14:	Reproducibility of Analyses	Medium	The description of analysis was sufficient and would be reproducible.
	Metric 15:	Statistical Analysis	High	The model to calculate risk estimates was transparent.

Additional Comments: This case-control study examined the risk of death from pancreatic cancer in different occupational settings. Exposure was solely assessed using occupation/industry at time of death (reported on death certificate) and the application of a job matrix assessing likely levels of exposure for different positions. This means of estimating exposure may not fully represent a participant's exposure history. Additionally, the number of impacted participants (exposed cases) was inadequate to perform quality analyses for some exposure levels.

Overall Quality Determination High

* No biomarkers were identified for this evaluation.

Study Citation:	Niehoff, N.M., Gammon, M.D., Keil, A.P., Nichols, H.B., Engel, L.S., Sandler, D.P., White, A.J. (2019). Airborne mammary carcinogens and breast cancer risk in the Sister Study. Environment International 130:104897.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Breast cancer diagnosis (overall), tumor characteristics, and estrogen receptor positive (ER+) invasive breast cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5440630

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	Data from the Sister Study were used. The Sister Study is "a prospective cohort of 50,884 women from across the US who were ages 35–74 at enrollment (Sandler et al., 2017). Participants were recruited from 2003 to 2009 using a national advertising campaign in English and Spanish. Women were eligible for the Sister Study if they had a sister who had been diagnosed with breast cancer, but no prior breast cancer themselves."Exclusions from the study occurred for the following reasons:-breast cancer diagnosed before enrollment was complete, or did not have follow-up information (n = 163)-Residential address couldn't be geocoded (n = 1003, < 2%) - This is a small perecentage, but all of those who were excluded for this reason were from Puerto Rico, West Virginia, Missouri, or Oklahoma.Key elements of the study design are reported. There is some potential for selection bias, but based on the small percentage of those eligible who were excluded, participation was not likely to be substantially biased.
	Metric 2:	Attrition	High	Response rates in the overall Sister study remained over 91% over follow-up. Reasons for non-response were not reported, and characteristics of those lost to follow up were not reported or compared with those included, but 9% loss to follow-up is minimal.
	Metric 3:	Comparison Group	High	Differences in baseline characteristics of groups were considered as potential confounding variables.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	The EPA NATA database of census-tract level modeled air toxics data was used. The study authors note the potential for exposure misclassification: "Concentrations at the census tract level do not fully account for variation in an individual's daily activities that could lead to higher or lower exposure, and all women within a census tract are assigned the same concentration."
	Metric 5:	Exposure Levels	Medium	There were five quintiles of exposure, so there was a sufficient range and distribution of exposure.
	Metric 6:	Temporality	Medium	This is a prospective cohort study.Exposure data from 2005 were chosen because they represented the middle of the enrollment period (2003-2009).The study reported that "94% of women enrolled in 2005 or later, and thus the exposure assessment primarily predated enrollment for the majority of Sister Study participants."The six percent of women who had the potential to have the outcome before exposure was measured in 2005 are a concern. But sensitivity analyses were used to assess whether the associations changed when restricted to those who enrolled in 2005 or later.The authors note that the study is making assumptions about the relevant exposure windows - therefore the exposure window is not certain.

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Study Citation:	Niehoff, N.M., Gammon, M.D., Keil, A.P., Nichols, H.B., Engel, L.S., Sandler, D.P., White, A.J. (2019). Airborne mammary carcinogens and breast cancer risk in the Sister Study. Environment International 130:104897.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Breast cancer diagnosis (overall), tumor characteristics, and estrogen receptor positive (ER+) invasive breast cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5440630

Domain	Metric		Rating	Comments
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Women who reported a breast cancer diagnosis on the annual health updates or follow-up questionnaires were asked to provide additional diagnosis information, and to grant permission for the study to obtain medical records and pathology reports. Medical records were obtained for 81% of breast cancer diagnoses. Agreement between self-reported breast cancers and medical records was high (positive predictive value > 99%) (Sandler et al., 2017), so self-report was used when medical records were not available. Tumor characteristics (stage; histology; and estrogen receptor (ER) status) were abstracted from medical records, or self-reported.
	Metric 8:	Reporting Bias	High	A description of measured outcomes is reported. Effect estimates are reported with confidence intervals.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Covariates considered included age, race, BMI, residence type, education, and smoking status. Potential confounders were identified using DAGs and literature review. Appropriate considerations were made for potential confounders.
	Metric 10:	Covariate Characterization	Medium	”Most covariates were assessed by self-report at the baseline interview.””At baseline, women completed a computer-assisted telephone interview and written questionnaires.”Previous publications might describe whether the questionnaires were validated, but validation was not specified in this publication.
	Metric 11:	Co-exposure Counfounding	Medium	Co-exposures to other air pollutants were assessed, but at the census tract level.Multipollutant classification trees were used, which might provide useful qualitative information.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design (large prospective cohort) and analysis method (Cox proportional hazard single and multi-pollutant models accounting for potential confounders) were appropriate to assess the association between exposure and disease.
	Metric 13:	Statistical Power	Medium	The study had an adequate sample size (1975 cancer cases) and follow-up time (mean=8.4 years).
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to be conceptually reproducible.

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Study Citation:	Niehoff, N.M., Gammon, M.D., Keil, A.P., Nichols, H.B., Engel, L.S., Sandler, D.P., White, A.J. (2019). Airborne mammary carcinogens and breast cancer risk in the Sister Study. Environment International 130:104897.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Breast cancer diagnosis (overall), tumor characteristics, and estrogen receptor positive (ER+) invasive breast cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5440630

Domain	Metric	Rating	Comments
	Metric 15: Statistical Analysis	High	Hazard ratios and 95% confidence intervals (CIs) are reported "comparing index categories of exposure to exposures below the first quintile using Cox proportional hazards regression, with age as the time scale." The method of calculating the hazard ratios is transparent. The authors reported that "the proportional hazards assumption was evaluated by conducting a Wald test for an interaction between the continuous form of the air toxic measure and time." Censoring times and times at-risk are described.

Additional Comments: This was a well-conducted study of a large prospective cohort, but the measurement of exposure at the census-tract rather than the individual level is a limitation.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Sobel, W., Bond, G.G., Skowronski, B.J., Brownson, P.J., Cook, R.R. (1987). A soft tissue sarcoma case control study in a large multi-chemical manufacturing facility. Chemosphere 16(8-9):2095-2099.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	soft-tissue sarcoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1357737

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	From a pool of > 37,000 subjects who worked at least 1 year at chemical company between January 1940-December 1979, the study identified 14 people who died due to soft-cell sarcoma (via death certificate, medical records, or histopathology report). Referents were matched 9:1 with cases (126 matched controls).
	Metric 2:	Attrition	High	There was minimal subject exclusion from the analysis sample; one case could not be matched to controls and was excluded from analysis.
	Metric 3:	Comparison Group	High	Cases and controls were recruited from the same eligible population within the same time frame and matched on sex, race, year of birth and year of hire. Both cases and controls had to have worked ≥1 yr at the plant during the study period.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Work histories for cases and referents were coded to determine an individual's potential exposure to chemical of interest and reviewed by an industrial hygienist blinded to case status.
	Metric 5:	Exposure Levels	Low	Exposure was considered dichotomous, ever exposed or never exposed. There is no quantitative information on exposure levels or range of exposures.
	Metric 6:	Temporality	Low	Temporality of exposure and outcome is established. It is unclear if the interval between exposure and outcome is sufficient for soft tissue sarcoma outcomes.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	The soft-tissue sarcoma outcome was assessed by information provided by death certificates, medical records, and histopathology reports, but study authors did not report the proportions determined by each method.
	Metric 8:	Reporting Bias	High	All outcomes outlined were reported. Authors reported the number of cases and controls in the table. Maximum likelihood estimate ORs with respective 95 % confidence intervals were reported.
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Sobel, W., Bond, G.G., Skowronski, B.J., Brownson, P.J., Cook, R.R. (1987). A soft tissue sarcoma case control study in a large multi-chemical manufacturing facility. Chemosphere 16(8-9):2095-2099.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	soft-tissue sarcoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1357737

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Low	Controls were matched with cases on age, sex, year of hire and survival information. There is indirect evidence that the considerations were made to identify potential confounders through evaluation of medical records of cases and controls (various heritable syndromes, family history of cancer, history of lymphedema, steroids, throrotrast, foreign body implants, chronic extensive scarring, radiation therapy, and immunological defects). Identified confounders between cases and controls were not reported and it is unclear if adjustments for these confounders were included in the final analyses.
	Metric 10:	Covariate Characterization	High	Potential covariates were assessed through evaluation of work histories and medical records.
	Metric 11:	Co-exposure Counfounding	Low	The study documented 13 chemicals, known to be associated with soft-tissue sarcoma (according to NTP, 1983) that were used at the manufacturing facility at some point since 1940. The authors note that some individuals were exposed to multiple chemicals during their employment history and were counted multiple times in the analysis for different chemical exposures. Co-exposures to chemicals to not appear to be adjusted for in analysis.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Low	The study design was adequate to assess the association between exposure and the outcome of interest (soft-tissue sarcoma). The study authors noted they used programs developed by Rothman and Boice to calculate odds ratios with CI intervals; the statistical methods are not further described. The page containing the Rothman and Boice reference appears to be missing from the PDF (or the citation is missing).
	Metric 13:	Statistical Power	Low	Statistical power was not calculated. For 1,2-dichloroethane, there was one case and 6 controls included in the analysis, which was not adequate to detect and effect.
	Metric 14:	Reproducibility of Analyses	Low	The study calculated odd ratios, and 95% CIs were calculated using point estimates and chi from hypothesis testing. The study authors noted they used programs developed by Rothman and Boice to calculate odds ratios with 95% CIs; the statistical methods are not further described and there was no reference for the programs cited.
	Metric 15:	Statistical Analysis	Low	A description of analyses/assumptions was not reported.

Additional Comments: A case-control study of workers at a chemical production facility who worked at least 1 year between January 1940-December 1979 (n=37,000) investigated the incidence of deaths due to soft-tissue sarcoma. The study identified 14 people who died due to soft-tissue sarcoma (through death certificate, medical records, or histopathology reports). Cases were matched to controls based on sex, race, year of birth and year of hire. 13 chemicals, including 1,2-dichloroethane, associated with soft-tissue sarcoma were used at the facility; it does not appear that co-exposures were adjusted for in the analysis. Odds ratios and corresponding CIs were calculated. No significant association was found between exposure to 1,2-DCE and soft-tissue sarcoma.

Overall Quality Determination Medium

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Study Citation:	Sobel, W., Bond, G.G., Skowronski, B.J., Brownson, P.J., Cook, R.R. (1987). A soft tissue sarcoma case control study in a large multi-chemical manufacturing facility. Chemosphere 16(8-9):2095-2099.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	soft-tissue sarcoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1357737

Domain	Metric	Rating	Comments

* No biomarkers were identified for this evaluation.

Study Citation:	Sobel, W., Bond, G.G., Skowronski, B.J., Brownson, P.J., Cook, R.R. (1987). A soft tissue sarcoma case control study in a large multi-chemical manufacturing facility. Chemosphere 16(8-9):2095-2099.
Health Outcome(s):	Skin and Connective Tissue
Reported Health Effect(s):	soft-tissue sarcoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1357737

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	From a pool of > 37,000 subjects who worked at least 1 year at chemical company between January 1940-December 1979, the study identified 14 people who died due to soft-cell sarcoma (via death certificate, medical records, or histopathology report). Referents were matched 9:1 with cases (126 matched controls).
	Metric 2:	Attrition	High	There was minimal subject exclusion from the analysis sample; one case could not be matched to controls and was excluded from analysis.
	Metric 3:	Comparison Group	High	Cases and controls were recruited from the same eligible population within the same time frame and matched on sex, race, year of birth and year of hire. Both cases and controls had to have worked ≥1 yr at the plant during the study period.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Work histories for cases and referents were coded to determine an individual's potential exposure to chemical of interest and reviewed by an industrial hygienist blinded to case status.
	Metric 5:	Exposure Levels	Low	Exposure was considered dichotomous, ever exposed or never exposed. There is no quantitative information on exposure levels or range of exposures.
	Metric 6:	Temporality	Low	Temporality of exposure and outcome is established. It is unclear if the interval between exposure and outcome is sufficient for soft tissue sarcoma outcomes.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	The soft-tissue sarcoma outcome was assessed by information provided by death certificates, medical records, and histopathology reports, but study authors did not report the proportions determined by each method.
	Metric 8:	Reporting Bias	High	All outcomes outlined were reported. Authors reported the number of cases and controls in the table. Maximum likelihood estimate ORs with respective confidence intervals were reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	Controls were matched with cases on age, sex, year of hire and survival information. There is indirect evidence that that considerations were made to identify potential confounders through evaluation of medical records of cases and controls (various heritable syndromes, family history of cancer, history of lymphedema, steroids, throrotrast, foreign body implants, chronic extensive scarring, radiation therapy, and immunological defects). Identified confounders between cases and controls were not reported and it is unclear if adjustments for these confounders were included in the final analyses.

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Study Citation:	Sobel, W., Bond, G.G., Skowronski, B.J., Brownson, P.J., Cook, R.R. (1987). A soft tissue sarcoma case control study in a large multi-chemical manufacturing facility. Chemosphere 16(8-9):2095-2099.
Health Outcome(s):	Skin and Connective Tissue
Reported Health Effect(s):	soft-tissue sarcoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1357737

Domain	Metric		Rating	Comments
	Metric 10:	Covariate Characterization	High	Potential covariates were assessed through evaluation of work histories and medical records.
	Metric 11:	Co-exposure Counfounding	Low	The study documented 13 chemicals, known to be associated with soft-tissue sarcoma (according to NTP, 1983) that were used at the manufacturing facility at some point since 1940. The authors note that some individuals were exposed to multiple chemicals during their employment history and were counted multiple times in the analysis for different chemical exposures. Co-exposures to chemicals to not appear to be adjusted for in analysis.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Low	The study design was adequate to assess the association between exposure and the outcome of interest (soft-tissue sarcoma). The study authors noted they used programs developed by Rothman and Boice to calculate odds ratios with (95% CIs; the statistical methods are not further described. The page containing the Rothman and Boice reference appears to be missing from the PDF (or the citation is missing).
	Metric 13:	Statistical Power	Low	Statistical power was not calculated. For 1,2-dichloroethane, there was one case and 6 controls included in the analysis, which was not adequate to detect and effect.
	Metric 14:	Reproducibility of Analyses	Low	The study calculated odd ratios, and 95% CIs were calculated using point estimates and chi from hypothesis testing. The study authors noted they used programs developed by Rothman and Boice to calculate odds ratios with CI intervals; the statistical methods are not further described and there was no reference for the programs cited.
	Metric 15:	Statistical Analysis	Low	A description of analyses/assumptions was not reported.

Additional Comments: A case-control study of workers at a chemical production facility who worked at least 1 year between January 1940-December 1979 (n=37,000) investigated the incidence of deaths due to soft-tissue sarcoma. The study identified 14 people who died due to soft-tissue sarcoma (through death certificate, medical records, or histopathology reports). Cases were matched to controls based on sex, race, year of birth and year of hire. 13 chemicals, including 1,2-dichloroethane, associated with soft-tissue sarcoma were used at the facility; it does not appear that co-exposures were adjusted for in the analysis. Odds ratios and corresponding CIs were calculated. No significant association was found between exposure to 1,2-DCE and soft-tissue sarcoma.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Teta, M. J., Ott, M. G., Schnatter, A. R. (1991). An update of mortality due to brain neoplasms and other causes among employees of a petrochemical facility. Journal of Occupational Medicine 33(1):45-51.
Health Outcome(s):	Mortality
Reported Health Effect(s):	all cause mortality, gastrointestinal cancer mortality, respiratory system cancer mortality, kidney and other urinary organ cancer mortality, skin cancer mortality, brain cancer mortality, lymphatic and hematopoietic tissue cancer mortality, benign neoplasm mortality, heart disease mortality, and liver cirrhosis mortality.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200633, 1629047
HERO ID:	200633

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	The facility was described in some detail. All male employees working for one day or more between 1941 and 1983 were included. There may be some healthy worker effect in this population.
	Metric 2:	Attrition	High	Study authors reported that vital status was complete for 99% of the population, and death certificates were obtained for 99% of decedents.
	Metric 3:	Comparison Group	High	SMRs were calculated using age-, race-, and calendar year-specific mortality rates of males in the United States. All included employees were male.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	All employees were treated as exposed. Table 4 indicates that relatively few employees were employed in areas designated as 1,2-DCA work areas. There is potential for substantial exposure misclassification.
	Metric 5:	Exposure Levels	Low	All employed individuals were categorized as exposed, and the reference population was described as unexposed. This represents two levels of exposure. The distribution of exposure within the employed population is unclear.
	Metric 6:	Temporality	Medium	Employees were followed from 1950 (or date of first hire) through 1983. The relevant timing of exposure is not entirely clear; however, this represents a sufficiently long period of follow-up.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Mortality was tracked using company records, Social Security Administration records, and the National Death Index. Specific ICD codes and use of a nosologist were not described, but there was no evidence to suggest the method had poor validity.
	Metric 8:	Reporting Bias	High	SMRs were provided with confidence intervals in addition to observed and expected cases. The authors state they did not carry out regional specific SMRs due to the higher prevalence of neoplasms in the surrounding area.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	SMRs were restricted to males. Rates were age-, race-, and calendar period-specific. No consideration was made for smoking.
	Metric 10:	Covariate Characterization	Medium	Demographic information was obtained from employment records. This was not a validated method, but there was no evidence to suggest it was an invalid method.

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Study Citation:	Teta, M. J., Ott, M. G., Schnatter, A. R. (1991). An update of mortality due to brain neoplasms and other causes among employees of a petrochemical facility. Journal of Occupational Medicine 33(1):45-51.
Health Outcome(s):	Mortality
Reported Health Effect(s):	all cause mortality, gastrointestinal cancer mortality, respiratory system cancer mortality, kidney and other urinary organ cancer mortality, skin cancer mortality, brain cancer mortality, lymphatic and hematopoietic tissue cancer mortality, benign neoplasm mortality, heart disease mortality, and liver cirrhosis mortality.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200633, 1629047
HERO ID:	200633

Domain	Metric		Rating	Comments
	Metric 11:	Co-exposure Counfounding	Low	Several other occupational exposures linked to cancer mortality were present, including vinyl chloride, butanol, and other petrochemicals.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	This study design was appropriate for the research question. Authors utilized retrospective occupational cohort data to determine standardized mortality rates for cancer-specific mortalities.
	Metric 13:	Statistical Power	Medium	While power was not calculated, there were over 1350 deaths from 7849 employees which was adequate to detect robust effect estimates.
	Metric 14:	Reproducibility of Analyses	Low	Most details were provided; however, ICD codes used to determine and group cancer mortality diagnoses were not provided.
	Metric 15:	Statistical Analysis	High	No issues identified.

Additional Comments: This study utilized an occupational cohort to retrospectively evaluate elevated rates of cancer mortality among petrochemical plant workers. There were numerous potentially hazardous chemicals mentioned in the plant description which may lead to co-exposure. Additionally, it appears that only a moderate portion of workers may have been exposed to 1,2-DCA or worked in 1,2-DCA areas which may lead to some exposure misclassification and limit the study's ability to inform hazard on 1,2-DCA.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Cases in this case-control study were former Union Carbide Corporation (UCC) chemical plant employees in Texas City, Texas. Cases were identified through death certificate searches and tumor registries, and may have included individuals formerly employed at UCC whose cause of death was unknown to the company. Additionally, control deaths were stated to be pulled from corporate employee benefits department and through locally published obituary notices routinely screened by the medical department - it is possible to assume that cases were identified in a similar manner. The study identified cases of brain tumors by searching death certificates primarily, although tumor registries throughout the state of Texas were also searched. The study clarifies that it is possible that some cases were not found if they survived or died due to another cause - while this is likely to have impacted selection, there is no evidence that this would be differential by exposure status. Overall, there is limited information on the source population of workers from which cases were identified.
	Metric 2:	Attrition	Medium	Attrition is not discussed in the study, and outcome data appear to be complete. There was a large proportion of missing exposure data (roughly 50%) due to workers being employed in roles such as maintenance, where exposure to any chemical is possible but unknown. Analyses were run separately where these ”unknown” individuals were a) treated as exposed, b) treated as unexposed, or c) treated as unknown and thus excluded. The study only presents results for when these individuals were excluded but specifies that the first scenario resulted in increased exposure estimates for controls relative to cases.

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Study Citation:	Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
	Metric 3:	Comparison Group	Medium	The study identifies two series of control groups, selected from all former Union Carbide Corporation (UCC) employees. However, the total number of employees is not stated. Only those who were deceased were used as controls since they had known causes of death and could thus be verified as non-brain tumors. One group of controls excluded employees whose cause of death was due to any malignant neoplasm to allow for the possibility that a general chemical carcinogen may have been associated with cancers of other sites. The other group of controls included deaths from all causes; this included malignant neoplasms other than brain tumors. Both control groups had 80 male employees randomly selected from 450 deceased employees known to the company in June 1979. Control deaths were stated to be pulled from corporate employee benefits department and through locally published obituary notices routinely screened by the medical department - it is possible to assume that cases were identified in a similar manner. The study reports that cases were slightly more likely to have been employed for less than 10 years than controls - the study attributes this in part to the fact that employees whose deaths were known to the company were more likely to have worked for longer - regardless the mean number of years employed was similar between cases and controls. However, cases were more likely to have been terminated from their job for reasons other than death, disability, or retirement (quitting, being fired, etc.), were generally younger at hire, and were less likely to survive to their 70th birthday. None of these factors are controlled for in statistical analyses - however, since controls and cases were pulled from the same population, there is indirect evidence that the groups were similar.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was determined based on official employment records. Records included job title and department assignment codes for each employment from date of hire to date of termination. For each unique department code, UCC and NIOSH industrial hygienists identified principal chemicals used or produced at any time in the history of the plant and correlated those with individual departments. This assessment was not performed on a year-by-year basis due to concerns for recall bias for longer-term employees where less detailed records were kept. An employee was categorized as ”exposed” to 1,2-dichloroethane if they ever worked in a department associated with that chemical. An ”unknown” exposure group was also created to account for employees who had only worked in departments for which no specific chemical could be identified.
	Metric 5:	Exposure Levels	Low	The study does not report any quantitative information and only splits exposure into ”exposed”, ”unexposed”, and ”unknown”.
	Metric 6:	Temporality	High	In this study exposure is confirmed to occur before the outcome is measured. The study reports latency periods, with subjects dichotomized into less than 15 years of latency or more than 15 years of latency. The majority of cases and controls had a latency of greater than 15 years, which is sufficiently long for brain tumors.

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Study Citation:	Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Cases were identified through death certificate searches and partially through tumor registries in the state of Texas. Case validation was performed by NIOSH, and 5 different levels of confirmation were reported: 1) tissue specimen interpreted by the Armed Forces Institute of Pathology; 2) autopsy report; 3) histopathology report; 4) clinical diagnosis from hospital record; 5) dearth certificate diagnosis. Codes 1-3 were considered to be ”confirmed” cases of brain tumors, while 4-5 were considered unconfirmed. 5/21 cases were only evaluated using ”unconfirmed methods”, meaning there is likely a high amount of accuracy in roughly 75% of cases. While no case validation is reported for controls, the study specifies that only controls who had died and thus could be confirmed to be non-brain tumors were included.
	Metric 8:	Reporting Bias	Medium	All primary and secondary outcomes that are outlined in the methods are reported in the results. However, the only statistical outcome of their analysis were unadjusted p-values that were not reported and were just described qualitatively.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	The only statistical analysis performed were Mantel-Haenszel chi-squared tests, which did not allow for confounder adjustment. The study does not present a distribution of potential confounders by exposure status but by case/control status. Several variables, such as reason for termination, age at hire, and age at death were significantly different between cases and controls and were not accounted for in statistical modeling. The study explains that these differences are not likely to have any epidemiologic significance and appear to be relatively small differences.
	Metric 10:	Covariate Characterization	Medium	While the study does not explain where they obtained covariate information, it is reasonable to assume that they gathered the information from company records.
	Metric 11:	Co-exposure Counfounding	Low	The study assesses a wide range of other potential occupational co-exposures. While these co-exposures are not adjusted for in any statistical models, effect estimates are presented separately for benzene, diethyl sulfate, ethylene oxide, and vinyl chloride. The distribution of co-exposures across cases and controls is demonstrated to be mostly balanced by comparing proportions of exposed/unexposed between cases and controls. The only notable instance of imbalance is for benzene, where 11.1% of cases were exposed whereas 37.9% of all controls and 19.2% of non-neoplasm related controls were exposed.
Domain 5: Analysis				

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Study Citation:	Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	The study chose a case-control design, which was appropriate to study the rare disease of brain tumors and its association with occupational exposures. The only statistical analysis conducted is a Mantzel-Haenszel chi-squared test, but there is no reason to suggest that this would be inappropriate.
	Metric 13:	Statistical Power	Medium	The study does not calculate statistical power, but the number of cases (n=21) and controls (n=80 in each analysis) is likely sufficient to detect an effect.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to understand what was done and could be reproduced given access to the analytic data.
	Metric 15:	Statistical Analysis	High	The only statistical analysis conducted is a Mantel-Haenszel chi-squared test, and all assumptions were met. The statistical process is transparent.

Additional Comments: This case-control study pulled deceased former employees of the Union Carbide Corporation in Texas City, Texas. The study examined dichotomous exposure to a wide range of occupational exposures, including 1,2-dichloroethane, in relation to brain tumor cases. There is no quantitative estimate of exposure. The only statistical analysis in the study is a Mantel-Haenszel chi-squared test statistic and no statistically significant differences in exposure between cases and controls were observed. The fact that there are no effect estimates, no adjustment for confounders, and no quantitative exposure estimates limits the usefulness of this paper.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Cases in this case-control study were former Union Carbide Corporation (UCC) chemical plant employees in Texas City, Texas. Cases were identified through death certificate searches and tumor registries, and may have included individuals formerly employed at UCC whose cause of death was unknown to the company. Additionally, control deaths were stated to be pulled from corporate employee benefits department and through locally published obituary notices routinely screened by the medical department - it is possible to assume that cases were identified in a similar manner. The study identified cases of brain tumors by searching death certificates primarily, although tumor registries throughout the state of Texas were also searched. The study clarifies that it is possible that some cases were not found if they survived or died due to another cause - while this is likely to have impacted selection, there is no evidence that this would be differential by exposure status. Overall, there is limited information on the source population of workers from which cases were identified.
	Metric 2:	Attrition	Medium	Attrition is not discussed in the study, and outcome data appear to be complete. There was a large proportion of missing exposure data (roughly 50%) due to workers being employed in roles such as maintenance, where exposure to any chemical is possible but unknown. Analyses were run separately where these ”unknown” individuals were a) treated as exposed, b) treated as unexposed, or c) treated as unknown and thus excluded. The study only presents results for when these individuals were excluded but specifies that the first scenario resulted in increased exposure estimates for controls relative to cases.

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Study Citation:	Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
	Metric 3:	Comparison Group	Medium	The study identifies two series of control groups, selected from all former Union Carbide Corporation (UCC) employees. However, the total number of employees is not stated. Only those who were deceased were used as controls since they had known causes of death and could thus be verified as non-brain tumors. One group of controls excluded employees whose cause of death was due to any malignant neoplasm to allow for the possibility that a general chemical carcinogen may have been associated with cancers of other sites. The other group of controls included deaths from all causes; this included malignant neoplasms other than brain tumors. Both control groups had 80 male employees randomly selected from 450 deceased employees known to the company in June 1979. Control deaths were stated to be pulled from corporate employee benefits department and through locally published obituary notices routinely screened by the medical department - it is possible to assume that cases were identified in a similar manner. The study reports that cases were slightly more likely to have been employed for less than 10 years than controls - the study attributes this in part to the fact that employees whose deaths were known to the company were more likely to have worked for longer - regardless the mean number of years employed was similar between cases and controls. However, cases were more likely to have been terminated from their job for reasons other than death, disability, or retirement (quitting, being fired, etc.), were generally younger at hire, and were less likely to survive to their 70th birthday. None of these factors are controlled for in statistical analyses - however, since controls and cases were pulled from the same population, there is indirect evidence that the groups were similar.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was determined based on official employment records. Records included job title and department assignment codes for each employment from date of hire to date of termination. For each unique department code, UCC and NIOSH industrial hygienists identified principal chemicals used or produced at any time in the history of the plant and correlated those with individual departments. This assessment was not performed on a year-by-year basis due to concerns for recall bias for longer-term employees where less detailed records were kept. An employee was categorized as ”exposed” to 1,2-dichloroethane if they ever worked in a department associated with that chemical. An ”unknown” exposure group was also created to account for employees who had only worked in departments for which no specific chemical could be identified.
	Metric 5:	Exposure Levels	Low	The study does not report any quantitative information and only splits exposure into ”exposed”, ”unexposed”, and ”unknown”.
	Metric 6:	Temporality	High	In this study exposure is confirmed to occur before the outcome is measured. The study reports latency periods, with subjects dichotomized into less than 15 years of latency or more than 15 years of latency. The majority of cases and controls had a latency of greater than 15 years, which is sufficiently long for brain tumors.

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Study Citation:	Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Cases were identified through death certificate searches and partially through tumor registries in the state of Texas. Case validation was performed by NIOSH, and 5 different levels of confirmation were reported: 1) tissue specimen interpreted by the Armed Forces Institute of Pathology; 2) autopsy report; 3) histopathology report; 4) clinical diagnosis from hospital record; 5) dearth certificate diagnosis. Codes 1-3 were considered to be ”confirmed” cases of brain tumors, while 4-5 were considered unconfirmed. 5/21 cases were only evaluated using ”unconfirmed methods”, meaning there is likely a high amount of accuracy in roughly 75% of cases. While no case validation is reported for controls, the study specifies that only controls who had died and thus could be confirmed to be non-brain tumors were included.
	Metric 8:	Reporting Bias	Medium	All primary and secondary outcomes that are outlined in the methods are reported in the results. However, the only statistical outcome of their analysis were unadjusted p-values that were not reported and were just described qualitatively.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	The only statistical analysis performed were Mantel-Haenszel chi-squared tests, which did not allow for confounder adjustment. The study does not present a distribution of potential confounders by exposure status but by case/control status. Several variables, such as reason for termination, age at hire, and age at death were significantly different between cases and controls and were not accounted for in statistical modeling. The study explains that these differences are not likely to have any epidemiologic significance and appear to be relatively small differences.
	Metric 10:	Covariate Characterization	Medium	While the study does not explain where they obtained covariate information, it is reasonable to assume that they gathered the information from company records.
	Metric 11:	Co-exposure Counfounding	Low	The study assesses a wide range of other potential occupational co-exposures. While these co-exposures are not adjusted for in any statistical models, effect estimates are presented separately for benzene, diethyl sulfate, ethylene oxide, and vinyl chloride. The distribution of co-exposures across cases and controls is demonstrated to be mostly balanced by comparing proportions of exposed/unexposed between cases and controls. The only notable instance of imbalance is for benzene, where 11.1% of cases were exposed whereas 37.9% of all controls and 19.2% of non-neoplasm related controls were exposed.
Domain 5: Analysis				

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Study Citation:	Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	The study chose a case-control design, which was appropriate to study the rare disease of brain tumors and its association with occupational exposures. The only statistical analysis conducted is a Mantzel-Haenszel chi-squared test, but there is no reason to suggest that this would be inappropriate.
	Metric 13:	Statistical Power	Medium	The study does not calculate statistical power, but the number of cases (n=21) and controls (n=80 in each analysis) is likely sufficient to detect an effect.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to understand what was done and could be reproduced given access to the analytic data.
	Metric 15:	Statistical Analysis	High	The only statistical analysis conducted is a Mantel-Haenszel chi-squared test, and all assumptions were met. The statistical process is transparent.

Additional Comments: This case-control study pulled deceased former employees of the Union Carbide Corporation in Texas City, Texas. The study examined dichotomous exposure to a wide range of occupational exposures, including 1,2-dichloroethane, in relation to brain tumor cases. There is no quantitative estimate of exposure. The only statistical analysis in the study is a Mantel-Haenszel chi-squared test statistic and no statistically significant differences in exposure between cases and controls were observed. The fact that there are no effect estimates, no adjustment for confounders, and no quantitative exposure estimates limits the usefulness of this paper.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	Urinary system cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	Urinary system cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	Urinary system cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Immune/Hematological
Reported Health Effect(s):	Lymphatic and hematopoietic tissue cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Health Outcome(s):	Immune/Hematological
Reported Health Effect(s):	Lymphatic and hematopoietic tissue cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Health Outcome(s):	Immune/Hematological
Reported Health Effect(s):	Lymphatic and hematopoietic tissue cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

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Health Outcome(s):	Other cancers (not specified)
Reported Health Effect(s):	Other cancers (not specified)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
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Domain 3: Outcome Assessment				

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Health Outcome(s):	Other cancers (not specified)
Reported Health Effect(s):	Other cancers (not specified)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
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	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
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	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Other cancers (not specified)
Reported Health Effect(s):	Other cancers (not specified)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Mortality
Reported Health Effect(s):	All-cause mortality
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Vital status was tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Medium	Death rates among unit employees were compared to death rates in the U.S. population adjusted for age and gender. Demographics of the exposed workers are not provided; therefore, it is not clear whether additional adjustment for race may have been appropriate. No justification is provided for the choice of the entire U.S. population as the comparison group. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis. Additional analyses are conducted limiting workers to those with the greatest likelihood of exposure (i.e., those working in jobs with high likelihood of contact with chemicals for more than a year, those working for the full year of 1979 during which chemical exposures were most frequently reported); these smaller groups are also compared to the unexposed general population.
	Metric 6:	Temporality	High	Temporality was established due to the longitudinal design and the use of mortality as the outcome. Exposures occurred between 1979 and 1987 and follow-up for vital status was conducted through 2003.
Domain 3: Outcome Assessment				

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Mortality
Reported Health Effect(s):	All-cause mortality
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Medium	The study did not provide information on how mortality was assessed either in the exposed population or in the comparison population; use of death certificates is implied but not stated.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected deaths are reported, but SIRs and 95% confidence intervals are not provided.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Comparisons of observed versus expected deaths were adjusted for age and gender. Demographics of the exposed workers are not provided; therefore, it is not clear whether additional adjustment for race may have been appropriate.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records or death records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed deaths among a population of exposed workers compared to expected deaths among the U.S. population, adjusted for age and gender.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected deaths; no SIR was provided. Expected death rates were adjusted for age and gender.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Mortality
Reported Health Effect(s):	All-cause mortality
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	All cancer (excluding non-melanoma skin cancer), digestive system cancer, colorectal cancer, respiratory cancer, prostate cancer, urinary system cancer, lymphatic and hematopoietic tissue cancer, other cancers (not specified)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	All cancer (excluding non-melanoma skin cancer), digestive system cancer, colorectal cancer, respiratory cancer, prostate cancer, urinary system cancer, lymphatic and hematopoietic tissue cancer, other cancers (not specified)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	All cancer (excluding non-melanoma skin cancer), digestive system cancer, colorectal cancer, respiratory cancer, prostate cancer, urinary system cancer, lymphatic and hematopoietic tissue cancer, other cancers (not specified)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Gastrointestinal
Reported Health Effect(s):	Digestive system cancer, colorectal cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Gastrointestinal
Reported Health Effect(s):	Digestive system cancer, colorectal cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Gastrointestinal
Reported Health Effect(s):	Digestive system cancer, colorectal cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Lung/Respiratory
Reported Health Effect(s):	Respiratory cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Health Outcome(s):	Lung/Respiratory
Reported Health Effect(s):	Respiratory cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Lung/Respiratory
Reported Health Effect(s):	Respiratory cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Prostate cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Prostate cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Prostate cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Male workers who had ever been assigned to the chlorohydrin unit between 1 January 1940 and 31 December 1967 at Union Carbide's South Charleston plant were enrolled and matched to the US National Death Index. Status on 5 workers could not be identified. Information on how workers were matched to death index was not specified.
	Metric 2:	Attrition	Medium	Rate of inclusion/participation was very high, as records were able to be matched for 98% of participants. Medium rating given because information on how participants whose vital status was not known was not specified.
	Metric 3:	Comparison Group	Uninformative	Unacceptable rating given because SMRs were calculated based on expected deaths from a reference population matched on sex, but not age.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Exposure was assessed based on duration of work in the plant. No information is provided on exposure levels, and a JEM was not used.
	Metric 5:	Exposure Levels	Uninformative	No information provided on levels of exposure.
	Metric 6:	Temporality	High	Temporality is well established; person-years stopped accumulating in 1967 and outcome was assessed beginning at that time.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar period, and interval since assignments, but distribution of these covariates was not reported.
	Metric 10:	Covariate Characterization	Medium	Information on covariate characterization not provided, but the selected covariates (age, calendar period, and interval since assignments) were likely extracted from employee records and unlikely to be largely problematic
	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.

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Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
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Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Study design was appropriate for the research method. Statistical methods were also appropriate.
	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.
	Metric 14:	Reproducibility of Analyses	Medium	Methods are well-enough described that study could be adequately reproduced.
	Metric 15:	Statistical Analysis	High	SMRs calculated based on US general population mortality for white males through 1988. RRs were ”evaluated over levels of duration of assignment to the chlorohydrin unit, stratified by age, calendar year, and interval since first assignment to the chlorohydrin unit”.

Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
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Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Male workers who had ever been assigned to the chlorohydrin unit between 1 January 1940 and 31 December 1967 at Union Carbide's South Charleston plant were enrolled and matched to the US National Death Index. Status on 5 workers could not be identified. Information on how workers were matched to death index was not specified.
	Metric 2:	Attrition	Medium	Rate of inclusion/participation was very high, as records were able to be matched for 98% of participants. Medium rating given because information on how participants whose vital status was not known was not specified.
	Metric 3:	Comparison Group	Uninformative	Unacceptable rating given because SMRs were calculated based on expected deaths from a reference population matched on sex, but not age.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Exposure was assessed based on duration of work in the plant. No information is provided on exposure levels, and a JEM was not used.
	Metric 5:	Exposure Levels	Uninformative	No information provided on levels of exposure.
	Metric 6:	Temporality	High	Temporality is well established; person-years stopped accumulating in 1967 and outcome was assessed beginning at that time.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar period, and interval since assignments, but distribution of these covariates was not reported.
	Metric 10:	Covariate Characterization	Medium	Information on covariate characterization not provided, but the selected covariates (age, calendar period, and interval since assignments) were likely extracted from employee records and unlikely to be largely problematic
	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.
Domain 5: Analysis				

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Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
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Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Study design was appropriate for the research method. Statistical methods were also appropriate.
	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.
	Metric 14:	Reproducibility of Analyses	Medium	Methods are well-enough described that study could be adequately reproduced.
	Metric 15:	Statistical Analysis	High	SMRs calculated based on US general population mortality for white males through 1988. RRs were ”evaluated over levels of duration of assignment to the chlorohydrin unit, stratified by age, calendar year, and interval since first assignment to the chlorohydrin unit”.

Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
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	Metric 2:	Attrition	Medium	Rate of inclusion/participation was very high, as records were able to be matched for 98% of participants. Medium rating given because information on how participants whose vital status was not known was not specified.
	Metric 3:	Comparison Group	Uninformative	Unacceptable rating given because SMRs were calculated based on expected deaths from a reference population matched on sex, but not age.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Exposure was assessed based on duration of work in the plant. No information is provided on exposure levels, and a JEM was not used.
	Metric 5:	Exposure Levels	Uninformative	No information provided on levels of exposure.
	Metric 6:	Temporality	High	Temporality is well established; person-years stopped accumulating in 1967 and outcome was assessed beginning at that time.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar period, and interval since assignments, but distribution of these covariates was not reported.
	Metric 10:	Covariate Characterization	Medium	Information on covariate characterization not provided, but the selected covariates (age, calendar period, and interval since assignments) were likely extracted from employee records and unlikely to be largely problematic
	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.
Domain 5: Analysis				

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Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Study design was appropriate for the research method. Statistical methods were also appropriate.
	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.
	Metric 14:	Reproducibility of Analyses	Medium	Methods are well-enough described that study could be adequately reproduced.
	Metric 15:	Statistical Analysis	High	SMRs calculated based on US general population mortality for white males through 1988. RRs were ”evaluated over levels of duration of assignment to the chlorohydrin unit, stratified by age, calendar year, and interval since first assignment to the chlorohydrin unit”.

Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

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Domain 1: Study Participation				
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	Metric 2:	Attrition	Medium	Rate of inclusion/participation was very high, as records were able to be matched for 98% of participants. Medium rating given because information on how participants whose vital status was not known was not specified.
	Metric 3:	Comparison Group	Uninformative	Unacceptable rating given because SMRs were calculated based on expected deaths from a reference population matched on sex, but not age.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Exposure was assessed based on duration of work in the plant. No information is provided on exposure levels, and a JEM was not used.
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	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar period, and interval since assignments, but distribution of these covariates was not reported.
	Metric 10:	Covariate Characterization	Medium	Information on covariate characterization not provided, but the selected covariates (age, calendar period, and interval since assignments) were likely extracted from employee records and unlikely to be largely problematic
	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.
Domain 5: Analysis				

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Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
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Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Study design was appropriate for the research method. Statistical methods were also appropriate.
	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.
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Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

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Domain 2: Exposure Characterization				
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Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar period, and interval since assignments, but distribution of these covariates was not reported.
	Metric 10:	Covariate Characterization	Medium	Information on covariate characterization not provided, but the selected covariates (age, calendar period, and interval since assignments) were likely extracted from employee records and unlikely to be largely problematic
	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.
Domain 5: Analysis				

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Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

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Domain 5: Analysis				

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Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

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Domain 5: Analysis				

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Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Study design was appropriate for the research method. Statistical methods were also appropriate.
	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.
	Metric 14:	Reproducibility of Analyses	Medium	Methods are well-enough described that study could be adequately reproduced.
	Metric 15:	Statistical Analysis	High	SMRs calculated based on US general population mortality for white males through 1988. RRs were ”evaluated over levels of duration of assignment to the chlorohydrin unit, stratified by age, calendar year, and interval since first assignment to the chlorohydrin unit”.

Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Male workers who had ever been assigned to the chlorohydrin unit between 1 January 1940 and 31 December 1967 at Union Carbide's South Charleston plant were enrolled and matched to the US National Death Index. Status on 5 workers could not be identified. Information on how workers were matched to death index was not specified.
	Metric 2:	Attrition	Medium	Rate of inclusion/participation was very high, as records were able to be matched for 98% of participants. Medium rating given because information on how participants whose vital status was not known was not specified.
	Metric 3:	Comparison Group	Uninformative	Unacceptable rating given because SMRs were calculated based on expected deaths from a reference population matched on sex, but not age.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Exposure was assessed based on duration of work in the plant. No information is provided on exposure levels, and a JEM was not used.
	Metric 5:	Exposure Levels	Uninformative	No information provided on levels of exposure.
	Metric 6:	Temporality	High	Temporality is well established; person-years stopped accumulating in 1967 and outcome was assessed beginning at that time.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar period, and interval since assignments, but distribution of these covariates was not reported.
	Metric 10:	Covariate Characterization	Medium	Information on covariate characterization not provided, but the selected covariates (age, calendar period, and interval since assignments) were likely extracted from employee records and unlikely to be largely problematic
	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.
Domain 5: Analysis				

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Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Study design was appropriate for the research method. Statistical methods were also appropriate.
	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.
	Metric 14:	Reproducibility of Analyses	Medium	Methods are well-enough described that study could be adequately reproduced.
	Metric 15:	Statistical Analysis	High	SMRs calculated based on US general population mortality for white males through 1988. RRs were ”evaluated over levels of duration of assignment to the chlorohydrin unit, stratified by age, calendar year, and interval since first assignment to the chlorohydrin unit”.

Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Bove, F. J. (1996). Public drinking water contamination and birthweight, prematurity, fetal deaths, and birth defects. Toxicology and Industrial Health 12(2):255-266.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	200239

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	This cross-sectional study (n=80,938) included all registered singleton live births and fetal deaths (>20 weeks' gestation) in 1985-88 in 75 New Jersey towns located in 4 counties with "some" water supplies contaminated with substances of interest and where: (i) residents were "mostly" served by public water systems; and (ii) births occurred "mostly" in state. Estimated proportions of residents served by public water systems, and of pregnancies/births captured, were not described. However, the inclusion of all eligible registered births, fetal deaths, and birth defects, as well as the selection of towns without knowledge of birth outcome prevalence, limited the likelihood of selection bias.
	Metric 2:	Attrition	Medium	All registered births and fetal deaths were included. Attrition due to missing values for multiple variables was not quantified and is therefore uncertain. However, attrition was likely modest as the proportion of missing values for individual variables was relatively low: (i) ~6% of subjects were excluded from analyses of outcomes such as preterm birth due to invalid or missing gestational ages; and (ii) other covariates evaluated as confounders had up to 4.9% missing values.
	Metric 3:	Comparison Group	High	After excluding plural pregnancies and chromosomal abnormalities, all registered live births during the study period in the areas included without the outcomes of interest were included in the comparison group. This comprehensive approach limited the potential for bias. Chromosomal abnormalities were not included as outcomes as they were not hypothesized to be associated with the exposures under study but were appropriately excluded given their uncertain etiology.
Domain 2: Exposure Characterization				

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Study Citation:	Bove, F. J. (1996). Public drinking water contamination and birthweight, prematurity, fetal deaths, and birth defects. Toxicology and Industrial Health 12(2):255-266.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	200239

Domain	Metric		Rating	Comments
	Metric 4:	Measurement of Exposure	Medium	Along with several other contaminants, residential drinking water exposure to 1,2-dichloroethane (as well as 1,1,1-trichloroethane and 'total dichloroethylenes') – was assigned based on maternal town of residence at birth. Exposure estimates were calculated using the average of water company sampling reports during the first trimester (for birth defects and fetal death) or the duration of pregnancy (for other outcomes). Detection limits and data availability were not specified in detail but were described as below 1 ppb, with reporting compliance >85%. A minimum of 1 sample per 6-month interval was required; variability in the number of measures available across water systems and towns was not described. Additional sources of measurement error included: changes in residence during pregnancy; water from alternate sources (ex. private wells, bottles, workplaces); variability in residential contaminant levels vs measured samples; unknown levels of tap water intake; and errors in estimated dermal and inhalation exposure while bathing or showering. While the extent of exposure misclassification is uncertain, there is no evidence to suggest it was differential rather than random.
	Metric 5:	Exposure Levels	Medium	Due to the high proportion of measures below detection limits, analyses relating exposure to health outcomes used only 2 categories for each of the chlorinated solvents of interest: cutoffs close to detection limits were used to define elevated exposure. Proportions defined as having elevated exposure was low (1.8% had 1,1-dichloroethylene ≥1 ppb). An important concern is that relatively low levels of exposure to these contaminants from sources other than residential drinking water, for which data were not available, could potentially have resulted in considerable misclassification.
	Metric 6:	Temporality	High	Exposure levels were assigned based on contaminant exposures estimated during: (i) the first trimester for analyses of birth defects and fetal deaths; and (ii) the duration of pregnancy for other pregnancy outcomes.

Domain 3: Outcome Assessment

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Study Citation:	Bove, F. J. (1996). Public drinking water contamination and birthweight, prematurity, fetal deaths, and birth defects. Toxicology and Industrial Health 12(2):255-266.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	200239

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcomes included measures of birthweight (continuous among term births, low term birthweight, very low birthweight), prematurity, fetal death, and congenital anomalies in live births or fetal deaths. The anomalies analyzed included defects of the central nervous system, neural tube, oral cleft, total cardiac, major cardiac, ventricular septum, and any surveillance defect excluding chromosomal defects. All outcomes were identified using birth certificates, fetal death certificates (>20 weeks' gestation), and the NJ congenital birth defect registry (ICD codes provided). These registry data are likely to be sufficiently valid for late pregnancy outcomes. However, their limited ability to capture early pregnancy losses is a weakness. The sample included only 594 fetal deaths (less than 1% of the >80,0000 sample). Typical estimates are that 10-20%, of recognized pregnancies ending in losses. Moreover, developmental defects contributing to early pregnancy losses were also not captured. A further limitation is that that potentially etiologically heterogeneous preterm birth types were analyzed together, as these data did not distinguish premature rupture of membranes vs idiopathic prematurity.
	Metric 8:	Reporting Bias	Medium	Models were constructed only for contaminants with associations > 1.0, and tables included only associations with odds ratios ≥1.5. No clear rationale was provided. Several positive odds ratios below the 1.5 cutoff were described in the results text (without confidence intervals), but no null/negative odds ratios were presented or described.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Potential confounding by maternal race, education, parity, and prior pregnancy loss, along with infant sex (for birth outcomes) and adequacy of prenatal care, was examined. Gestational age was addressed by analyzing birthweight among full term births, term low birth weight, and small size for gestational age. Only fully adjusted models were presented. In a companion case-control study (with low participation rates), adjustment for other variables not available on birth certificates (ex. maternal smoking, occupational exposures, medical history, and gestational weight gain) did not influence associations with other studied contaminants. This separate study reduces concerns for important confounding bias, but confounding cannot be ruled out.
	Metric 10:	Covariate Characterization	Medium	Data on covariates came from registry data: birth certificates, fetal death certificates, and the NJ congenital birth defects registry.
	Metric 11:	Co-exposure Counfounding	Medium	Co-exposure confounding by drinking water trihalomethane concentrations was evaluated. There was no evidence to suggest substantial confounding by this or other co-exposures.
Domain 5: Analysis				

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Study Citation:	Bove, F. J. (1996). Public drinking water contamination and birthweight, prematurity, fetal deaths, and birth defects. Toxicology and Industrial Health 12(2):255-266.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	200239

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Methods were appropriate. The study used logistic regression models to estimate odds ratios and confidence intervals for dichotomous outcomes, and linear regression for analysis of continuous birth weight.
	Metric 13:	Statistical Power	Medium	Statistical power was likely to have been limited as a consequence of the small proportion of the sample defined as having "elevated" residential water concentrations of the chemicals of interest. The range of exposure examined was limited, as cutoffs for elevated levels were close to the detection limits of 1 ppb. In addition, for most birth defect outcomes, fewer than 10 cases had elevated exposure.
	Metric 14:	Reproducibility of Analyses	Medium	The authors clearly described steps used to estimate exposure-outcome associations, including exposure category cutoffs and criteria for confounding. However, many results were not shown as tables included odds ratios ≥1.5.
	Metric 15:	Statistical Analysis	High	The authors estimated coefficients, odds ratios and 95% confidence intervals using adequate methods. Confounding was based on 15% change-in-estimate comparing nested models. Effect modification (ex by infant sex) was not evaluated as there was no a priori evidence to suggest such analyses at that time.

Additional Comments: This study analyzed the association between estimated residential drinking water concentrations of several chlorinated solvents including 1,2-dichloroethane (as well as 1,1,1-trichloroethane; ∑[trans-1,2-dichloroethylene and 1,1-dichloroethylene]) and pregnancy outcomes (size at birth, prematurity, fetal deaths, and congenital birth defects). The sample included more than 80,000 births during 1985-88 for residents of 75 towns in NJ using public water system records to estimate exposure during gestation, and registry data (birth certificate, fetal death certificates for pregnancies >20 weeks, state birth defect registry) to characterize outcomes. Strengths included the large sample size and inclusion of all eligible registered births and fetal deaths in the study period. A critical concern is the inability to capture early fetal deaths and any related malformations (1% of the sample had fetal deaths vs typical estimates of >10%). An important limitation was the low percentage of the sample with detectable (> 1ppb) concentrations of these contaminants (<1% to 6.2%). Small numbers for birth defect outcomes also limited power. Exposure misclassification (ex. drinking water from wells/ work/ bottles, changes in residence, exposure from other sources) is also a concern. However, such misclassification was likely non-differential, and thus more likely to under- vs. to over-estimate associations.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Bove, F. J., Fulcomer, M. C., Klotz, J. B., Esmart, J., Dufficy, E. M., Savrin, J. E. (1995). Public drinking water contamination and birth outcomes. American Journal of Epidemiology 141(9):850-862.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	194932

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	This semi-ecological study (n=80,938) included all registered singleton live births and fetal deaths (>20 weeks) in 1985-88 in 75 New Jersey towns located in 4 counties with "some" water supplies contaminated with substances of interest and where: (i) residents were "mostly" served by public water systems; and (ii) births occurred "mostly" in state. Estimated proportions of residents served by public water systems, and of pregnancies/births captured, were not described. However, the inclusion of all eligible registered births, fetal deaths, and birth defects, as well as the selection of towns without knowledge of birth outcome prevalence, limited the likelihood of selection bias.
	Metric 2:	Attrition	Medium	All registered births and fetal deaths were included. Attrition due to missing values for multiple variables was not quantified and is therefore uncertain. However, attrition was likely modest as the proportion of missing values for individual variables was relatively low: (i) ~6% of subjects were excluded from analyses of outcomes such as preterm birth due to invalid or missing gestational ages; and (ii) other covariates evaluated as confounders had up to 4.9% missing values.
	Metric 3:	Comparison Group	High	After excluding plural pregnancies and chromosomal abnormalities, all registered live births during the study period in the areas included without the outcomes of interest were included in the comparison group. This comprehensive approach limited the potential for bias. Chromosomal abnormalities were not included as outcomes as they were not hypothesized to be associated with the exposures under study but were appropriately excluded given their uncertain etiology.
Domain 2: Exposure Characterization				

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Study Citation:	Bove, F. J., Fulcomer, M. C., Klotz, J. B., Esmart, J., Dufficy, E. M., Savrin, J. E. (1995). Public drinking water contamination and birth outcomes. American Journal of Epidemiology 141(9):850-862.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	194932

Domain	Metric		Rating	Comments
	Metric 4:	Measurement of Exposure	Medium	Along with several other contaminants, residential drinking water exposure to 1,2-dichloroethane (as well as 1,1,1-trichloroethane and 'total dichloroethylenes') was assigned based on maternal town of residence at birth. Exposure estimates were calculated using the average of water company sampling reports during the first trimester (for birth defects and fetal death) or the duration of pregnancy (for other outcomes). Detection limits and data availability were not specified in detail but were described as below 1 ppb, with reporting compliance >85%. A minimum of 1 sample per 6-month interval was required; variability in the number of measures available across water systems and towns was not described. Additional sources of measurement error included: changes in residence during pregnancy; water from alternate sources (ex. private wells, bottles, workplaces); variability in residential contaminant levels vs measured samples; unknown levels of tap water intake; and errors in estimated dermal and inhalation exposure while bathing or showering. While the extent of exposure misclassification is uncertain, there is no evidence to suggest it was differential rather than random.
	Metric 5:	Exposure Levels	Low	Due to the high proportion of measures below detection limits, analyses relating exposure to health outcomes used only 2 categories for each of the three chemicals of interest: cutoffs close to detection limits were used to define elevated exposure. Proportions defined as having elevated exposure were low (1.8% had 1,1-dichloroethylene ≥1 ppb). An important concern is that relatively low levels of exposure to this contaminant from sources other than residential drinking water, for which data were not available, could potentially have resulted in considerable misclassification.
	Metric 6:	Temporality	High	Exposure levels were assigned based on contaminant exposures estimated during: (i) the first trimester for analyses of birth defects and fetal deaths; and (ii) the duration of pregnancy for other pregnancy outcomes.

Domain 3: Outcome Assessment

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Study Citation:	Bove, F. J., Fulcomer, M. C., Klotz, J. B., Esmart, J., Dufficy, E. M., Savrin, J. E. (1995). Public drinking water contamination and birth outcomes. American Journal of Epidemiology 141(9):850-862.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	194932

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcomes included measures of birthweight (continuous among term births, low term birthweight, very low birthweight), prematurity, fetal death, and congenital anomalies in live births or fetal deaths. The anomalies analyzed included defects of the central nervous system, neural tube, oral cleft, total cardiac, major cardiac, ventricular septum, and any surveillance defect excluding chromosomal defects. All outcomes were identified using birth certificates, fetal death certificates (>20 weeks' gestation), and the NJ congenital birth defect registry (ICD codes provided). These registry data are likely to be sufficiently valid for late pregnancy outcomes. However, their limited ability to capture early pregnancy losses is a weakness. The sample included only 594 fetal deaths (less than 1% of the >80,0000 sample). Typical estimates are that 10-20%, of recognized pregnancies ending in losses. Moreover, developmental defects contributing to early pregnancy losses were also not captured. A further limitation is that that potentially etiologically heterogeneous preterm birth types were analyzed together, as these data did not distinguish premature rupture of membranes vs idiopathic prematurity.
	Metric 8:	Reporting Bias	Low	Models were constructed only for contaminants with associations > 1.0, and tables included only associations with odds ratios ≥1.5. No clear rationale was provided. Several positive odds ratios below the 1.5 cutoff were described in the results text (without confidence intervals), but no null/negative odds ratios were presented or described.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Potential confounding by maternal race, education, parity, and prior pregnancy loss, along with infant sex (for birth outcomes) and adequacy of prenatal care, was examined. Gestational age was addressed by analyzing birthweight among full term births, term low birth weight, and small size for gestational age. Only fully adjusted models were presented. In a companion case-control study (with low participation rates), adjustment for other variables not available on birth certificates (ex. maternal smoking, occupational exposures, medical history, and gestational weight gain) did not influence associations with other studied contaminants. This separate study reduces concerns for important confounding bias, but confounding cannot be ruled out.
	Metric 10:	Covariate Characterization	Medium	Data on covariates came from registry data: birth certificates, fetal death certificates, and the NJ congenital birth defects registry.
	Metric 11:	Co-exposure Counfounding	Medium	Co-exposure confounding by drinking water trihalomethane concentrations was evaluated. There was no evidence to suggest substantial confounding by this or other co-exposures.
Domain 5: Analysis				

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Study Citation:	Bove, F. J., Fulcomer, M. C., Klotz, J. B., Esmart, J., Dufficy, E. M., Savrin, J. E. (1995). Public drinking water contamination and birth outcomes. American Journal of Epidemiology 141(9):850-862.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	194932

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Methods were appropriate. The study used logistic regression models to estimate odds ratios and confidence intervals for dichotomous outcomes, and linear regression for analysis of continuous birth weight.
	Metric 13:	Statistical Power	Low	Statistical power was likely to have been limited as a consequence of the small proportion of the sample defined as having "elevated" residential water concentrations of the chemicals of interest. The range of exposure examined was limited, as cutoffs for elevated levels were close to the detection limits of 1 ppb. In addition, for most birth defect outcomes, fewer than 10 cases had elevated exposure. However, the authors emphasized the magnitude of associations rather than statistical significance and presented multiple confidence intervals to aid interpretation of the precision of estimates (50%, 90% and 99%).
	Metric 14:	Reproducibility of Analyses	Medium	The authors clearly described steps used to estimate exposure-outcome associations, including exposure category cutoffs and criteria for confounding. However, many results were not shown as tables included odds ratios ≥1.5.
	Metric 15:	Statistical Analysis	High	The authors estimated coefficients, odds ratios and confidence intervals using adequate methods. Confounding was based on 15% change-in-estimate comparing nested models. Effect modification (ex by infant sex) was not evaluated as there was no a priori evidence to suggest such analyses at that time.

Additional Comments: This study analyzed the association between estimated residential drinking water concentrations of several chlorinated solvents including 1,2-dichloroethane (as well as 1,1,1-trichloroethane and the ∑[trans-1,2-dichloroethylene & 1,1-dichloroethylene]) and pregnancy outcomes (size at birth, prematurity, fetal deaths, and congenital birth defects). The sample included more than 80,000 births during 1985-88 for residents of 75 towns in NJ using public water system records to estimate exposure during gestation, and registry data (birth certificate, fetal death certificates for pregnancies >20 weeks' gestation, state birth defect registry) to characterize outcomes. Strengths included the large sample size and inclusion of all eligible registered births and fetal deaths in the study period. A critical concern is the inability to capture early fetal deaths and any related malformations (1% of the sample had fetal deaths vs typical estimates of >10%). An important limitation was the low percentage of the sample with detectable (> 1ppb) concentrations of this solvent (<2%), which likely limited power. Small numbers for birth defect outcomes also limited power. Exposure misclassification (ex. drinking water from wells/ work/ bottles, changes in residence, exposure from other sources) is also a concern. However, such misclassification was likely non-differential, and thus more likely to under- vs. to over-estimate associations.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Bowler, R.M., Gysens, S., Hartney, C. (2003). Neuropsychological effects of ethylene dichloride exposure. NeuroToxicology 24(4-5):553-562.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Wechsler Adult Intelligence Scale III (WAIS-III), Wechsler Memory Scale III (WMS-III), Boston Naming Test (BNT), Trail Making Test (TMT), Stroop Color-Word Test, Grooved Pegboard, Dynamometer, Wide Range Achievement Test (WRAT), Finger tapping, Beck Anxiety Index, Beck Depression Index, Symptom Checklist-90 (SCL-90).
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	200241

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Uninformative	221 workers that had been exposed to 1,2-DCE in the Southern United States were initially included. Exclusion criteria were provided, including the number of individuals excluded for each reason. The study authors note that those initially included in the analysis sample were referred by physicians after neurological complaints were documented. Detailed criteria for referral were not provided. Referral-based recruitment of neurological cases will likely result in an analysis sample with an exposure-outcome distribution that is not representative of the eligible population (i.e., contamination site clean-up workers).
	Metric 2:	Attrition	Medium	There was moderate subject loss. Reasons for exclusion from the analysis sample are provided, and only those with complete information were included in the analysis.
	Metric 3:	Comparison Group	Low	Impairment scores were compared to normative data from manuals and/or a "demographically similar control group" cited to Bowler et al. (2001). The controls from this study appeared similar (albeit somewhat older) than 1,2-DCE-exposed workers and reported no prior chemical exposure.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	A job-exposure matrix was not considered plausible; variables considered as surrogates of exposure were obtained from interviews. This method is expected to have poor validity because it relies on workers' recall of subjective events and their frequency (e.g., contact with water); workers (who are taking part in a lawsuit) may overestimate their exposure.
	Metric 5:	Exposure Levels	Low	Two levels of exposure (exposed and not exposed) were used to evaluate neurophysiological effects.
	Metric 6:	Temporality	Medium	Exposures primarily occurred between 1993 and 1995 and neurophysiological effects were evaluated in 2000. Temporality is established, but it is unclear whether exposures fall within relevant exposure windows for the outcome of interest.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Neurophysiological effects were evaluated using a number of standardized tests, including (but not limited to) the Wechsler Adult Intelligence Scale (WAIS-III), the Wechsler Memory Scale (WMS-III), and the Symptom Checklist 90-Revised (SCL90-R). There was no information whether tests were performed using the same methods for exposed and referent groups (e.g., timing and order of tests).

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Study Citation:	Bowler, R.M., Gysens, S., Hartney, C. (2003). Neuropsychological effects of ethylene dichloride exposure. NeuroToxicology 24(4-5):553-562.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Wechsler Adult Intelligence Scale III (WAIS-III), Wechsler Memory Scale III (WMS-III), Boston Naming Test (BNT), Trail Making Test (TMT), Stroop Color-Word Test, Grooved Pegboard, Dynamometer, Wide Range Achievement Test (WRAT), Finger tapping, Beck Anxiety Index, Beck Depression Index, Symptom Checklist-90 (SCL-90).
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	200241

Domain	Metric		Rating	Comments
	Metric 8:	Reporting Bias	Low	Neurobehavioral outcomes mentioned in the methods were reported for 1,2-DCE-exposed workers (as mean score, standard deviation, and percentage impaired); results for controls/normative data were not shown and/or p-values from t-tests were not provided. Control data were used to define impairment (based on z-score) but these values were not reported. Data pertaining to specific exposure variables were reported in the text only; no data were shown in a table.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Normative data permitted adjustments based on age, education, and gender. The control group was "socio-demographically" similar but specific parameters used to define similarity were not indicated. Separate ANCOVA analyses on workers only were stratified by race (citation provided), and adjusted for ethnicity, age, and education. The methods for identifying and including potential confounders in the analytic approach was not described.
	Metric 10:	Covariate Characterization	Low	No description of the covariate collection method was provided. It was not clear whether the method used was valid or not.
	Metric 11:	Co-exposure Counfounding	Low	A number of workers (18%) reported current exposure to chemicals in their work environment. These potential co-exposures were not were not appropriately adjusted for in the analytical approach used.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Low	The study design was appropriate to evaluate the neurophysiological status of 1,2-DCE-exposed workers; however, statistical methods were not comprehensive.
	Metric 13:	Statistical Power	Medium	The report indicates "significant impairments" were observed on various neurophysiological tests using t-tests, and significant exposure relationships were reported based on test scores and specific exposure variables (used as surrogates of exposure). Therefore, the number of participants was sufficient to detect an effect.
	Metric 14:	Reproducibility of Analyses	Low	Tests were scored according to relevant manuals; the calculation of z-scores, used in all impairment comparisons and analyses of exposure relationships, was not explained in adequate detail. The methods used to determine relationships between specific exposure variables and test scores (i.e., ANCOVA analyses) were not fully described.
	Metric 15:	Statistical Analysis	Low	Description of the ANCOVA analysis was largely not present. It is not clear whether model assumptions were met.

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Study Citation:	Bowler, R.M., Gysens, S., Hartney, C. (2003). Neuropsychological effects of ethylene dichloride exposure. NeuroToxicology 24(4-5):553-562.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Wechsler Adult Intelligence Scale III (WAIS-III), Wechsler Memory Scale III (WMS-III), Boston Naming Test (BNT), Trail Making Test (TMT), Stroop Color-Word Test, Grooved Pegboard, Dynamometer, Wide Range Achievement Test (WRAT), Finger tapping, Beck Anxiety Index, Beck Depression Index, Symptom Checklist-90 (SCL-90).
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	200241

Domain	Metric	Rating	Comments
Additional Comments:	The study evaluated the neurobehavioral status of a group of workers with known exposure to 1,2-DCE at a clean-up site. Impairments related to processing speed, attention, cognitive flexibility, motor coordination and speed, verbal memory/fluency, vision and visual-spatial abilities, and mood were reported in exposed workers. Serious and consequential flaws are associated with the study including methods of participant selection and retention, and exposure characterization among others.		

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Brender, J.D., Shinde, M.U., Zhan, F.B., Gong, X., Langlois, P.H. (2014). Maternal residential proximity to chlorinated solvent emissions and birth defects in offspring: A case-control study. Environmental Health: A Global Access Science Source 13(1):96.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	birth defects (neural tube defects, limbs deficiencies, oral cleft defects, heart defects, spina bifida, anencephaly)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	2799700

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Participants were drawn from the Texas Birth Defects Registry (TBDR) for years 1996-2008. Controls were frequency matched from the same registry. Study authors state that neural tube cases were more likely to not be successfully geocoded which may introduce selection bias, however, the authors note that both cases and controls with addresses that could not be geocoded were similar. In spite of that, the inclusion criteria, methods of participant selection, and frequency match were reported.
	Metric 2:	Attrition	Medium	13.3% case mother addresses and 12.8% control mother addresses were unable to be geocoded, however this most likely only lowered the precision of the study and most likely does not vary based on exposure level.
	Metric 3:	Comparison Group	Medium	Controls were matched to cases and pulled from the same eligible population by year of delivery and public health service region. Other demographic factors, e.g., race was not matched in population selection. However, statistical analyses were adjusted for year of delivery, maternal age, race/ethnicity, education, and public health region of residence.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Used Emission Weighted Proximity Model to estimate exposure at a given address based on proximity to emission sources and the specific amount or type of pollutant emitted. There may be some exposure misclassification due to mothers moving away from geocoded addresses. Previous studies indicate ~67% of mothers do not move between conception and delivery.
	Metric 5:	Exposure Levels	Medium	Reports exposure as "exposure risk value" and groups the risk values into quartiles, with exposure risk values < 0 being the referent group
	Metric 6:	Temporality	Medium	The study authors estimated exposure based on residence during pregnancy and evaluated birth outcomes. Temporality is established. Previous studies indicate ~67% mothers don't move between trimester and delivery. For mothers who moved during the pregnancy, the temporality is unknown.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Outcomes determined by Texas Birth Defect Registry, checking for birth defect diagnosis. Birth certificates came from Center for Health Statistics at Texas Department of State Health Services
	Metric 8:	Reporting Bias	High	Outcome data measured and reported clearly, stratified by specific type of birth defect
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Brender, J.D., Shinde, M.U., Zhan, F.B., Gong, X., Langlois, P.H. (2014). Maternal residential proximity to chlorinated solvent emissions and birth defects in offspring: A case-control study. Environmental Health: A Global Access Science Source 13(1):96.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	birth defects (neural tube defects, limbs deficiencies, oral cleft defects, heart defects, spina bifida, anencephaly)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	2799700

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	High	Cases were frequency matched by year of delivery and public health service region. Final models were adjusted for year of delivery, public health region, maternal age (<20, 20-24, 25-29, 30-34, 35-39, >39 years), education (<12 years, 12 years, >12 years), and race/ethnicity (Whit non-Hispanic, Black non-Hispanic, Hispanic, other non-Hispanic).
	Metric 10:	Covariate Characterization	High	Used birth and death certificates for demographic information
	Metric 11:	Co-exposure Counfounding	Medium	other co-exposures were not described
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	study used logistic regression to measure association between exposure and birth defects
	Metric 13:	Statistical Power	Medium	Overall adequate number of cases and controls - some effects have low cell counts, but at least one health effect has sufficient statistical power.
	Metric 14:	Reproducibility of Analyses	Medium	Methods sufficiently detailed for reproducibility
	Metric 15:	Statistical Analysis	High	No logistic regression model assumption violations were identified.

Additional Comments: This study examined the association between proximity to several point sources of chlorinated solvents and birth defects. Exposure was assessed using EPA's Toxic Release Inventory, and birth defects were assessed using Texas birth registries. The geocoded address of mothers on day of delivery and the amount of solvent was plugged into the Emission Weighted Probability model to assign each mother an exposure risk value. Limitations include limited evidence of temporality. Additionally, elective terminations lacked a vital record, which meant only 69% of mothers with neural tube defects were geocoded. Mothers highly exposed to 1,2-dichloroethane were 1.85 times more likely to have the spina bifida birth defect than mothers who were not significantly exposed.

Overall Quality Determination High

* No biomarkers were identified for this evaluation.

Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Nested case-control design; cases selected from deaths in cohort study was described by Rinsky et al (1988; HERO 597923) (29,139 workers in Union Carbide facilities in West Virginia followed from 1940 to 1978). Vital status complete for 95% of cohort members.
	Metric 2:	Attrition	High	There was minimal exclusion of subjects/missing data, because vital status follow-up was complete for 96% of the 29,139 men in the cohort study.
	Metric 3:	Comparison Group	Medium	Controls were randomly selected in a 5:1 ratio to cases from the total employee cohort such that they were first employed in the same decade and survived to the same five-year survival period as cases. Controls survived at least to the beginning of the five-year interval in which cases died. Controls were independently selected for each of the individual disease subcategories. However, the demographic information between cases and controls were not compared in the paper.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was partially described: (1) Potential employee contact with a specific substance was determined by tracing each employee's work assignments and linking these assignment records to a separate computer file that contained a history of departmental usage for each substance; (2) Potential exposure to each chemical group was assumed on the basis of assignment o a production unit with a history of usage of any member of that chemical group. However, exposure level either based on work assignment in departments such as job exposure matrix or on the chemical levels were not presented.
	Metric 5:	Exposure Levels	Low	The range of exposure is limited. For example, exposure was presented by the duration of work in two categories: <5 years and 5+ years.
	Metric 6:	Temporality	Medium	Temporality is established, but it is unclear whether the exposures fall within the relevant exposure window. Authors used a lag time of 5 years; since controls were selected for 5 yr intervals, the effective lag time ranged from 5-9 years with an average of 7.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Case definition was based on death certificate diagnosis; but no method validation was conducted against this well-established methods.
	Metric 8:	Reporting Bias	Medium	All outcomes reported, but ORs for many analyses presented without CIs (some CIs reported in text).
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Low	There is indirect evidence that considerations were not made for potential confounders (ORs not adjusted, controls not age- or race-matched). Even though authors note that "Age-adjusted stratified analyses, which were also conducted, did not materially modify the odds ratio estimates". Also stratified examination of odds ratios were conducted to assess duration of exposure effects. However, other key confounders e.g., smoking status and race were not accounted for.
	Metric 10:	Covariate Characterization	Medium	The only potential confounder considered was age; this was presumably evaluated based on employment records (no discussion presented). Age-adjusted stratified analyses were conducted.
	Metric 11:	Co-exposure Counfounding	Low	Co-exposures were present and were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Nested case-control study design is appropriate for research question. Initial data analysis included crude odds ratio and then stratified examination of odds ratios was conducted to ass duration of exposure effect. Also, age-adjusted stratified analysis was conducted.
	Metric 13:	Statistical Power	Low	Statistical power calculations were not reported. Case numbers for each disease were low. The number of subjects was not sufficient to detect an effect of 1,2-dichloroethylene exposure.
	Metric 14:	Reproducibility of Analyses	Medium	Description was sufficient to be conceptually reproducible.
	Metric 15:	Statistical Analysis	Low	Statistical model to calculate odds ratio was not described.

Additional Comments: This nested case-control study within a cohort study is a good study design to answer the research question regarding the association between multiple chemical exposures and four cancer sites. Cases and controls are selected appropriate. However, there are several limitations in this study: (1) confounders were not all considered and adjusted for, except that age-adjusted odds ratios were conducted; (2) it is not described if co-exposures were adjusted for; (3) numbers of cancer cases for each cancer type were small, so the statistical power is limited; (4) statistical models for calculating odds ratios were not described.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Nested case-control design; cases selected from deaths in cohort study was described by Rinsky et al (1988; HERO 597923) (29,139 workers in Union Carbide facilities in West Virginia followed from 1940 to 1978). Vital status complete for 95% of cohort members.
	Metric 2:	Attrition	High	There was minimal exclusion of subjects/missing data, because vital status follow-up was complete for 96% of the 29,139 men in the cohort study.
	Metric 3:	Comparison Group	Medium	Controls were randomly selected in a 5:1 ratio to cases from the total employee cohort such that they were first employed in the same decade and survived to the same five-year survival period as cases. Controls survived at least to the beginning of the five-year interval in which cases died. Controls were independently selected for each of the individual disease subcategories. However, the demographic information between cases and controls were not compared in the paper.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was partially described: (1) Potential employee contact with a specific substance was determined by tracing each employee's work assignments and linking these assignment records to a separate computer file that contained a history of departmental usage for each substance; (2) Potential exposure to each chemical group was assumed on the basis of assignment o a production unit with a history of usage of any member of that chemical group. However, exposure level either based on work assignment in departments such as job exposure matrix or on the chemical levels were not presented.
	Metric 5:	Exposure Levels	Low	The range of exposure is limited. For example, exposure was presented by the duration of work in two categories: <5 years and 5+ years.
	Metric 6:	Temporality	Medium	Temporality is established, but it is unclear whether the exposures fall within the relevant exposure window. Authors used a lag time of 5 years; since controls were selected for 5 yr intervals, the effective lag time ranged from 5-9 years with an average of 7.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Case definition was based on death certificate diagnosis; but no method validation was conducted against this well-established methods.
	Metric 8:	Reporting Bias	Medium	All outcomes reported, but ORs for many analyses presented without CIs (some CIs reported in text).
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Low	There is indirect evidence that considerations were not made for potential confounders (ORs not adjusted, controls not age- or race-matched). Even though authors note that "Age-adjusted stratified analyses, which were also conducted, did not materially modify the odds ratio estimates". Also stratified examination of odds ratios were conducted to assess duration of exposure effects. However, other key confounders e.g., smoking status and race were not accounted for.
	Metric 10:	Covariate Characterization	Medium	The only potential confounder considered was age; this was presumably evaluated based on employment records (no discussion presented). Age-adjusted stratified analyses were conducted.
	Metric 11:	Co-exposure Counfounding	Low	Co-exposures were present and were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Nested case-control study design is appropriate for research question. Initial data analysis included crude odds ratio and then stratified examination of odds ratios was conducted to ass duration of exposure effect. Also, age-adjusted stratified analysis was conducted.
	Metric 13:	Statistical Power	Low	Statistical power calculations were not reported. Case numbers for each disease were low. The number of subjects was not sufficient to detect an effect of 1,2-dichloroethylene exposure.
	Metric 14:	Reproducibility of Analyses	Medium	Description was sufficient to be conceptually reproducible.
	Metric 15:	Statistical Analysis	Low	Statistical model to calculate odds ratio was not described.

Additional Comments: This nested case-control study within a cohort study is a good study design to answer the research question regarding the association between multiple chemical exposures and four cancer sites. Cases and controls are selected appropriate. However, there are several limitations in this study: (1) confounders were not all considered and adjusted for, except that age-adjusted odds ratios were conducted; (2) it is not described if co-exposures were adjusted for; (3) numbers of cancer cases for each cancer type were small, so the statistical power is limited; (4) statistical models for calculating odds ratios were not described.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Nested case-control design; cases selected from deaths in cohort study was described by Rinsky et al (1988; HERO 597923) (29,139 workers in Union Carbide facilities in West Virginia followed from 1940 to 1978). Vital status complete for 95% of cohort members.
	Metric 2:	Attrition	High	There was minimal exclusion of subjects/missing data, because vital status follow-up was complete for 96% of the 29,139 men in the cohort study.
	Metric 3:	Comparison Group	Medium	Controls were randomly selected in a 5:1 ratio to cases from the total employee cohort such that they were first employed in the same decade and survived to the same five-year survival period as cases. Controls survived at least to the beginning of the five-year interval in which cases died. Controls were independently selected for each of the individual disease subcategories. However, the demographic information between cases and controls were not compared in the paper.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was partially described: (1) Potential employee contact with a specific substance was determined by tracing each employee's work assignments and linking these assignment records to a separate computer file that contained a history of departmental usage for each substance; (2) Potential exposure to each chemical group was assumed on the basis of assignment o a production unit with a history of usage of any member of that chemical group. However, exposure level either based on work assignment in departments such as job exposure matrix or on the chemical levels were not presented.
	Metric 5:	Exposure Levels	Low	The range of exposure is limited. For example, exposure was presented by the duration of work in two categories: <5 years and 5+ years.
	Metric 6:	Temporality	Medium	Temporality is established, but it is unclear whether the exposures fall within the relevant exposure window. Authors used a lag time of 5 years; since controls were selected for 5 yr intervals, the effective lag time ranged from 5-9 years with an average of 7.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Case definition was based on death certificate diagnosis; but no method validation was conducted against this well-established methods.
	Metric 8:	Reporting Bias	Medium	All outcomes reported, but ORs for many analyses presented without CIs (some CIs reported in text).
Domain 4: Potential Confounding / Variability Control				

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Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Low	There is indirect evidence that considerations were not made for potential confounders (ORs not adjusted, controls not age- or race-matched). Even though authors note that "Age-adjusted stratified analyses, which were also conducted, did not materially modify the odds ratio estimates". Also stratified examination of odds ratios were conducted to assess duration of exposure effects. However, other key confounders e.g., smoking status and race were not accounted for.
	Metric 10:	Covariate Characterization	Medium	The only potential confounder considered was age; this was presumably evaluated based on employment records (no discussion presented). Age-adjusted stratified analyses were conducted.
	Metric 11:	Co-exposure Counfounding	Low	Co-exposures were present and were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Nested case-control study design is appropriate for research question. Initial data analysis included crude odds ratio and then stratified examination of odds ratios was conducted to ass duration of exposure effect. Also, age-adjusted stratified analysis was conducted.
	Metric 13:	Statistical Power	Low	Statistical power calculations were not reported. Case numbers for each disease were low. The number of subjects was not sufficient to detect an effect of 1,2-dichloroethylene exposure.
	Metric 14:	Reproducibility of Analyses	Medium	Description was sufficient to be conceptually reproducible.
	Metric 15:	Statistical Analysis	Low	Statistical model to calculate odds ratio was not described.

Additional Comments: This nested case-control study within a cohort study is a good study design to answer the research question regarding the association between multiple chemical exposures and four cancer sites. Cases and controls are selected appropriate. However, there are several limitations in this study: (1) confounders were not all considered and adjusted for, except that age-adjusted odds ratios were conducted; (2) it is not described if co-exposures were adjusted for; (3) numbers of cancer cases for each cancer type were small, so the statistical power is limited; (4) statistical models for calculating odds ratios were not described.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Nested case-control design; cases selected from deaths in cohort study was described by Rinsky et al (1988; HERO 597923) (29,139 workers in Union Carbide facilities in West Virginia followed from 1940 to 1978). Vital status complete for 95% of cohort members.
	Metric 2:	Attrition	High	There was minimal exclusion of subjects/missing data, because vital status follow-up was complete for 96% of the 29,139 men in the cohort study.
	Metric 3:	Comparison Group	Medium	Controls were randomly selected in a 5:1 ratio to cases from the total employee cohort such that they were first employed in the same decade and survived to the same five-year survival period as cases. Controls survived at least to the beginning of the five-year interval in which cases died. Controls were independently selected for each of the individual disease subcategories. However, the demographic information between cases and controls were not compared in the paper.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was partially described: (1) Potential employee contact with a specific substance was determined by tracing each employee's work assignments and linking these assignment records to a separate computer file that contained a history of departmental usage for each substance; (2) Potential exposure to each chemical group was assumed on the basis of assignment o a production unit with a history of usage of any member of that chemical group. However, exposure level either based on work assignment in departments such as job exposure matrix or on the chemical levels were not presented.
	Metric 5:	Exposure Levels	Low	The range of exposure is limited. For example, exposure was presented by the duration of work in two categories: <5 years and 5+ years.
	Metric 6:	Temporality	Medium	Temporality is established, but it is unclear whether the exposures fall within the relevant exposure window. Authors used a lag time of 5 years; since controls were selected for 5 yr intervals, the effective lag time ranged from 5-9 years with an average of 7.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Case definition was based on death certificate diagnosis; but no method validation was conducted against this well-established methods.
	Metric 8:	Reporting Bias	Medium	All outcomes reported, but ORs for many analyses presented without CIs (some CIs reported in text).
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Low	There is indirect evidence that considerations were not made for potential confounders (ORs not adjusted, controls not age- or race-matched). Even though authors note that "Age-adjusted stratified analyses, which were also conducted, did not materially modify the odds ratio estimates". Also stratified examination of odds ratios were conducted to assess duration of exposure effects. However, other key confounders e.g., smoking status and race were not accounted for.
	Metric 10:	Covariate Characterization	Medium	The only potential confounder considered was age; this was presumably evaluated based on employment records (no discussion presented). Age-adjusted stratified analyses were conducted.
	Metric 11:	Co-exposure Counfounding	Low	Co-exposures were present and were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Nested case-control study design is appropriate for research question. Initial data analysis included crude odds ratio and then stratified examination of odds ratios was conducted to ass duration of exposure effect. Also, age-adjusted stratified analysis was conducted.
	Metric 13:	Statistical Power	Low	Statistical power calculations were not reported. Case numbers for each disease were low. The number of subjects was not sufficient to detect an effect of 1,2-dichloroethylene exposure.
	Metric 14:	Reproducibility of Analyses	Medium	Description was sufficient to be conceptually reproducible.
	Metric 15:	Statistical Analysis	Low	Statistical model to calculate odds ratio was not described.

Additional Comments: This nested case-control study within a cohort study is a good study design to answer the research question regarding the association between multiple chemical exposures and four cancer sites. Cases and controls are selected appropriate. However, there are several limitations in this study: (1) confounders were not all considered and adjusted for, except that age-adjusted odds ratios were conducted; (2) it is not described if co-exposures were adjusted for; (3) numbers of cancer cases for each cancer type were small, so the statistical power is limited; (4) statistical models for calculating odds ratios were not described.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Cheng, T.J., Huang, M.L., You, N.C., Du, C.L., Chau, T.T. (1999). Abnormal liver function in workers exposed to low levels of ethylene dichloride and vinyl chloride monomer. Journal of Occupational and Environmental Medicine 41(12):1128-1133.
Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	AST, ALT, GGT, Hepatitis B virus surface antigen (HBsAg), and anti-hepatitis C virus antibody (anti-HCV).
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	200266

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	A total of 251 male workers were included from 4 vinyl chloride monomer manufacturing plants. Other details on recruitment strategy, eligibility criteria, year of enrollment, and participation rates were not provided.
	Metric 2:	Attrition	Low	There was no indication of attrition and details on the number of eligible participants throughout the study was limited. Attrition could not be adequately assessed due to a lack of information regarding recruitment and selection.
	Metric 3:	Comparison Group	Medium	The low-EDC-low-VCM group (187 participants) was used as the comparison group, and there is indirect evidence groups are similar. Limited details were provided for setting, inclusion and exclusion criteria, and methods of participant selection.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	NIOSH recommended methods 1003 and 1007 were used for personal and area sampling, respectively. Air samples were collected, stored at 4 deg. C, and analyzed within 2 weeks of the sampling event. However, historical job changes, changes in exposure levels over time, and timing (year or days during work week) or duration of area or personal sampling were not reported.
	Metric 5:	Exposure Levels	Medium	EDC and VCM levels were reported for the different categories of jobs, which were classified into low-EDC-low-VCM, mod-EDC-low-VCM, and low-EDC-mod-VCM groups.
	Metric 6:	Temporality	High	The age of participants (mean age 33.7-40.1 years) and employment duration (mean 7.5-14.3 years) were reported, and the temporality between the exposure and outcome appears to be appropriate.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	AST, ALT, and GGT "were analyzed with a Hitachi 7050 autoanalyzer". A basis for the cutoff values used in Table 4 to determine "abnormal" AST, ALT, and GGT levels was not provided.
	Metric 8:	Reporting Bias	High	Odds ratios for abnormal liver function were provided with 95% confidence intervals, the number per exposure level, and significance when applicable.
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Cheng, T.J., Huang, M.L., You, N.C., Du, C.L., Chau, T.T. (1999). Abnormal liver function in workers exposed to low levels of ethylene dichloride and vinyl chloride monomer. Journal of Occupational and Environmental Medicine 41(12):1128-1133.
Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	AST, ALT, GGT, Hepatitis B virus surface antigen (HBsAg), and anti-hepatitis C virus antibody (anti-HCV).
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	200266

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Medium	The study reports information on potential confounders (age, hepatitis, BMI, alcohol use, and employment duration), and controls for hepatitis, BMI and alcohol consumption in the multiple logistic regression analyses. There is indirect evidence that appropriate adjustments were made.
	Metric 10:	Covariate Characterization	Medium	An interviewer administered the questionnaires to collect information about potential confounders and occupational history.
	Metric 11:	Co-exposure Counfounding	Low	Exposure to ethylene dichloride was evaluated in a vinyl chloride monomer (VCM) manufacturing facility, and VCM was also subsequently analyzed using personal and area sampling. Results for VCM exposure concentrations were provided. VCM is also suspected to cause liver damage.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design (cohort) was appropriate to assess the outcome of interest (”markers of liver damage”). Chi-squared (X2) test and multiple logistic regression were used for statistical analyses.
	Metric 13:	Statistical Power	Medium	The number of participants was adequate to detect an effect in the exposed populations, although power calculations were not provided. There were >20 participants in each group.
	Metric 14:	Reproducibility of Analyses	Low	A description of the logistic regression analysis was provided, however, study authors do not provide information on categorization of abnormal liver function.
	Metric 15:	Statistical Analysis	High	There were no identifiable logistic regression model assumption violations.
Domain 6: Other (if applicable) Considerations for Biomarker Selection and Measurement (Lakind et al. 2014)				
	Metric 16:	Use of Biomarker of Exposure	N/A	Biomarker of exposures were not assessed.
	Metric 17:	Effect Biomarker	High	This study uses aspartate aminotransferase, alanine aminotransferase, and y-glutamyltransferase as biomarkers of effect. While these no works cited to explain their connection to liver function, all three are well-known marker of liver function. Similarly, Hepatitis B virus surface antigen and antihepatitis C virus anitbody are also well-known measures of liver function and health.
	Metric 18:	Method Sensitivity	Low	No limit of detection information is provided for any of the effect biomarkers.
	Metric 19:	Biomarker Stability	Medium	While the study does not provide a lot of information regarding biomarker storage or stability, the authors do mention that venous blood used to detect biomarkers was stored at 4 degrees C.
	Metric 20:	Sample Contamination	Medium	No specific information regarding potential sample contamination was provided.
	Metric 21:	Method Requirements	Medium	Aspartate aminotransferase, alanine aminotransferase, and y-glutamyltransferase were analyzed using a Hitachi 7050 autoanalyzer. Hepatitis B virus surface antibody and antihepatitis C virus antibody were assessed with radioimmunoassay and enzyme-linked immunosorbent assay.

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Study Citation:	Cheng, T.J., Huang, M.L., You, N.C., Du, C.L., Chau, T.T. (1999). Abnormal liver function in workers exposed to low levels of ethylene dichloride and vinyl chloride monomer. Journal of Occupational and Environmental Medicine 41(12):1128-1133.
Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	AST, ALT, GGT, Hepatitis B virus surface antigen (HBsAg), and anti-hepatitis C virus antibody (anti-HCV).
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	200266

Domain	Metric	Rating	Comments
	Metric 22: Matrix Adjustment	N/A	No information on matrix adjustment was provided/available.

Additional Comments: A group of 251 male workers from 4 vinyl chloride monomer (VCM) manufacturing plants were included in this assessment to examine if occupational exposure to VCM and ethylene dichloride (EDC) "resulted in increased risk of liver damage" by examining AST, ALT, and GGT levels in the blood. Increased ORs for abnormal AST (>37 IU/L) and ALT (>41 IU/L) in the mod-EDC-low-VCM group (0.17-333.7 ppm EDC, 0.18-0.34 ppm VCM), compared with the low-EDC-low-VCM group, was reported. Exposure levels were measured using area and personal sampling, but the timing and duration of the sampling events were not reported.

Overall Quality Determination Medium

Study Citation:	Dosemeci, M., Cocco, P., Chow, W.H. (1999). Gender differences in risk of renal cell carcinoma and occupational exposures to chlorinated aliphatic hydrocarbons. American Journal of Industrial Medicine 36(1):54-59.
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	renal cell carcinoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	4697224

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	The details of the study design were reported elsewhere (Chow et al. 1994, HERO ID 701514). Brief details about the setting, date, number of eligible participants, and control matching were reported. Reasons for exclusions/non-participation were described with details by Chow et al. (1994).
	Metric 2:	Attrition	High	For the details of the study design and attrition of study subjects, the study authors referred to another publication by Chow et al., 1994. Chow et al. (1994) mentioned that at the end of the personal interview, the respondents were given a self-administered food-frequency questionnaire. Of the subjects interviewed for the study, 632 patients (79% of 796 eligible patients) and 653 control subjects (79% of 707 eligible control subjects) returned the diet questionnaire. A number of subjects, whose responses were considered unreliable, were excluded from the analysis, including 48 patients and three control subjects who had seven or more skipped food items or had questionable data and 50 patients whose next-of-kin respondent was not a spouse. Also excluded were two patients with unknown smoking status, since smoking is a risk factor.
	Metric 3:	Comparison Group	Medium	The cases were pulled from the Minnesota Cancer Surveillance System. Controls were selected from the general population of Minnesota; controls age 20-64 years were selected through random digital dialing and controls age 65-85 years were collected from files through the Health Care Financing Administration. Controls were age- and gender-stratified and were of the same race. Characteristics of cases and controls were not provided in the text or a table.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	High	Occupational histories including the most recent and usual occupation and industry, job activities, started-year and ended-year, and part-time/full-time status were collected. Occupations and industries were coded according to the standard occupational classification (SOC) and standard industrial classification (SIC) schemes. The National Cancer Institute developed job exposure matrices (JEM) for nine individual chlorinated aliphatic hydrocarbons (CAHCs), all CAHCs-combined, and all organic solvents-combined. These JEMs were merged with assigned SOC and SIC to determine the exposure status to these chemicals for each study subject. Application of the JEM was described elsewhere (Dosemeci et al. 1994, HERO ID 632334; Gomez et al. 1994, HERO ID 702154).
	Metric 5:	Exposure Levels	Medium	Details of the application of the JEM were described elsewhere (Dosemeci et al. 1994, HERO ID 632334; Gomez et al. 1994, HERO ID 702154). Dosemeci et al. (1994) described more details about that this study assigned three levels of probability (low, medium, high) to industries and occupations for chemical exposure levels.

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Study Citation:	Dosemeci, M., Cocco, P., Chow, W.H. (1999). Gender differences in risk of renal cell carcinoma and occupational exposures to chlorinated aliphatic hydrocarbons. American Journal of Industrial Medicine 36(1):54-59.
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	renal cell carcinoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	4697224

Domain	Metric		Rating	Comments
	Metric 6:	Temporality	Medium	Occupational questionnaires identified prior exposures based on reported recent and usual occupations as well as duration of employment. Outcome status was determined from registry data. The authors note that some occupational history was incomplete which may result in some uncertainty in regard to temporality.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Cases were identified as newly diagnosed and histologically confirmed renal cell carcinoma through the Minnesota Cancer Surveillance System and information about each participant was collected using a questionnaire. Validation was not specified.
	Metric 8:	Reporting Bias	Medium	A description of measured outcomes is reported and ORs were stratified by sex. Effect estimates are reported with a confidence interval. One table showed the total numbers of men and women respectively for each chemical, but numbers of cases/controls were not reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Appropriate adjustments were made in the final analysis, including age, gender, smoking, hypertension and the use of diuretics and/or anti-hypertension drugs, and BMI. Results were stratified by sex.
	Metric 10:	Covariate Characterization	Medium	Information about participants was collected using a questionnaire, and it includes potential confounders, e.g., smoking habits. Validation was not specified.
	Metric 11:	Co-exposure Counfounding	Medium	Co-exposures were identified through the job exposure matrices. Chemicals were evaluated individually and as a group.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen (case-control) was appropriate for the research question (renal cell carcinoma risk from occupational organic solvent exposure). Logistic regression models were used to estimate the relative risk and 95% CI.
	Metric 13:	Statistical Power	Low	Statistical power calculations were not provided. No significant effects were observed with 1,2-dichloroethane. The number of participated women to calculate odds ratio was inadequate to detect an effect in the participants for other chemicals or the combined risk, because it was very low.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis was brief, but is sufficient to understand precisely what has been done and to be conceptually reproducible with access to the analytic data.
	Metric 15:	Statistical Analysis	High	Model assumptions for logistic regression were met. The odds ratios were adjusted for age, smoking, hypertension status and/or use of diuretic and/or anti-hypertension drugs, and body mass index for men and women separately.

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Study Citation:	Dosemeci, M., Cocco, P., Chow, W.H. (1999). Gender differences in risk of renal cell carcinoma and occupational exposures to chlorinated aliphatic hydrocarbons. American Journal of Industrial Medicine 36(1):54-59.
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	renal cell carcinoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	4697224

Domain	Metric	Rating	Comments
Additional Comments:	A group of 438 cases (273 men and 165 women) were selected from the Minnesota Cancer Surveillance System that had been newly diagnosed with renal cell carcinoma. Controls included 687 participants (462 men and 225 women) age- and gender- stratified that were selected from either the general population of Minnesota (age 20-64 years) or from the Health Care Financing Administration files (age 65-85). No significant increase in the risk of renal cell carcinoma was observed with exposure to 1,2-dichloroethane among men or women separately, or for all participants exposed.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Dosemeci, M., Cocco, P., Chow, W.H. (1999). Gender differences in risk of renal cell carcinoma and occupational exposures to chlorinated aliphatic hydrocarbons. American Journal of Industrial Medicine 36(1):54-59.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	renal cell carcinoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	4697224

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	The details of the study design were reported elsewhere (Chow et al. 1994, HERO ID 701514). Brief details about the setting, date, number of eligible participants, and control matching were reported. Reasons for exclusions/non-participation were described with details by Chow et al. (1994).
	Metric 2:	Attrition	Medium	For the details of the study design and attrition of study subjects, the study authors referred to another publication by Chow et al., 1994. Chow et al. (1994) mentioned that at the end of the personal interview, the respondents were given a self-administered food-frequency questionnaire. Of the subjects interviewed for the study, 632 patients (79% of 796 eligible patients) and 653 control subjects (79% of 707 eligible control subjects) returned the diet questionnaire. A number of subjects, whose responses were considered unreliable, were excluded from the analysis, including 48 patients and three control subjects who had seven or more skipped food items or had questionable data and 50 patients whose next-of-kin respondent was not a spouse. Also excluded were two patients with unknown smoking status, since smoking is a risk factor.
	Metric 3:	Comparison Group	Medium	The cases were pulled from the Minnesota Cancer Surveillance System. Controls were selected from the general population of Minnesota; controls age 20-64 years were selected through random digital dialing and controls age 65-85 years were collected from files through the Health Care Financing Administration. Controls were age- and gender-stratified and were of the same race. Characteristics of cases and controls were not provided in the text or a table.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	High	Occupational histories including the most recent and usual occupation and industry, job activities, started-year and ended-year, and part-time/full-time status were collected. Occupations and industries were coded according to the standard occupational classification (SOC) and standard industrial classification (SIC) schemes. The National Cancer Institute developed job exposure matrices (JEM) for nine individual chlorinated aliphatic hydrocarbons (CAHCs), all CAHCs-combined, and all organic solvents-combined. These JEMs were merged with assigned SOC and SIC to determine the exposure status to these chemicals for each study subject. Application of the JEM was described elsewhere (Dosemeci et al. 1994, HERO ID 632334; Gomez et al. 1994, HERO ID 702154).
	Metric 5:	Exposure Levels	Medium	Details of the application of the JEM were described elsewhere (Dosemeci et al. 1994, HERO ID 632334; Gomez et al. 1994, HERO ID 702154). Dosemeci et al. (1994) described more details about that this study assigned three levels of probability (low, medium, high) to industries and occupations for chemical exposure levels.

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Study Citation:	Dosemeci, M., Cocco, P., Chow, W.H. (1999). Gender differences in risk of renal cell carcinoma and occupational exposures to chlorinated aliphatic hydrocarbons. American Journal of Industrial Medicine 36(1):54-59.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	renal cell carcinoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	4697224

Domain	Metric		Rating	Comments
	Metric 6:	Temporality	Medium	Occupational questionnaires identified prior exposures based on reported recent and usual occupations as well as duration of employment. Outcome status was determined from registry data. The authors note that some occupational history was incomplete which may result in some uncertainty in regard to temporality.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Cases were identified as newly diagnosed and histologically confirmed renal cell carcinoma through the Minnesota Cancer Surveillance System and information about each participant was collected using a questionnaire. Validation was not specified.
	Metric 8:	Reporting Bias	Medium	A description of measured outcomes is reported and ORs were stratified by sex. Effect estimates are reported with a confidence interval. One table showed the total numbers of men and women respectively for each chemical, but numbers of cases/controls were not reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Appropriate adjustments were made in the final analysis, including age, gender, smoking, hypertension and the use of diuretics and/or anti-hypertension drugs, and BMI. Results were stratified by sex.
	Metric 10:	Covariate Characterization	Medium	Information about participants was collected using a questionnaire, and it includes potential confounders, e.g., smoking habits. Validation was not specified.
	Metric 11:	Co-exposure Counfounding	Medium	Co-exposures were identified through the job exposure matrices. Chemicals were evaluated individually and as a group.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen (case-control) was appropriate for the research question (renal cell carcinoma risk from occupational organic solvent exposure). Logistic regression models were used to estimate the relative risk and 95% CI.
	Metric 13:	Statistical Power	Low	Statistical power calculations were not provided. No significant effects were observed with 1,2-dichloroethane. The number of participated women to calculate odds ratio was inadequate to detect an effect in the participants for other chemicals or the combined risk, because it was very low.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis was brief, but is sufficient to understand precisely what has been done and to be conceptually reproducible with access to the analytic data.
	Metric 15:	Statistical Analysis	High	Model assumptions for logistic regression were met. The odds ratios were adjusted for age, smoking, hypertension status and/or use of diuretic and/or anti-hypertension drugs, and body mass index for men and women separately.

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Study Citation:	Dosemeci, M., Cocco, P., Chow, W.H. (1999). Gender differences in risk of renal cell carcinoma and occupational exposures to chlorinated aliphatic hydrocarbons. American Journal of Industrial Medicine 36(1):54-59.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	renal cell carcinoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	4697224

Domain	Metric	Rating	Comments
Additional Comments:	A group of 438 cases (273 men and 165 women) were selected from the Minnesota Cancer Surveillance System that had been newly diagnosed with renal cell carcinoma. Controls included 687 participants (462 men and 225 women) age- and gender- stratified that were selected from either the general population of Minnesota (age 20-64 years) or from the Health Care Financing Administration files (age 65-85). No significant increase in the risk of renal cell carcinoma was observed with exposure to 1,2-dichloroethane among men or women separately, or for all participants exposed.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Garcia, E., Hurley, S., Nelson, D.O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health: A Global Access Science Source 14(1):14.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	breast cancer in females
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	3014082

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	A total of 112,378 women were included in this study out of 133,479 eligible female participants from the California Teacher Study cohort. A full description of the cohort is provided in Bernstein et al. 2002 (HERO ID 808446). Reasons for exclusion were provided. The reported information indicates that participant selection in or out of the study and participation was not likely to be biased.
	Metric 2:	Attrition	High	112,378/133,479 participants were included in the study. Exclusions were for the purpose of the study and analysis. Exclusion criteria were documented. Included participants had completed questionnaires. The California Cancer Registry is estimated to be 99% complete.
	Metric 3:	Comparison Group	Medium	There is only indirect evidence that groups are similar. Participants were recruited from the same eligible population with the same method of ascertainment. Comparisons were provided for participants with and without breast cancer. Characteristics between these two groups were generally similar. 5 Quintiles of exposure were used, and Q2-5 were compared with Q1.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	High	The Assessment System for Population Exposure Nationwide and the Human Exposure Model are used as part of the National-Scale Air Toxics Assessment produced by the EPA and was used to estimate ambient HAP concentrations for geographic locations. Methods are described online through the US EPA Assessment Methods.
	Metric 5:	Exposure Levels	Medium	The distribution of the NATA annual ambient concentration for each compound was plotted in Figure 1 using a box plot, and 5 Quintiles were used in the analyses.
	Metric 6:	Temporality	Medium	The follow-up period was from 1995-2011, and the NATA estimates were made in 2002 because it was approximately half way between the start and end of the follow-up period. However, it is unclear whether exposures fall within relevant exposure windows for the outcome of interest.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Annual linkage between the CTS cohort and the California Cancer Registry (CCR) was used to identify cases of invasive breast cancer. The CCR is estimated to be 99% complete. The case of invasive breast cancer was defined by ICD codes.

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Study Citation:	Garcia, E., Hurley, S., Nelson, D.O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health: A Global Access Science Source 14(1):14.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	breast cancer in females
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	3014082

Domain	Metric		Rating	Comments
	Metric 8:	Reporting Bias	Medium	A description of measured outcome is reported for adjustments by age and race, and effect estimates are reported with a 95% confidence interval. The measured outcomes using multiple comparisons were generally described in the text, but non-significant results were excluded from Table 3.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	The models were stratified by age and race. Additionally, adjustments were made for multiple comparisons among subsets of the participants (significant results reported in Table 3). Socioeconomic status (SES) of each participant was not evaluated, however, cohort SES characteristics were thought to be similar by study authors.
	Metric 10:	Covariate Characterization	Medium	Information about baseline characteristics for each participant was collected through a questionnaire. It is unknown if the questionnaire was validated.
	Metric 11:	Co-exposure Counfounding	Medium	A total of 37 compounds were identified as mammary gland carcinogens, but 13 were not included in this analysis. Thirteen compounds were excluded from the analysis due to insufficient variability (nine because they had the same value for all census tracts in the state of California; and four because they had less than 25% non-zero values). Ethylene dichloride (1,2-dichloroethane) was among the 24 compounds evaluated in this assessment, and evaluations for breast cancer were conducted for each of these 24 individual compounds.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen (prospective cohort) was appropriate for the research question (incidence of breast cancer). Cox proportional hazard models and SAS 9.3 were used in this assessment. Data analysis was described.
	Metric 13:	Statistical Power	Medium	Statistical power calculations were not provided. No significant effects were observed with ethylene dichloride (1,2-dichloroethane), however, this study utilized a large cohort, approximately 112,000 individuals. Distributions of chemicals of interest suggest there were sufficient numbers of participants in exposure subgroups.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to understand precisely what has been done and to be conceptually reproducible with access to the analytic data.
	Metric 15:	Statistical Analysis	High	The statistical models that were used were identified and described. ”No apparent violation of the underlying assumption of proportional hazards was detected”.

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Study Citation:	Garcia, E., Hurley, S., Nelson, D.O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health: A Global Access Science Source 14(1):14.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	breast cancer in females
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	3014082

Domain	Metric	Rating	Comments
Additional Comments:	A group of 112,378 female participants from the California Teacher Study cohort were assessed for their estimated exposure to ambient air pollutants, including ethylene dichloride (1,2-dichloroethane), and the incidence of invasive breast cancer. Air contaminant concentrations were estimated using the US EPA NATA and the ASPEN and HEM models. The approximate median concentration of 1,2-dichloroethane is between 1E-4 and 1E-2 (estimated from Figure 1). Exposures were categorized into 5 Quintiles, and compared against Quintile 1. No significant increase in the estimated hazard rate ratio for invasive breast cancer was observed with Quintile 2-5 exposure estimates for 1,2-dichloroethane, adjusted for age and race, when compared against Quintile 1, or when further adjusted using multiple comparisons.		

Overall Quality Determination High

* No biomarkers were identified for this evaluation.

Study Citation:	Garcia, E., Hurley, S., Nelson, D.O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health: A Global Access Science Source 14(1):14.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	breast cancer in females
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	3014082

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	A total of 112,378 women were included in this study out of 133,479 eligible female participants from the California Teacher Study cohort. A full description of the cohort is provided in Bernstein et al. 2002 (HERO ID 808446). Reasons for exclusion were provided. The reported information indicates that participant selection in or out of the study and participation was not likely to be biased.
	Metric 2:	Attrition	High	112,378/133,479 participants were included in the study. Exclusions were for the purpose of the study and analysis. Exclusion criteria were documented. Included participants had completed questionnaires. The California Cancer Registry is estimated to be 99% complete.
	Metric 3:	Comparison Group	Medium	There is only indirect evidence that groups are similar. Participants were recruited from the same eligible population with the same method of ascertainment. Comparisons were provided for participants with and without breast cancer. Characteristics between these two groups were generally similar. 5 Quintiles of exposure were used, and Q2-5 were compared with Q1.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	High	The Assessment System for Population Exposure Nationwide and the Human Exposure Model are used as part of the National-Scale Air Toxics Assessment produced by the EPA and was used to estimate ambient HAP concentrations for geographic locations. Methods are described online through the US EPA Assessment Methods.
	Metric 5:	Exposure Levels	Medium	The distribution of the NATA annual ambient concentration for each compound was plotted in Figure 1 using a box plot, and 5 Quintiles were used in the analyses.
	Metric 6:	Temporality	Medium	The follow-up period was from 1995-2011, and the NATA estimates were made in 2002 because it was approximately half way between the start and end of the follow-up period. However, it is unclear whether exposures fall within relevant exposure windows for the outcome of interest.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Annual linkage between the CTS cohort and the California Cancer Registry (CCR) was used to identify cases of invasive breast cancer. The CCR is estimated to be 99% complete. The case of invasive breast cancer was defined by ICD codes.
	Metric 8:	Reporting Bias	Medium	A description of measured outcome is reported for adjustments by age and race, and effect estimates are reported with a 95% confidence interval. The measured outcomes using multiple comparisons were generally described in the text, but non-significant results were excluded from Table 3.

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Study Citation:	Garcia, E., Hurley, S., Nelson, D.O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health: A Global Access Science Source 14(1):14.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	breast cancer in females
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	3014082

Domain	Metric		Rating	Comments
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	The models were stratified by age and race. Additionally, adjustments were made for multiple comparisons among subsets of the participants (significant results reported in Table 3). Socioeconomic status (SES) of each participant was not evaluated, however, cohort SES characteristics were thought to be similar by study authors.
	Metric 10:	Covariate Characterization	Medium	Information about baseline characteristics for each participant was collected through a questionnaire. It is unknown if the questionnaire was validated.
	Metric 11:	Co-exposure Counfounding	Medium	A total of 37 compounds were identified as mammary gland carcinogens, but 13 were not included in this analysis. Thirteen compounds were excluded from the analysis due to insufficient variability (nine because they had the same value for all census tracts in the state of California; and four because they had less than 25% non-zero values). Ethylene dichloride (1,2-dichloroethane) was among the 24 compounds evaluated in this assessment, and evaluations for breast cancer were conducted for each of these 24 individual compounds.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen (prospective cohort) was appropriate for the research question (incidence of breast cancer). Cox proportional hazard models and SAS 9.3 were used in this assessment. Data analysis was described.
	Metric 13:	Statistical Power	Medium	Statistical power calculations were not provided. No significant effects were observed with ethylene dichloride (1,2-dichloroethane), however, this study utilized a large cohort, approximately 112,000 individuals. Distributions of chemicals of interest suggest there were sufficient numbers of participants in exposure subgroups.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to understand precisely what has been done and to be conceptually reproducible with access to the analytic data.
	Metric 15:	Statistical Analysis	High	The statistical models that were used were identified and described. ”No apparent violation of the underlying assumption of proportional hazards was detected”.

Additional Comments: A group of 112,378 female participants from the California Teacher Study cohort were assessed for their estimated exposure to ambient air pollutants, including ethylene dichloride (1,2-dichloroethane), and the incidence of invasive breast cancer. Air contaminant concentrations were estimated using the US EPA NATA and the ASPEN and HEM models. The approximate median concentration of 1,2-dichloroethane is between 1E-4 and 1E-2 (estimated from Figure 1). Exposures were categorized into 5 Quintiles, and compared against Quintile 1. No significant increase in the estimated hazard rate ratio for invasive breast cancer was observed with Quintile 2-5 exposure estimates for 1,2-dichloroethane, adjusted for age and race, when compared against Quintile 1, or when further adjusted using multiple comparisons.

Overall Quality Determination High

* No biomarkers were identified for this evaluation.

Study Citation:	Guo, P., Yokoyama, K., Piao, F., Sakai, K., Khalequzzaman, M., Kamijima, M., Nakajima, T., Kitamura, F. (2013). Sick building syndrome by indoor air pollution in Dalian, China. International Journal of Environmental Research and Public Health 10(4):1489-1504.
Health Outcome(s):	sick building syndrome
Reported Health Effect(s):	The statistical analysis considers all subjective self-reported symptoms together (not segregated by health outcome) as a group health outcome –sick building syndrome. The study compared two conditions for each studied chemical: combined self-reported symptoms to no symptoms. Therefore, only one form 3 was completed.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1938385

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Residents of a housing estate of 3000 homes were invited to a community meeting to explain the purpose of the study and volunteers were invited to participate. It was not reported whether these volunteers were different from the overall eligible population.
	Metric 2:	Attrition	Low	Of the 70 families that agreed to participate, questionnaires were provided by 59. Reasons of uncompleted questionnaires were not fully provided, and there was no comparison between those who participated and those who did not.
	Metric 3:	Comparison Group	Low	The overall description of the analysis sample indicated a wide range of ages and lengths of stay at the current residence. Thus it is hard to know that subjects in all exposure groups were similar. In addition, the methods of selecting participants in all exposure groups were not fully reported. The numbers of male and female smokers were reported, respectively, but the smoking status and age were not controlled in the statistical analysis.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure concentrations for each home were obtained by diffusion sampling over 24 hrs in the bedroom, kitchen, and outdoors; temperature, the vertical height of samplers, and ventilation (hours windows left open) were reported. Samples were analyzed by GC/MS. The number of samples per home is unclear. The frequency of measurements for each house was not reported.
	Metric 5:	Exposure Levels	Low	The frequency of detection was not reported, so it is difficult to ascertain the actual exposure range. In addition, the reported exposure levels were median, geometric mean, and 95% CI, so they are inadequate to develop an exposure-response estimate.
	Metric 6:	Temporality	Uninformative	For 1,2-dichloroethane, the study evaluated self-reported symptoms in the past (”since they moved into their flats”) and their association with sampling conducted during the study; thus, exposure was measured after the outcome.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Low	Participants provided self-reported symptoms using a questionnaire. Study authors cited a previous study, Kamijima et al., 2005 (in Japanese, HERO ID 1598645) for further details on the questionnaire. It was not clear whether the questionnaire was validated.

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Study Citation: Guo, P., Yokoyama, K., Piao, F., Sakai, K., Khalequzzaman, M., Kamijima, M., Nakajima, T., Kitamura, F. (2013). Sick building syndrome by indoor air pollution in Dalian, China. International Journal of Environmental Research and Public Health 10(4):1489-1504.

Health Outcome(s): sick building syndrome

Reported Health Effect(s): The statistical analysis considers all subjective self-reported symptoms together (not segregated by health outcome) as a group health outcome –sick building syndrome. The study compared two conditions for each studied chemical: combined self-reported symptoms to no symptoms. Therefore, only one form 3 was completed.

Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

Linked HERO ID(s): No linked references.

HERO ID: 1938385

Domain	Metric		Rating	Comments
	Metric 8:	Reporting Bias	Low	The study only mentioned subjective symptoms in the abstract or methods. The abstract and method sections did not report the specific symptoms included in the questionnaire or whether the questionnaire was open-ended for symptoms. The questionnaire was cited to Kamijima et al. 2005 (in Japanese).
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	Comparisons were made separately by sex. The distribution of age and time spent living in residence differed greatly between those reporting symptoms and those not reporting symptoms. Smoking was indicated but not controlled for in the analysis. In short, the statistical analysis did not consider these three potential confounders, age, time spent living in residence, and smoking.
	Metric 10:	Covariate Characterization	Low	Covariates were presumably evaluated via a questionnaire that was cited to Kamijima et al. 2005 (in Japanese).
	Metric 11:	Co-exposure Counfounding	Low	The analysis did not account for other exposures. A number of other VOCs, HCHO, and NO2 were measured in the homes. The concentrations of several other VOCs and HCHO were much higher (5-30x) than 1,2-dichloroethane and may also be associated with these symptoms.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Low	The study design is best characterized as cross-sectional. Only one analysis to compare exposure concentrations between those with and without symptoms was adjusted for a confounder, sex, via stratification. Other potential confounders were not adjusted for. Study authors combine responses for symptoms reported before and during the sampling period in one statistical analysis, which may not reflect the relationship between symptoms and contaminants' exposure at each period.
	Metric 13:	Statistical Power	Medium	Statistical power was not reported. The number of participants was sufficient to detect a difference in median concentration between those with and without symptoms.
	Metric 14:	Reproducibility of Analyses	Medium	Study presents sufficient description of analysis (statistical methods) to be conceptually reproducible with access to the raw data.
	Metric 15:	Statistical Analysis	Low	Study uses a Wilcoxon's rank sum test to compare exposure concentrations in persons with and without symptoms; test for equal variance is not reported.

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Study Citation:	Guo, P., Yokoyama, K., Piao, F., Sakai, K., Khalequzzaman, M., Kamijima, M., Nakajima, T., Kitamura, F. (2013). Sick building syndrome by indoor air pollution in Dalian, China. International Journal of Environmental Research and Public Health 10(4):1489-1504.
Health Outcome(s):	sick building syndrome
Reported Health Effect(s):	The statistical analysis considers all subjective self-reported symptoms together (not segregated by health outcome) as a group health outcome –sick building syndrome. The study compared two conditions for each studied chemical: combined self-reported symptoms to no symptoms. Therefore, only one form 3 was completed.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1938385

Domain	Metric	Rating	Comments
Additional Comments:	Concentrations of VOCs (including 1,2-dichloroethane), HCHO, and NO2 were measured in the 59 homes of families that agreed to participate after being informed of the nature of the study. Participants completed questionnaires asking about symptoms since they moved into the homes and the concentrations of selected compounds were compared among men and women reporting any symptoms vs no symptoms. Concentrations of 1,2-dichloroethane in homes of people with symptoms were higher than in homes without. p-Dichlorobenzene was measured in the homes as well, but median concentration was <DL and no further analysis was made. Unacceptable due to selection bias, lack of confounding control, inadequate outcome characterization, and lack of temporality.		

Overall Quality Determination — Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Kernan, G.J., Ji, B.T., Dosemeci, M., Silverman, D.T., Balbus, J., Zahm, S.H. (1999). Occupational risk factors for pancreatic cancer: A case-control study based on death certificates from 24 U.S. states. American Journal of Industrial Medicine 36(2):260-270.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Death from pancreatic cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	194820

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	The National Cancer Institute, National Institute of Occupational Safety and Health, and the National Center for Health Statistics reviewed death certificates from 24 states to select cases from those that had died from pancreatic cancer and matched controls. Controls with cause of death related to the outcome of interest (i.e. pancreatic diseases) were excluded from the study. All key elements of the study design were reported.
	Metric 2:	Attrition	Medium	There was no direct evidence of subject loss or exclusion of subgroups from analyses. The authors provide the total number of cases and controls in the analysis. Case and control data were taken from a registry. It can be assumed that the data are complete for each subject.
	Metric 3:	Comparison Group	High	Controls were selected from the same pool of death certificates from 24 states that cases were selected from. Controls with cause of death related to the outcome of interest were eliminated. Differences in baseline characteristics were controlled for via matching, stratification, and adjustment.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure was assessed via occupation and industry data on death certificates. A job matrix was further applied to assess the likely levels of exposure. Probability and intensity of exposure were estimated across four levels for each occupation. Only employment captured on the death certificate could be considered. The exposure assessment needs exposure information before the job listed on the death certificates.
	Metric 5:	Exposure Levels	Medium	The study offers 4 levels of estimated probability and intensity of exposure (referent, low, medium, high).
	Metric 6:	Temporality	Medium	Exposure was determined by occupational and industry codes on death certificates and indicate that exposure would precede disease, however, the timing and latency period is less clear.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Causes of mortality were determined from death certificates for both cases and controls. Death certificates were drawn from death registries of participating states (n=24). Causes of death were coded using ICD-9 codes, and pancreatic cancer was identified as ICD 157.
	Metric 8:	Reporting Bias	Medium	Measured outcomes, effect estimates and confidence intervals are reported. Number of exposed cases is reported for each analysis, however the number of controls (exposed and unexposed) are not reported for analyses.

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Study Citation:	Kernan, G.J., Ji, B.T., Dosemeci, M., Silverman, D.T., Balbus, J., Zahm, S.H. (1999). Occupational risk factors for pancreatic cancer: A case-control study based on death certificates from 24 U.S. states. American Journal of Industrial Medicine 36(2):260-270.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Death from pancreatic cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	194820

Domain	Metric		Rating	Comments
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Potential confounders were accounted for in the following ways: matching (five year age group, state, race, and gender); adjustment in models (age, marital status, metropolitan, and residential status); and stratification (race and gender). Smoking was not included as a confounder.
	Metric 10:	Covariate Characterization	Medium	Data used to assess potential confounders was derived from death certificates, an adequate measure. However, no information about cigarette smoking and other lifestyle factors were available for adjustment in the analysis.
	Metric 11:	Co-exposure Counfounding	Medium	The variety of industries considered in the analysis diminishes concerns about co-exposures.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The case-control study design and statistical analysis methods were appropriate to assess the exposures/outcome of interest.
	Metric 13:	Statistical Power	Medium	This study had an adequate sample size to detect an effect (n for cases = 63,097; n for controls = 252,386).
	Metric 14:	Reproducibility of Analyses	Medium	The description of analysis was sufficient and would be reproducible.
	Metric 15:	Statistical Analysis	High	The model to calculate risk estimates was transparent.

Additional Comments: This case-control study examined the risk of death from pancreatic cancer in different occupational settings. Exposure was solely assessed using occupation/industry at time of death (reported on death certificate) and the application of a job matrix assessing likely levels of exposure for different positions. This means of estimating exposure may not fully represent a participant's exposure history. Additionally, the number of impacted participants (exposed cases) was inadequate to perform quality analyses for some exposure levels.

Overall Quality Determination High

* No biomarkers were identified for this evaluation.

Study Citation:	Kernan, G.J., Ji, B.T., Dosemeci, M., Silverman, D.T., Balbus, J., Zahm, S.H. (1999). Occupational risk factors for pancreatic cancer: A case-control study based on death certificates from 24 U.S. states. American Journal of Industrial Medicine 36(2):260-270.
Health Outcome(s):	Endocrine
Reported Health Effect(s):	Death from pancreatic cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	194820

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	The National Cancer Institute, National Institute of Occupational Safety and Health, and the National Center for Health Statistics reviewed death certificates from 24 states to select cases from those that had died from pancreatic cancer and matched controls. Controls with cause of death related to the outcome of interest (i.e. pancreatic diseases) were excluded from the study. All key elements of the study design were reported.
	Metric 2:	Attrition	Medium	There was no direct evidence of subject loss or exclusion of subgroups from analyses. The authors provide the total number of cases and controls in the analysis. Case and control data were taken from a registry. It can be assumed that the data are complete for each subject.
	Metric 3:	Comparison Group	High	Controls were selected from the same pool of death certificates from 24 states that cases were selected from. Controls with cause of death related to the outcome of interest were eliminated. Differences in baseline characteristics were controlled for via matching, stratification, and adjustment.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure was assessed via occupation and industry data on death certificates. A job matrix was further applied to assess the likely levels of exposure. Probability and intensity of exposure were estimated across four levels for each occupation. Only employment captured on the death certificate could be considered. The exposure assessment needs exposure information before the job listed on the death certificates.
	Metric 5:	Exposure Levels	Medium	The study offers 4 levels of estimated probability and intensity of exposure (referent, low, medium, high).
	Metric 6:	Temporality	Medium	Exposure was determined by occupational and industry codes on death certificates and indicate that exposure would precede disease, however, the timing and latency period is less clear.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Causes of mortality were determined from death certificates for both cases and controls. Death certificates were drawn from death registries of participating states (n=24). Causes of death were coded using ICD-9 codes, and pancreatic cancer was identified as ICD 157.
	Metric 8:	Reporting Bias	Medium	Measured outcomes, effect estimates and confidence intervals are reported. Number of exposed cases is reported for each analysis, however the number of controls (exposed and unexposed) are not reported for analyses.
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Kernan, G.J., Ji, B.T., Dosemeci, M., Silverman, D.T., Balbus, J., Zahm, S.H. (1999). Occupational risk factors for pancreatic cancer: A case-control study based on death certificates from 24 U.S. states. American Journal of Industrial Medicine 36(2):260-270.
Health Outcome(s):	Endocrine
Reported Health Effect(s):	Death from pancreatic cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	194820

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Medium	Potential confounders were accounted for in the following ways: matching (five year age group, state, race, and gender); adjustment in models (age, marital status, metropolitan, and residential status); and stratification (race and gender). Smoking was not included as a confounder.
	Metric 10:	Covariate Characterization	Medium	Data used to assess potential confounders was derived from death certificates, an adequate measure. However, no information about cigarette smoking and other lifestyle factors were available for adjustment in the analysis.
	Metric 11:	Co-exposure Counfounding	Medium	The variety of industries considered in the analysis diminishes concerns about co-exposures.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The case-control study design and statistical analysis methods were appropriate to assess the exposures/outcome of interest.
	Metric 13:	Statistical Power	Medium	This study had an adequate sample size to detect an effect (n for cases = 63,097; n for controls = 252,386).
	Metric 14:	Reproducibility of Analyses	Medium	The description of analysis was sufficient and would be reproducible.
	Metric 15:	Statistical Analysis	High	The model to calculate risk estimates was transparent.

Additional Comments: This case-control study examined the risk of death from pancreatic cancer in different occupational settings. Exposure was solely assessed using occupation/industry at time of death (reported on death certificate) and the application of a job matrix assessing likely levels of exposure for different positions. This means of estimating exposure may not fully represent a participant's exposure history. Additionally, the number of impacted participants (exposed cases) was inadequate to perform quality analyses for some exposure levels.

Overall Quality Determination High

* No biomarkers were identified for this evaluation.

Study Citation:	Niehoff, N.M., Gammon, M.D., Keil, A.P., Nichols, H.B., Engel, L.S., Sandler, D.P., White, A.J. (2019). Airborne mammary carcinogens and breast cancer risk in the Sister Study. Environment International 130:104897.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Breast cancer diagnosis (overall), tumor characteristics, and estrogen receptor positive (ER+) invasive breast cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5440630

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	Data from the Sister Study were used. The Sister Study is "a prospective cohort of 50,884 women from across the US who were ages 35–74 at enrollment (Sandler et al., 2017). Participants were recruited from 2003 to 2009 using a national advertising campaign in English and Spanish. Women were eligible for the Sister Study if they had a sister who had been diagnosed with breast cancer, but no prior breast cancer themselves."Exclusions from the study occurred for the following reasons:-breast cancer diagnosed before enrollment was complete, or did not have follow-up information (n = 163)-Residential address couldn't be geocoded (n = 1003, < 2%) - This is a small perecentage, but all of those who were excluded for this reason were from Puerto Rico, West Virginia, Missouri, or Oklahoma.Key elements of the study design are reported. There is some potential for selection bias, but based on the small percentage of those eligible who were excluded, participation was not likely to be substantially biased.
	Metric 2:	Attrition	High	Response rates in the overall Sister study remained over 91% over follow-up. Reasons for non-response were not reported, and characteristics of those lost to follow up were not reported or compared with those included, but 9% loss to follow-up is minimal.
	Metric 3:	Comparison Group	High	Differences in baseline characteristics of groups were considered as potential confounding variables.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	The EPA NATA database of census-tract level modeled air toxics data was used. The study authors note the potential for exposure misclassification: "Concentrations at the census tract level do not fully account for variation in an individual's daily activities that could lead to higher or lower exposure, and all women within a census tract are assigned the same concentration."
	Metric 5:	Exposure Levels	Medium	There were five quintiles of exposure, so there was a sufficient range and distribution of exposure.
	Metric 6:	Temporality	Medium	This is a prospective cohort study.Exposure data from 2005 were chosen because they represented the middle of the enrollment period (2003-2009).The study reported that "94% of women enrolled in 2005 or later, and thus the exposure assessment primarily predated enrollment for the majority of Sister Study participants."The six percent of women who had the potential to have the outcome before exposure was measured in 2005 are a concern. But sensitivity analyses were used to assess whether the associations changed when restricted to those who enrolled in 2005 or later.The authors note that the study is making assumptions about the relevant exposure windows - therefore the exposure window is not certain.

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Study Citation:	Niehoff, N.M., Gammon, M.D., Keil, A.P., Nichols, H.B., Engel, L.S., Sandler, D.P., White, A.J. (2019). Airborne mammary carcinogens and breast cancer risk in the Sister Study. Environment International 130:104897.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Breast cancer diagnosis (overall), tumor characteristics, and estrogen receptor positive (ER+) invasive breast cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5440630

Domain	Metric		Rating	Comments
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Women who reported a breast cancer diagnosis on the annual health updates or follow-up questionnaires were asked to provide additional diagnosis information, and to grant permission for the study to obtain medical records and pathology reports. Medical records were obtained for 81% of breast cancer diagnoses. Agreement between self-reported breast cancers and medical records was high (positive predictive value > 99%) (Sandler et al., 2017), so self-report was used when medical records were not available. Tumor characteristics (stage; histology; and estrogen receptor (ER) status) were abstracted from medical records, or self-reported.
	Metric 8:	Reporting Bias	High	A description of measured outcomes is reported. Effect estimates are reported with confidence intervals.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Covariates considered included age, race, BMI, residence type, education, and smoking status. Potential confounders were identified using DAGs and literature review. Appropriate considerations were made for potential confounders.
	Metric 10:	Covariate Characterization	Medium	”Most covariates were assessed by self-report at the baseline interview.””At baseline, women completed a computer-assisted telephone interview and written questionnaires.”Previous publications might describe whether the questionnaires were validated, but validation was not specified in this publication.
	Metric 11:	Co-exposure Counfounding	Medium	Co-exposures to other air pollutants were assessed, but at the census tract level.Multipollutant classification trees were used, which might provide useful qualitative information.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design (large prospective cohort) and analysis method (Cox proportional hazard single and multi-pollutant models accounting for potential confounders) were appropriate to assess the association between exposure and disease.
	Metric 13:	Statistical Power	Medium	The study had an adequate sample size (1975 cancer cases) and follow-up time (mean=8.4 years).
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to be conceptually reproducible.

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Study Citation:	Niehoff, N.M., Gammon, M.D., Keil, A.P., Nichols, H.B., Engel, L.S., Sandler, D.P., White, A.J. (2019). Airborne mammary carcinogens and breast cancer risk in the Sister Study. Environment International 130:104897.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Breast cancer diagnosis (overall), tumor characteristics, and estrogen receptor positive (ER+) invasive breast cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5440630

Domain	Metric	Rating	Comments
	Metric 15: Statistical Analysis	High	Hazard ratios and 95% confidence intervals (CIs) are reported "comparing index categories of exposure to exposures below the first quintile using Cox proportional hazards regression, with age as the time scale." The method of calculating the hazard ratios is transparent. The authors reported that "the proportional hazards assumption was evaluated by conducting a Wald test for an interaction between the continuous form of the air toxic measure and time." Censoring times and times at-risk are described.

Additional Comments: This was a well-conducted study of a large prospective cohort, but the measurement of exposure at the census-tract rather than the individual level is a limitation.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Sobel, W., Bond, G.G., Skowronski, B.J., Brownson, P.J., Cook, R.R. (1987). A soft tissue sarcoma case control study in a large multi-chemical manufacturing facility. Chemosphere 16(8-9):2095-2099.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	soft-tissue sarcoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1357737

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	From a pool of > 37,000 subjects who worked at least 1 year at chemical company between January 1940-December 1979, the study identified 14 people who died due to soft-cell sarcoma (via death certificate, medical records, or histopathology report). Referents were matched 9:1 with cases (126 matched controls).
	Metric 2:	Attrition	High	There was minimal subject exclusion from the analysis sample; one case could not be matched to controls and was excluded from analysis.
	Metric 3:	Comparison Group	High	Cases and controls were recruited from the same eligible population within the same time frame and matched on sex, race, year of birth and year of hire. Both cases and controls had to have worked ≥1 yr at the plant during the study period.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Work histories for cases and referents were coded to determine an individual's potential exposure to chemical of interest and reviewed by an industrial hygienist blinded to case status.
	Metric 5:	Exposure Levels	Low	Exposure was considered dichotomous, ever exposed or never exposed. There is no quantitative information on exposure levels or range of exposures.
	Metric 6:	Temporality	Low	Temporality of exposure and outcome is established. It is unclear if the interval between exposure and outcome is sufficient for soft tissue sarcoma outcomes.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	The soft-tissue sarcoma outcome was assessed by information provided by death certificates, medical records, and histopathology reports, but study authors did not report the proportions determined by each method.
	Metric 8:	Reporting Bias	High	All outcomes outlined were reported. Authors reported the number of cases and controls in the table. Maximum likelihood estimate ORs with respective 95 % confidence intervals were reported.
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Sobel, W., Bond, G.G., Skowronski, B.J., Brownson, P.J., Cook, R.R. (1987). A soft tissue sarcoma case control study in a large multi-chemical manufacturing facility. Chemosphere 16(8-9):2095-2099.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	soft-tissue sarcoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1357737

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Low	Controls were matched with cases on age, sex, year of hire and survival information. There is indirect evidence that the considerations were made to identify potential confounders through evaluation of medical records of cases and controls (various heritable syndromes, family history of cancer, history of lymphedema, steroids, throrotrast, foreign body implants, chronic extensive scarring, radiation therapy, and immunological defects). Identified confounders between cases and controls were not reported and it is unclear if adjustments for these confounders were included in the final analyses.
	Metric 10:	Covariate Characterization	High	Potential covariates were assessed through evaluation of work histories and medical records.
	Metric 11:	Co-exposure Counfounding	Low	The study documented 13 chemicals, known to be associated with soft-tissue sarcoma (according to NTP, 1983) that were used at the manufacturing facility at some point since 1940. The authors note that some individuals were exposed to multiple chemicals during their employment history and were counted multiple times in the analysis for different chemical exposures. Co-exposures to chemicals to not appear to be adjusted for in analysis.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Low	The study design was adequate to assess the association between exposure and the outcome of interest (soft-tissue sarcoma). The study authors noted they used programs developed by Rothman and Boice to calculate odds ratios with CI intervals; the statistical methods are not further described. The page containing the Rothman and Boice reference appears to be missing from the PDF (or the citation is missing).
	Metric 13:	Statistical Power	Low	Statistical power was not calculated. For 1,2-dichloroethane, there was one case and 6 controls included in the analysis, which was not adequate to detect and effect.
	Metric 14:	Reproducibility of Analyses	Low	The study calculated odd ratios, and 95% CIs were calculated using point estimates and chi from hypothesis testing. The study authors noted they used programs developed by Rothman and Boice to calculate odds ratios with 95% CIs; the statistical methods are not further described and there was no reference for the programs cited.
	Metric 15:	Statistical Analysis	Low	A description of analyses/assumptions was not reported.

Additional Comments: A case-control study of workers at a chemical production facility who worked at least 1 year between January 1940-December 1979 (n=37,000) investigated the incidence of deaths due to soft-tissue sarcoma. The study identified 14 people who died due to soft-tissue sarcoma (through death certificate, medical records, or histopathology reports). Cases were matched to controls based on sex, race, year of birth and year of hire. 13 chemicals, including 1,2-dichloroethane, associated with soft-tissue sarcoma were used at the facility; it does not appear that co-exposures were adjusted for in the analysis. Odds ratios and corresponding CIs were calculated. No significant association was found between exposure to 1,2-DCE and soft-tissue sarcoma.

Overall Quality Determination Medium

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Study Citation:	Sobel, W., Bond, G.G., Skowronski, B.J., Brownson, P.J., Cook, R.R. (1987). A soft tissue sarcoma case control study in a large multi-chemical manufacturing facility. Chemosphere 16(8-9):2095-2099.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	soft-tissue sarcoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1357737

Domain	Metric	Rating	Comments

* No biomarkers were identified for this evaluation.

Study Citation:	Sobel, W., Bond, G.G., Skowronski, B.J., Brownson, P.J., Cook, R.R. (1987). A soft tissue sarcoma case control study in a large multi-chemical manufacturing facility. Chemosphere 16(8-9):2095-2099.
Health Outcome(s):	Skin and Connective Tissue
Reported Health Effect(s):	soft-tissue sarcoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1357737

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	From a pool of > 37,000 subjects who worked at least 1 year at chemical company between January 1940-December 1979, the study identified 14 people who died due to soft-cell sarcoma (via death certificate, medical records, or histopathology report). Referents were matched 9:1 with cases (126 matched controls).
	Metric 2:	Attrition	High	There was minimal subject exclusion from the analysis sample; one case could not be matched to controls and was excluded from analysis.
	Metric 3:	Comparison Group	High	Cases and controls were recruited from the same eligible population within the same time frame and matched on sex, race, year of birth and year of hire. Both cases and controls had to have worked ≥1 yr at the plant during the study period.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Work histories for cases and referents were coded to determine an individual's potential exposure to chemical of interest and reviewed by an industrial hygienist blinded to case status.
	Metric 5:	Exposure Levels	Low	Exposure was considered dichotomous, ever exposed or never exposed. There is no quantitative information on exposure levels or range of exposures.
	Metric 6:	Temporality	Low	Temporality of exposure and outcome is established. It is unclear if the interval between exposure and outcome is sufficient for soft tissue sarcoma outcomes.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	The soft-tissue sarcoma outcome was assessed by information provided by death certificates, medical records, and histopathology reports, but study authors did not report the proportions determined by each method.
	Metric 8:	Reporting Bias	High	All outcomes outlined were reported. Authors reported the number of cases and controls in the table. Maximum likelihood estimate ORs with respective confidence intervals were reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	Controls were matched with cases on age, sex, year of hire and survival information. There is indirect evidence that that considerations were made to identify potential confounders through evaluation of medical records of cases and controls (various heritable syndromes, family history of cancer, history of lymphedema, steroids, throrotrast, foreign body implants, chronic extensive scarring, radiation therapy, and immunological defects). Identified confounders between cases and controls were not reported and it is unclear if adjustments for these confounders were included in the final analyses.

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Study Citation:	Sobel, W., Bond, G.G., Skowronski, B.J., Brownson, P.J., Cook, R.R. (1987). A soft tissue sarcoma case control study in a large multi-chemical manufacturing facility. Chemosphere 16(8-9):2095-2099.
Health Outcome(s):	Skin and Connective Tissue
Reported Health Effect(s):	soft-tissue sarcoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1357737

Domain	Metric		Rating	Comments
	Metric 10:	Covariate Characterization	High	Potential covariates were assessed through evaluation of work histories and medical records.
	Metric 11:	Co-exposure Counfounding	Low	The study documented 13 chemicals, known to be associated with soft-tissue sarcoma (according to NTP, 1983) that were used at the manufacturing facility at some point since 1940. The authors note that some individuals were exposed to multiple chemicals during their employment history and were counted multiple times in the analysis for different chemical exposures. Co-exposures to chemicals to not appear to be adjusted for in analysis.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Low	The study design was adequate to assess the association between exposure and the outcome of interest (soft-tissue sarcoma). The study authors noted they used programs developed by Rothman and Boice to calculate odds ratios with (95% CIs; the statistical methods are not further described. The page containing the Rothman and Boice reference appears to be missing from the PDF (or the citation is missing).
	Metric 13:	Statistical Power	Low	Statistical power was not calculated. For 1,2-dichloroethane, there was one case and 6 controls included in the analysis, which was not adequate to detect and effect.
	Metric 14:	Reproducibility of Analyses	Low	The study calculated odd ratios, and 95% CIs were calculated using point estimates and chi from hypothesis testing. The study authors noted they used programs developed by Rothman and Boice to calculate odds ratios with CI intervals; the statistical methods are not further described and there was no reference for the programs cited.
	Metric 15:	Statistical Analysis	Low	A description of analyses/assumptions was not reported.

Additional Comments: A case-control study of workers at a chemical production facility who worked at least 1 year between January 1940-December 1979 (n=37,000) investigated the incidence of deaths due to soft-tissue sarcoma. The study identified 14 people who died due to soft-tissue sarcoma (through death certificate, medical records, or histopathology reports). Cases were matched to controls based on sex, race, year of birth and year of hire. 13 chemicals, including 1,2-dichloroethane, associated with soft-tissue sarcoma were used at the facility; it does not appear that co-exposures were adjusted for in the analysis. Odds ratios and corresponding CIs were calculated. No significant association was found between exposure to 1,2-DCE and soft-tissue sarcoma.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Teta, M. J., Ott, M. G., Schnatter, A. R. (1991). An update of mortality due to brain neoplasms and other causes among employees of a petrochemical facility. Journal of Occupational Medicine 33(1):45-51.
Health Outcome(s):	Mortality
Reported Health Effect(s):	all cause mortality, gastrointestinal cancer mortality, respiratory system cancer mortality, kidney and other urinary organ cancer mortality, skin cancer mortality, brain cancer mortality, lymphatic and hematopoietic tissue cancer mortality, benign neoplasm mortality, heart disease mortality, and liver cirrhosis mortality.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200633, 1629047
HERO ID:	200633

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	The facility was described in some detail. All male employees working for one day or more between 1941 and 1983 were included. There may be some healthy worker effect in this population.
	Metric 2:	Attrition	High	Study authors reported that vital status was complete for 99% of the population, and death certificates were obtained for 99% of decedents.
	Metric 3:	Comparison Group	High	SMRs were calculated using age-, race-, and calendar year-specific mortality rates of males in the United States. All included employees were male.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	All employees were treated as exposed. Table 4 indicates that relatively few employees were employed in areas designated as 1,2-DCA work areas. There is potential for substantial exposure misclassification.
	Metric 5:	Exposure Levels	Low	All employed individuals were categorized as exposed, and the reference population was described as unexposed. This represents two levels of exposure. The distribution of exposure within the employed population is unclear.
	Metric 6:	Temporality	Medium	Employees were followed from 1950 (or date of first hire) through 1983. The relevant timing of exposure is not entirely clear; however, this represents a sufficiently long period of follow-up.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Mortality was tracked using company records, Social Security Administration records, and the National Death Index. Specific ICD codes and use of a nosologist were not described, but there was no evidence to suggest the method had poor validity.
	Metric 8:	Reporting Bias	High	SMRs were provided with confidence intervals in addition to observed and expected cases. The authors state they did not carry out regional specific SMRs due to the higher prevalence of neoplasms in the surrounding area.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	SMRs were restricted to males. Rates were age-, race-, and calendar period-specific. No consideration was made for smoking.
	Metric 10:	Covariate Characterization	Medium	Demographic information was obtained from employment records. This was not a validated method, but there was no evidence to suggest it was an invalid method.

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Study Citation:	Teta, M. J., Ott, M. G., Schnatter, A. R. (1991). An update of mortality due to brain neoplasms and other causes among employees of a petrochemical facility. Journal of Occupational Medicine 33(1):45-51.
Health Outcome(s):	Mortality
Reported Health Effect(s):	all cause mortality, gastrointestinal cancer mortality, respiratory system cancer mortality, kidney and other urinary organ cancer mortality, skin cancer mortality, brain cancer mortality, lymphatic and hematopoietic tissue cancer mortality, benign neoplasm mortality, heart disease mortality, and liver cirrhosis mortality.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200633, 1629047
HERO ID:	200633

Domain	Metric		Rating	Comments
	Metric 11:	Co-exposure Counfounding	Low	Several other occupational exposures linked to cancer mortality were present, including vinyl chloride, butanol, and other petrochemicals.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	This study design was appropriate for the research question. Authors utilized retrospective occupational cohort data to determine standardized mortality rates for cancer-specific mortalities.
	Metric 13:	Statistical Power	Medium	While power was not calculated, there were over 1350 deaths from 7849 employees which was adequate to detect robust effect estimates.
	Metric 14:	Reproducibility of Analyses	Low	Most details were provided; however, ICD codes used to determine and group cancer mortality diagnoses were not provided.
	Metric 15:	Statistical Analysis	High	No issues identified.

Additional Comments: This study utilized an occupational cohort to retrospectively evaluate elevated rates of cancer mortality among petrochemical plant workers. There were numerous potentially hazardous chemicals mentioned in the plant description which may lead to co-exposure. Additionally, it appears that only a moderate portion of workers may have been exposed to 1,2-DCA or worked in 1,2-DCA areas which may lead to some exposure misclassification and limit the study's ability to inform hazard on 1,2-DCA.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Cases in this case-control study were former Union Carbide Corporation (UCC) chemical plant employees in Texas City, Texas. Cases were identified through death certificate searches and tumor registries, and may have included individuals formerly employed at UCC whose cause of death was unknown to the company. Additionally, control deaths were stated to be pulled from corporate employee benefits department and through locally published obituary notices routinely screened by the medical department - it is possible to assume that cases were identified in a similar manner. The study identified cases of brain tumors by searching death certificates primarily, although tumor registries throughout the state of Texas were also searched. The study clarifies that it is possible that some cases were not found if they survived or died due to another cause - while this is likely to have impacted selection, there is no evidence that this would be differential by exposure status. Overall, there is limited information on the source population of workers from which cases were identified.
	Metric 2:	Attrition	Medium	Attrition is not discussed in the study, and outcome data appear to be complete. There was a large proportion of missing exposure data (roughly 50%) due to workers being employed in roles such as maintenance, where exposure to any chemical is possible but unknown. Analyses were run separately where these ”unknown” individuals were a) treated as exposed, b) treated as unexposed, or c) treated as unknown and thus excluded. The study only presents results for when these individuals were excluded but specifies that the first scenario resulted in increased exposure estimates for controls relative to cases.

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Study Citation:	Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
	Metric 3:	Comparison Group	Medium	The study identifies two series of control groups, selected from all former Union Carbide Corporation (UCC) employees. However, the total number of employees is not stated. Only those who were deceased were used as controls since they had known causes of death and could thus be verified as non-brain tumors. One group of controls excluded employees whose cause of death was due to any malignant neoplasm to allow for the possibility that a general chemical carcinogen may have been associated with cancers of other sites. The other group of controls included deaths from all causes; this included malignant neoplasms other than brain tumors. Both control groups had 80 male employees randomly selected from 450 deceased employees known to the company in June 1979. Control deaths were stated to be pulled from corporate employee benefits department and through locally published obituary notices routinely screened by the medical department - it is possible to assume that cases were identified in a similar manner. The study reports that cases were slightly more likely to have been employed for less than 10 years than controls - the study attributes this in part to the fact that employees whose deaths were known to the company were more likely to have worked for longer - regardless the mean number of years employed was similar between cases and controls. However, cases were more likely to have been terminated from their job for reasons other than death, disability, or retirement (quitting, being fired, etc.), were generally younger at hire, and were less likely to survive to their 70th birthday. None of these factors are controlled for in statistical analyses - however, since controls and cases were pulled from the same population, there is indirect evidence that the groups were similar.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was determined based on official employment records. Records included job title and department assignment codes for each employment from date of hire to date of termination. For each unique department code, UCC and NIOSH industrial hygienists identified principal chemicals used or produced at any time in the history of the plant and correlated those with individual departments. This assessment was not performed on a year-by-year basis due to concerns for recall bias for longer-term employees where less detailed records were kept. An employee was categorized as ”exposed” to 1,2-dichloroethane if they ever worked in a department associated with that chemical. An ”unknown” exposure group was also created to account for employees who had only worked in departments for which no specific chemical could be identified.
	Metric 5:	Exposure Levels	Low	The study does not report any quantitative information and only splits exposure into ”exposed”, ”unexposed”, and ”unknown”.
	Metric 6:	Temporality	High	In this study exposure is confirmed to occur before the outcome is measured. The study reports latency periods, with subjects dichotomized into less than 15 years of latency or more than 15 years of latency. The majority of cases and controls had a latency of greater than 15 years, which is sufficiently long for brain tumors.

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Study Citation:	Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Cases were identified through death certificate searches and partially through tumor registries in the state of Texas. Case validation was performed by NIOSH, and 5 different levels of confirmation were reported: 1) tissue specimen interpreted by the Armed Forces Institute of Pathology; 2) autopsy report; 3) histopathology report; 4) clinical diagnosis from hospital record; 5) dearth certificate diagnosis. Codes 1-3 were considered to be ”confirmed” cases of brain tumors, while 4-5 were considered unconfirmed. 5/21 cases were only evaluated using ”unconfirmed methods”, meaning there is likely a high amount of accuracy in roughly 75% of cases. While no case validation is reported for controls, the study specifies that only controls who had died and thus could be confirmed to be non-brain tumors were included.
	Metric 8:	Reporting Bias	Medium	All primary and secondary outcomes that are outlined in the methods are reported in the results. However, the only statistical outcome of their analysis were unadjusted p-values that were not reported and were just described qualitatively.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	The only statistical analysis performed were Mantel-Haenszel chi-squared tests, which did not allow for confounder adjustment. The study does not present a distribution of potential confounders by exposure status but by case/control status. Several variables, such as reason for termination, age at hire, and age at death were significantly different between cases and controls and were not accounted for in statistical modeling. The study explains that these differences are not likely to have any epidemiologic significance and appear to be relatively small differences.
	Metric 10:	Covariate Characterization	Medium	While the study does not explain where they obtained covariate information, it is reasonable to assume that they gathered the information from company records.
	Metric 11:	Co-exposure Counfounding	Low	The study assesses a wide range of other potential occupational co-exposures. While these co-exposures are not adjusted for in any statistical models, effect estimates are presented separately for benzene, diethyl sulfate, ethylene oxide, and vinyl chloride. The distribution of co-exposures across cases and controls is demonstrated to be mostly balanced by comparing proportions of exposed/unexposed between cases and controls. The only notable instance of imbalance is for benzene, where 11.1% of cases were exposed whereas 37.9% of all controls and 19.2% of non-neoplasm related controls were exposed.
Domain 5: Analysis				

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Study Citation:	Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	The study chose a case-control design, which was appropriate to study the rare disease of brain tumors and its association with occupational exposures. The only statistical analysis conducted is a Mantzel-Haenszel chi-squared test, but there is no reason to suggest that this would be inappropriate.
	Metric 13:	Statistical Power	Medium	The study does not calculate statistical power, but the number of cases (n=21) and controls (n=80 in each analysis) is likely sufficient to detect an effect.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to understand what was done and could be reproduced given access to the analytic data.
	Metric 15:	Statistical Analysis	High	The only statistical analysis conducted is a Mantel-Haenszel chi-squared test, and all assumptions were met. The statistical process is transparent.

Additional Comments: This case-control study pulled deceased former employees of the Union Carbide Corporation in Texas City, Texas. The study examined dichotomous exposure to a wide range of occupational exposures, including 1,2-dichloroethane, in relation to brain tumor cases. There is no quantitative estimate of exposure. The only statistical analysis in the study is a Mantel-Haenszel chi-squared test statistic and no statistically significant differences in exposure between cases and controls were observed. The fact that there are no effect estimates, no adjustment for confounders, and no quantitative exposure estimates limits the usefulness of this paper.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Cases in this case-control study were former Union Carbide Corporation (UCC) chemical plant employees in Texas City, Texas. Cases were identified through death certificate searches and tumor registries, and may have included individuals formerly employed at UCC whose cause of death was unknown to the company. Additionally, control deaths were stated to be pulled from corporate employee benefits department and through locally published obituary notices routinely screened by the medical department - it is possible to assume that cases were identified in a similar manner. The study identified cases of brain tumors by searching death certificates primarily, although tumor registries throughout the state of Texas were also searched. The study clarifies that it is possible that some cases were not found if they survived or died due to another cause - while this is likely to have impacted selection, there is no evidence that this would be differential by exposure status. Overall, there is limited information on the source population of workers from which cases were identified.
	Metric 2:	Attrition	Medium	Attrition is not discussed in the study, and outcome data appear to be complete. There was a large proportion of missing exposure data (roughly 50%) due to workers being employed in roles such as maintenance, where exposure to any chemical is possible but unknown. Analyses were run separately where these ”unknown” individuals were a) treated as exposed, b) treated as unexposed, or c) treated as unknown and thus excluded. The study only presents results for when these individuals were excluded but specifies that the first scenario resulted in increased exposure estimates for controls relative to cases.

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Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
	Metric 3:	Comparison Group	Medium	The study identifies two series of control groups, selected from all former Union Carbide Corporation (UCC) employees. However, the total number of employees is not stated. Only those who were deceased were used as controls since they had known causes of death and could thus be verified as non-brain tumors. One group of controls excluded employees whose cause of death was due to any malignant neoplasm to allow for the possibility that a general chemical carcinogen may have been associated with cancers of other sites. The other group of controls included deaths from all causes; this included malignant neoplasms other than brain tumors. Both control groups had 80 male employees randomly selected from 450 deceased employees known to the company in June 1979. Control deaths were stated to be pulled from corporate employee benefits department and through locally published obituary notices routinely screened by the medical department - it is possible to assume that cases were identified in a similar manner. The study reports that cases were slightly more likely to have been employed for less than 10 years than controls - the study attributes this in part to the fact that employees whose deaths were known to the company were more likely to have worked for longer - regardless the mean number of years employed was similar between cases and controls. However, cases were more likely to have been terminated from their job for reasons other than death, disability, or retirement (quitting, being fired, etc.), were generally younger at hire, and were less likely to survive to their 70th birthday. None of these factors are controlled for in statistical analyses - however, since controls and cases were pulled from the same population, there is indirect evidence that the groups were similar.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was determined based on official employment records. Records included job title and department assignment codes for each employment from date of hire to date of termination. For each unique department code, UCC and NIOSH industrial hygienists identified principal chemicals used or produced at any time in the history of the plant and correlated those with individual departments. This assessment was not performed on a year-by-year basis due to concerns for recall bias for longer-term employees where less detailed records were kept. An employee was categorized as ”exposed” to 1,2-dichloroethane if they ever worked in a department associated with that chemical. An ”unknown” exposure group was also created to account for employees who had only worked in departments for which no specific chemical could be identified.
	Metric 5:	Exposure Levels	Low	The study does not report any quantitative information and only splits exposure into ”exposed”, ”unexposed”, and ”unknown”.
	Metric 6:	Temporality	High	In this study exposure is confirmed to occur before the outcome is measured. The study reports latency periods, with subjects dichotomized into less than 15 years of latency or more than 15 years of latency. The majority of cases and controls had a latency of greater than 15 years, which is sufficiently long for brain tumors.

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Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Cases were identified through death certificate searches and partially through tumor registries in the state of Texas. Case validation was performed by NIOSH, and 5 different levels of confirmation were reported: 1) tissue specimen interpreted by the Armed Forces Institute of Pathology; 2) autopsy report; 3) histopathology report; 4) clinical diagnosis from hospital record; 5) dearth certificate diagnosis. Codes 1-3 were considered to be ”confirmed” cases of brain tumors, while 4-5 were considered unconfirmed. 5/21 cases were only evaluated using ”unconfirmed methods”, meaning there is likely a high amount of accuracy in roughly 75% of cases. While no case validation is reported for controls, the study specifies that only controls who had died and thus could be confirmed to be non-brain tumors were included.
	Metric 8:	Reporting Bias	Medium	All primary and secondary outcomes that are outlined in the methods are reported in the results. However, the only statistical outcome of their analysis were unadjusted p-values that were not reported and were just described qualitatively.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	The only statistical analysis performed were Mantel-Haenszel chi-squared tests, which did not allow for confounder adjustment. The study does not present a distribution of potential confounders by exposure status but by case/control status. Several variables, such as reason for termination, age at hire, and age at death were significantly different between cases and controls and were not accounted for in statistical modeling. The study explains that these differences are not likely to have any epidemiologic significance and appear to be relatively small differences.
	Metric 10:	Covariate Characterization	Medium	While the study does not explain where they obtained covariate information, it is reasonable to assume that they gathered the information from company records.
	Metric 11:	Co-exposure Counfounding	Low	The study assesses a wide range of other potential occupational co-exposures. While these co-exposures are not adjusted for in any statistical models, effect estimates are presented separately for benzene, diethyl sulfate, ethylene oxide, and vinyl chloride. The distribution of co-exposures across cases and controls is demonstrated to be mostly balanced by comparing proportions of exposed/unexposed between cases and controls. The only notable instance of imbalance is for benzene, where 11.1% of cases were exposed whereas 37.9% of all controls and 19.2% of non-neoplasm related controls were exposed.
Domain 5: Analysis				

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Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	The study chose a case-control design, which was appropriate to study the rare disease of brain tumors and its association with occupational exposures. The only statistical analysis conducted is a Mantzel-Haenszel chi-squared test, but there is no reason to suggest that this would be inappropriate.
	Metric 13:	Statistical Power	Medium	The study does not calculate statistical power, but the number of cases (n=21) and controls (n=80 in each analysis) is likely sufficient to detect an effect.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to understand what was done and could be reproduced given access to the analytic data.
	Metric 15:	Statistical Analysis	High	The only statistical analysis conducted is a Mantel-Haenszel chi-squared test, and all assumptions were met. The statistical process is transparent.

Additional Comments: This case-control study pulled deceased former employees of the Union Carbide Corporation in Texas City, Texas. The study examined dichotomous exposure to a wide range of occupational exposures, including 1,2-dichloroethane, in relation to brain tumor cases. There is no quantitative estimate of exposure. The only statistical analysis in the study is a Mantel-Haenszel chi-squared test statistic and no statistically significant differences in exposure between cases and controls were observed. The fact that there are no effect estimates, no adjustment for confounders, and no quantitative exposure estimates limits the usefulness of this paper.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	Urinary system cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	Urinary system cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	Urinary system cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Immune/Hematological
Reported Health Effect(s):	Lymphatic and hematopoietic tissue cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Immune/Hematological
Reported Health Effect(s):	Lymphatic and hematopoietic tissue cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Immune/Hematological
Reported Health Effect(s):	Lymphatic and hematopoietic tissue cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Other cancers (not specified)
Reported Health Effect(s):	Other cancers (not specified)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Other cancers (not specified)
Reported Health Effect(s):	Other cancers (not specified)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Other cancers (not specified)
Reported Health Effect(s):	Other cancers (not specified)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Mortality
Reported Health Effect(s):	All-cause mortality
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Vital status was tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Medium	Death rates among unit employees were compared to death rates in the U.S. population adjusted for age and gender. Demographics of the exposed workers are not provided; therefore, it is not clear whether additional adjustment for race may have been appropriate. No justification is provided for the choice of the entire U.S. population as the comparison group. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis. Additional analyses are conducted limiting workers to those with the greatest likelihood of exposure (i.e., those working in jobs with high likelihood of contact with chemicals for more than a year, those working for the full year of 1979 during which chemical exposures were most frequently reported); these smaller groups are also compared to the unexposed general population.
	Metric 6:	Temporality	High	Temporality was established due to the longitudinal design and the use of mortality as the outcome. Exposures occurred between 1979 and 1987 and follow-up for vital status was conducted through 2003.
Domain 3: Outcome Assessment				

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Mortality
Reported Health Effect(s):	All-cause mortality
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Medium	The study did not provide information on how mortality was assessed either in the exposed population or in the comparison population; use of death certificates is implied but not stated.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected deaths are reported, but SIRs and 95% confidence intervals are not provided.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Comparisons of observed versus expected deaths were adjusted for age and gender. Demographics of the exposed workers are not provided; therefore, it is not clear whether additional adjustment for race may have been appropriate.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records or death records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed deaths among a population of exposed workers compared to expected deaths among the U.S. population, adjusted for age and gender.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected deaths; no SIR was provided. Expected death rates were adjusted for age and gender.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Mortality
Reported Health Effect(s):	All-cause mortality
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	All cancer (excluding non-melanoma skin cancer), digestive system cancer, colorectal cancer, respiratory cancer, prostate cancer, urinary system cancer, lymphatic and hematopoietic tissue cancer, other cancers (not specified)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
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	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	All cancer (excluding non-melanoma skin cancer), digestive system cancer, colorectal cancer, respiratory cancer, prostate cancer, urinary system cancer, lymphatic and hematopoietic tissue cancer, other cancers (not specified)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	All cancer (excluding non-melanoma skin cancer), digestive system cancer, colorectal cancer, respiratory cancer, prostate cancer, urinary system cancer, lymphatic and hematopoietic tissue cancer, other cancers (not specified)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Gastrointestinal
Reported Health Effect(s):	Digestive system cancer, colorectal cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Gastrointestinal
Reported Health Effect(s):	Digestive system cancer, colorectal cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Gastrointestinal
Reported Health Effect(s):	Digestive system cancer, colorectal cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Lung/Respiratory
Reported Health Effect(s):	Respiratory cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Lung/Respiratory
Reported Health Effect(s):	Respiratory cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Lung/Respiratory
Reported Health Effect(s):	Respiratory cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Prostate cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Prostate cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Prostate cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Male workers who had ever been assigned to the chlorohydrin unit between 1 January 1940 and 31 December 1967 at Union Carbide's South Charleston plant were enrolled and matched to the US National Death Index. Status on 5 workers could not be identified. Information on how workers were matched to death index was not specified.
	Metric 2:	Attrition	Medium	Rate of inclusion/participation was very high, as records were able to be matched for 98% of participants. Medium rating given because information on how participants whose vital status was not known was not specified.
	Metric 3:	Comparison Group	Uninformative	Unacceptable rating given because SMRs were calculated based on expected deaths from a reference population matched on sex, but not age.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Exposure was assessed based on duration of work in the plant. No information is provided on exposure levels, and a JEM was not used.
	Metric 5:	Exposure Levels	Uninformative	No information provided on levels of exposure.
	Metric 6:	Temporality	High	Temporality is well established; person-years stopped accumulating in 1967 and outcome was assessed beginning at that time.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar period, and interval since assignments, but distribution of these covariates was not reported.
	Metric 10:	Covariate Characterization	Medium	Information on covariate characterization not provided, but the selected covariates (age, calendar period, and interval since assignments) were likely extracted from employee records and unlikely to be largely problematic
	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.

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Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Study design was appropriate for the research method. Statistical methods were also appropriate.
	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.
	Metric 14:	Reproducibility of Analyses	Medium	Methods are well-enough described that study could be adequately reproduced.
	Metric 15:	Statistical Analysis	High	SMRs calculated based on US general population mortality for white males through 1988. RRs were ”evaluated over levels of duration of assignment to the chlorohydrin unit, stratified by age, calendar year, and interval since first assignment to the chlorohydrin unit”.

Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Male workers who had ever been assigned to the chlorohydrin unit between 1 January 1940 and 31 December 1967 at Union Carbide's South Charleston plant were enrolled and matched to the US National Death Index. Status on 5 workers could not be identified. Information on how workers were matched to death index was not specified.
	Metric 2:	Attrition	Medium	Rate of inclusion/participation was very high, as records were able to be matched for 98% of participants. Medium rating given because information on how participants whose vital status was not known was not specified.
	Metric 3:	Comparison Group	Uninformative	Unacceptable rating given because SMRs were calculated based on expected deaths from a reference population matched on sex, but not age.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Exposure was assessed based on duration of work in the plant. No information is provided on exposure levels, and a JEM was not used.
	Metric 5:	Exposure Levels	Uninformative	No information provided on levels of exposure.
	Metric 6:	Temporality	High	Temporality is well established; person-years stopped accumulating in 1967 and outcome was assessed beginning at that time.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar period, and interval since assignments, but distribution of these covariates was not reported.
	Metric 10:	Covariate Characterization	Medium	Information on covariate characterization not provided, but the selected covariates (age, calendar period, and interval since assignments) were likely extracted from employee records and unlikely to be largely problematic
	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.
Domain 5: Analysis				

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Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Study design was appropriate for the research method. Statistical methods were also appropriate.
	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.
	Metric 14:	Reproducibility of Analyses	Medium	Methods are well-enough described that study could be adequately reproduced.
	Metric 15:	Statistical Analysis	High	SMRs calculated based on US general population mortality for white males through 1988. RRs were ”evaluated over levels of duration of assignment to the chlorohydrin unit, stratified by age, calendar year, and interval since first assignment to the chlorohydrin unit”.

Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

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Linked HERO ID(s):	200224, 5447107
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Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Male workers who had ever been assigned to the chlorohydrin unit between 1 January 1940 and 31 December 1967 at Union Carbide's South Charleston plant were enrolled and matched to the US National Death Index. Status on 5 workers could not be identified. Information on how workers were matched to death index was not specified.
	Metric 2:	Attrition	Medium	Rate of inclusion/participation was very high, as records were able to be matched for 98% of participants. Medium rating given because information on how participants whose vital status was not known was not specified.
	Metric 3:	Comparison Group	Uninformative	Unacceptable rating given because SMRs were calculated based on expected deaths from a reference population matched on sex, but not age.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Exposure was assessed based on duration of work in the plant. No information is provided on exposure levels, and a JEM was not used.
	Metric 5:	Exposure Levels	Uninformative	No information provided on levels of exposure.
	Metric 6:	Temporality	High	Temporality is well established; person-years stopped accumulating in 1967 and outcome was assessed beginning at that time.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar period, and interval since assignments, but distribution of these covariates was not reported.
	Metric 10:	Covariate Characterization	Medium	Information on covariate characterization not provided, but the selected covariates (age, calendar period, and interval since assignments) were likely extracted from employee records and unlikely to be largely problematic
	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.
Domain 5: Analysis				

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Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
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	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.
	Metric 14:	Reproducibility of Analyses	Medium	Methods are well-enough described that study could be adequately reproduced.
	Metric 15:	Statistical Analysis	High	SMRs calculated based on US general population mortality for white males through 1988. RRs were ”evaluated over levels of duration of assignment to the chlorohydrin unit, stratified by age, calendar year, and interval since first assignment to the chlorohydrin unit”.

Additional Comments: None

Overall Quality Determination Uninformative

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	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.
Domain 4: Potential Confounding / Variability Control				
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Domain 5: Analysis				

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Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Study design was appropriate for the research method. Statistical methods were also appropriate.
	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.
	Metric 14:	Reproducibility of Analyses	Medium	Methods are well-enough described that study could be adequately reproduced.
	Metric 15:	Statistical Analysis	High	SMRs calculated based on US general population mortality for white males through 1988. RRs were ”evaluated over levels of duration of assignment to the chlorohydrin unit, stratified by age, calendar year, and interval since first assignment to the chlorohydrin unit”.

Additional Comments: None

Overall Quality Determination Uninformative

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Domain 5: Analysis				

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Additional Comments: None

Overall Quality Determination Uninformative

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Domain 5: Analysis				

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Additional Comments: None

Overall Quality Determination Uninformative

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Domain 1: Study Participation				
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Domain 5: Analysis				

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Additional Comments: None

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Domain 5: Analysis				

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Domain	Metric		Rating	Comments
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Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Bove, F. J. (1996). Public drinking water contamination and birthweight, prematurity, fetal deaths, and birth defects. Toxicology and Industrial Health 12(2):255-266.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	200239

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	This cross-sectional study (n=80,938) included all registered singleton live births and fetal deaths (>20 weeks' gestation) in 1985-88 in 75 New Jersey towns located in 4 counties with "some" water supplies contaminated with substances of interest and where: (i) residents were "mostly" served by public water systems; and (ii) births occurred "mostly" in state. Estimated proportions of residents served by public water systems, and of pregnancies/births captured, were not described. However, the inclusion of all eligible registered births, fetal deaths, and birth defects, as well as the selection of towns without knowledge of birth outcome prevalence, limited the likelihood of selection bias.
	Metric 2:	Attrition	Medium	All registered births and fetal deaths were included. Attrition due to missing values for multiple variables was not quantified and is therefore uncertain. However, attrition was likely modest as the proportion of missing values for individual variables was relatively low: (i) ~6% of subjects were excluded from analyses of outcomes such as preterm birth due to invalid or missing gestational ages; and (ii) other covariates evaluated as confounders had up to 4.9% missing values.
	Metric 3:	Comparison Group	High	After excluding plural pregnancies and chromosomal abnormalities, all registered live births during the study period in the areas included without the outcomes of interest were included in the comparison group. This comprehensive approach limited the potential for bias. Chromosomal abnormalities were not included as outcomes as they were not hypothesized to be associated with the exposures under study but were appropriately excluded given their uncertain etiology.
Domain 2: Exposure Characterization				

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Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
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Domain	Metric		Rating	Comments
	Metric 4:	Measurement of Exposure	Medium	Along with several other contaminants, residential drinking water exposure to 1,2-dichloroethane (as well as 1,1,1-trichloroethane and 'total dichloroethylenes') – was assigned based on maternal town of residence at birth. Exposure estimates were calculated using the average of water company sampling reports during the first trimester (for birth defects and fetal death) or the duration of pregnancy (for other outcomes). Detection limits and data availability were not specified in detail but were described as below 1 ppb, with reporting compliance >85%. A minimum of 1 sample per 6-month interval was required; variability in the number of measures available across water systems and towns was not described. Additional sources of measurement error included: changes in residence during pregnancy; water from alternate sources (ex. private wells, bottles, workplaces); variability in residential contaminant levels vs measured samples; unknown levels of tap water intake; and errors in estimated dermal and inhalation exposure while bathing or showering. While the extent of exposure misclassification is uncertain, there is no evidence to suggest it was differential rather than random.
	Metric 5:	Exposure Levels	Medium	Due to the high proportion of measures below detection limits, analyses relating exposure to health outcomes used only 2 categories for each of the chlorinated solvents of interest: cutoffs close to detection limits were used to define elevated exposure. Proportions defined as having elevated exposure was low (1.8% had 1,1-dichloroethylene ≥1 ppb). An important concern is that relatively low levels of exposure to these contaminants from sources other than residential drinking water, for which data were not available, could potentially have resulted in considerable misclassification.
	Metric 6:	Temporality	High	Exposure levels were assigned based on contaminant exposures estimated during: (i) the first trimester for analyses of birth defects and fetal deaths; and (ii) the duration of pregnancy for other pregnancy outcomes.

Domain 3: Outcome Assessment

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Study Citation:	Bove, F. J. (1996). Public drinking water contamination and birthweight, prematurity, fetal deaths, and birth defects. Toxicology and Industrial Health 12(2):255-266.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	200239

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcomes included measures of birthweight (continuous among term births, low term birthweight, very low birthweight), prematurity, fetal death, and congenital anomalies in live births or fetal deaths. The anomalies analyzed included defects of the central nervous system, neural tube, oral cleft, total cardiac, major cardiac, ventricular septum, and any surveillance defect excluding chromosomal defects. All outcomes were identified using birth certificates, fetal death certificates (>20 weeks' gestation), and the NJ congenital birth defect registry (ICD codes provided). These registry data are likely to be sufficiently valid for late pregnancy outcomes. However, their limited ability to capture early pregnancy losses is a weakness. The sample included only 594 fetal deaths (less than 1% of the >80,0000 sample). Typical estimates are that 10-20%, of recognized pregnancies ending in losses. Moreover, developmental defects contributing to early pregnancy losses were also not captured. A further limitation is that that potentially etiologically heterogeneous preterm birth types were analyzed together, as these data did not distinguish premature rupture of membranes vs idiopathic prematurity.
	Metric 8:	Reporting Bias	Medium	Models were constructed only for contaminants with associations > 1.0, and tables included only associations with odds ratios ≥1.5. No clear rationale was provided. Several positive odds ratios below the 1.5 cutoff were described in the results text (without confidence intervals), but no null/negative odds ratios were presented or described.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Potential confounding by maternal race, education, parity, and prior pregnancy loss, along with infant sex (for birth outcomes) and adequacy of prenatal care, was examined. Gestational age was addressed by analyzing birthweight among full term births, term low birth weight, and small size for gestational age. Only fully adjusted models were presented. In a companion case-control study (with low participation rates), adjustment for other variables not available on birth certificates (ex. maternal smoking, occupational exposures, medical history, and gestational weight gain) did not influence associations with other studied contaminants. This separate study reduces concerns for important confounding bias, but confounding cannot be ruled out.
	Metric 10:	Covariate Characterization	Medium	Data on covariates came from registry data: birth certificates, fetal death certificates, and the NJ congenital birth defects registry.
	Metric 11:	Co-exposure Counfounding	Medium	Co-exposure confounding by drinking water trihalomethane concentrations was evaluated. There was no evidence to suggest substantial confounding by this or other co-exposures.
Domain 5: Analysis				

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Study Citation: Bove, F. J. (1996). Public drinking water contamination and birthweight, prematurity, fetal deaths, and birth defects. Toxicology and Industrial Health 12(2):255-266.

Health Outcome(s): Reproductive/Developmental

Reported Health Effect(s): Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.

Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

Linked HERO ID(s): 194932, 200239

HERO ID: 200239

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Methods were appropriate. The study used logistic regression models to estimate odds ratios and confidence intervals for dichotomous outcomes, and linear regression for analysis of continuous birth weight.
	Metric 13:	Statistical Power	Medium	Statistical power was likely to have been limited as a consequence of the small proportion of the sample defined as having "elevated" residential water concentrations of the chemicals of interest. The range of exposure examined was limited, as cutoffs for elevated levels were close to the detection limits of 1 ppb. In addition, for most birth defect outcomes, fewer than 10 cases had elevated exposure.
	Metric 14:	Reproducibility of Analyses	Medium	The authors clearly described steps used to estimate exposure-outcome associations, including exposure category cutoffs and criteria for confounding. However, many results were not shown as tables included odds ratios ≥1.5.
	Metric 15:	Statistical Analysis	High	The authors estimated coefficients, odds ratios and 95% confidence intervals using adequate methods. Confounding was based on 15% change-in-estimate comparing nested models. Effect modification (ex by infant sex) was not evaluated as there was no a priori evidence to suggest such analyses at that time.

Additional Comments: This study analyzed the association between estimated residential drinking water concentrations of several chlorinated solvents including 1,2-dichloroethane (as well as 1,1,1-trichloroethane; ∑[trans-1,2-dichloroethylene and 1,1-dichloroethylene]) and pregnancy outcomes (size at birth, prematurity, fetal deaths, and congenital birth defects). The sample included more than 80,000 births during 1985-88 for residents of 75 towns in NJ using public water system records to estimate exposure during gestation, and registry data (birth certificate, fetal death certificates for pregnancies >20 weeks, state birth defect registry) to characterize outcomes. Strengths included the large sample size and inclusion of all eligible registered births and fetal deaths in the study period. A critical concern is the inability to capture early fetal deaths and any related malformations (1% of the sample had fetal deaths vs typical estimates of >10%). An important limitation was the low percentage of the sample with detectable (> 1ppb) concentrations of these contaminants (<1% to 6.2%). Small numbers for birth defect outcomes also limited power. Exposure misclassification (ex. drinking water from wells/ work/ bottles, changes in residence, exposure from other sources) is also a concern. However, such misclassification was likely non-differential, and thus more likely to under- vs. to over-estimate associations.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Bove, F. J., Fulcomer, M. C., Klotz, J. B., Esmart, J., Dufficy, E. M., Savrin, J. E. (1995). Public drinking water contamination and birth outcomes. American Journal of Epidemiology 141(9):850-862.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	194932

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	This semi-ecological study (n=80,938) included all registered singleton live births and fetal deaths (>20 weeks) in 1985-88 in 75 New Jersey towns located in 4 counties with "some" water supplies contaminated with substances of interest and where: (i) residents were "mostly" served by public water systems; and (ii) births occurred "mostly" in state. Estimated proportions of residents served by public water systems, and of pregnancies/births captured, were not described. However, the inclusion of all eligible registered births, fetal deaths, and birth defects, as well as the selection of towns without knowledge of birth outcome prevalence, limited the likelihood of selection bias.
	Metric 2:	Attrition	Medium	All registered births and fetal deaths were included. Attrition due to missing values for multiple variables was not quantified and is therefore uncertain. However, attrition was likely modest as the proportion of missing values for individual variables was relatively low: (i) ~6% of subjects were excluded from analyses of outcomes such as preterm birth due to invalid or missing gestational ages; and (ii) other covariates evaluated as confounders had up to 4.9% missing values.
	Metric 3:	Comparison Group	High	After excluding plural pregnancies and chromosomal abnormalities, all registered live births during the study period in the areas included without the outcomes of interest were included in the comparison group. This comprehensive approach limited the potential for bias. Chromosomal abnormalities were not included as outcomes as they were not hypothesized to be associated with the exposures under study but were appropriately excluded given their uncertain etiology.
Domain 2: Exposure Characterization				

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Study Citation:	Bove, F. J., Fulcomer, M. C., Klotz, J. B., Esmart, J., Dufficy, E. M., Savrin, J. E. (1995). Public drinking water contamination and birth outcomes. American Journal of Epidemiology 141(9):850-862.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	194932

Domain	Metric		Rating	Comments
	Metric 4:	Measurement of Exposure	Medium	Along with several other contaminants, residential drinking water exposure to 1,2-dichloroethane (as well as 1,1,1-trichloroethane and 'total dichloroethylenes') was assigned based on maternal town of residence at birth. Exposure estimates were calculated using the average of water company sampling reports during the first trimester (for birth defects and fetal death) or the duration of pregnancy (for other outcomes). Detection limits and data availability were not specified in detail but were described as below 1 ppb, with reporting compliance >85%. A minimum of 1 sample per 6-month interval was required; variability in the number of measures available across water systems and towns was not described. Additional sources of measurement error included: changes in residence during pregnancy; water from alternate sources (ex. private wells, bottles, workplaces); variability in residential contaminant levels vs measured samples; unknown levels of tap water intake; and errors in estimated dermal and inhalation exposure while bathing or showering. While the extent of exposure misclassification is uncertain, there is no evidence to suggest it was differential rather than random.
	Metric 5:	Exposure Levels	Low	Due to the high proportion of measures below detection limits, analyses relating exposure to health outcomes used only 2 categories for each of the three chemicals of interest: cutoffs close to detection limits were used to define elevated exposure. Proportions defined as having elevated exposure were low (1.8% had 1,1-dichloroethylene ≥1 ppb). An important concern is that relatively low levels of exposure to this contaminant from sources other than residential drinking water, for which data were not available, could potentially have resulted in considerable misclassification.
	Metric 6:	Temporality	High	Exposure levels were assigned based on contaminant exposures estimated during: (i) the first trimester for analyses of birth defects and fetal deaths; and (ii) the duration of pregnancy for other pregnancy outcomes.

Domain 3: Outcome Assessment

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Study Citation:	Bove, F. J., Fulcomer, M. C., Klotz, J. B., Esmart, J., Dufficy, E. M., Savrin, J. E. (1995). Public drinking water contamination and birth outcomes. American Journal of Epidemiology 141(9):850-862.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	194932

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcomes included measures of birthweight (continuous among term births, low term birthweight, very low birthweight), prematurity, fetal death, and congenital anomalies in live births or fetal deaths. The anomalies analyzed included defects of the central nervous system, neural tube, oral cleft, total cardiac, major cardiac, ventricular septum, and any surveillance defect excluding chromosomal defects. All outcomes were identified using birth certificates, fetal death certificates (>20 weeks' gestation), and the NJ congenital birth defect registry (ICD codes provided). These registry data are likely to be sufficiently valid for late pregnancy outcomes. However, their limited ability to capture early pregnancy losses is a weakness. The sample included only 594 fetal deaths (less than 1% of the >80,0000 sample). Typical estimates are that 10-20%, of recognized pregnancies ending in losses. Moreover, developmental defects contributing to early pregnancy losses were also not captured. A further limitation is that that potentially etiologically heterogeneous preterm birth types were analyzed together, as these data did not distinguish premature rupture of membranes vs idiopathic prematurity.
	Metric 8:	Reporting Bias	Low	Models were constructed only for contaminants with associations > 1.0, and tables included only associations with odds ratios ≥1.5. No clear rationale was provided. Several positive odds ratios below the 1.5 cutoff were described in the results text (without confidence intervals), but no null/negative odds ratios were presented or described.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Potential confounding by maternal race, education, parity, and prior pregnancy loss, along with infant sex (for birth outcomes) and adequacy of prenatal care, was examined. Gestational age was addressed by analyzing birthweight among full term births, term low birth weight, and small size for gestational age. Only fully adjusted models were presented. In a companion case-control study (with low participation rates), adjustment for other variables not available on birth certificates (ex. maternal smoking, occupational exposures, medical history, and gestational weight gain) did not influence associations with other studied contaminants. This separate study reduces concerns for important confounding bias, but confounding cannot be ruled out.
	Metric 10:	Covariate Characterization	Medium	Data on covariates came from registry data: birth certificates, fetal death certificates, and the NJ congenital birth defects registry.
	Metric 11:	Co-exposure Counfounding	Medium	Co-exposure confounding by drinking water trihalomethane concentrations was evaluated. There was no evidence to suggest substantial confounding by this or other co-exposures.
Domain 5: Analysis				

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Study Citation:	Bove, F. J., Fulcomer, M. C., Klotz, J. B., Esmart, J., Dufficy, E. M., Savrin, J. E. (1995). Public drinking water contamination and birth outcomes. American Journal of Epidemiology 141(9):850-862.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	194932

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Methods were appropriate. The study used logistic regression models to estimate odds ratios and confidence intervals for dichotomous outcomes, and linear regression for analysis of continuous birth weight.
	Metric 13:	Statistical Power	Low	Statistical power was likely to have been limited as a consequence of the small proportion of the sample defined as having "elevated" residential water concentrations of the chemicals of interest. The range of exposure examined was limited, as cutoffs for elevated levels were close to the detection limits of 1 ppb. In addition, for most birth defect outcomes, fewer than 10 cases had elevated exposure. However, the authors emphasized the magnitude of associations rather than statistical significance and presented multiple confidence intervals to aid interpretation of the precision of estimates (50%, 90% and 99%).
	Metric 14:	Reproducibility of Analyses	Medium	The authors clearly described steps used to estimate exposure-outcome associations, including exposure category cutoffs and criteria for confounding. However, many results were not shown as tables included odds ratios ≥1.5.
	Metric 15:	Statistical Analysis	High	The authors estimated coefficients, odds ratios and confidence intervals using adequate methods. Confounding was based on 15% change-in-estimate comparing nested models. Effect modification (ex by infant sex) was not evaluated as there was no a priori evidence to suggest such analyses at that time.

Additional Comments: This study analyzed the association between estimated residential drinking water concentrations of several chlorinated solvents including 1,2-dichloroethane (as well as 1,1,1-trichloroethane and the ∑[trans-1,2-dichloroethylene & 1,1-dichloroethylene]) and pregnancy outcomes (size at birth, prematurity, fetal deaths, and congenital birth defects). The sample included more than 80,000 births during 1985-88 for residents of 75 towns in NJ using public water system records to estimate exposure during gestation, and registry data (birth certificate, fetal death certificates for pregnancies >20 weeks' gestation, state birth defect registry) to characterize outcomes. Strengths included the large sample size and inclusion of all eligible registered births and fetal deaths in the study period. A critical concern is the inability to capture early fetal deaths and any related malformations (1% of the sample had fetal deaths vs typical estimates of >10%). An important limitation was the low percentage of the sample with detectable (> 1ppb) concentrations of this solvent (<2%), which likely limited power. Small numbers for birth defect outcomes also limited power. Exposure misclassification (ex. drinking water from wells/ work/ bottles, changes in residence, exposure from other sources) is also a concern. However, such misclassification was likely non-differential, and thus more likely to under- vs. to over-estimate associations.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Bowler, R.M., Gysens, S., Hartney, C. (2003). Neuropsychological effects of ethylene dichloride exposure. NeuroToxicology 24(4-5):553-562.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Wechsler Adult Intelligence Scale III (WAIS-III), Wechsler Memory Scale III (WMS-III), Boston Naming Test (BNT), Trail Making Test (TMT), Stroop Color-Word Test, Grooved Pegboard, Dynamometer, Wide Range Achievement Test (WRAT), Finger tapping, Beck Anxiety Index, Beck Depression Index, Symptom Checklist-90 (SCL-90).
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	200241

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Uninformative	221 workers that had been exposed to 1,2-DCE in the Southern United States were initially included. Exclusion criteria were provided, including the number of individuals excluded for each reason. The study authors note that those initially included in the analysis sample were referred by physicians after neurological complaints were documented. Detailed criteria for referral were not provided. Referral-based recruitment of neurological cases will likely result in an analysis sample with an exposure-outcome distribution that is not representative of the eligible population (i.e., contamination site clean-up workers).
	Metric 2:	Attrition	Medium	There was moderate subject loss. Reasons for exclusion from the analysis sample are provided, and only those with complete information were included in the analysis.
	Metric 3:	Comparison Group	Low	Impairment scores were compared to normative data from manuals and/or a "demographically similar control group" cited to Bowler et al. (2001). The controls from this study appeared similar (albeit somewhat older) than 1,2-DCE-exposed workers and reported no prior chemical exposure.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	A job-exposure matrix was not considered plausible; variables considered as surrogates of exposure were obtained from interviews. This method is expected to have poor validity because it relies on workers' recall of subjective events and their frequency (e.g., contact with water); workers (who are taking part in a lawsuit) may overestimate their exposure.
	Metric 5:	Exposure Levels	Low	Two levels of exposure (exposed and not exposed) were used to evaluate neurophysiological effects.
	Metric 6:	Temporality	Medium	Exposures primarily occurred between 1993 and 1995 and neurophysiological effects were evaluated in 2000. Temporality is established, but it is unclear whether exposures fall within relevant exposure windows for the outcome of interest.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Neurophysiological effects were evaluated using a number of standardized tests, including (but not limited to) the Wechsler Adult Intelligence Scale (WAIS-III), the Wechsler Memory Scale (WMS-III), and the Symptom Checklist 90-Revised (SCL90-R). There was no information whether tests were performed using the same methods for exposed and referent groups (e.g., timing and order of tests).

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Study Citation:	Bowler, R.M., Gysens, S., Hartney, C. (2003). Neuropsychological effects of ethylene dichloride exposure. NeuroToxicology 24(4-5):553-562.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Wechsler Adult Intelligence Scale III (WAIS-III), Wechsler Memory Scale III (WMS-III), Boston Naming Test (BNT), Trail Making Test (TMT), Stroop Color-Word Test, Grooved Pegboard, Dynamometer, Wide Range Achievement Test (WRAT), Finger tapping, Beck Anxiety Index, Beck Depression Index, Symptom Checklist-90 (SCL-90).
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	200241

Domain	Metric		Rating	Comments
	Metric 8:	Reporting Bias	Low	Neurobehavioral outcomes mentioned in the methods were reported for 1,2-DCE-exposed workers (as mean score, standard deviation, and percentage impaired); results for controls/normative data were not shown and/or p-values from t-tests were not provided. Control data were used to define impairment (based on z-score) but these values were not reported. Data pertaining to specific exposure variables were reported in the text only; no data were shown in a table.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Normative data permitted adjustments based on age, education, and gender. The control group was "socio-demographically" similar but specific parameters used to define similarity were not indicated. Separate ANCOVA analyses on workers only were stratified by race (citation provided), and adjusted for ethnicity, age, and education. The methods for identifying and including potential confounders in the analytic approach was not described.
	Metric 10:	Covariate Characterization	Low	No description of the covariate collection method was provided. It was not clear whether the method used was valid or not.
	Metric 11:	Co-exposure Counfounding	Low	A number of workers (18%) reported current exposure to chemicals in their work environment. These potential co-exposures were not were not appropriately adjusted for in the analytical approach used.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Low	The study design was appropriate to evaluate the neurophysiological status of 1,2-DCE-exposed workers; however, statistical methods were not comprehensive.
	Metric 13:	Statistical Power	Medium	The report indicates "significant impairments" were observed on various neurophysiological tests using t-tests, and significant exposure relationships were reported based on test scores and specific exposure variables (used as surrogates of exposure). Therefore, the number of participants was sufficient to detect an effect.
	Metric 14:	Reproducibility of Analyses	Low	Tests were scored according to relevant manuals; the calculation of z-scores, used in all impairment comparisons and analyses of exposure relationships, was not explained in adequate detail. The methods used to determine relationships between specific exposure variables and test scores (i.e., ANCOVA analyses) were not fully described.
	Metric 15:	Statistical Analysis	Low	Description of the ANCOVA analysis was largely not present. It is not clear whether model assumptions were met.

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Study Citation:	Bowler, R.M., Gysens, S., Hartney, C. (2003). Neuropsychological effects of ethylene dichloride exposure. NeuroToxicology 24(4-5):553-562.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Wechsler Adult Intelligence Scale III (WAIS-III), Wechsler Memory Scale III (WMS-III), Boston Naming Test (BNT), Trail Making Test (TMT), Stroop Color-Word Test, Grooved Pegboard, Dynamometer, Wide Range Achievement Test (WRAT), Finger tapping, Beck Anxiety Index, Beck Depression Index, Symptom Checklist-90 (SCL-90).
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	200241

Domain	Metric	Rating	Comments
Additional Comments:	The study evaluated the neurobehavioral status of a group of workers with known exposure to 1,2-DCE at a clean-up site. Impairments related to processing speed, attention, cognitive flexibility, motor coordination and speed, verbal memory/fluency, vision and visual-spatial abilities, and mood were reported in exposed workers. Serious and consequential flaws are associated with the study including methods of participant selection and retention, and exposure characterization among others.		

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Brender, J.D., Shinde, M.U., Zhan, F.B., Gong, X., Langlois, P.H. (2014). Maternal residential proximity to chlorinated solvent emissions and birth defects in offspring: A case-control study. Environmental Health: A Global Access Science Source 13(1):96.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	birth defects (neural tube defects, limbs deficiencies, oral cleft defects, heart defects, spina bifida, anencephaly)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	2799700

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Participants were drawn from the Texas Birth Defects Registry (TBDR) for years 1996-2008. Controls were frequency matched from the same registry. Study authors state that neural tube cases were more likely to not be successfully geocoded which may introduce selection bias, however, the authors note that both cases and controls with addresses that could not be geocoded were similar. In spite of that, the inclusion criteria, methods of participant selection, and frequency match were reported.
	Metric 2:	Attrition	Medium	13.3% case mother addresses and 12.8% control mother addresses were unable to be geocoded, however this most likely only lowered the precision of the study and most likely does not vary based on exposure level.
	Metric 3:	Comparison Group	Medium	Controls were matched to cases and pulled from the same eligible population by year of delivery and public health service region. Other demographic factors, e.g., race was not matched in population selection. However, statistical analyses were adjusted for year of delivery, maternal age, race/ethnicity, education, and public health region of residence.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Used Emission Weighted Proximity Model to estimate exposure at a given address based on proximity to emission sources and the specific amount or type of pollutant emitted. There may be some exposure misclassification due to mothers moving away from geocoded addresses. Previous studies indicate ~67% of mothers do not move between conception and delivery.
	Metric 5:	Exposure Levels	Medium	Reports exposure as "exposure risk value" and groups the risk values into quartiles, with exposure risk values < 0 being the referent group
	Metric 6:	Temporality	Medium	The study authors estimated exposure based on residence during pregnancy and evaluated birth outcomes. Temporality is established. Previous studies indicate ~67% mothers don't move between trimester and delivery. For mothers who moved during the pregnancy, the temporality is unknown.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Outcomes determined by Texas Birth Defect Registry, checking for birth defect diagnosis. Birth certificates came from Center for Health Statistics at Texas Department of State Health Services
	Metric 8:	Reporting Bias	High	Outcome data measured and reported clearly, stratified by specific type of birth defect
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Brender, J.D., Shinde, M.U., Zhan, F.B., Gong, X., Langlois, P.H. (2014). Maternal residential proximity to chlorinated solvent emissions and birth defects in offspring: A case-control study. Environmental Health: A Global Access Science Source 13(1):96.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	birth defects (neural tube defects, limbs deficiencies, oral cleft defects, heart defects, spina bifida, anencephaly)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	2799700

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	High	Cases were frequency matched by year of delivery and public health service region. Final models were adjusted for year of delivery, public health region, maternal age (<20, 20-24, 25-29, 30-34, 35-39, >39 years), education (<12 years, 12 years, >12 years), and race/ethnicity (Whit non-Hispanic, Black non-Hispanic, Hispanic, other non-Hispanic).
	Metric 10:	Covariate Characterization	High	Used birth and death certificates for demographic information
	Metric 11:	Co-exposure Counfounding	Medium	other co-exposures were not described
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	study used logistic regression to measure association between exposure and birth defects
	Metric 13:	Statistical Power	Medium	Overall adequate number of cases and controls - some effects have low cell counts, but at least one health effect has sufficient statistical power.
	Metric 14:	Reproducibility of Analyses	Medium	Methods sufficiently detailed for reproducibility
	Metric 15:	Statistical Analysis	High	No logistic regression model assumption violations were identified.

Additional Comments: This study examined the association between proximity to several point sources of chlorinated solvents and birth defects. Exposure was assessed using EPA's Toxic Release Inventory, and birth defects were assessed using Texas birth registries. The geocoded address of mothers on day of delivery and the amount of solvent was plugged into the Emission Weighted Probability model to assign each mother an exposure risk value. Limitations include limited evidence of temporality. Additionally, elective terminations lacked a vital record, which meant only 69% of mothers with neural tube defects were geocoded. Mothers highly exposed to 1,2-dichloroethane were 1.85 times more likely to have the spina bifida birth defect than mothers who were not significantly exposed.

Overall Quality Determination High

* No biomarkers were identified for this evaluation.

Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Nested case-control design; cases selected from deaths in cohort study was described by Rinsky et al (1988; HERO 597923) (29,139 workers in Union Carbide facilities in West Virginia followed from 1940 to 1978). Vital status complete for 95% of cohort members.
	Metric 2:	Attrition	High	There was minimal exclusion of subjects/missing data, because vital status follow-up was complete for 96% of the 29,139 men in the cohort study.
	Metric 3:	Comparison Group	Medium	Controls were randomly selected in a 5:1 ratio to cases from the total employee cohort such that they were first employed in the same decade and survived to the same five-year survival period as cases. Controls survived at least to the beginning of the five-year interval in which cases died. Controls were independently selected for each of the individual disease subcategories. However, the demographic information between cases and controls were not compared in the paper.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was partially described: (1) Potential employee contact with a specific substance was determined by tracing each employee's work assignments and linking these assignment records to a separate computer file that contained a history of departmental usage for each substance; (2) Potential exposure to each chemical group was assumed on the basis of assignment o a production unit with a history of usage of any member of that chemical group. However, exposure level either based on work assignment in departments such as job exposure matrix or on the chemical levels were not presented.
	Metric 5:	Exposure Levels	Low	The range of exposure is limited. For example, exposure was presented by the duration of work in two categories: <5 years and 5+ years.
	Metric 6:	Temporality	Medium	Temporality is established, but it is unclear whether the exposures fall within the relevant exposure window. Authors used a lag time of 5 years; since controls were selected for 5 yr intervals, the effective lag time ranged from 5-9 years with an average of 7.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Case definition was based on death certificate diagnosis; but no method validation was conducted against this well-established methods.
	Metric 8:	Reporting Bias	Medium	All outcomes reported, but ORs for many analyses presented without CIs (some CIs reported in text).
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Low	There is indirect evidence that considerations were not made for potential confounders (ORs not adjusted, controls not age- or race-matched). Even though authors note that "Age-adjusted stratified analyses, which were also conducted, did not materially modify the odds ratio estimates". Also stratified examination of odds ratios were conducted to assess duration of exposure effects. However, other key confounders e.g., smoking status and race were not accounted for.
	Metric 10:	Covariate Characterization	Medium	The only potential confounder considered was age; this was presumably evaluated based on employment records (no discussion presented). Age-adjusted stratified analyses were conducted.
	Metric 11:	Co-exposure Counfounding	Low	Co-exposures were present and were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Nested case-control study design is appropriate for research question. Initial data analysis included crude odds ratio and then stratified examination of odds ratios was conducted to ass duration of exposure effect. Also, age-adjusted stratified analysis was conducted.
	Metric 13:	Statistical Power	Low	Statistical power calculations were not reported. Case numbers for each disease were low. The number of subjects was not sufficient to detect an effect of 1,2-dichloroethylene exposure.
	Metric 14:	Reproducibility of Analyses	Medium	Description was sufficient to be conceptually reproducible.
	Metric 15:	Statistical Analysis	Low	Statistical model to calculate odds ratio was not described.

Additional Comments: This nested case-control study within a cohort study is a good study design to answer the research question regarding the association between multiple chemical exposures and four cancer sites. Cases and controls are selected appropriate. However, there are several limitations in this study: (1) confounders were not all considered and adjusted for, except that age-adjusted odds ratios were conducted; (2) it is not described if co-exposures were adjusted for; (3) numbers of cancer cases for each cancer type were small, so the statistical power is limited; (4) statistical models for calculating odds ratios were not described.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Nested case-control design; cases selected from deaths in cohort study was described by Rinsky et al (1988; HERO 597923) (29,139 workers in Union Carbide facilities in West Virginia followed from 1940 to 1978). Vital status complete for 95% of cohort members.
	Metric 2:	Attrition	High	There was minimal exclusion of subjects/missing data, because vital status follow-up was complete for 96% of the 29,139 men in the cohort study.
	Metric 3:	Comparison Group	Medium	Controls were randomly selected in a 5:1 ratio to cases from the total employee cohort such that they were first employed in the same decade and survived to the same five-year survival period as cases. Controls survived at least to the beginning of the five-year interval in which cases died. Controls were independently selected for each of the individual disease subcategories. However, the demographic information between cases and controls were not compared in the paper.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was partially described: (1) Potential employee contact with a specific substance was determined by tracing each employee's work assignments and linking these assignment records to a separate computer file that contained a history of departmental usage for each substance; (2) Potential exposure to each chemical group was assumed on the basis of assignment o a production unit with a history of usage of any member of that chemical group. However, exposure level either based on work assignment in departments such as job exposure matrix or on the chemical levels were not presented.
	Metric 5:	Exposure Levels	Low	The range of exposure is limited. For example, exposure was presented by the duration of work in two categories: <5 years and 5+ years.
	Metric 6:	Temporality	Medium	Temporality is established, but it is unclear whether the exposures fall within the relevant exposure window. Authors used a lag time of 5 years; since controls were selected for 5 yr intervals, the effective lag time ranged from 5-9 years with an average of 7.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Case definition was based on death certificate diagnosis; but no method validation was conducted against this well-established methods.
	Metric 8:	Reporting Bias	Medium	All outcomes reported, but ORs for many analyses presented without CIs (some CIs reported in text).
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Low	There is indirect evidence that considerations were not made for potential confounders (ORs not adjusted, controls not age- or race-matched). Even though authors note that "Age-adjusted stratified analyses, which were also conducted, did not materially modify the odds ratio estimates". Also stratified examination of odds ratios were conducted to assess duration of exposure effects. However, other key confounders e.g., smoking status and race were not accounted for.
	Metric 10:	Covariate Characterization	Medium	The only potential confounder considered was age; this was presumably evaluated based on employment records (no discussion presented). Age-adjusted stratified analyses were conducted.
	Metric 11:	Co-exposure Counfounding	Low	Co-exposures were present and were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Nested case-control study design is appropriate for research question. Initial data analysis included crude odds ratio and then stratified examination of odds ratios was conducted to ass duration of exposure effect. Also, age-adjusted stratified analysis was conducted.
	Metric 13:	Statistical Power	Low	Statistical power calculations were not reported. Case numbers for each disease were low. The number of subjects was not sufficient to detect an effect of 1,2-dichloroethylene exposure.
	Metric 14:	Reproducibility of Analyses	Medium	Description was sufficient to be conceptually reproducible.
	Metric 15:	Statistical Analysis	Low	Statistical model to calculate odds ratio was not described.

Additional Comments: This nested case-control study within a cohort study is a good study design to answer the research question regarding the association between multiple chemical exposures and four cancer sites. Cases and controls are selected appropriate. However, there are several limitations in this study: (1) confounders were not all considered and adjusted for, except that age-adjusted odds ratios were conducted; (2) it is not described if co-exposures were adjusted for; (3) numbers of cancer cases for each cancer type were small, so the statistical power is limited; (4) statistical models for calculating odds ratios were not described.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Nested case-control design; cases selected from deaths in cohort study was described by Rinsky et al (1988; HERO 597923) (29,139 workers in Union Carbide facilities in West Virginia followed from 1940 to 1978). Vital status complete for 95% of cohort members.
	Metric 2:	Attrition	High	There was minimal exclusion of subjects/missing data, because vital status follow-up was complete for 96% of the 29,139 men in the cohort study.
	Metric 3:	Comparison Group	Medium	Controls were randomly selected in a 5:1 ratio to cases from the total employee cohort such that they were first employed in the same decade and survived to the same five-year survival period as cases. Controls survived at least to the beginning of the five-year interval in which cases died. Controls were independently selected for each of the individual disease subcategories. However, the demographic information between cases and controls were not compared in the paper.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was partially described: (1) Potential employee contact with a specific substance was determined by tracing each employee's work assignments and linking these assignment records to a separate computer file that contained a history of departmental usage for each substance; (2) Potential exposure to each chemical group was assumed on the basis of assignment o a production unit with a history of usage of any member of that chemical group. However, exposure level either based on work assignment in departments such as job exposure matrix or on the chemical levels were not presented.
	Metric 5:	Exposure Levels	Low	The range of exposure is limited. For example, exposure was presented by the duration of work in two categories: <5 years and 5+ years.
	Metric 6:	Temporality	Medium	Temporality is established, but it is unclear whether the exposures fall within the relevant exposure window. Authors used a lag time of 5 years; since controls were selected for 5 yr intervals, the effective lag time ranged from 5-9 years with an average of 7.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Case definition was based on death certificate diagnosis; but no method validation was conducted against this well-established methods.
	Metric 8:	Reporting Bias	Medium	All outcomes reported, but ORs for many analyses presented without CIs (some CIs reported in text).
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
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Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Low	There is indirect evidence that considerations were not made for potential confounders (ORs not adjusted, controls not age- or race-matched). Even though authors note that "Age-adjusted stratified analyses, which were also conducted, did not materially modify the odds ratio estimates". Also stratified examination of odds ratios were conducted to assess duration of exposure effects. However, other key confounders e.g., smoking status and race were not accounted for.
	Metric 10:	Covariate Characterization	Medium	The only potential confounder considered was age; this was presumably evaluated based on employment records (no discussion presented). Age-adjusted stratified analyses were conducted.
	Metric 11:	Co-exposure Counfounding	Low	Co-exposures were present and were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Nested case-control study design is appropriate for research question. Initial data analysis included crude odds ratio and then stratified examination of odds ratios was conducted to ass duration of exposure effect. Also, age-adjusted stratified analysis was conducted.
	Metric 13:	Statistical Power	Low	Statistical power calculations were not reported. Case numbers for each disease were low. The number of subjects was not sufficient to detect an effect of 1,2-dichloroethylene exposure.
	Metric 14:	Reproducibility of Analyses	Medium	Description was sufficient to be conceptually reproducible.
	Metric 15:	Statistical Analysis	Low	Statistical model to calculate odds ratio was not described.

Additional Comments: This nested case-control study within a cohort study is a good study design to answer the research question regarding the association between multiple chemical exposures and four cancer sites. Cases and controls are selected appropriate. However, there are several limitations in this study: (1) confounders were not all considered and adjusted for, except that age-adjusted odds ratios were conducted; (2) it is not described if co-exposures were adjusted for; (3) numbers of cancer cases for each cancer type were small, so the statistical power is limited; (4) statistical models for calculating odds ratios were not described.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Nested case-control design; cases selected from deaths in cohort study was described by Rinsky et al (1988; HERO 597923) (29,139 workers in Union Carbide facilities in West Virginia followed from 1940 to 1978). Vital status complete for 95% of cohort members.
	Metric 2:	Attrition	High	There was minimal exclusion of subjects/missing data, because vital status follow-up was complete for 96% of the 29,139 men in the cohort study.
	Metric 3:	Comparison Group	Medium	Controls were randomly selected in a 5:1 ratio to cases from the total employee cohort such that they were first employed in the same decade and survived to the same five-year survival period as cases. Controls survived at least to the beginning of the five-year interval in which cases died. Controls were independently selected for each of the individual disease subcategories. However, the demographic information between cases and controls were not compared in the paper.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was partially described: (1) Potential employee contact with a specific substance was determined by tracing each employee's work assignments and linking these assignment records to a separate computer file that contained a history of departmental usage for each substance; (2) Potential exposure to each chemical group was assumed on the basis of assignment o a production unit with a history of usage of any member of that chemical group. However, exposure level either based on work assignment in departments such as job exposure matrix or on the chemical levels were not presented.
	Metric 5:	Exposure Levels	Low	The range of exposure is limited. For example, exposure was presented by the duration of work in two categories: <5 years and 5+ years.
	Metric 6:	Temporality	Medium	Temporality is established, but it is unclear whether the exposures fall within the relevant exposure window. Authors used a lag time of 5 years; since controls were selected for 5 yr intervals, the effective lag time ranged from 5-9 years with an average of 7.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Case definition was based on death certificate diagnosis; but no method validation was conducted against this well-established methods.
	Metric 8:	Reporting Bias	Medium	All outcomes reported, but ORs for many analyses presented without CIs (some CIs reported in text).
Domain 4: Potential Confounding / Variability Control				

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Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Low	There is indirect evidence that considerations were not made for potential confounders (ORs not adjusted, controls not age- or race-matched). Even though authors note that "Age-adjusted stratified analyses, which were also conducted, did not materially modify the odds ratio estimates". Also stratified examination of odds ratios were conducted to assess duration of exposure effects. However, other key confounders e.g., smoking status and race were not accounted for.
	Metric 10:	Covariate Characterization	Medium	The only potential confounder considered was age; this was presumably evaluated based on employment records (no discussion presented). Age-adjusted stratified analyses were conducted.
	Metric 11:	Co-exposure Counfounding	Low	Co-exposures were present and were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Nested case-control study design is appropriate for research question. Initial data analysis included crude odds ratio and then stratified examination of odds ratios was conducted to ass duration of exposure effect. Also, age-adjusted stratified analysis was conducted.
	Metric 13:	Statistical Power	Low	Statistical power calculations were not reported. Case numbers for each disease were low. The number of subjects was not sufficient to detect an effect of 1,2-dichloroethylene exposure.
	Metric 14:	Reproducibility of Analyses	Medium	Description was sufficient to be conceptually reproducible.
	Metric 15:	Statistical Analysis	Low	Statistical model to calculate odds ratio was not described.

Additional Comments: This nested case-control study within a cohort study is a good study design to answer the research question regarding the association between multiple chemical exposures and four cancer sites. Cases and controls are selected appropriate. However, there are several limitations in this study: (1) confounders were not all considered and adjusted for, except that age-adjusted odds ratios were conducted; (2) it is not described if co-exposures were adjusted for; (3) numbers of cancer cases for each cancer type were small, so the statistical power is limited; (4) statistical models for calculating odds ratios were not described.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Cheng, T.J., Huang, M.L., You, N.C., Du, C.L., Chau, T.T. (1999). Abnormal liver function in workers exposed to low levels of ethylene dichloride and vinyl chloride monomer. Journal of Occupational and Environmental Medicine 41(12):1128-1133.
Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	AST, ALT, GGT, Hepatitis B virus surface antigen (HBsAg), and anti-hepatitis C virus antibody (anti-HCV).
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	200266

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	A total of 251 male workers were included from 4 vinyl chloride monomer manufacturing plants. Other details on recruitment strategy, eligibility criteria, year of enrollment, and participation rates were not provided.
	Metric 2:	Attrition	Low	There was no indication of attrition and details on the number of eligible participants throughout the study was limited. Attrition could not be adequately assessed due to a lack of information regarding recruitment and selection.
	Metric 3:	Comparison Group	Medium	The low-EDC-low-VCM group (187 participants) was used as the comparison group, and there is indirect evidence groups are similar. Limited details were provided for setting, inclusion and exclusion criteria, and methods of participant selection.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	NIOSH recommended methods 1003 and 1007 were used for personal and area sampling, respectively. Air samples were collected, stored at 4 deg. C, and analyzed within 2 weeks of the sampling event. However, historical job changes, changes in exposure levels over time, and timing (year or days during work week) or duration of area or personal sampling were not reported.
	Metric 5:	Exposure Levels	Medium	EDC and VCM levels were reported for the different categories of jobs, which were classified into low-EDC-low-VCM, mod-EDC-low-VCM, and low-EDC-mod-VCM groups.
	Metric 6:	Temporality	High	The age of participants (mean age 33.7-40.1 years) and employment duration (mean 7.5-14.3 years) were reported, and the temporality between the exposure and outcome appears to be appropriate.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	AST, ALT, and GGT "were analyzed with a Hitachi 7050 autoanalyzer". A basis for the cutoff values used in Table 4 to determine "abnormal" AST, ALT, and GGT levels was not provided.
	Metric 8:	Reporting Bias	High	Odds ratios for abnormal liver function were provided with 95% confidence intervals, the number per exposure level, and significance when applicable.
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Cheng, T.J., Huang, M.L., You, N.C., Du, C.L., Chau, T.T. (1999). Abnormal liver function in workers exposed to low levels of ethylene dichloride and vinyl chloride monomer. Journal of Occupational and Environmental Medicine 41(12):1128-1133.
Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	AST, ALT, GGT, Hepatitis B virus surface antigen (HBsAg), and anti-hepatitis C virus antibody (anti-HCV).
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	200266

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Medium	The study reports information on potential confounders (age, hepatitis, BMI, alcohol use, and employment duration), and controls for hepatitis, BMI and alcohol consumption in the multiple logistic regression analyses. There is indirect evidence that appropriate adjustments were made.
	Metric 10:	Covariate Characterization	Medium	An interviewer administered the questionnaires to collect information about potential confounders and occupational history.
	Metric 11:	Co-exposure Counfounding	Low	Exposure to ethylene dichloride was evaluated in a vinyl chloride monomer (VCM) manufacturing facility, and VCM was also subsequently analyzed using personal and area sampling. Results for VCM exposure concentrations were provided. VCM is also suspected to cause liver damage.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design (cohort) was appropriate to assess the outcome of interest (”markers of liver damage”). Chi-squared (X2) test and multiple logistic regression were used for statistical analyses.
	Metric 13:	Statistical Power	Medium	The number of participants was adequate to detect an effect in the exposed populations, although power calculations were not provided. There were >20 participants in each group.
	Metric 14:	Reproducibility of Analyses	Low	A description of the logistic regression analysis was provided, however, study authors do not provide information on categorization of abnormal liver function.
	Metric 15:	Statistical Analysis	High	There were no identifiable logistic regression model assumption violations.
Domain 6: Other (if applicable) Considerations for Biomarker Selection and Measurement (Lakind et al. 2014)				
	Metric 16:	Use of Biomarker of Exposure	N/A	Biomarker of exposures were not assessed.
	Metric 17:	Effect Biomarker	High	This study uses aspartate aminotransferase, alanine aminotransferase, and y-glutamyltransferase as biomarkers of effect. While these no works cited to explain their connection to liver function, all three are well-known marker of liver function. Similarly, Hepatitis B virus surface antigen and antihepatitis C virus anitbody are also well-known measures of liver function and health.
	Metric 18:	Method Sensitivity	Low	No limit of detection information is provided for any of the effect biomarkers.
	Metric 19:	Biomarker Stability	Medium	While the study does not provide a lot of information regarding biomarker storage or stability, the authors do mention that venous blood used to detect biomarkers was stored at 4 degrees C.
	Metric 20:	Sample Contamination	Medium	No specific information regarding potential sample contamination was provided.
	Metric 21:	Method Requirements	Medium	Aspartate aminotransferase, alanine aminotransferase, and y-glutamyltransferase were analyzed using a Hitachi 7050 autoanalyzer. Hepatitis B virus surface antibody and antihepatitis C virus antibody were assessed with radioimmunoassay and enzyme-linked immunosorbent assay.

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Study Citation:	Cheng, T.J., Huang, M.L., You, N.C., Du, C.L., Chau, T.T. (1999). Abnormal liver function in workers exposed to low levels of ethylene dichloride and vinyl chloride monomer. Journal of Occupational and Environmental Medicine 41(12):1128-1133.
Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	AST, ALT, GGT, Hepatitis B virus surface antigen (HBsAg), and anti-hepatitis C virus antibody (anti-HCV).
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	200266

Domain	Metric	Rating	Comments
	Metric 22: Matrix Adjustment	N/A	No information on matrix adjustment was provided/available.

Additional Comments: A group of 251 male workers from 4 vinyl chloride monomer (VCM) manufacturing plants were included in this assessment to examine if occupational exposure to VCM and ethylene dichloride (EDC) ”resulted in increased risk of liver damage” by examining AST, ALT, and GGT levels in the blood. Increased ORs for abnormal AST (>37 IU/L) and ALT (>41 IU/L) in the mod-EDC-low-VCM group (0.17-333.7 ppm EDC, 0.18-0.34 ppm VCM), compared with the low-EDC-low-VCM group, was reported. Exposure levels were measured using area and personal sampling, but the timing and duration of the sampling events were not reported.

Overall Quality Determination Medium

Study Citation:	Dosemeci, M., Cocco, P., Chow, W.H. (1999). Gender differences in risk of renal cell carcinoma and occupational exposures to chlorinated aliphatic hydrocarbons. American Journal of Industrial Medicine 36(1):54-59.
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	renal cell carcinoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	4697224

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	The details of the study design were reported elsewhere (Chow et al. 1994, HERO ID 701514). Brief details about the setting, date, number of eligible participants, and control matching were reported. Reasons for exclusions/non-participation were described with details by Chow et al. (1994).
	Metric 2:	Attrition	High	For the details of the study design and attrition of study subjects, the study authors referred to another publication by Chow et al., 1994. Chow et al. (1994) mentioned that at the end of the personal interview, the respondents were given a self-administered food-frequency questionnaire. Of the subjects interviewed for the study, 632 patients (79% of 796 eligible patients) and 653 control subjects (79% of 707 eligible control subjects) returned the diet questionnaire. A number of subjects, whose responses were considered unreliable, were excluded from the analysis, including 48 patients and three control subjects who had seven or more skipped food items or had questionable data and 50 patients whose next-of-kin respondent was not a spouse. Also excluded were two patients with unknown smoking status, since smoking is a risk factor.
	Metric 3:	Comparison Group	Medium	The cases were pulled from the Minnesota Cancer Surveillance System. Controls were selected from the general population of Minnesota; controls age 20-64 years were selected through random digital dialing and controls age 65-85 years were collected from files through the Health Care Financing Administration. Controls were age- and gender-stratified and were of the same race. Characteristics of cases and controls were not provided in the text or a table.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	High	Occupational histories including the most recent and usual occupation and industry, job activities, started-year and ended-year, and part-time/full-time status were collected. Occupations and industries were coded according to the standard occupational classification (SOC) and standard industrial classification (SIC) schemes. The National Cancer Institute developed job exposure matrices (JEM) for nine individual chlorinated aliphatic hydrocarbons (CAHCs), all CAHCs-combined, and all organic solvents-combined. These JEMs were merged with assigned SOC and SIC to determine the exposure status to these chemicals for each study subject. Application of the JEM was described elsewhere (Dosemeci et al. 1994, HERO ID 632334; Gomez et al. 1994, HERO ID 702154).
	Metric 5:	Exposure Levels	Medium	Details of the application of the JEM were described elsewhere (Dosemeci et al. 1994, HERO ID 632334; Gomez et al. 1994, HERO ID 702154). Dosemeci et al. (1994) described more details about that this study assigned three levels of probability (low, medium, high) to industries and occupations for chemical exposure levels.

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Study Citation:	Dosemeci, M., Cocco, P., Chow, W.H. (1999). Gender differences in risk of renal cell carcinoma and occupational exposures to chlorinated aliphatic hydrocarbons. American Journal of Industrial Medicine 36(1):54-59.
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	renal cell carcinoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	4697224

Domain	Metric		Rating	Comments
	Metric 6:	Temporality	Medium	Occupational questionnaires identified prior exposures based on reported recent and usual occupations as well as duration of employment. Outcome status was determined from registry data. The authors note that some occupational history was incomplete which may result in some uncertainty in regard to temporality.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Cases were identified as newly diagnosed and histologically confirmed renal cell carcinoma through the Minnesota Cancer Surveillance System and information about each participant was collected using a questionnaire. Validation was not specified.
	Metric 8:	Reporting Bias	Medium	A description of measured outcomes is reported and ORs were stratified by sex. Effect estimates are reported with a confidence interval. One table showed the total numbers of men and women respectively for each chemical, but numbers of cases/controls were not reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Appropriate adjustments were made in the final analysis, including age, gender, smoking, hypertension and the use of diuretics and/or anti-hypertension drugs, and BMI. Results were stratified by sex.
	Metric 10:	Covariate Characterization	Medium	Information about participants was collected using a questionnaire, and it includes potential confounders, e.g., smoking habits. Validation was not specified.
	Metric 11:	Co-exposure Counfounding	Medium	Co-exposures were identified through the job exposure matrices. Chemicals were evaluated individually and as a group.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen (case-control) was appropriate for the research question (renal cell carcinoma risk from occupational organic solvent exposure). Logistic regression models were used to estimate the relative risk and 95% CI.
	Metric 13:	Statistical Power	Low	Statistical power calculations were not provided. No significant effects were observed with 1,2-dichloroethane. The number of participated women to calculate odds ratio was inadequate to detect an effect in the participants for other chemicals or the combined risk, because it was very low.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis was brief, but is sufficient to understand precisely what has been done and to be conceptually reproducible with access to the analytic data.
	Metric 15:	Statistical Analysis	High	Model assumptions for logistic regression were met. The odds ratios were adjusted for age, smoking, hypertension status and/or use of diuretic and/or anti-hypertension drugs, and body mass index for men and women separately.

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Study Citation:	Dosemeci, M., Cocco, P., Chow, W.H. (1999). Gender differences in risk of renal cell carcinoma and occupational exposures to chlorinated aliphatic hydrocarbons. American Journal of Industrial Medicine 36(1):54-59.
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	renal cell carcinoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	4697224

Domain	Metric	Rating	Comments
Additional Comments:	A group of 438 cases (273 men and 165 women) were selected from the Minnesota Cancer Surveillance System that had been newly diagnosed with renal cell carcinoma. Controls included 687 participants (462 men and 225 women) age- and gender- stratified that were selected from either the general population of Minnesota (age 20-64 years) or from the Health Care Financing Administration files (age 65-85). No significant increase in the risk of renal cell carcinoma was observed with exposure to 1,2-dichloroethane among men or women separately, or for all participants exposed.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Dosemeci, M., Cocco, P., Chow, W.H. (1999). Gender differences in risk of renal cell carcinoma and occupational exposures to chlorinated aliphatic hydrocarbons. American Journal of Industrial Medicine 36(1):54-59.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	renal cell carcinoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	4697224

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	The details of the study design were reported elsewhere (Chow et al. 1994, HERO ID 701514). Brief details about the setting, date, number of eligible participants, and control matching were reported. Reasons for exclusions/non-participation were described with details by Chow et al. (1994).
	Metric 2:	Attrition	Medium	For the details of the study design and attrition of study subjects, the study authors referred to another publication by Chow et al., 1994. Chow et al. (1994) mentioned that at the end of the personal interview, the respondents were given a self-administered food-frequency questionnaire. Of the subjects interviewed for the study, 632 patients (79% of 796 eligible patients) and 653 control subjects (79% of 707 eligible control subjects) returned the diet questionnaire. A number of subjects, whose responses were considered unreliable, were excluded from the analysis, including 48 patients and three control subjects who had seven or more skipped food items or had questionable data and 50 patients whose next-of-kin respondent was not a spouse. Also excluded were two patients with unknown smoking status, since smoking is a risk factor.
	Metric 3:	Comparison Group	Medium	The cases were pulled from the Minnesota Cancer Surveillance System. Controls were selected from the general population of Minnesota; controls age 20-64 years were selected through random digital dialing and controls age 65-85 years were collected from files through the Health Care Financing Administration. Controls were age- and gender-stratified and were of the same race. Characteristics of cases and controls were not provided in the text or a table.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	High	Occupational histories including the most recent and usual occupation and industry, job activities, started-year and ended-year, and part-time/full-time status were collected. Occupations and industries were coded according to the standard occupational classification (SOC) and standard industrial classification (SIC) schemes. The National Cancer Institute developed job exposure matrices (JEM) for nine individual chlorinated aliphatic hydrocarbons (CAHCs), all CAHCs-combined, and all organic solvents-combined. These JEMs were merged with assigned SOC and SIC to determine the exposure status to these chemicals for each study subject. Application of the JEM was described elsewhere (Dosemeci et al. 1994, HERO ID 632334; Gomez et al. 1994, HERO ID 702154).
	Metric 5:	Exposure Levels	Medium	Details of the application of the JEM were described elsewhere (Dosemeci et al. 1994, HERO ID 632334; Gomez et al. 1994, HERO ID 702154). Dosemeci et al. (1994) described more details about that this study assigned three levels of probability (low, medium, high) to industries and occupations for chemical exposure levels.

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Study Citation:	Dosemeci, M., Cocco, P., Chow, W.H. (1999). Gender differences in risk of renal cell carcinoma and occupational exposures to chlorinated aliphatic hydrocarbons. American Journal of Industrial Medicine 36(1):54-59.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	renal cell carcinoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	4697224

Domain	Metric		Rating	Comments
	Metric 6:	Temporality	Medium	Occupational questionnaires identified prior exposures based on reported recent and usual occupations as well as duration of employment. Outcome status was determined from registry data. The authors note that some occupational history was incomplete which may result in some uncertainty in regard to temporality.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Cases were identified as newly diagnosed and histologically confirmed renal cell carcinoma through the Minnesota Cancer Surveillance System and information about each participant was collected using a questionnaire. Validation was not specified.
	Metric 8:	Reporting Bias	Medium	A description of measured outcomes is reported and ORs were stratified by sex. Effect estimates are reported with a confidence interval. One table showed the total numbers of men and women respectively for each chemical, but numbers of cases/controls were not reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Appropriate adjustments were made in the final analysis, including age, gender, smoking, hypertension and the use of diuretics and/or anti-hypertension drugs, and BMI. Results were stratified by sex.
	Metric 10:	Covariate Characterization	Medium	Information about participants was collected using a questionnaire, and it includes potential confounders, e.g., smoking habits. Validation was not specified.
	Metric 11:	Co-exposure Counfounding	Medium	Co-exposures were identified through the job exposure matrices. Chemicals were evaluated individually and as a group.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen (case-control) was appropriate for the research question (renal cell carcinoma risk from occupational organic solvent exposure). Logistic regression models were used to estimate the relative risk and 95% CI.
	Metric 13:	Statistical Power	Low	Statistical power calculations were not provided. No significant effects were observed with 1,2-dichloroethane. The number of participated women to calculate odds ratio was inadequate to detect an effect in the participants for other chemicals or the combined risk, because it was very low.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis was brief, but is sufficient to understand precisely what has been done and to be conceptually reproducible with access to the analytic data.
	Metric 15:	Statistical Analysis	High	Model assumptions for logistic regression were met. The odds ratios were adjusted for age, smoking, hypertension status and/or use of diuretic and/or anti-hypertension drugs, and body mass index for men and women separately.

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Study Citation:	Dosemeci, M., Cocco, P., Chow, W.H. (1999). Gender differences in risk of renal cell carcinoma and occupational exposures to chlorinated aliphatic hydrocarbons. American Journal of Industrial Medicine 36(1):54-59.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	renal cell carcinoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	4697224

Domain	Metric	Rating	Comments
Additional Comments:	A group of 438 cases (273 men and 165 women) were selected from the Minnesota Cancer Surveillance System that had been newly diagnosed with renal cell carcinoma. Controls included 687 participants (462 men and 225 women) age- and gender- stratified that were selected from either the general population of Minnesota (age 20-64 years) or from the Health Care Financing Administration files (age 65-85). No significant increase in the risk of renal cell carcinoma was observed with exposure to 1,2-dichloroethane among men or women separately, or for all participants exposed.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Garcia, E., Hurley, S., Nelson, D.O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health: A Global Access Science Source 14(1):14.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	breast cancer in females
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	3014082

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	A total of 112,378 women were included in this study out of 133,479 eligible female participants from the California Teacher Study cohort. A full description of the cohort is provided in Bernstein et al. 2002 (HERO ID 808446). Reasons for exclusion were provided. The reported information indicates that participant selection in or out of the study and participation was not likely to be biased.
	Metric 2:	Attrition	High	112,378/133,479 participants were included in the study. Exclusions were for the purpose of the study and analysis. Exclusion criteria were documented. Included participants had completed questionnaires. The California Cancer Registry is estimated to be 99% complete.
	Metric 3:	Comparison Group	Medium	There is only indirect evidence that groups are similar. Participants were recruited from the same eligible population with the same method of ascertainment. Comparisons were provided for participants with and without breast cancer. Characteristics between these two groups were generally similar. 5 Quintiles of exposure were used, and Q2-5 were compared with Q1.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	High	The Assessment System for Population Exposure Nationwide and the Human Exposure Model are used as part of the National-Scale Air Toxics Assessment produced by the EPA and was used to estimate ambient HAP concentrations for geographic locations. Methods are described online through the US EPA Assessment Methods.
	Metric 5:	Exposure Levels	Medium	The distribution of the NATA annual ambient concentration for each compound was plotted in Figure 1 using a box plot, and 5 Quintiles were used in the analyses.
	Metric 6:	Temporality	Medium	The follow-up period was from 1995-2011, and the NATA estimates were made in 2002 because it was approximately half way between the start and end of the follow-up period. However, it is unclear whether exposures fall within relevant exposure windows for the outcome of interest.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Annual linkage between the CTS cohort and the California Cancer Registry (CCR) was used to identify cases of invasive breast cancer. The CCR is estimated to be 99% complete. The case of invasive breast cancer was defined by ICD codes.

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Study Citation:	Garcia, E., Hurley, S., Nelson, D.O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health: A Global Access Science Source 14(1):14.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	breast cancer in females
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	3014082

Domain	Metric		Rating	Comments
	Metric 8:	Reporting Bias	Medium	A description of measured outcome is reported for adjustments by age and race, and effect estimates are reported with a 95% confidence interval. The measured outcomes using multiple comparisons were generally described in the text, but non-significant results were excluded from Table 3.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	The models were stratified by age and race. Additionally, adjustments were made for multiple comparisons among subsets of the participants (significant results reported in Table 3). Socioeconomic status (SES) of each participant was not evaluated, however, cohort SES characteristics were thought to be similar by study authors.
	Metric 10:	Covariate Characterization	Medium	Information about baseline characteristics for each participant was collected through a questionnaire. It is unknown if the questionnaire was validated.
	Metric 11:	Co-exposure Counfounding	Medium	A total of 37 compounds were identified as mammary gland carcinogens, but 13 were not included in this analysis. Thirteen compounds were excluded from the analysis due to insufficient variability (nine because they had the same value for all census tracts in the state of California; and four because they had less than 25% non-zero values). Ethylene dichloride (1,2-dichloroethane) was among the 24 compounds evaluated in this assessment, and evaluations for breast cancer were conducted for each of these 24 individual compounds.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen (prospective cohort) was appropriate for the research question (incidence of breast cancer). Cox proportional hazard models and SAS 9.3 were used in this assessment. Data analysis was described.
	Metric 13:	Statistical Power	Medium	Statistical power calculations were not provided. No significant effects were observed with ethylene dichloride (1,2-dichloroethane), however, this study utilized a large cohort, approximately 112,000 individuals. Distributions of chemicals of interest suggest there were sufficient numbers of participants in exposure subgroups.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to understand precisely what has been done and to be conceptually reproducible with access to the analytic data.
	Metric 15:	Statistical Analysis	High	The statistical models that were used were identified and described. ”No apparent violation of the underlying assumption of proportional hazards was detected”.

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Study Citation:	Garcia, E., Hurley, S., Nelson, D.O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health: A Global Access Science Source 14(1):14.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	breast cancer in females
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	3014082

Domain	Metric	Rating	Comments
Additional Comments:	A group of 112,378 female participants from the California Teacher Study cohort were assessed for their estimated exposure to ambient air pollutants, including ethylene dichloride (1,2-dichloroethane), and the incidence of invasive breast cancer. Air contaminant concentrations were estimated using the US EPA NATA and the ASPEN and HEM models. The approximate median concentration of 1,2-dichloroethane is between 1E-4 and 1E-2 (estimated from Figure 1). Exposures were categorized into 5 Quintiles, and compared against Quintile 1. No significant increase in the estimated hazard rate ratio for invasive breast cancer was observed with Quintile 2-5 exposure estimates for 1,2-dichloroethane, adjusted for age and race, when compared against Quintile 1, or when further adjusted using multiple comparisons.		

Overall Quality Determination High

* No biomarkers were identified for this evaluation.

Study Citation:	Garcia, E., Hurley, S., Nelson, D.O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health: A Global Access Science Source 14(1):14.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	breast cancer in females
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	3014082

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	A total of 112,378 women were included in this study out of 133,479 eligible female participants from the California Teacher Study cohort. A full description of the cohort is provided in Bernstein et al. 2002 (HERO ID 808446). Reasons for exclusion were provided. The reported information indicates that participant selection in or out of the study and participation was not likely to be biased.
	Metric 2:	Attrition	High	112,378/133,479 participants were included in the study. Exclusions were for the purpose of the study and analysis. Exclusion criteria were documented. Included participants had completed questionnaires. The California Cancer Registry is estimated to be 99% complete.
	Metric 3:	Comparison Group	Medium	There is only indirect evidence that groups are similar. Participants were recruited from the same eligible population with the same method of ascertainment. Comparisons were provided for participants with and without breast cancer. Characteristics between these two groups were generally similar. 5 Quintiles of exposure were used, and Q2-5 were compared with Q1.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	High	The Assessment System for Population Exposure Nationwide and the Human Exposure Model are used as part of the National-Scale Air Toxics Assessment produced by the EPA and was used to estimate ambient HAP concentrations for geographic locations. Methods are described online through the US EPA Assessment Methods.
	Metric 5:	Exposure Levels	Medium	The distribution of the NATA annual ambient concentration for each compound was plotted in Figure 1 using a box plot, and 5 Quintiles were used in the analyses.
	Metric 6:	Temporality	Medium	The follow-up period was from 1995-2011, and the NATA estimates were made in 2002 because it was approximately half way between the start and end of the follow-up period. However, it is unclear whether exposures fall within relevant exposure windows for the outcome of interest.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Annual linkage between the CTS cohort and the California Cancer Registry (CCR) was used to identify cases of invasive breast cancer. The CCR is estimated to be 99% complete. The case of invasive breast cancer was defined by ICD codes.
	Metric 8:	Reporting Bias	Medium	A description of measured outcome is reported for adjustments by age and race, and effect estimates are reported with a 95% confidence interval. The measured outcomes using multiple comparisons were generally described in the text, but non-significant results were excluded from Table 3.

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Study Citation:	Garcia, E., Hurley, S., Nelson, D.O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health: A Global Access Science Source 14(1):14.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	breast cancer in females
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	3014082

Domain	Metric		Rating	Comments
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	The models were stratified by age and race. Additionally, adjustments were made for multiple comparisons among subsets of the participants (significant results reported in Table 3). Socioeconomic status (SES) of each participant was not evaluated, however, cohort SES characteristics were thought to be similar by study authors.
	Metric 10:	Covariate Characterization	Medium	Information about baseline characteristics for each participant was collected through a questionnaire. It is unknown if the questionnaire was validated.
	Metric 11:	Co-exposure Counfounding	Medium	A total of 37 compounds were identified as mammary gland carcinogens, but 13 were not included in this analysis. Thirteen compounds were excluded from the analysis due to insufficient variability (nine because they had the same value for all census tracts in the state of California; and four because they had less than 25% non-zero values). Ethylene dichloride (1,2-dichloroethane) was among the 24 compounds evaluated in this assessment, and evaluations for breast cancer were conducted for each of these 24 individual compounds.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen (prospective cohort) was appropriate for the research question (incidence of breast cancer). Cox proportional hazard models and SAS 9.3 were used in this assessment. Data analysis was described.
	Metric 13:	Statistical Power	Medium	Statistical power calculations were not provided. No significant effects were observed with ethylene dichloride (1,2-dichloroethane), however, this study utilized a large cohort, approximately 112,000 individuals. Distributions of chemicals of interest suggest there were sufficient numbers of participants in exposure subgroups.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to understand precisely what has been done and to be conceptually reproducible with access to the analytic data.
	Metric 15:	Statistical Analysis	High	The statistical models that were used were identified and described. ”No apparent violation of the underlying assumption of proportional hazards was detected”.

Additional Comments: A group of 112,378 female participants from the California Teacher Study cohort were assessed for their estimated exposure to ambient air pollutants, including ethylene dichloride (1,2-dichloroethane), and the incidence of invasive breast cancer. Air contaminant concentrations were estimated using the US EPA NATA and the ASPEN and HEM models. The approximate median concentration of 1,2-dichloroethane is between 1E-4 and 1E-2 (estimated from Figure 1). Exposures were categorized into 5 Quintiles, and compared against Quintile 1. No significant increase in the estimated hazard rate ratio for invasive breast cancer was observed with Quintile 2-5 exposure estimates for 1,2-dichloroethane, adjusted for age and race, when compared against Quintile 1, or when further adjusted using multiple comparisons.

Overall Quality Determination High

* No biomarkers were identified for this evaluation.

Study Citation:	Guo, P., Yokoyama, K., Piao, F., Sakai, K., Khalequzzaman, M., Kamijima, M., Nakajima, T., Kitamura, F. (2013). Sick building syndrome by indoor air pollution in Dalian, China. International Journal of Environmental Research and Public Health 10(4):1489-1504.
Health Outcome(s):	sick building syndrome
Reported Health Effect(s):	The statistical analysis considers all subjective self-reported symptoms together (not segregated by health outcome) as a group health outcome –sick building syndrome. The study compared two conditions for each studied chemical: combined self-reported symptoms to no symptoms. Therefore, only one form 3 was completed.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1938385

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Residents of a housing estate of 3000 homes were invited to a community meeting to explain the purpose of the study and volunteers were invited to participate. It was not reported whether these volunteers were different from the overall eligible population.
	Metric 2:	Attrition	Low	Of the 70 families that agreed to participate, questionnaires were provided by 59. Reasons of uncompleted questionnaires were not fully provided, and there was no comparison between those who participated and those who did not.
	Metric 3:	Comparison Group	Low	The overall description of the analysis sample indicated a wide range of ages and lengths of stay at the current residence. Thus it is hard to know that subjects in all exposure groups were similar. In addition, the methods of selecting participants in all exposure groups were not fully reported. The numbers of male and female smokers were reported, respectively, but the smoking status and age were not controlled in the statistical analysis.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure concentrations for each home were obtained by diffusion sampling over 24 hrs in the bedroom, kitchen, and outdoors; temperature, the vertical height of samplers, and ventilation (hours windows left open) were reported. Samples were analyzed by GC/MS. The number of samples per home is unclear. The frequency of measurements for each house was not reported.
	Metric 5:	Exposure Levels	Low	The frequency of detection was not reported, so it is difficult to ascertain the actual exposure range. In addition, the reported exposure levels were median, geometric mean, and 95% CI, so they are inadequate to develop an exposure-response estimate.
	Metric 6:	Temporality	Uninformative	For 1,2-dichloroethane, the study evaluated self-reported symptoms in the past (”since they moved into their flats”) and their association with sampling conducted during the study; thus, exposure was measured after the outcome.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Low	Participants provided self-reported symptoms using a questionnaire. Study authors cited a previous study, Kamijima et al., 2005 (in Japanese, HERO ID 1598645) for further details on the questionnaire. It was not clear whether the questionnaire was validated.

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Study Citation:	Guo, P., Yokoyama, K., Piao, F., Sakai, K., Khalequzzaman, M., Kamijima, M., Nakajima, T., Kitamura, F. (2013). Sick building syndrome by indoor air pollution in Dalian, China. International Journal of Environmental Research and Public Health 10(4):1489-1504.
Health Outcome(s):	sick building syndrome
Reported Health Effect(s):	The statistical analysis considers all subjective self-reported symptoms together (not segregated by health outcome) as a group health outcome –sick building syndrome. The study compared two conditions for each studied chemical: combined self-reported symptoms to no symptoms. Therefore, only one form 3 was completed.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1938385

Domain	Metric		Rating	Comments
	Metric 8:	Reporting Bias	Low	The study only mentioned subjective symptoms in the abstract or methods. The abstract and method sections did not report the specific symptoms included in the questionnaire or whether the questionnaire was open-ended for symptoms. The questionnaire was cited to Kamijima et al. 2005 (in Japanese).
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	Comparisons were made separately by sex. The distribution of age and time spent living in residence differed greatly between those reporting symptoms and those not reporting symptoms. Smoking was indicated but not controlled for in the analysis. In short, the statistical analysis did not consider these three potential confounders, age, time spent living in residence, and smoking.
	Metric 10:	Covariate Characterization	Low	Covariates were presumably evaluated via a questionnaire that was cited to Kamijima et al. 2005 (in Japanese).
	Metric 11:	Co-exposure Counfounding	Low	The analysis did not account for other exposures. A number of other VOCs, HCHO, and NO2 were measured in the homes. The concentrations of several other VOCs and HCHO were much higher (5-30x) than 1,2-dichloroethane and may also be associated with these symptoms.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Low	The study design is best characterized as cross-sectional. Only one analysis to compare exposure concentrations between those with and without symptoms was adjusted for a confounder, sex, via stratification. Other potential confounders were not adjusted for. Study authors combine responses for symptoms reported before and during the sampling period in one statistical analysis, which may not reflect the relationship between symptoms and contaminants' exposure at each period.
	Metric 13:	Statistical Power	Medium	Statistical power was not reported. The number of participants was sufficient to detect a difference in median concentration between those with and without symptoms.
	Metric 14:	Reproducibility of Analyses	Medium	Study presents sufficient description of analysis (statistical methods) to be conceptually reproducible with access to the raw data.
	Metric 15:	Statistical Analysis	Low	Study uses a Wilcoxon's rank sum test to compare exposure concentrations in persons with and without symptoms; test for equal variance is not reported.

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Study Citation:	Guo, P., Yokoyama, K., Piao, F., Sakai, K., Khalequzzaman, M., Kamijima, M., Nakajima, T., Kitamura, F. (2013). Sick building syndrome by indoor air pollution in Dalian, China. International Journal of Environmental Research and Public Health 10(4):1489-1504.
Health Outcome(s):	sick building syndrome
Reported Health Effect(s):	The statistical analysis considers all subjective self-reported symptoms together (not segregated by health outcome) as a group health outcome –sick building syndrome. The study compared two conditions for each studied chemical: combined self-reported symptoms to no symptoms. Therefore, only one form 3 was completed.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1938385

Domain	Metric	Rating	Comments
Additional Comments:	Concentrations of VOCs (including 1,2-dichloroethane), HCHO, and NO2 were measured in the 59 homes of families that agreed to participate after being informed of the nature of the study. Participants completed questionnaires asking about symptoms since they moved into the homes and the concentrations of selected compounds were compared among men and women reporting any symptoms vs no symptoms. Concentrations of 1,2-dichloroethane in homes of people with symptoms were higher than in homes without. p-Dichlorobenzene was measured in the homes as well, but median concentration was <DL and no further analysis was made. Unacceptable due to selection bias, lack of confounding control, inadequate outcome characterization, and lack of temporality.		

Overall Quality Determination — Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Kernan, G.J., Ji, B.T., Dosemeci, M., Silverman, D.T., Balbus, J., Zahm, S.H. (1999). Occupational risk factors for pancreatic cancer: A case-control study based on death certificates from 24 U.S. states. American Journal of Industrial Medicine 36(2):260-270.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Death from pancreatic cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	194820

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	The National Cancer Institute, National Institute of Occupational Safety and Health, and the National Center for Health Statistics reviewed death certificates from 24 states to select cases from those that had died from pancreatic cancer and matched controls. Controls with cause of death related to the outcome of interest (i.e. pancreatic diseases) were excluded from the study. All key elements of the study design were reported.
	Metric 2:	Attrition	Medium	There was no direct evidence of subject loss or exclusion of subgroups from analyses. The authors provide the total number of cases and controls in the analysis. Case and control data were taken from a registry. It can be assumed that the data are complete for each subject.
	Metric 3:	Comparison Group	High	Controls were selected from the same pool of death certificates from 24 states that cases were selected from. Controls with cause of death related to the outcome of interest were eliminated. Differences in baseline characteristics were controlled for via matching, stratification, and adjustment.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure was assessed via occupation and industry data on death certificates. A job matrix was further applied to assess the likely levels of exposure. Probability and intensity of exposure were estimated across four levels for each occupation. Only employment captured on the death certificate could be considered. The exposure assessment needs exposure information before the job listed on the death certificates.
	Metric 5:	Exposure Levels	Medium	The study offers 4 levels of estimated probability and intensity of exposure (referent, low, medium, high).
	Metric 6:	Temporality	Medium	Exposure was determined by occupational and industry codes on death certificates and indicate that exposure would precede disease, however, the timing and latency period is less clear.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Causes of mortality were determined from death certificates for both cases and controls. Death certificates were drawn from death registries of participating states (n=24). Causes of death were coded using ICD-9 codes, and pancreatic cancer was identified as ICD 157.
	Metric 8:	Reporting Bias	Medium	Measured outcomes, effect estimates and confidence intervals are reported. Number of exposed cases is reported for each analysis, however the number of controls (exposed and unexposed) are not reported for analyses.

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Study Citation:	Kernan, G.J., Ji, B.T., Dosemeci, M., Silverman, D.T., Balbus, J., Zahm, S.H. (1999). Occupational risk factors for pancreatic cancer: A case-control study based on death certificates from 24 U.S. states. American Journal of Industrial Medicine 36(2):260-270.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Death from pancreatic cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	194820

Domain	Metric		Rating	Comments
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Potential confounders were accounted for in the following ways: matching (five year age group, state, race, and gender); adjustment in models (age, marital status, metropolitan, and residential status); and stratification (race and gender). Smoking was not included as a confounder.
	Metric 10:	Covariate Characterization	Medium	Data used to assess potential confounders was derived from death certificates, an adequate measure. However, no information about cigarette smoking and other lifestyle factors were available for adjustment in the analysis.
	Metric 11:	Co-exposure Counfounding	Medium	The variety of industries considered in the analysis diminishes concerns about co-exposures.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The case-control study design and statistical analysis methods were appropriate to assess the exposures/outcome of interest.
	Metric 13:	Statistical Power	Medium	This study had an adequate sample size to detect an effect (n for cases = 63,097; n for controls = 252,386).
	Metric 14:	Reproducibility of Analyses	Medium	The description of analysis was sufficient and would be reproducible.
	Metric 15:	Statistical Analysis	High	The model to calculate risk estimates was transparent.

Additional Comments: This case-control study examined the risk of death from pancreatic cancer in different occupational settings. Exposure was solely assessed using occupation/industry at time of death (reported on death certificate) and the application of a job matrix assessing likely levels of exposure for different positions. This means of estimating exposure may not fully represent a participant's exposure history. Additionally, the number of impacted participants (exposed cases) was inadequate to perform quality analyses for some exposure levels.

Overall Quality Determination High

* No biomarkers were identified for this evaluation.

Study Citation:	Kernan, G.J., Ji, B.T., Dosemeci, M., Silverman, D.T., Balbus, J., Zahm, S.H. (1999). Occupational risk factors for pancreatic cancer: A case-control study based on death certificates from 24 U.S. states. American Journal of Industrial Medicine 36(2):260-270.
Health Outcome(s):	Endocrine
Reported Health Effect(s):	Death from pancreatic cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	194820

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	The National Cancer Institute, National Institute of Occupational Safety and Health, and the National Center for Health Statistics reviewed death certificates from 24 states to select cases from those that had died from pancreatic cancer and matched controls. Controls with cause of death related to the outcome of interest (i.e. pancreatic diseases) were excluded from the study. All key elements of the study design were reported.
	Metric 2:	Attrition	Medium	There was no direct evidence of subject loss or exclusion of subgroups from analyses. The authors provide the total number of cases and controls in the analysis. Case and control data were taken from a registry. It can be assumed that the data are complete for each subject.
	Metric 3:	Comparison Group	High	Controls were selected from the same pool of death certificates from 24 states that cases were selected from. Controls with cause of death related to the outcome of interest were eliminated. Differences in baseline characteristics were controlled for via matching, stratification, and adjustment.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure was assessed via occupation and industry data on death certificates. A job matrix was further applied to assess the likely levels of exposure. Probability and intensity of exposure were estimated across four levels for each occupation. Only employment captured on the death certificate could be considered. The exposure assessment needs exposure information before the job listed on the death certificates.
	Metric 5:	Exposure Levels	Medium	The study offers 4 levels of estimated probability and intensity of exposure (referent, low, medium, high).
	Metric 6:	Temporality	Medium	Exposure was determined by occupational and industry codes on death certificates and indicate that exposure would precede disease, however, the timing and latency period is less clear.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Causes of mortality were determined from death certificates for both cases and controls. Death certificates were drawn from death registries of participating states (n=24). Causes of death were coded using ICD-9 codes, and pancreatic cancer was identified as ICD 157.
	Metric 8:	Reporting Bias	Medium	Measured outcomes, effect estimates and confidence intervals are reported. Number of exposed cases is reported for each analysis, however the number of controls (exposed and unexposed) are not reported for analyses.
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Kernan, G.J., Ji, B.T., Dosemeci, M., Silverman, D.T., Balbus, J., Zahm, S.H. (1999). Occupational risk factors for pancreatic cancer: A case-control study based on death certificates from 24 U.S. states. American Journal of Industrial Medicine 36(2):260-270.
Health Outcome(s):	Endocrine
Reported Health Effect(s):	Death from pancreatic cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	194820

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Medium	Potential confounders were accounted for in the following ways: matching (five year age group, state, race, and gender); adjustment in models (age, marital status, metropolitan, and residential status); and stratification (race and gender). Smoking was not included as a confounder.
	Metric 10:	Covariate Characterization	Medium	Data used to assess potential confounders was derived from death certificates, an adequate measure. However, no information about cigarette smoking and other lifestyle factors were available for adjustment in the analysis.
	Metric 11:	Co-exposure Counfounding	Medium	The variety of industries considered in the analysis diminishes concerns about co-exposures.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The case-control study design and statistical analysis methods were appropriate to assess the exposures/outcome of interest.
	Metric 13:	Statistical Power	Medium	This study had an adequate sample size to detect an effect (n for cases = 63,097; n for controls = 252,386).
	Metric 14:	Reproducibility of Analyses	Medium	The description of analysis was sufficient and would be reproducible.
	Metric 15:	Statistical Analysis	High	The model to calculate risk estimates was transparent.

Additional Comments: This case-control study examined the risk of death from pancreatic cancer in different occupational settings. Exposure was solely assessed using occupation/industry at time of death (reported on death certificate) and the application of a job matrix assessing likely levels of exposure for different positions. This means of estimating exposure may not fully represent a participant's exposure history. Additionally, the number of impacted participants (exposed cases) was inadequate to perform quality analyses for some exposure levels.

Overall Quality Determination High

* No biomarkers were identified for this evaluation.

Study Citation:	Niehoff, N.M., Gammon, M.D., Keil, A.P., Nichols, H.B., Engel, L.S., Sandler, D.P., White, A.J. (2019). Airborne mammary carcinogens and breast cancer risk in the Sister Study. Environment International 130:104897.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Breast cancer diagnosis (overall), tumor characteristics, and estrogen receptor positive (ER+) invasive breast cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5440630

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	Data from the Sister Study were used. The Sister Study is "a prospective cohort of 50,884 women from across the US who were ages 35–74 at enrollment (Sandler et al., 2017). Participants were recruited from 2003 to 2009 using a national advertising campaign in English and Spanish. Women were eligible for the Sister Study if they had a sister who had been diagnosed with breast cancer, but no prior breast cancer themselves."Exclusions from the study occurred for the following reasons:-breast cancer diagnosed before enrollment was complete, or did not have follow-up information (n = 163)-Residential address couldn't be geocoded (n = 1003, < 2%) - This is a small perecentage, but all of those who were excluded for this reason were from Puerto Rico, West Virginia, Missouri, or Oklahoma.Key elements of the study design are reported. There is some potential for selection bias, but based on the small percentage of those eligible who were excluded, participation was not likely to be substantially biased.
	Metric 2:	Attrition	High	Response rates in the overall Sister study remained over 91% over follow-up. Reasons for non-response were not reported, and characteristics of those lost to follow up were not reported or compared with those included, but 9% loss to follow-up is minimal.
	Metric 3:	Comparison Group	High	Differences in baseline characteristics of groups were considered as potential confounding variables.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	The EPA NATA database of census-tract level modeled air toxics data was used. The study authors note the potential for exposure misclassification: "Concentrations at the census tract level do not fully account for variation in an individual's daily activities that could lead to higher or lower exposure, and all women within a census tract are assigned the same concentration."
	Metric 5:	Exposure Levels	Medium	There were five quintiles of exposure, so there was a sufficient range and distribution of exposure.
	Metric 6:	Temporality	Medium	This is a prospective cohort study.Exposure data from 2005 were chosen because they represented the middle of the enrollment period (2003-2009).The study reported that "94% of women enrolled in 2005 or later, and thus the exposure assessment primarily predated enrollment for the majority of Sister Study participants."The six percent of women who had the potential to have the outcome before exposure was measured in 2005 are a concern. But sensitivity analyses were used to assess whether the associations changed when restricted to those who enrolled in 2005 or later.The authors note that the study is making assumptions about the relevant exposure windows - therefore the exposure window is not certain.

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Study Citation:	Niehoff, N.M., Gammon, M.D., Keil, A.P., Nichols, H.B., Engel, L.S., Sandler, D.P., White, A.J. (2019). Airborne mammary carcinogens and breast cancer risk in the Sister Study. Environment International 130:104897.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Breast cancer diagnosis (overall), tumor characteristics, and estrogen receptor positive (ER+) invasive breast cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5440630

Domain	Metric		Rating	Comments
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Women who reported a breast cancer diagnosis on the annual health updates or follow-up questionnaires were asked to provide additional diagnosis information, and to grant permission for the study to obtain medical records and pathology reports. Medical records were obtained for 81% of breast cancer diagnoses. Agreement between self-reported breast cancers and medical records was high (positive predictive value > 99%) (Sandler et al., 2017), so self-report was used when medical records were not available. Tumor characteristics (stage; histology; and estrogen receptor (ER) status) were abstracted from medical records, or self-reported.
	Metric 8:	Reporting Bias	High	A description of measured outcomes is reported. Effect estimates are reported with confidence intervals.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Covariates considered included age, race, BMI, residence type, education, and smoking status. Potential confounders were identified using DAGs and literature review. Appropriate considerations were made for potential confounders.
	Metric 10:	Covariate Characterization	Medium	”Most covariates were assessed by self-report at the baseline interview.””At baseline, women completed a computer-assisted telephone interview and written questionnaires.”Previous publications might describe whether the questionnaires were validated, but validation was not specified in this publication.
	Metric 11:	Co-exposure Counfounding	Medium	Co-exposures to other air pollutants were assessed, but at the census tract level.Multipollutant classification trees were used, which might provide useful qualitative information.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design (large prospective cohort) and analysis method (Cox proportional hazard single and multi-pollutant models accounting for potential confounders) were appropriate to assess the association between exposure and disease.
	Metric 13:	Statistical Power	Medium	The study had an adequate sample size (1975 cancer cases) and follow-up time (mean=8.4 years).
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to be conceptually reproducible.

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Study Citation:	Niehoff, N.M., Gammon, M.D., Keil, A.P., Nichols, H.B., Engel, L.S., Sandler, D.P., White, A.J. (2019). Airborne mammary carcinogens and breast cancer risk in the Sister Study. Environment International 130:104897.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Breast cancer diagnosis (overall), tumor characteristics, and estrogen receptor positive (ER+) invasive breast cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5440630

Domain	Metric	Rating	Comments
	Metric 15: Statistical Analysis	High	Hazard ratios and 95% confidence intervals (CIs) are reported "comparing index categories of exposure to exposures below the first quintile using Cox proportional hazards regression, with age as the time scale." The method of calculating the hazard ratios is transparent. The authors reported that "the proportional hazards assumption was evaluated by conducting a Wald test for an interaction between the continuous form of the air toxic measure and time." Censoring times and times at-risk are described.

Additional Comments: This was a well-conducted study of a large prospective cohort, but the measurement of exposure at the census-tract rather than the individual level is a limitation.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Sobel, W., Bond, G.G., Skowronski, B.J., Brownson, P.J., Cook, R.R. (1987). A soft tissue sarcoma case control study in a large multi-chemical manufacturing facility. Chemosphere 16(8-9):2095-2099.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	soft-tissue sarcoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1357737

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	From a pool of > 37,000 subjects who worked at least 1 year at chemical company between January 1940-December 1979, the study identified 14 people who died due to soft-cell sarcoma (via death certificate, medical records, or histopathology report). Referents were matched 9:1 with cases (126 matched controls).
	Metric 2:	Attrition	High	There was minimal subject exclusion from the analysis sample; one case could not be matched to controls and was excluded from analysis.
	Metric 3:	Comparison Group	High	Cases and controls were recruited from the same eligible population within the same time frame and matched on sex, race, year of birth and year of hire. Both cases and controls had to have worked ≥1 yr at the plant during the study period.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Work histories for cases and referents were coded to determine an individual's potential exposure to chemical of interest and reviewed by an industrial hygienist blinded to case status.
	Metric 5:	Exposure Levels	Low	Exposure was considered dichotomous, ever exposed or never exposed. There is no quantitative information on exposure levels or range of exposures.
	Metric 6:	Temporality	Low	Temporality of exposure and outcome is established. It is unclear if the interval between exposure and outcome is sufficient for soft tissue sarcoma outcomes.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	The soft-tissue sarcoma outcome was assessed by information provided by death certificates, medical records, and histopathology reports, but study authors did not report the proportions determined by each method.
	Metric 8:	Reporting Bias	High	All outcomes outlined were reported. Authors reported the number of cases and controls in the table. Maximum likelihood estimate ORs with respective 95 % confidence intervals were reported.
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Sobel, W., Bond, G.G., Skowronski, B.J., Brownson, P.J., Cook, R.R. (1987). A soft tissue sarcoma case control study in a large multi-chemical manufacturing facility. Chemosphere 16(8-9):2095-2099.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	soft-tissue sarcoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1357737

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Low	Controls were matched with cases on age, sex, year of hire and survival information. There is indirect evidence that the considerations were made to identify potential confounders through evaluation of medical records of cases and controls (various heritable syndromes, family history of cancer, history of lymphedema, steroids, throrotrast, foreign body implants, chronic extensive scarring, radiation therapy, and immunological defects). Identified confounders between cases and controls were not reported and it is unclear if adjustments for these confounders were included in the final analyses.
	Metric 10:	Covariate Characterization	High	Potential covariates were assessed through evaluation of work histories and medical records.
	Metric 11:	Co-exposure Counfounding	Low	The study documented 13 chemicals, known to be associated with soft-tissue sarcoma (according to NTP, 1983) that were used at the manufacturing facility at some point since 1940. The authors note that some individuals were exposed to multiple chemicals during their employment history and were counted multiple times in the analysis for different chemical exposures. Co-exposures to chemicals to not appear to be adjusted for in analysis.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Low	The study design was adequate to assess the association between exposure and the outcome of interest (soft-tissue sarcoma). The study authors noted they used programs developed by Rothman and Boice to calculate odds ratios with CI intervals; the statistical methods are not further described. The page containing the Rothman and Boice reference appears to be missing from the PDF (or the citation is missing).
	Metric 13:	Statistical Power	Low	Statistical power was not calculated. For 1,2-dichloroethane, there was one case and 6 controls included in the analysis, which was not adequate to detect and effect.
	Metric 14:	Reproducibility of Analyses	Low	The study calculated odd ratios, and 95% CIs were calculated using point estimates and chi from hypothesis testing. The study authors noted they used programs developed by Rothman and Boice to calculate odds ratios with 95% CIs; the statistical methods are not further described and there was no reference for the programs cited.
	Metric 15:	Statistical Analysis	Low	A description of analyses/assumptions was not reported.

Additional Comments: A case-control study of workers at a chemical production facility who worked at least 1 year between January 1940-December 1979 (n=37,000) investigated the incidence of deaths due to soft-tissue sarcoma. The study identified 14 people who died due to soft-tissue sarcoma (through death certificate, medical records, or histopathology reports). Cases were matched to controls based on sex, race, year of birth and year of hire. 13 chemicals, including 1,2-dichloroethane, associated with soft-tissue sarcoma were used at the facility; it does not appear that co-exposures were adjusted for in the analysis. Odds ratios and corresponding CIs were calculated. No significant association was found between exposure to 1,2-DCE and soft-tissue sarcoma.

Overall Quality Determination Medium

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Study Citation:	Sobel, W., Bond, G.G., Skowronski, B.J., Brownson, P.J., Cook, R.R. (1987). A soft tissue sarcoma case control study in a large multi-chemical manufacturing facility. Chemosphere 16(8-9):2095-2099.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	soft-tissue sarcoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1357737

Domain	Metric	Rating	Comments

* No biomarkers were identified for this evaluation.

Study Citation:	Sobel, W., Bond, G.G., Skowronski, B.J., Brownson, P.J., Cook, R.R. (1987). A soft tissue sarcoma case control study in a large multi-chemical manufacturing facility. Chemosphere 16(8-9):2095-2099.
Health Outcome(s):	Skin and Connective Tissue
Reported Health Effect(s):	soft-tissue sarcoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1357737

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	From a pool of > 37,000 subjects who worked at least 1 year at chemical company between January 1940-December 1979, the study identified 14 people who died due to soft-cell sarcoma (via death certificate, medical records, or histopathology report). Referents were matched 9:1 with cases (126 matched controls).
	Metric 2:	Attrition	High	There was minimal subject exclusion from the analysis sample; one case could not be matched to controls and was excluded from analysis.
	Metric 3:	Comparison Group	High	Cases and controls were recruited from the same eligible population within the same time frame and matched on sex, race, year of birth and year of hire. Both cases and controls had to have worked ≥1 yr at the plant during the study period.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Work histories for cases and referents were coded to determine an individual's potential exposure to chemical of interest and reviewed by an industrial hygienist blinded to case status.
	Metric 5:	Exposure Levels	Low	Exposure was considered dichotomous, ever exposed or never exposed. There is no quantitative information on exposure levels or range of exposures.
	Metric 6:	Temporality	Low	Temporality of exposure and outcome is established. It is unclear if the interval between exposure and outcome is sufficient for soft tissue sarcoma outcomes.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	The soft-tissue sarcoma outcome was assessed by information provided by death certificates, medical records, and histopathology reports, but study authors did not report the proportions determined by each method.
	Metric 8:	Reporting Bias	High	All outcomes outlined were reported. Authors reported the number of cases and controls in the table. Maximum likelihood estimate ORs with respective confidence intervals were reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	Controls were matched with cases on age, sex, year of hire and survival information. There is indirect evidence that that considerations were made to identify potential confounders through evaluation of medical records of cases and controls (various heritable syndromes, family history of cancer, history of lymphedema, steroids, throrotrast, foreign body implants, chronic extensive scarring, radiation therapy, and immunological defects). Identified confounders between cases and controls were not reported and it is unclear if adjustments for these confounders were included in the final analyses.

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Study Citation:	Sobel, W., Bond, G.G., Skowronski, B.J., Brownson, P.J., Cook, R.R. (1987). A soft tissue sarcoma case control study in a large multi-chemical manufacturing facility. Chemosphere 16(8-9):2095-2099.
Health Outcome(s):	Skin and Connective Tissue
Reported Health Effect(s):	soft-tissue sarcoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1357737

Domain	Metric		Rating	Comments
	Metric 10:	Covariate Characterization	High	Potential covariates were assessed through evaluation of work histories and medical records.
	Metric 11:	Co-exposure Counfounding	Low	The study documented 13 chemicals, known to be associated with soft-tissue sarcoma (according to NTP, 1983) that were used at the manufacturing facility at some point since 1940. The authors note that some individuals were exposed to multiple chemicals during their employment history and were counted multiple times in the analysis for different chemical exposures. Co-exposures to chemicals to not appear to be adjusted for in analysis.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Low	The study design was adequate to assess the association between exposure and the outcome of interest (soft-tissue sarcoma). The study authors noted they used programs developed by Rothman and Boice to calculate odds ratios with (95% CIs; the statistical methods are not further described. The page containing the Rothman and Boice reference appears to be missing from the PDF (or the citation is missing).
	Metric 13:	Statistical Power	Low	Statistical power was not calculated. For 1,2-dichloroethane, there was one case and 6 controls included in the analysis, which was not adequate to detect and effect.
	Metric 14:	Reproducibility of Analyses	Low	The study calculated odd ratios, and 95% CIs were calculated using point estimates and chi from hypothesis testing. The study authors noted they used programs developed by Rothman and Boice to calculate odds ratios with CI intervals; the statistical methods are not further described and there was no reference for the programs cited.
	Metric 15:	Statistical Analysis	Low	A description of analyses/assumptions was not reported.

Additional Comments: A case-control study of workers at a chemical production facility who worked at least 1 year between January 1940-December 1979 (n=37,000) investigated the incidence of deaths due to soft-tissue sarcoma. The study identified 14 people who died due to soft-tissue sarcoma (through death certificate, medical records, or histopathology reports). Cases were matched to controls based on sex, race, year of birth and year of hire. 13 chemicals, including 1,2-dichloroethane, associated with soft-tissue sarcoma were used at the facility; it does not appear that co-exposures were adjusted for in the analysis. Odds ratios and corresponding CIs were calculated. No significant association was found between exposure to 1,2-DCE and soft-tissue sarcoma.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Teta, M. J., Ott, M. G., Schnatter, A. R. (1991). An update of mortality due to brain neoplasms and other causes among employees of a petrochemical facility. Journal of Occupational Medicine 33(1):45-51.
Health Outcome(s):	Mortality
Reported Health Effect(s):	all cause mortality, gastrointestinal cancer mortality, respiratory system cancer mortality, kidney and other urinary organ cancer mortality, skin cancer mortality, brain cancer mortality, lymphatic and hematopoietic tissue cancer mortality, benign neoplasm mortality, heart disease mortality, and liver cirrhosis mortality.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200633, 1629047
HERO ID:	200633

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	The facility was described in some detail. All male employees working for one day or more between 1941 and 1983 were included. There may be some healthy worker effect in this population.
	Metric 2:	Attrition	High	Study authors reported that vital status was complete for 99% of the population, and death certificates were obtained for 99% of decedents.
	Metric 3:	Comparison Group	High	SMRs were calculated using age-, race-, and calendar year-specific mortality rates of males in the United States. All included employees were male.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	All employees were treated as exposed. Table 4 indicates that relatively few employees were employed in areas designated as 1,2-DCA work areas. There is potential for substantial exposure misclassification.
	Metric 5:	Exposure Levels	Low	All employed individuals were categorized as exposed, and the reference population was described as unexposed. This represents two levels of exposure. The distribution of exposure within the employed population is unclear.
	Metric 6:	Temporality	Medium	Employees were followed from 1950 (or date of first hire) through 1983. The relevant timing of exposure is not entirely clear; however, this represents a sufficiently long period of follow-up.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Mortality was tracked using company records, Social Security Administration records, and the National Death Index. Specific ICD codes and use of a nosologist were not described, but there was no evidence to suggest the method had poor validity.
	Metric 8:	Reporting Bias	High	SMRs were provided with confidence intervals in addition to observed and expected cases. The authors state they did not carry out regional specific SMRs due to the higher prevalence of neoplasms in the surrounding area.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	SMRs were restricted to males. Rates were age-, race-, and calendar period-specific. No consideration was made for smoking.
	Metric 10:	Covariate Characterization	Medium	Demographic information was obtained from employment records. This was not a validated method, but there was no evidence to suggest it was an invalid method.

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Study Citation:	Teta, M. J., Ott, M. G., Schnatter, A. R. (1991). An update of mortality due to brain neoplasms and other causes among employees of a petrochemical facility. Journal of Occupational Medicine 33(1):45-51.
Health Outcome(s):	Mortality
Reported Health Effect(s):	all cause mortality, gastrointestinal cancer mortality, respiratory system cancer mortality, kidney and other urinary organ cancer mortality, skin cancer mortality, brain cancer mortality, lymphatic and hematopoietic tissue cancer mortality, benign neoplasm mortality, heart disease mortality, and liver cirrhosis mortality.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200633, 1629047
HERO ID:	200633

Domain	Metric		Rating	Comments
	Metric 11:	Co-exposure Counfounding	Low	Several other occupational exposures linked to cancer mortality were present, including vinyl chloride, butanol, and other petrochemicals.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	This study design was appropriate for the research question. Authors utilized retrospective occupational cohort data to determine standardized mortality rates for cancer-specific mortalities.
	Metric 13:	Statistical Power	Medium	While power was not calculated, there were over 1350 deaths from 7849 employees which was adequate to detect robust effect estimates.
	Metric 14:	Reproducibility of Analyses	Low	Most details were provided; however, ICD codes used to determine and group cancer mortality diagnoses were not provided.
	Metric 15:	Statistical Analysis	High	No issues identified.

Additional Comments: This study utilized an occupational cohort to retrospectively evaluate elevated rates of cancer mortality among petrochemical plant workers. There were numerous potentially hazardous chemicals mentioned in the plant description which may lead to co-exposure. Additionally, it appears that only a moderate portion of workers may have been exposed to 1,2-DCA or worked in 1,2-DCA areas which may lead to some exposure misclassification and limit the study's ability to inform hazard on 1,2-DCA.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Cases in this case-control study were former Union Carbide Corporation (UCC) chemical plant employees in Texas City, Texas. Cases were identified through death certificate searches and tumor registries, and may have included individuals formerly employed at UCC whose cause of death was unknown to the company. Additionally, control deaths were stated to be pulled from corporate employee benefits department and through locally published obituary notices routinely screened by the medical department - it is possible to assume that cases were identified in a similar manner. The study identified cases of brain tumors by searching death certificates primarily, although tumor registries throughout the state of Texas were also searched. The study clarifies that it is possible that some cases were not found if they survived or died due to another cause - while this is likely to have impacted selection, there is no evidence that this would be differential by exposure status. Overall, there is limited information on the source population of workers from which cases were identified.
	Metric 2:	Attrition	Medium	Attrition is not discussed in the study, and outcome data appear to be complete. There was a large proportion of missing exposure data (roughly 50%) due to workers being employed in roles such as maintenance, where exposure to any chemical is possible but unknown. Analyses were run separately where these ”unknown” individuals were a) treated as exposed, b) treated as unexposed, or c) treated as unknown and thus excluded. The study only presents results for when these individuals were excluded but specifies that the first scenario resulted in increased exposure estimates for controls relative to cases.

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Study Citation:	Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
	Metric 3:	Comparison Group	Medium	The study identifies two series of control groups, selected from all former Union Carbide Corporation (UCC) employees. However, the total number of employees is not stated. Only those who were deceased were used as controls since they had known causes of death and could thus be verified as non-brain tumors. One group of controls excluded employees whose cause of death was due to any malignant neoplasm to allow for the possibility that a general chemical carcinogen may have been associated with cancers of other sites. The other group of controls included deaths from all causes; this included malignant neoplasms other than brain tumors. Both control groups had 80 male employees randomly selected from 450 deceased employees known to the company in June 1979. Control deaths were stated to be pulled from corporate employee benefits department and through locally published obituary notices routinely screened by the medical department - it is possible to assume that cases were identified in a similar manner. The study reports that cases were slightly more likely to have been employed for less than 10 years than controls - the study attributes this in part to the fact that employees whose deaths were known to the company were more likely to have worked for longer - regardless the mean number of years employed was similar between cases and controls. However, cases were more likely to have been terminated from their job for reasons other than death, disability, or retirement (quitting, being fired, etc.), were generally younger at hire, and were less likely to survive to their 70th birthday. None of these factors are controlled for in statistical analyses - however, since controls and cases were pulled from the same population, there is indirect evidence that the groups were similar.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was determined based on official employment records. Records included job title and department assignment codes for each employment from date of hire to date of termination. For each unique department code, UCC and NIOSH industrial hygienists identified principal chemicals used or produced at any time in the history of the plant and correlated those with individual departments. This assessment was not performed on a year-by-year basis due to concerns for recall bias for longer-term employees where less detailed records were kept. An employee was categorized as ”exposed” to 1,2-dichloroethane if they ever worked in a department associated with that chemical. An ”unknown” exposure group was also created to account for employees who had only worked in departments for which no specific chemical could be identified.
	Metric 5:	Exposure Levels	Low	The study does not report any quantitative information and only splits exposure into ”exposed”, ”unexposed”, and ”unknown”.
	Metric 6:	Temporality	High	In this study exposure is confirmed to occur before the outcome is measured. The study reports latency periods, with subjects dichotomized into less than 15 years of latency or more than 15 years of latency. The majority of cases and controls had a latency of greater than 15 years, which is sufficiently long for brain tumors.

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Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Cases were identified through death certificate searches and partially through tumor registries in the state of Texas. Case validation was performed by NIOSH, and 5 different levels of confirmation were reported: 1) tissue specimen interpreted by the Armed Forces Institute of Pathology; 2) autopsy report; 3) histopathology report; 4) clinical diagnosis from hospital record; 5) dearth certificate diagnosis. Codes 1-3 were considered to be ”confirmed” cases of brain tumors, while 4-5 were considered unconfirmed. 5/21 cases were only evaluated using ”unconfirmed methods”, meaning there is likely a high amount of accuracy in roughly 75% of cases. While no case validation is reported for controls, the study specifies that only controls who had died and thus could be confirmed to be non-brain tumors were included.
	Metric 8:	Reporting Bias	Medium	All primary and secondary outcomes that are outlined in the methods are reported in the results. However, the only statistical outcome of their analysis were unadjusted p-values that were not reported and were just described qualitatively.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	The only statistical analysis performed were Mantel-Haenszel chi-squared tests, which did not allow for confounder adjustment. The study does not present a distribution of potential confounders by exposure status but by case/control status. Several variables, such as reason for termination, age at hire, and age at death were significantly different between cases and controls and were not accounted for in statistical modeling. The study explains that these differences are not likely to have any epidemiologic significance and appear to be relatively small differences.
	Metric 10:	Covariate Characterization	Medium	While the study does not explain where they obtained covariate information, it is reasonable to assume that they gathered the information from company records.
	Metric 11:	Co-exposure Counfounding	Low	The study assesses a wide range of other potential occupational co-exposures. While these co-exposures are not adjusted for in any statistical models, effect estimates are presented separately for benzene, diethyl sulfate, ethylene oxide, and vinyl chloride. The distribution of co-exposures across cases and controls is demonstrated to be mostly balanced by comparing proportions of exposed/unexposed between cases and controls. The only notable instance of imbalance is for benzene, where 11.1% of cases were exposed whereas 37.9% of all controls and 19.2% of non-neoplasm related controls were exposed.
Domain 5: Analysis				

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Study Citation:	Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	The study chose a case-control design, which was appropriate to study the rare disease of brain tumors and its association with occupational exposures. The only statistical analysis conducted is a Mantzel-Haenszel chi-squared test, but there is no reason to suggest that this would be inappropriate.
	Metric 13:	Statistical Power	Medium	The study does not calculate statistical power, but the number of cases (n=21) and controls (n=80 in each analysis) is likely sufficient to detect an effect.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to understand what was done and could be reproduced given access to the analytic data.
	Metric 15:	Statistical Analysis	High	The only statistical analysis conducted is a Mantel-Haenszel chi-squared test, and all assumptions were met. The statistical process is transparent.

Additional Comments: This case-control study pulled deceased former employees of the Union Carbide Corporation in Texas City, Texas. The study examined dichotomous exposure to a wide range of occupational exposures, including 1,2-dichloroethane, in relation to brain tumor cases. There is no quantitative estimate of exposure. The only statistical analysis in the study is a Mantel-Haenszel chi-squared test statistic and no statistically significant differences in exposure between cases and controls were observed. The fact that there are no effect estimates, no adjustment for confounders, and no quantitative exposure estimates limits the usefulness of this paper.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Cases in this case-control study were former Union Carbide Corporation (UCC) chemical plant employees in Texas City, Texas. Cases were identified through death certificate searches and tumor registries, and may have included individuals formerly employed at UCC whose cause of death was unknown to the company. Additionally, control deaths were stated to be pulled from corporate employee benefits department and through locally published obituary notices routinely screened by the medical department - it is possible to assume that cases were identified in a similar manner. The study identified cases of brain tumors by searching death certificates primarily, although tumor registries throughout the state of Texas were also searched. The study clarifies that it is possible that some cases were not found if they survived or died due to another cause - while this is likely to have impacted selection, there is no evidence that this would be differential by exposure status. Overall, there is limited information on the source population of workers from which cases were identified.
	Metric 2:	Attrition	Medium	Attrition is not discussed in the study, and outcome data appear to be complete. There was a large proportion of missing exposure data (roughly 50%) due to workers being employed in roles such as maintenance, where exposure to any chemical is possible but unknown. Analyses were run separately where these ”unknown” individuals were a) treated as exposed, b) treated as unexposed, or c) treated as unknown and thus excluded. The study only presents results for when these individuals were excluded but specifies that the first scenario resulted in increased exposure estimates for controls relative to cases.

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Linked HERO ID(s):	No linked references.
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Domain	Metric		Rating	Comments
	Metric 3:	Comparison Group	Medium	The study identifies two series of control groups, selected from all former Union Carbide Corporation (UCC) employees. However, the total number of employees is not stated. Only those who were deceased were used as controls since they had known causes of death and could thus be verified as non-brain tumors. One group of controls excluded employees whose cause of death was due to any malignant neoplasm to allow for the possibility that a general chemical carcinogen may have been associated with cancers of other sites. The other group of controls included deaths from all causes; this included malignant neoplasms other than brain tumors. Both control groups had 80 male employees randomly selected from 450 deceased employees known to the company in June 1979. Control deaths were stated to be pulled from corporate employee benefits department and through locally published obituary notices routinely screened by the medical department - it is possible to assume that cases were identified in a similar manner. The study reports that cases were slightly more likely to have been employed for less than 10 years than controls - the study attributes this in part to the fact that employees whose deaths were known to the company were more likely to have worked for longer - regardless the mean number of years employed was similar between cases and controls. However, cases were more likely to have been terminated from their job for reasons other than death, disability, or retirement (quitting, being fired, etc.), were generally younger at hire, and were less likely to survive to their 70th birthday. None of these factors are controlled for in statistical analyses - however, since controls and cases were pulled from the same population, there is indirect evidence that the groups were similar.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was determined based on official employment records. Records included job title and department assignment codes for each employment from date of hire to date of termination. For each unique department code, UCC and NIOSH industrial hygienists identified principal chemicals used or produced at any time in the history of the plant and correlated those with individual departments. This assessment was not performed on a year-by-year basis due to concerns for recall bias for longer-term employees where less detailed records were kept. An employee was categorized as ”exposed” to 1,2-dichloroethane if they ever worked in a department associated with that chemical. An ”unknown” exposure group was also created to account for employees who had only worked in departments for which no specific chemical could be identified.
	Metric 5:	Exposure Levels	Low	The study does not report any quantitative information and only splits exposure into ”exposed”, ”unexposed”, and ”unknown”.
	Metric 6:	Temporality	High	In this study exposure is confirmed to occur before the outcome is measured. The study reports latency periods, with subjects dichotomized into less than 15 years of latency or more than 15 years of latency. The majority of cases and controls had a latency of greater than 15 years, which is sufficiently long for brain tumors.

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Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Cases were identified through death certificate searches and partially through tumor registries in the state of Texas. Case validation was performed by NIOSH, and 5 different levels of confirmation were reported: 1) tissue specimen interpreted by the Armed Forces Institute of Pathology; 2) autopsy report; 3) histopathology report; 4) clinical diagnosis from hospital record; 5) dearth certificate diagnosis. Codes 1-3 were considered to be ”confirmed” cases of brain tumors, while 4-5 were considered unconfirmed. 5/21 cases were only evaluated using ”unconfirmed methods”, meaning there is likely a high amount of accuracy in roughly 75% of cases. While no case validation is reported for controls, the study specifies that only controls who had died and thus could be confirmed to be non-brain tumors were included.
	Metric 8:	Reporting Bias	Medium	All primary and secondary outcomes that are outlined in the methods are reported in the results. However, the only statistical outcome of their analysis were unadjusted p-values that were not reported and were just described qualitatively.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	The only statistical analysis performed were Mantel-Haenszel chi-squared tests, which did not allow for confounder adjustment. The study does not present a distribution of potential confounders by exposure status but by case/control status. Several variables, such as reason for termination, age at hire, and age at death were significantly different between cases and controls and were not accounted for in statistical modeling. The study explains that these differences are not likely to have any epidemiologic significance and appear to be relatively small differences.
	Metric 10:	Covariate Characterization	Medium	While the study does not explain where they obtained covariate information, it is reasonable to assume that they gathered the information from company records.
	Metric 11:	Co-exposure Counfounding	Low	The study assesses a wide range of other potential occupational co-exposures. While these co-exposures are not adjusted for in any statistical models, effect estimates are presented separately for benzene, diethyl sulfate, ethylene oxide, and vinyl chloride. The distribution of co-exposures across cases and controls is demonstrated to be mostly balanced by comparing proportions of exposed/unexposed between cases and controls. The only notable instance of imbalance is for benzene, where 11.1% of cases were exposed whereas 37.9% of all controls and 19.2% of non-neoplasm related controls were exposed.
Domain 5: Analysis				

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Study Citation:	Austin, S. G., Schnatter, A. R. (1983). A case-control study of chemical exposures and brain tumors in petrochemical workers. Journal of Occupational and Environmental Medicine 25(4):313-320.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Brain tumors
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	32901

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	The study chose a case-control design, which was appropriate to study the rare disease of brain tumors and its association with occupational exposures. The only statistical analysis conducted is a Mantzel-Haenszel chi-squared test, but there is no reason to suggest that this would be inappropriate.
	Metric 13:	Statistical Power	Medium	The study does not calculate statistical power, but the number of cases (n=21) and controls (n=80 in each analysis) is likely sufficient to detect an effect.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to understand what was done and could be reproduced given access to the analytic data.
	Metric 15:	Statistical Analysis	High	The only statistical analysis conducted is a Mantel-Haenszel chi-squared test, and all assumptions were met. The statistical process is transparent.

Additional Comments: This case-control study pulled deceased former employees of the Union Carbide Corporation in Texas City, Texas. The study examined dichotomous exposure to a wide range of occupational exposures, including 1,2-dichloroethane, in relation to brain tumor cases. There is no quantitative estimate of exposure. The only statistical analysis in the study is a Mantel-Haenszel chi-squared test statistic and no statistically significant differences in exposure between cases and controls were observed. The fact that there are no effect estimates, no adjustment for confounders, and no quantitative exposure estimates limits the usefulness of this paper.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	Urinary system cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	Urinary system cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	Urinary system cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Immune/Hematological
Reported Health Effect(s):	Lymphatic and hematopoietic tissue cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Immune/Hematological
Reported Health Effect(s):	Lymphatic and hematopoietic tissue cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Immune/Hematological
Reported Health Effect(s):	Lymphatic and hematopoietic tissue cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Other cancers (not specified)
Reported Health Effect(s):	Other cancers (not specified)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Other cancers (not specified)
Reported Health Effect(s):	Other cancers (not specified)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Other cancers (not specified)
Reported Health Effect(s):	Other cancers (not specified)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Mortality
Reported Health Effect(s):	All-cause mortality
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Vital status was tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Medium	Death rates among unit employees were compared to death rates in the U.S. population adjusted for age and gender. Demographics of the exposed workers are not provided; therefore, it is not clear whether additional adjustment for race may have been appropriate. No justification is provided for the choice of the entire U.S. population as the comparison group. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis. Additional analyses are conducted limiting workers to those with the greatest likelihood of exposure (i.e., those working in jobs with high likelihood of contact with chemicals for more than a year, those working for the full year of 1979 during which chemical exposures were most frequently reported); these smaller groups are also compared to the unexposed general population.
	Metric 6:	Temporality	High	Temporality was established due to the longitudinal design and the use of mortality as the outcome. Exposures occurred between 1979 and 1987 and follow-up for vital status was conducted through 2003.
Domain 3: Outcome Assessment				

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Mortality
Reported Health Effect(s):	All-cause mortality
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Medium	The study did not provide information on how mortality was assessed either in the exposed population or in the comparison population; use of death certificates is implied but not stated.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected deaths are reported, but SIRs and 95% confidence intervals are not provided.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Comparisons of observed versus expected deaths were adjusted for age and gender. Demographics of the exposed workers are not provided; therefore, it is not clear whether additional adjustment for race may have been appropriate.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records or death records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed deaths among a population of exposed workers compared to expected deaths among the U.S. population, adjusted for age and gender.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected deaths; no SIR was provided. Expected death rates were adjusted for age and gender.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Mortality
Reported Health Effect(s):	All-cause mortality
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	All cancer (excluding non-melanoma skin cancer), digestive system cancer, colorectal cancer, respiratory cancer, prostate cancer, urinary system cancer, lymphatic and hematopoietic tissue cancer, other cancers (not specified)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	All cancer (excluding non-melanoma skin cancer), digestive system cancer, colorectal cancer, respiratory cancer, prostate cancer, urinary system cancer, lymphatic and hematopoietic tissue cancer, other cancers (not specified)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	All cancer (excluding non-melanoma skin cancer), digestive system cancer, colorectal cancer, respiratory cancer, prostate cancer, urinary system cancer, lymphatic and hematopoietic tissue cancer, other cancers (not specified)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Gastrointestinal
Reported Health Effect(s):	Digestive system cancer, colorectal cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Gastrointestinal
Reported Health Effect(s):	Digestive system cancer, colorectal cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Health Outcome(s):	Gastrointestinal
Reported Health Effect(s):	Digestive system cancer, colorectal cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Lung/Respiratory
Reported Health Effect(s):	Respiratory cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Reported Health Effect(s):	Respiratory cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Health Outcome(s):	Lung/Respiratory
Reported Health Effect(s):	Respiratory cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	BASF, (2005). Letter: Subject: Supplemental information regarding prior TSCA Section 8(e) submission - Preliminary results from a cancer incidence study of employees assigned to a BASF Corporation former chemical manufacturing unit in Geismar, LA that ceased operations in 1987 (EPA Control number: 8EHQ-02-15135).
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Prostate cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Participants were workers at a chemical manufacturing unit in Geimar, Louisiana that manufactured bentazon. The study included 251 employees that had been assigned to work in the unit for at least 3 months during its years of operation (1979-1987). Participants were identified "using multiple record sources" (BASF 2002, HERO ID: 6570014). No other information on inclusion/exclusion criteria is provided. No information on participation rates or demographics is provided.
	Metric 2:	Attrition	High	Cancer diagnoses were tracked for participants through 2003. No loss to follow-up is described, and no missingness in exposure or outcome data is described.
	Metric 3:	Comparison Group	Low	Cancer incidence rates among unit employees were compared to incidence rates in the South Louisiana population, adjusted for age, gender, and race. Bias due to the healthy worker effect is plausible, as the comparison group is not limited to workers.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	Exposures in this occupational study population were assigned based on job type. No quantitative measurement of exposure was conducted. Specifically, individuals were considered exposed if they worked in the chemical manufacturing unit for at least 3 months between 1979 and 1987. No information on the completeness of employment records was provided. Exposure assessment was not specific to a particular chemical, but rather was intended to reflect general exposure to chemicals used in the process of manufacturing bentazon.
	Metric 5:	Exposure Levels	Low	Exposures levels were classified into two groups (exposed vs. unexposed) for the main analysis for all cancer outcomes. Additional analyses for all cancers considered together were conducted among sets of workers with varying exposures compared to the unexposed population (e.g., production employees vs. unexposed, maintenance and service employees vs. unexposed, those working in jobs with high likelihood of contact with chemicals for more than a year vs. unexposed, those working for the full year of 1979 during which chemical exposures were most frequently reported vs. unexposed).
	Metric 6:	Temporality	Medium	Temporality was established due to the longitudinal design, although the cancer status of workers prior to the start of the study was not specified. Exposures occurred between 1979 and 1987 and follow-up for cancer status was conducted through 2003. No information was provided on when cancer diagnoses occurred following exposure; it is thus not fully clear if exposure occurred during the relevant time window for all cases.
Domain 3: Outcome Assessment				

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Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Low	Outcome measurement methods and follow-up length varied by exposure group. Cancer cases among employees were assessed using "self-report by employees or their spouses, and through death certificates." Cancer cases in the general population of South Louisiana (used as a comparison population) were ascertained through the Louisiana Tumor Registry. Employees were followed for cancer through 2003, while information on cancer in the South Louisiana population via the registry were only available through 2000; the study did not state if or how this difference in follow-up time was addressed in analysis.
	Metric 8:	Reporting Bias	Medium	All of the outcomes described in the introduction are reported. Numbers of observed versus expected cancers are reported, but SIRs and 95% confidence intervals are inconsistently reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Comparisons of observed versus expected cancer incidence were adjusted for age, gender, and race.
	Metric 10:	Covariate Characterization	Medium	The source of information on covariates that were considered in this analysis (age, gender, race) was not discussed; however, based on the information available to the study authors it is reasonable to assume that the information came from either personnel records, death records, or tumor registry records.
	Metric 11:	Co-exposure Counfounding	Low	Exposure assessment in this study reflected whether workers were exposed to chemicals used to manufacture bentazon. Acute exposures to multiple chemicals were reported to the employer's medical department (i.e., direct evidence that exposure to other chemicals occurred in this population). Co-exposures to other chemicals were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen was appropriate for the research question. The study reported observed cancers among a population of exposed workers compared to expected deaths among the South Louisiana population, adjusted for age, gender, and race.
	Metric 13:	Statistical Power	Medium	The study population included 251 exposed workers with no reported loss to follow-up.
	Metric 14:	Reproducibility of Analyses	Low	The description of the analysis is limited. In particular, additional information on participant selection, outcome assessment methods, and details of the statistical analysis would be needed to reproduce the analysis.
	Metric 15:	Statistical Analysis	High	The main results of this analysis were observed versus expected cancers; SIRs adjusted for age, gender, and race were reported for some analyses.

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Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	6570017, 6570014
HERO ID:	6570017

Domain	Metric	Rating	Comments
Additional Comments:	This occupational study examined deaths and cancer incidence among employees who worked in a chemical manufacturing unit, compared to expected deaths among the U.S. population and expected cancers among the South Louisiana population. The study found lower death rates among employees compared to the U.S. population. Observed cancer incidence was generally higher than expected, although the study did not consistently present information on statistical significance. The exposure measurement approach was limited to assignment based on job history, with no quantitative measurement of exposure. Detailed information on most aspects of the study design and analysis was not provided.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Male workers who had ever been assigned to the chlorohydrin unit between 1 January 1940 and 31 December 1967 at Union Carbide's South Charleston plant were enrolled and matched to the US National Death Index. Status on 5 workers could not be identified. Information on how workers were matched to death index was not specified.
	Metric 2:	Attrition	Medium	Rate of inclusion/participation was very high, as records were able to be matched for 98% of participants. Medium rating given because information on how participants whose vital status was not known was not specified.
	Metric 3:	Comparison Group	Uninformative	Unacceptable rating given because SMRs were calculated based on expected deaths from a reference population matched on sex, but not age.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Exposure was assessed based on duration of work in the plant. No information is provided on exposure levels, and a JEM was not used.
	Metric 5:	Exposure Levels	Uninformative	No information provided on levels of exposure.
	Metric 6:	Temporality	High	Temporality is well established; person-years stopped accumulating in 1967 and outcome was assessed beginning at that time.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar period, and interval since assignments, but distribution of these covariates was not reported.
	Metric 10:	Covariate Characterization	Medium	Information on covariate characterization not provided, but the selected covariates (age, calendar period, and interval since assignments) were likely extracted from employee records and unlikely to be largely problematic
	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.

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Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Study design was appropriate for the research method. Statistical methods were also appropriate.
	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.
	Metric 14:	Reproducibility of Analyses	Medium	Methods are well-enough described that study could be adequately reproduced.
	Metric 15:	Statistical Analysis	High	SMRs calculated based on US general population mortality for white males through 1988. RRs were ”evaluated over levels of duration of assignment to the chlorohydrin unit, stratified by age, calendar year, and interval since first assignment to the chlorohydrin unit”.

Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
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Linked HERO ID(s):	200224, 5447107
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Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Male workers who had ever been assigned to the chlorohydrin unit between 1 January 1940 and 31 December 1967 at Union Carbide's South Charleston plant were enrolled and matched to the US National Death Index. Status on 5 workers could not be identified. Information on how workers were matched to death index was not specified.
	Metric 2:	Attrition	Medium	Rate of inclusion/participation was very high, as records were able to be matched for 98% of participants. Medium rating given because information on how participants whose vital status was not known was not specified.
	Metric 3:	Comparison Group	Uninformative	Unacceptable rating given because SMRs were calculated based on expected deaths from a reference population matched on sex, but not age.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Exposure was assessed based on duration of work in the plant. No information is provided on exposure levels, and a JEM was not used.
	Metric 5:	Exposure Levels	Uninformative	No information provided on levels of exposure.
	Metric 6:	Temporality	High	Temporality is well established; person-years stopped accumulating in 1967 and outcome was assessed beginning at that time.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar period, and interval since assignments, but distribution of these covariates was not reported.
	Metric 10:	Covariate Characterization	Medium	Information on covariate characterization not provided, but the selected covariates (age, calendar period, and interval since assignments) were likely extracted from employee records and unlikely to be largely problematic
	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.
Domain 5: Analysis				

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Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
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Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Study design was appropriate for the research method. Statistical methods were also appropriate.
	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.
	Metric 14:	Reproducibility of Analyses	Medium	Methods are well-enough described that study could be adequately reproduced.
	Metric 15:	Statistical Analysis	High	SMRs calculated based on US general population mortality for white males through 1988. RRs were ”evaluated over levels of duration of assignment to the chlorohydrin unit, stratified by age, calendar year, and interval since first assignment to the chlorohydrin unit”.

Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
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Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Male workers who had ever been assigned to the chlorohydrin unit between 1 January 1940 and 31 December 1967 at Union Carbide's South Charleston plant were enrolled and matched to the US National Death Index. Status on 5 workers could not be identified. Information on how workers were matched to death index was not specified.
	Metric 2:	Attrition	Medium	Rate of inclusion/participation was very high, as records were able to be matched for 98% of participants. Medium rating given because information on how participants whose vital status was not known was not specified.
	Metric 3:	Comparison Group	Uninformative	Unacceptable rating given because SMRs were calculated based on expected deaths from a reference population matched on sex, but not age.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Exposure was assessed based on duration of work in the plant. No information is provided on exposure levels, and a JEM was not used.
	Metric 5:	Exposure Levels	Uninformative	No information provided on levels of exposure.
	Metric 6:	Temporality	High	Temporality is well established; person-years stopped accumulating in 1967 and outcome was assessed beginning at that time.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar period, and interval since assignments, but distribution of these covariates was not reported.
	Metric 10:	Covariate Characterization	Medium	Information on covariate characterization not provided, but the selected covariates (age, calendar period, and interval since assignments) were likely extracted from employee records and unlikely to be largely problematic
	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.
Domain 5: Analysis				

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Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
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Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Study design was appropriate for the research method. Statistical methods were also appropriate.
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Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
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Domain	Metric		Rating	Comments
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	Metric 2:	Attrition	Medium	Rate of inclusion/participation was very high, as records were able to be matched for 98% of participants. Medium rating given because information on how participants whose vital status was not known was not specified.
	Metric 3:	Comparison Group	Uninformative	Unacceptable rating given because SMRs were calculated based on expected deaths from a reference population matched on sex, but not age.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Exposure was assessed based on duration of work in the plant. No information is provided on exposure levels, and a JEM was not used.
	Metric 5:	Exposure Levels	Uninformative	No information provided on levels of exposure.
	Metric 6:	Temporality	High	Temporality is well established; person-years stopped accumulating in 1967 and outcome was assessed beginning at that time.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar period, and interval since assignments, but distribution of these covariates was not reported.
	Metric 10:	Covariate Characterization	Medium	Information on covariate characterization not provided, but the selected covariates (age, calendar period, and interval since assignments) were likely extracted from employee records and unlikely to be largely problematic
	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.
Domain 5: Analysis				

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Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Study design was appropriate for the research method. Statistical methods were also appropriate.
	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.
	Metric 14:	Reproducibility of Analyses	Medium	Methods are well-enough described that study could be adequately reproduced.
	Metric 15:	Statistical Analysis	High	SMRs calculated based on US general population mortality for white males through 1988. RRs were ”evaluated over levels of duration of assignment to the chlorohydrin unit, stratified by age, calendar year, and interval since first assignment to the chlorohydrin unit”.

Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
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Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Male workers who had ever been assigned to the chlorohydrin unit between 1 January 1940 and 31 December 1967 at Union Carbide's South Charleston plant were enrolled and matched to the US National Death Index. Status on 5 workers could not be identified. Information on how workers were matched to death index was not specified.
	Metric 2:	Attrition	Medium	Rate of inclusion/participation was very high, as records were able to be matched for 98% of participants. Medium rating given because information on how participants whose vital status was not known was not specified.
	Metric 3:	Comparison Group	Uninformative	Unacceptable rating given because SMRs were calculated based on expected deaths from a reference population matched on sex, but not age.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Exposure was assessed based on duration of work in the plant. No information is provided on exposure levels, and a JEM was not used.
	Metric 5:	Exposure Levels	Uninformative	No information provided on levels of exposure.
	Metric 6:	Temporality	High	Temporality is well established; person-years stopped accumulating in 1967 and outcome was assessed beginning at that time.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar period, and interval since assignments, but distribution of these covariates was not reported.
	Metric 10:	Covariate Characterization	Medium	Information on covariate characterization not provided, but the selected covariates (age, calendar period, and interval since assignments) were likely extracted from employee records and unlikely to be largely problematic
	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.
Domain 5: Analysis				

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Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Study design was appropriate for the research method. Statistical methods were also appropriate.
	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.
	Metric 14:	Reproducibility of Analyses	Medium	Methods are well-enough described that study could be adequately reproduced.
	Metric 15:	Statistical Analysis	High	SMRs calculated based on US general population mortality for white males through 1988. RRs were ”evaluated over levels of duration of assignment to the chlorohydrin unit, stratified by age, calendar year, and interval since first assignment to the chlorohydrin unit”.

Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
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Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Male workers who had ever been assigned to the chlorohydrin unit between 1 January 1940 and 31 December 1967 at Union Carbide's South Charleston plant were enrolled and matched to the US National Death Index. Status on 5 workers could not be identified. Information on how workers were matched to death index was not specified.
	Metric 2:	Attrition	Medium	Rate of inclusion/participation was very high, as records were able to be matched for 98% of participants. Medium rating given because information on how participants whose vital status was not known was not specified.
	Metric 3:	Comparison Group	Uninformative	Unacceptable rating given because SMRs were calculated based on expected deaths from a reference population matched on sex, but not age.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Exposure was assessed based on duration of work in the plant. No information is provided on exposure levels, and a JEM was not used.
	Metric 5:	Exposure Levels	Uninformative	No information provided on levels of exposure.
	Metric 6:	Temporality	High	Temporality is well established; person-years stopped accumulating in 1967 and outcome was assessed beginning at that time.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar period, and interval since assignments, but distribution of these covariates was not reported.
	Metric 10:	Covariate Characterization	Medium	Information on covariate characterization not provided, but the selected covariates (age, calendar period, and interval since assignments) were likely extracted from employee records and unlikely to be largely problematic
	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.
Domain 5: Analysis				

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Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Study design was appropriate for the research method. Statistical methods were also appropriate.
	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.
	Metric 14:	Reproducibility of Analyses	Medium	Methods are well-enough described that study could be adequately reproduced.
	Metric 15:	Statistical Analysis	High	SMRs calculated based on US general population mortality for white males through 1988. RRs were ”evaluated over levels of duration of assignment to the chlorohydrin unit, stratified by age, calendar year, and interval since first assignment to the chlorohydrin unit”.

Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
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Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Male workers who had ever been assigned to the chlorohydrin unit between 1 January 1940 and 31 December 1967 at Union Carbide's South Charleston plant were enrolled and matched to the US National Death Index. Status on 5 workers could not be identified. Information on how workers were matched to death index was not specified.
	Metric 2:	Attrition	Medium	Rate of inclusion/participation was very high, as records were able to be matched for 98% of participants. Medium rating given because information on how participants whose vital status was not known was not specified.
	Metric 3:	Comparison Group	Uninformative	Unacceptable rating given because SMRs were calculated based on expected deaths from a reference population matched on sex, but not age.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Exposure was assessed based on duration of work in the plant. No information is provided on exposure levels, and a JEM was not used.
	Metric 5:	Exposure Levels	Uninformative	No information provided on levels of exposure.
	Metric 6:	Temporality	High	Temporality is well established; person-years stopped accumulating in 1967 and outcome was assessed beginning at that time.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar period, and interval since assignments, but distribution of these covariates was not reported.
	Metric 10:	Covariate Characterization	Medium	Information on covariate characterization not provided, but the selected covariates (age, calendar period, and interval since assignments) were likely extracted from employee records and unlikely to be largely problematic
	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.
Domain 5: Analysis				

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Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Study design was appropriate for the research method. Statistical methods were also appropriate.
	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.
	Metric 14:	Reproducibility of Analyses	Medium	Methods are well-enough described that study could be adequately reproduced.
	Metric 15:	Statistical Analysis	High	SMRs calculated based on US general population mortality for white males through 1988. RRs were ”evaluated over levels of duration of assignment to the chlorohydrin unit, stratified by age, calendar year, and interval since first assignment to the chlorohydrin unit”.

Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
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Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Male workers who had ever been assigned to the chlorohydrin unit between 1 January 1940 and 31 December 1967 at Union Carbide's South Charleston plant were enrolled and matched to the US National Death Index. Status on 5 workers could not be identified. Information on how workers were matched to death index was not specified.
	Metric 2:	Attrition	Medium	Rate of inclusion/participation was very high, as records were able to be matched for 98% of participants. Medium rating given because information on how participants whose vital status was not known was not specified.
	Metric 3:	Comparison Group	Uninformative	Unacceptable rating given because SMRs were calculated based on expected deaths from a reference population matched on sex, but not age.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	Exposure was assessed based on duration of work in the plant. No information is provided on exposure levels, and a JEM was not used.
	Metric 5:	Exposure Levels	Uninformative	No information provided on levels of exposure.
	Metric 6:	Temporality	High	Temporality is well established; person-years stopped accumulating in 1967 and outcome was assessed beginning at that time.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcome was assessed using vital records, which raises very little concern. Medium rating given over high because information on what employee information was used to match to vital records was not specified.
	Metric 8:	Reporting Bias	Low	All results reported appropriately with a measure of variance. Sample size reported for each analysis.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	SMRs sex-restricted but no discussion of age. RRs were adjusted for age, calendar period, and interval since assignments, but distribution of these covariates was not reported.
	Metric 10:	Covariate Characterization	Medium	Information on covariate characterization not provided, but the selected covariates (age, calendar period, and interval since assignments) were likely extracted from employee records and unlikely to be largely problematic
	Metric 11:	Co-exposure Counfounding	Low	No discussion of co-exposures, but authors note that other carcinogens were present in the chlorohydrin unit.
Domain 5: Analysis				

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Study Citation:	Benson, L.O., Teta, M.J. (1993). Mortality due to pancreatic and lymphopoietic cancers in chlorohydrin production workers. British Journal of Industrial Medicine 50(8):710-716.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Pancreatic cancer, lymphatic and haematopoietic cancer, Leukemia, lymphosarcoma, lymphoma, multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200224, 5447107
HERO ID:	200224

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Study design was appropriate for the research method. Statistical methods were also appropriate.
	Metric 13:	Statistical Power	Medium	Over 50 years of follow-up ensured that the study was adequately powered.
	Metric 14:	Reproducibility of Analyses	Medium	Methods are well-enough described that study could be adequately reproduced.
	Metric 15:	Statistical Analysis	High	SMRs calculated based on US general population mortality for white males through 1988. RRs were ”evaluated over levels of duration of assignment to the chlorohydrin unit, stratified by age, calendar year, and interval since first assignment to the chlorohydrin unit”.

Additional Comments: None

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Bove, F. J. (1996). Public drinking water contamination and birthweight, prematurity, fetal deaths, and birth defects. Toxicology and Industrial Health 12(2):255-266.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	200239

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	This cross-sectional study (n=80,938) included all registered singleton live births and fetal deaths (>20 weeks' gestation) in 1985-88 in 75 New Jersey towns located in 4 counties with "some" water supplies contaminated with substances of interest and where: (i) residents were "mostly" served by public water systems; and (ii) births occurred "mostly" in state. Estimated proportions of residents served by public water systems, and of pregnancies/births captured, were not described. However, the inclusion of all eligible registered births, fetal deaths, and birth defects, as well as the selection of towns without knowledge of birth outcome prevalence, limited the likelihood of selection bias.
	Metric 2:	Attrition	Medium	All registered births and fetal deaths were included. Attrition due to missing values for multiple variables was not quantified and is therefore uncertain. However, attrition was likely modest as the proportion of missing values for individual variables was relatively low: (i) ~6% of subjects were excluded from analyses of outcomes such as preterm birth due to invalid or missing gestational ages; and (ii) other covariates evaluated as confounders had up to 4.9% missing values.
	Metric 3:	Comparison Group	High	After excluding plural pregnancies and chromosomal abnormalities, all registered live births during the study period in the areas included without the outcomes of interest were included in the comparison group. This comprehensive approach limited the potential for bias. Chromosomal abnormalities were not included as outcomes as they were not hypothesized to be associated with the exposures under study but were appropriately excluded given their uncertain etiology.
Domain 2: Exposure Characterization				

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Study Citation:	Bove, F. J. (1996). Public drinking water contamination and birthweight, prematurity, fetal deaths, and birth defects. Toxicology and Industrial Health 12(2):255-266.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	200239

Domain	Metric		Rating	Comments
	Metric 4:	Measurement of Exposure	Medium	Along with several other contaminants, residential drinking water exposure to 1,2-dichloroethane (as well as 1,1,1-trichloroethane and 'total dichloroethylenes') – was assigned based on maternal town of residence at birth. Exposure estimates were calculated using the average of water company sampling reports during the first trimester (for birth defects and fetal death) or the duration of pregnancy (for other outcomes). Detection limits and data availability were not specified in detail but were described as below 1 ppb, with reporting compliance >85%. A minimum of 1 sample per 6-month interval was required; variability in the number of measures available across water systems and towns was not described. Additional sources of measurement error included: changes in residence during pregnancy; water from alternate sources (ex. private wells, bottles, workplaces); variability in residential contaminant levels vs measured samples; unknown levels of tap water intake; and errors in estimated dermal and inhalation exposure while bathing or showering. While the extent of exposure misclassification is uncertain, there is no evidence to suggest it was differential rather than random.
	Metric 5:	Exposure Levels	Medium	Due to the high proportion of measures below detection limits, analyses relating exposure to health outcomes used only 2 categories for each of the chlorinated solvents of interest: cutoffs close to detection limits were used to define elevated exposure. Proportions defined as having elevated exposure was low (1.8% had 1,1-dichloroethylene ≥1 ppb). An important concern is that relatively low levels of exposure to these contaminants from sources other than residential drinking water, for which data were not available, could potentially have resulted in considerable misclassification.
	Metric 6:	Temporality	High	Exposure levels were assigned based on contaminant exposures estimated during: (i) the first trimester for analyses of birth defects and fetal deaths; and (ii) the duration of pregnancy for other pregnancy outcomes.

Domain 3: Outcome Assessment

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Study Citation:	Bove, F. J. (1996). Public drinking water contamination and birthweight, prematurity, fetal deaths, and birth defects. Toxicology and Industrial Health 12(2):255-266.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	200239

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcomes included measures of birthweight (continuous among term births, low term birthweight, very low birthweight), prematurity, fetal death, and congenital anomalies in live births or fetal deaths. The anomalies analyzed included defects of the central nervous system, neural tube, oral cleft, total cardiac, major cardiac, ventricular septum, and any surveillance defect excluding chromosomal defects. All outcomes were identified using birth certificates, fetal death certificates (>20 weeks' gestation), and the NJ congenital birth defect registry (ICD codes provided). These registry data are likely to be sufficiently valid for late pregnancy outcomes. However, their limited ability to capture early pregnancy losses is a weakness. The sample included only 594 fetal deaths (less than 1% of the >80,0000 sample). Typical estimates are that 10-20%, of recognized pregnancies ending in losses. Moreover, developmental defects contributing to early pregnancy losses were also not captured. A further limitation is that that potentially etiologically heterogeneous preterm birth types were analyzed together, as these data did not distinguish premature rupture of membranes vs idiopathic prematurity.
	Metric 8:	Reporting Bias	Medium	Models were constructed only for contaminants with associations > 1.0, and tables included only associations with odds ratios ≥1.5. No clear rationale was provided. Several positive odds ratios below the 1.5 cutoff were described in the results text (without confidence intervals), but no null/negative odds ratios were presented or described.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Potential confounding by maternal race, education, parity, and prior pregnancy loss, along with infant sex (for birth outcomes) and adequacy of prenatal care, was examined. Gestational age was addressed by analyzing birthweight among full term births, term low birth weight, and small size for gestational age. Only fully adjusted models were presented. In a companion case-control study (with low participation rates), adjustment for other variables not available on birth certificates (ex. maternal smoking, occupational exposures, medical history, and gestational weight gain) did not influence associations with other studied contaminants. This separate study reduces concerns for important confounding bias, but confounding cannot be ruled out.
	Metric 10:	Covariate Characterization	Medium	Data on covariates came from registry data: birth certificates, fetal death certificates, and the NJ congenital birth defects registry.
	Metric 11:	Co-exposure Counfounding	Medium	Co-exposure confounding by drinking water trihalomethane concentrations was evaluated. There was no evidence to suggest substantial confounding by this or other co-exposures.
Domain 5: Analysis				

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Study Citation: Bove, F. J. (1996). Public drinking water contamination and birthweight, prematurity, fetal deaths, and birth defects. Toxicology and Industrial Health 12(2):255-266.

Health Outcome(s): Reproductive/Developmental

Reported Health Effect(s): Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.

Chemical: 1,1-Dichloroethane- Isomer: 1,2-Dichloroethane

Linked HERO ID(s): 194932, 200239

HERO ID: 200239

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Methods were appropriate. The study used logistic regression models to estimate odds ratios and confidence intervals for dichotomous outcomes, and linear regression for analysis of continuous birth weight.
	Metric 13:	Statistical Power	Medium	Statistical power was likely to have been limited as a consequence of the small proportion of the sample defined as having "elevated" residential water concentrations of the chemicals of interest. The range of exposure examined was limited, as cutoffs for elevated levels were close to the detection limits of 1 ppb. In addition, for most birth defect outcomes, fewer than 10 cases had elevated exposure.
	Metric 14:	Reproducibility of Analyses	Medium	The authors clearly described steps used to estimate exposure-outcome associations, including exposure category cutoffs and criteria for confounding. However, many results were not shown as tables included odds ratios ≥1.5.
	Metric 15:	Statistical Analysis	High	The authors estimated coefficients, odds ratios and 95% confidence intervals using adequate methods. Confounding was based on 15% change-in-estimate comparing nested models. Effect modification (ex by infant sex) was not evaluated as there was no a priori evidence to suggest such analyses at that time.

Additional Comments: This study analyzed the association between estimated residential drinking water concentrations of several chlorinated solvents including 1,2-dichloroethane (as well as 1,1,1-trichloroethane; ∑[trans-1,2-dichloroethylene and 1,1-dichloroethylene]) and pregnancy outcomes (size at birth, prematurity, fetal deaths, and congenital birth defects). The sample included more than 80,000 births during 1985-88 for residents of 75 towns in NJ using public water system records to estimate exposure during gestation, and registry data (birth certificate, fetal death certificates for pregnancies >20 weeks, state birth defect registry) to characterize outcomes. Strengths included the large sample size and inclusion of all eligible registered births and fetal deaths in the study period. A critical concern is the inability to capture early fetal deaths and any related malformations (1% of the sample had fetal deaths vs typical estimates of >10%). An important limitation was the low percentage of the sample with detectable (> 1ppb) concentrations of these contaminants (<1% to 6.2%). Small numbers for birth defect outcomes also limited power. Exposure misclassification (ex. drinking water from wells/ work/ bottles, changes in residence, exposure from other sources) is also a concern. However, such misclassification was likely non-differential, and thus more likely to under- vs. to over-estimate associations.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Bove, F. J., Fulcomer, M. C., Klotz, J. B., Esmart, J., Dufficy, E. M., Savrin, J. E. (1995). Public drinking water contamination and birth outcomes. American Journal of Epidemiology 141(9):850-862.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	194932

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	This semi-ecological study (n=80,938) included all registered singleton live births and fetal deaths (>20 weeks) in 1985-88 in 75 New Jersey towns located in 4 counties with "some" water supplies contaminated with substances of interest and where: (i) residents were "mostly" served by public water systems; and (ii) births occurred "mostly" in state. Estimated proportions of residents served by public water systems, and of pregnancies/births captured, were not described. However, the inclusion of all eligible registered births, fetal deaths, and birth defects, as well as the selection of towns without knowledge of birth outcome prevalence, limited the likelihood of selection bias.
	Metric 2:	Attrition	Medium	All registered births and fetal deaths were included. Attrition due to missing values for multiple variables was not quantified and is therefore uncertain. However, attrition was likely modest as the proportion of missing values for individual variables was relatively low: (i) ~6% of subjects were excluded from analyses of outcomes such as preterm birth due to invalid or missing gestational ages; and (ii) other covariates evaluated as confounders had up to 4.9% missing values.
	Metric 3:	Comparison Group	High	After excluding plural pregnancies and chromosomal abnormalities, all registered live births during the study period in the areas included without the outcomes of interest were included in the comparison group. This comprehensive approach limited the potential for bias. Chromosomal abnormalities were not included as outcomes as they were not hypothesized to be associated with the exposures under study but were appropriately excluded given their uncertain etiology.
Domain 2: Exposure Characterization				

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Study Citation:	Bove, F. J., Fulcomer, M. C., Klotz, J. B., Esmart, J., Dufficy, E. M., Savrin, J. E. (1995). Public drinking water contamination and birth outcomes. American Journal of Epidemiology 141(9):850-862.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	194932

Domain	Metric		Rating	Comments
	Metric 4:	Measurement of Exposure	Medium	Along with several other contaminants, residential drinking water exposure to 1,2-dichloroethane (as well as 1,1,1-trichloroethane and 'total dichloroethylenes') was assigned based on maternal town of residence at birth. Exposure estimates were calculated using the average of water company sampling reports during the first trimester (for birth defects and fetal death) or the duration of pregnancy (for other outcomes). Detection limits and data availability were not specified in detail but were described as below 1 ppb, with reporting compliance >85%. A minimum of 1 sample per 6-month interval was required; variability in the number of measures available across water systems and towns was not described. Additional sources of measurement error included: changes in residence during pregnancy; water from alternate sources (ex. private wells, bottles, workplaces); variability in residential contaminant levels vs measured samples; unknown levels of tap water intake; and errors in estimated dermal and inhalation exposure while bathing or showering. While the extent of exposure misclassification is uncertain, there is no evidence to suggest it was differential rather than random.
	Metric 5:	Exposure Levels	Low	Due to the high proportion of measures below detection limits, analyses relating exposure to health outcomes used only 2 categories for each of the three chemicals of interest: cutoffs close to detection limits were used to define elevated exposure. Proportions defined as having elevated exposure were low (1.8% had 1,1-dichloroethylene ≥1 ppb). An important concern is that relatively low levels of exposure to this contaminant from sources other than residential drinking water, for which data were not available, could potentially have resulted in considerable misclassification.
	Metric 6:	Temporality	High	Exposure levels were assigned based on contaminant exposures estimated during: (i) the first trimester for analyses of birth defects and fetal deaths; and (ii) the duration of pregnancy for other pregnancy outcomes.

Domain 3: Outcome Assessment

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Study Citation:	Bove, F. J., Fulcomer, M. C., Klotz, J. B., Esmart, J., Dufficy, E. M., Savrin, J. E. (1995). Public drinking water contamination and birth outcomes. American Journal of Epidemiology 141(9):850-862.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	194932

Domain	Metric		Rating	Comments
	Metric 7:	Outcome Measurement or Characterization	Medium	Outcomes included measures of birthweight (continuous among term births, low term birthweight, very low birthweight), prematurity, fetal death, and congenital anomalies in live births or fetal deaths. The anomalies analyzed included defects of the central nervous system, neural tube, oral cleft, total cardiac, major cardiac, ventricular septum, and any surveillance defect excluding chromosomal defects. All outcomes were identified using birth certificates, fetal death certificates (>20 weeks' gestation), and the NJ congenital birth defect registry (ICD codes provided). These registry data are likely to be sufficiently valid for late pregnancy outcomes. However, their limited ability to capture early pregnancy losses is a weakness. The sample included only 594 fetal deaths (less than 1% of the >80,0000 sample). Typical estimates are that 10-20%, of recognized pregnancies ending in losses. Moreover, developmental defects contributing to early pregnancy losses were also not captured. A further limitation is that that potentially etiologically heterogeneous preterm birth types were analyzed together, as these data did not distinguish premature rupture of membranes vs idiopathic prematurity.
	Metric 8:	Reporting Bias	Low	Models were constructed only for contaminants with associations > 1.0, and tables included only associations with odds ratios ≥1.5. No clear rationale was provided. Several positive odds ratios below the 1.5 cutoff were described in the results text (without confidence intervals), but no null/negative odds ratios were presented or described.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Potential confounding by maternal race, education, parity, and prior pregnancy loss, along with infant sex (for birth outcomes) and adequacy of prenatal care, was examined. Gestational age was addressed by analyzing birthweight among full term births, term low birth weight, and small size for gestational age. Only fully adjusted models were presented. In a companion case-control study (with low participation rates), adjustment for other variables not available on birth certificates (ex. maternal smoking, occupational exposures, medical history, and gestational weight gain) did not influence associations with other studied contaminants. This separate study reduces concerns for important confounding bias, but confounding cannot be ruled out.
	Metric 10:	Covariate Characterization	Medium	Data on covariates came from registry data: birth certificates, fetal death certificates, and the NJ congenital birth defects registry.
	Metric 11:	Co-exposure Counfounding	Medium	Co-exposure confounding by drinking water trihalomethane concentrations was evaluated. There was no evidence to suggest substantial confounding by this or other co-exposures.
Domain 5: Analysis				

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Study Citation:	Bove, F. J., Fulcomer, M. C., Klotz, J. B., Esmart, J., Dufficy, E. M., Savrin, J. E. (1995). Public drinking water contamination and birth outcomes. American Journal of Epidemiology 141(9):850-862.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	Fetal growth and development: -Birthweight (term births), low birthweight (term births), very low birthweight, small for gestational age-Preterm birth-Fetal death (>20 weeks' gestation)-Congenital anomalies: (i) nervous system (central nervous system, neural tube defects); (ii) oral cleft; (iii) cardiovascular (total cardiac, major cardiac, ventricular septum defects); and (iv) any surveillance defect excluding chromosomal defects.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	194932, 200239
HERO ID:	194932

Domain	Metric		Rating	Comments
	Metric 12:	Study Design and Methods	High	Methods were appropriate. The study used logistic regression models to estimate odds ratios and confidence intervals for dichotomous outcomes, and linear regression for analysis of continuous birth weight.
	Metric 13:	Statistical Power	Low	Statistical power was likely to have been limited as a consequence of the small proportion of the sample defined as having "elevated" residential water concentrations of the chemicals of interest. The range of exposure examined was limited, as cutoffs for elevated levels were close to the detection limits of 1 ppb. In addition, for most birth defect outcomes, fewer than 10 cases had elevated exposure. However, the authors emphasized the magnitude of associations rather than statistical significance and presented multiple confidence intervals to aid interpretation of the precision of estimates (50%, 90% and 99%).
	Metric 14:	Reproducibility of Analyses	Medium	The authors clearly described steps used to estimate exposure-outcome associations, including exposure category cutoffs and criteria for confounding. However, many results were not shown as tables included odds ratios ≥1.5.
	Metric 15:	Statistical Analysis	High	The authors estimated coefficients, odds ratios and confidence intervals using adequate methods. Confounding was based on 15% change-in-estimate comparing nested models. Effect modification (ex by infant sex) was not evaluated as there was no a priori evidence to suggest such analyses at that time.

Additional Comments: This study analyzed the association between estimated residential drinking water concentrations of several chlorinated solvents including 1,2-dichloroethane (as well as 1,1,1-trichloroethane and the ∑[trans-1,2-dichloroethylene & 1,1-dichloroethylene]) and pregnancy outcomes (size at birth, prematurity, fetal deaths, and congenital birth defects). The sample included more than 80,000 births during 1985-88 for residents of 75 towns in NJ using public water system records to estimate exposure during gestation, and registry data (birth certificate, fetal death certificates for pregnancies >20 weeks' gestation, state birth defect registry) to characterize outcomes. Strengths included the large sample size and inclusion of all eligible registered births and fetal deaths in the study period. A critical concern is the inability to capture early fetal deaths and any related malformations (1% of the sample had fetal deaths vs typical estimates of >10%). An important limitation was the low percentage of the sample with detectable (> 1ppb) concentrations of this solvent (<2%), which likely limited power. Small numbers for birth defect outcomes also limited power. Exposure misclassification (ex. drinking water from wells/ work/ bottles, changes in residence, exposure from other sources) is also a concern. However, such misclassification was likely non-differential, and thus more likely to under- vs. to over-estimate associations.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Bowler, R.M., Gysens, S., Hartney, C. (2003). Neuropsychological effects of ethylene dichloride exposure. NeuroToxicology 24(4-5):553-562.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Wechsler Adult Intelligence Scale III (WAIS-III), Wechsler Memory Scale III (WMS-III), Boston Naming Test (BNT), Trail Making Test (TMT), Stroop Color-Word Test, Grooved Pegboard, Dynamometer, Wide Range Achievement Test (WRAT), Finger tapping, Beck Anxiety Index, Beck Depression Index, Symptom Checklist-90 (SCL-90).
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	200241

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Uninformative	221 workers that had been exposed to 1,2-DCE in the Southern United States were initially included. Exclusion criteria were provided, including the number of individuals excluded for each reason. The study authors note that those initially included in the analysis sample were referred by physicians after neurological complaints were documented. Detailed criteria for referral were not provided. Referral-based recruitment of neurological cases will likely result in an analysis sample with an exposure-outcome distribution that is not representative of the eligible population (i.e., contamination site clean-up workers).
	Metric 2:	Attrition	Medium	There was moderate subject loss. Reasons for exclusion from the analysis sample are provided, and only those with complete information were included in the analysis.
	Metric 3:	Comparison Group	Low	Impairment scores were compared to normative data from manuals and/or a "demographically similar control group" cited to Bowler et al. (2001). The controls from this study appeared similar (albeit somewhat older) than 1,2-DCE-exposed workers and reported no prior chemical exposure.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Uninformative	A job-exposure matrix was not considered plausible; variables considered as surrogates of exposure were obtained from interviews. This method is expected to have poor validity because it relies on workers' recall of subjective events and their frequency (e.g., contact with water); workers (who are taking part in a lawsuit) may overestimate their exposure.
	Metric 5:	Exposure Levels	Low	Two levels of exposure (exposed and not exposed) were used to evaluate neurophysiological effects.
	Metric 6:	Temporality	Medium	Exposures primarily occurred between 1993 and 1995 and neurophysiological effects were evaluated in 2000. Temporality is established, but it is unclear whether exposures fall within relevant exposure windows for the outcome of interest.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Neurophysiological effects were evaluated using a number of standardized tests, including (but not limited to) the Wechsler Adult Intelligence Scale (WAIS-III), the Wechsler Memory Scale (WMS-III), and the Symptom Checklist 90-Revised (SCL90-R). There was no information whether tests were performed using the same methods for exposed and referent groups (e.g., timing and order of tests).

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Study Citation:	Bowler, R.M., Gysens, S., Hartney, C. (2003). Neuropsychological effects of ethylene dichloride exposure. NeuroToxicology 24(4-5):553-562.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Wechsler Adult Intelligence Scale III (WAIS-III), Wechsler Memory Scale III (WMS-III), Boston Naming Test (BNT), Trail Making Test (TMT), Stroop Color-Word Test, Grooved Pegboard, Dynamometer, Wide Range Achievement Test (WRAT), Finger tapping, Beck Anxiety Index, Beck Depression Index, Symptom Checklist-90 (SCL-90).
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	200241

Domain	Metric		Rating	Comments
	Metric 8:	Reporting Bias	Low	Neurobehavioral outcomes mentioned in the methods were reported for 1,2-DCE-exposed workers (as mean score, standard deviation, and percentage impaired); results for controls/normative data were not shown and/or p-values from t-tests were not provided. Control data were used to define impairment (based on z-score) but these values were not reported. Data pertaining to specific exposure variables were reported in the text only; no data were shown in a table.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Normative data permitted adjustments based on age, education, and gender. The control group was "socio-demographically" similar but specific parameters used to define similarity were not indicated. Separate ANCOVA analyses on workers only were stratified by race (citation provided), and adjusted for ethnicity, age, and education. The methods for identifying and including potential confounders in the analytic approach was not described.
	Metric 10:	Covariate Characterization	Low	No description of the covariate collection method was provided. It was not clear whether the method used was valid or not.
	Metric 11:	Co-exposure Counfounding	Low	A number of workers (18%) reported current exposure to chemicals in their work environment. These potential co-exposures were not were not appropriately adjusted for in the analytical approach used.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Low	The study design was appropriate to evaluate the neurophysiological status of 1,2-DCE-exposed workers; however, statistical methods were not comprehensive.
	Metric 13:	Statistical Power	Medium	The report indicates "significant impairments" were observed on various neurophysiological tests using t-tests, and significant exposure relationships were reported based on test scores and specific exposure variables (used as surrogates of exposure). Therefore, the number of participants was sufficient to detect an effect.
	Metric 14:	Reproducibility of Analyses	Low	Tests were scored according to relevant manuals; the calculation of z-scores, used in all impairment comparisons and analyses of exposure relationships, was not explained in adequate detail. The methods used to determine relationships between specific exposure variables and test scores (i.e., ANCOVA analyses) were not fully described.
	Metric 15:	Statistical Analysis	Low	Description of the ANCOVA analysis was largely not present. It is not clear whether model assumptions were met.

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Study Citation:	Bowler, R.M., Gysens, S., Hartney, C. (2003). Neuropsychological effects of ethylene dichloride exposure. NeuroToxicology 24(4-5):553-562.
Health Outcome(s):	Neurological/Behavioral
Reported Health Effect(s):	Wechsler Adult Intelligence Scale III (WAIS-III), Wechsler Memory Scale III (WMS-III), Boston Naming Test (BNT), Trail Making Test (TMT), Stroop Color-Word Test, Grooved Pegboard, Dynamometer, Wide Range Achievement Test (WRAT), Finger tapping, Beck Anxiety Index, Beck Depression Index, Symptom Checklist-90 (SCL-90).
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	200241

Domain	Metric	Rating	Comments
Additional Comments:	The study evaluated the neurobehavioral status of a group of workers with known exposure to 1,2-DCE at a clean-up site. Impairments related to processing speed, attention, cognitive flexibility, motor coordination and speed, verbal memory/fluency, vision and visual-spatial abilities, and mood were reported in exposed workers. Serious and consequential flaws are associated with the study including methods of participant selection and retention, and exposure characterization among others.		

Overall Quality Determination Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Brender, J.D., Shinde, M.U., Zhan, F.B., Gong, X., Langlois, P.H. (2014). Maternal residential proximity to chlorinated solvent emissions and birth defects in offspring: A case-control study. Environmental Health: A Global Access Science Source 13(1):96.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	birth defects (neural tube defects, limbs deficiencies, oral cleft defects, heart defects, spina bifida, anencephaly)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	2799700

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Participants were drawn from the Texas Birth Defects Registry (TBDR) for years 1996-2008. Controls were frequency matched from the same registry. Study authors state that neural tube cases were more likely to not be successfully geocoded which may introduce selection bias, however, the authors note that both cases and controls with addresses that could not be geocoded were similar. In spite of that, the inclusion criteria, methods of participant selection, and frequency match were reported.
	Metric 2:	Attrition	Medium	13.3% case mother addresses and 12.8% control mother addresses were unable to be geocoded, however this most likely only lowered the precision of the study and most likely does not vary based on exposure level.
	Metric 3:	Comparison Group	Medium	Controls were matched to cases and pulled from the same eligible population by year of delivery and public health service region. Other demographic factors, e.g., race was not matched in population selection. However, statistical analyses were adjusted for year of delivery, maternal age, race/ethnicity, education, and public health region of residence.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Used Emission Weighted Proximity Model to estimate exposure at a given address based on proximity to emission sources and the specific amount or type of pollutant emitted. There may be some exposure misclassification due to mothers moving away from geocoded addresses. Previous studies indicate ~67% of mothers do not move between conception and delivery.
	Metric 5:	Exposure Levels	Medium	Reports exposure as "exposure risk value" and groups the risk values into quartiles, with exposure risk values < 0 being the referent group
	Metric 6:	Temporality	Medium	The study authors estimated exposure based on residence during pregnancy and evaluated birth outcomes. Temporality is established. Previous studies indicate ~67% mothers don't move between trimester and delivery. For mothers who moved during the pregnancy, the temporality is unknown.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Outcomes determined by Texas Birth Defect Registry, checking for birth defect diagnosis. Birth certificates came from Center for Health Statistics at Texas Department of State Health Services
	Metric 8:	Reporting Bias	High	Outcome data measured and reported clearly, stratified by specific type of birth defect
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Brender, J.D., Shinde, M.U., Zhan, F.B., Gong, X., Langlois, P.H. (2014). Maternal residential proximity to chlorinated solvent emissions and birth defects in offspring: A case-control study. Environmental Health: A Global Access Science Source 13(1):96.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	birth defects (neural tube defects, limbs deficiencies, oral cleft defects, heart defects, spina bifida, anencephaly)
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	2799700

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	High	Cases were frequency matched by year of delivery and public health service region. Final models were adjusted for year of delivery, public health region, maternal age (<20, 20-24, 25-29, 30-34, 35-39, >39 years), education (<12 years, 12 years, >12 years), and race/ethnicity (Whit non-Hispanic, Black non-Hispanic, Hispanic, other non-Hispanic).
	Metric 10:	Covariate Characterization	High	Used birth and death certificates for demographic information
	Metric 11:	Co-exposure Counfounding	Medium	other co-exposures were not described
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	study used logistic regression to measure association between exposure and birth defects
	Metric 13:	Statistical Power	Medium	Overall adequate number of cases and controls - some effects have low cell counts, but at least one health effect has sufficient statistical power.
	Metric 14:	Reproducibility of Analyses	Medium	Methods sufficiently detailed for reproducibility
	Metric 15:	Statistical Analysis	High	No logistic regression model assumption violations were identified.

Additional Comments: This study examined the association between proximity to several point sources of chlorinated solvents and birth defects. Exposure was assessed using EPA's Toxic Release Inventory, and birth defects were assessed using Texas birth registries. The geocoded address of mothers on day of delivery and the amount of solvent was plugged into the Emission Weighted Probability model to assign each mother an exposure risk value. Limitations include limited evidence of temporality. Additionally, elective terminations lacked a vital record, which meant only 69% of mothers with neural tube defects were geocoded. Mothers highly exposed to 1,2-dichloroethane were 1.85 times more likely to have the spina bifida birth defect than mothers who were not significantly exposed.

Overall Quality Determination High

* No biomarkers were identified for this evaluation.

Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Nested case-control design; cases selected from deaths in cohort study was described by Rinsky et al (1988; HERO 597923) (29,139 workers in Union Carbide facilities in West Virginia followed from 1940 to 1978). Vital status complete for 95% of cohort members.
	Metric 2:	Attrition	High	There was minimal exclusion of subjects/missing data, because vital status follow-up was complete for 96% of the 29,139 men in the cohort study.
	Metric 3:	Comparison Group	Medium	Controls were randomly selected in a 5:1 ratio to cases from the total employee cohort such that they were first employed in the same decade and survived to the same five-year survival period as cases. Controls survived at least to the beginning of the five-year interval in which cases died. Controls were independently selected for each of the individual disease subcategories. However, the demographic information between cases and controls were not compared in the paper.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was partially described: (1) Potential employee contact with a specific substance was determined by tracing each employee's work assignments and linking these assignment records to a separate computer file that contained a history of departmental usage for each substance; (2) Potential exposure to each chemical group was assumed on the basis of assignment o a production unit with a history of usage of any member of that chemical group. However, exposure level either based on work assignment in departments such as job exposure matrix or on the chemical levels were not presented.
	Metric 5:	Exposure Levels	Low	The range of exposure is limited. For example, exposure was presented by the duration of work in two categories: <5 years and 5+ years.
	Metric 6:	Temporality	Medium	Temporality is established, but it is unclear whether the exposures fall within the relevant exposure window. Authors used a lag time of 5 years; since controls were selected for 5 yr intervals, the effective lag time ranged from 5-9 years with an average of 7.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Case definition was based on death certificate diagnosis; but no method validation was conducted against this well-established methods.
	Metric 8:	Reporting Bias	Medium	All outcomes reported, but ORs for many analyses presented without CIs (some CIs reported in text).
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Low	There is indirect evidence that considerations were not made for potential confounders (ORs not adjusted, controls not age- or race-matched). Even though authors note that "Age-adjusted stratified analyses, which were also conducted, did not materially modify the odds ratio estimates". Also stratified examination of odds ratios were conducted to assess duration of exposure effects. However, other key confounders e.g., smoking status and race were not accounted for.
	Metric 10:	Covariate Characterization	Medium	The only potential confounder considered was age; this was presumably evaluated based on employment records (no discussion presented). Age-adjusted stratified analyses were conducted.
	Metric 11:	Co-exposure Counfounding	Low	Co-exposures were present and were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Nested case-control study design is appropriate for research question. Initial data analysis included crude odds ratio and then stratified examination of odds ratios was conducted to ass duration of exposure effect. Also, age-adjusted stratified analysis was conducted.
	Metric 13:	Statistical Power	Low	Statistical power calculations were not reported. Case numbers for each disease were low. The number of subjects was not sufficient to detect an effect of 1,2-dichloroethylene exposure.
	Metric 14:	Reproducibility of Analyses	Medium	Description was sufficient to be conceptually reproducible.
	Metric 15:	Statistical Analysis	Low	Statistical model to calculate odds ratio was not described.

Additional Comments: This nested case-control study within a cohort study is a good study design to answer the research question regarding the association between multiple chemical exposures and four cancer sites. Cases and controls are selected appropriate. However, there are several limitations in this study: (1) confounders were not all considered and adjusted for, except that age-adjusted odds ratios were conducted; (2) it is not described if co-exposures were adjusted for; (3) numbers of cancer cases for each cancer type were small, so the statistical power is limited; (4) statistical models for calculating odds ratios were not described.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Nested case-control design; cases selected from deaths in cohort study was described by Rinsky et al (1988; HERO 597923) (29,139 workers in Union Carbide facilities in West Virginia followed from 1940 to 1978). Vital status complete for 95% of cohort members.
	Metric 2:	Attrition	High	There was minimal exclusion of subjects/missing data, because vital status follow-up was complete for 96% of the 29,139 men in the cohort study.
	Metric 3:	Comparison Group	Medium	Controls were randomly selected in a 5:1 ratio to cases from the total employee cohort such that they were first employed in the same decade and survived to the same five-year survival period as cases. Controls survived at least to the beginning of the five-year interval in which cases died. Controls were independently selected for each of the individual disease subcategories. However, the demographic information between cases and controls were not compared in the paper.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was partially described: (1) Potential employee contact with a specific substance was determined by tracing each employee's work assignments and linking these assignment records to a separate computer file that contained a history of departmental usage for each substance; (2) Potential exposure to each chemical group was assumed on the basis of assignment o a production unit with a history of usage of any member of that chemical group. However, exposure level either based on work assignment in departments such as job exposure matrix or on the chemical levels were not presented.
	Metric 5:	Exposure Levels	Low	The range of exposure is limited. For example, exposure was presented by the duration of work in two categories: <5 years and 5+ years.
	Metric 6:	Temporality	Medium	Temporality is established, but it is unclear whether the exposures fall within the relevant exposure window. Authors used a lag time of 5 years; since controls were selected for 5 yr intervals, the effective lag time ranged from 5-9 years with an average of 7.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Case definition was based on death certificate diagnosis; but no method validation was conducted against this well-established methods.
	Metric 8:	Reporting Bias	Medium	All outcomes reported, but ORs for many analyses presented without CIs (some CIs reported in text).
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Low	There is indirect evidence that considerations were not made for potential confounders (ORs not adjusted, controls not age- or race-matched). Even though authors note that "Age-adjusted stratified analyses, which were also conducted, did not materially modify the odds ratio estimates". Also stratified examination of odds ratios were conducted to assess duration of exposure effects. However, other key confounders e.g., smoking status and race were not accounted for.
	Metric 10:	Covariate Characterization	Medium	The only potential confounder considered was age; this was presumably evaluated based on employment records (no discussion presented). Age-adjusted stratified analyses were conducted.
	Metric 11:	Co-exposure Counfounding	Low	Co-exposures were present and were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Nested case-control study design is appropriate for research question. Initial data analysis included crude odds ratio and then stratified examination of odds ratios was conducted to ass duration of exposure effect. Also, age-adjusted stratified analysis was conducted.
	Metric 13:	Statistical Power	Low	Statistical power calculations were not reported. Case numbers for each disease were low. The number of subjects was not sufficient to detect an effect of 1,2-dichloroethylene exposure.
	Metric 14:	Reproducibility of Analyses	Medium	Description was sufficient to be conceptually reproducible.
	Metric 15:	Statistical Analysis	Low	Statistical model to calculate odds ratio was not described.

Additional Comments: This nested case-control study within a cohort study is a good study design to answer the research question regarding the association between multiple chemical exposures and four cancer sites. Cases and controls are selected appropriate. However, there are several limitations in this study: (1) confounders were not all considered and adjusted for, except that age-adjusted odds ratios were conducted; (2) it is not described if co-exposures were adjusted for; (3) numbers of cancer cases for each cancer type were small, so the statistical power is limited; (4) statistical models for calculating odds ratios were not described.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
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Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Nested case-control design; cases selected from deaths in cohort study was described by Rinsky et al (1988; HERO 597923) (29,139 workers in Union Carbide facilities in West Virginia followed from 1940 to 1978). Vital status complete for 95% of cohort members.
	Metric 2:	Attrition	High	There was minimal exclusion of subjects/missing data, because vital status follow-up was complete for 96% of the 29,139 men in the cohort study.
	Metric 3:	Comparison Group	Medium	Controls were randomly selected in a 5:1 ratio to cases from the total employee cohort such that they were first employed in the same decade and survived to the same five-year survival period as cases. Controls survived at least to the beginning of the five-year interval in which cases died. Controls were independently selected for each of the individual disease subcategories. However, the demographic information between cases and controls were not compared in the paper.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was partially described: (1) Potential employee contact with a specific substance was determined by tracing each employee's work assignments and linking these assignment records to a separate computer file that contained a history of departmental usage for each substance; (2) Potential exposure to each chemical group was assumed on the basis of assignment o a production unit with a history of usage of any member of that chemical group. However, exposure level either based on work assignment in departments such as job exposure matrix or on the chemical levels were not presented.
	Metric 5:	Exposure Levels	Low	The range of exposure is limited. For example, exposure was presented by the duration of work in two categories: <5 years and 5+ years.
	Metric 6:	Temporality	Medium	Temporality is established, but it is unclear whether the exposures fall within the relevant exposure window. Authors used a lag time of 5 years; since controls were selected for 5 yr intervals, the effective lag time ranged from 5-9 years with an average of 7.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Case definition was based on death certificate diagnosis; but no method validation was conducted against this well-established methods.
	Metric 8:	Reporting Bias	Medium	All outcomes reported, but ORs for many analyses presented without CIs (some CIs reported in text).
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Low	There is indirect evidence that considerations were not made for potential confounders (ORs not adjusted, controls not age- or race-matched). Even though authors note that "Age-adjusted stratified analyses, which were also conducted, did not materially modify the odds ratio estimates". Also stratified examination of odds ratios were conducted to assess duration of exposure effects. However, other key confounders e.g., smoking status and race were not accounted for.
	Metric 10:	Covariate Characterization	Medium	The only potential confounder considered was age; this was presumably evaluated based on employment records (no discussion presented). Age-adjusted stratified analyses were conducted.
	Metric 11:	Co-exposure Counfounding	Low	Co-exposures were present and were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Nested case-control study design is appropriate for research question. Initial data analysis included crude odds ratio and then stratified examination of odds ratios was conducted to ass duration of exposure effect. Also, age-adjusted stratified analysis was conducted.
	Metric 13:	Statistical Power	Low	Statistical power calculations were not reported. Case numbers for each disease were low. The number of subjects was not sufficient to detect an effect of 1,2-dichloroethylene exposure.
	Metric 14:	Reproducibility of Analyses	Medium	Description was sufficient to be conceptually reproducible.
	Metric 15:	Statistical Analysis	Low	Statistical model to calculate odds ratio was not described.

Additional Comments: This nested case-control study within a cohort study is a good study design to answer the research question regarding the association between multiple chemical exposures and four cancer sites. Cases and controls are selected appropriate. However, there are several limitations in this study: (1) confounders were not all considered and adjusted for, except that age-adjusted odds ratios were conducted; (2) it is not described if co-exposures were adjusted for; (3) numbers of cancer cases for each cancer type were small, so the statistical power is limited; (4) statistical models for calculating odds ratios were not described.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Carbide, Union (1989). Lymphatic and hematopoietic tissue cancer in a chemical manufacturing environment with attached tables and cover letter dated 022189.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	Nested case-control design; cases selected from deaths in cohort study was described by Rinsky et al (1988; HERO 597923) (29,139 workers in Union Carbide facilities in West Virginia followed from 1940 to 1978). Vital status complete for 95% of cohort members.
	Metric 2:	Attrition	High	There was minimal exclusion of subjects/missing data, because vital status follow-up was complete for 96% of the 29,139 men in the cohort study.
	Metric 3:	Comparison Group	Medium	Controls were randomly selected in a 5:1 ratio to cases from the total employee cohort such that they were first employed in the same decade and survived to the same five-year survival period as cases. Controls survived at least to the beginning of the five-year interval in which cases died. Controls were independently selected for each of the individual disease subcategories. However, the demographic information between cases and controls were not compared in the paper.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure assessment was partially described: (1) Potential employee contact with a specific substance was determined by tracing each employee's work assignments and linking these assignment records to a separate computer file that contained a history of departmental usage for each substance; (2) Potential exposure to each chemical group was assumed on the basis of assignment o a production unit with a history of usage of any member of that chemical group. However, exposure level either based on work assignment in departments such as job exposure matrix or on the chemical levels were not presented.
	Metric 5:	Exposure Levels	Low	The range of exposure is limited. For example, exposure was presented by the duration of work in two categories: <5 years and 5+ years.
	Metric 6:	Temporality	Medium	Temporality is established, but it is unclear whether the exposures fall within the relevant exposure window. Authors used a lag time of 5 years; since controls were selected for 5 yr intervals, the effective lag time ranged from 5-9 years with an average of 7.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Case definition was based on death certificate diagnosis; but no method validation was conducted against this well-established methods.
	Metric 8:	Reporting Bias	Medium	All outcomes reported, but ORs for many analyses presented without CIs (some CIs reported in text).
Domain 4: Potential Confounding / Variability Control				

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Reported Health Effect(s):	Mortality from non-Hodgkin's lymphoma, non-lymphocytic leukemia, lymphocytic leukemia, or multiple myeloma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5451581

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Low	There is indirect evidence that considerations were not made for potential confounders (ORs not adjusted, controls not age- or race-matched). Even though authors note that "Age-adjusted stratified analyses, which were also conducted, did not materially modify the odds ratio estimates". Also stratified examination of odds ratios were conducted to assess duration of exposure effects. However, other key confounders e.g., smoking status and race were not accounted for.
	Metric 10:	Covariate Characterization	Medium	The only potential confounder considered was age; this was presumably evaluated based on employment records (no discussion presented). Age-adjusted stratified analyses were conducted.
	Metric 11:	Co-exposure Counfounding	Low	Co-exposures were present and were not adjusted for.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	Nested case-control study design is appropriate for research question. Initial data analysis included crude odds ratio and then stratified examination of odds ratios was conducted to ass duration of exposure effect. Also, age-adjusted stratified analysis was conducted.
	Metric 13:	Statistical Power	Low	Statistical power calculations were not reported. Case numbers for each disease were low. The number of subjects was not sufficient to detect an effect of 1,2-dichloroethylene exposure.
	Metric 14:	Reproducibility of Analyses	Medium	Description was sufficient to be conceptually reproducible.
	Metric 15:	Statistical Analysis	Low	Statistical model to calculate odds ratio was not described.

Additional Comments: This nested case-control study within a cohort study is a good study design to answer the research question regarding the association between multiple chemical exposures and four cancer sites. Cases and controls are selected appropriate. However, there are several limitations in this study: (1) confounders were not all considered and adjusted for, except that age-adjusted odds ratios were conducted; (2) it is not described if co-exposures were adjusted for; (3) numbers of cancer cases for each cancer type were small, so the statistical power is limited; (4) statistical models for calculating odds ratios were not described.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Cheng, T.J., Huang, M.L., You, N.C., Du, C.L., Chau, T.T. (1999). Abnormal liver function in workers exposed to low levels of ethylene dichloride and vinyl chloride monomer. Journal of Occupational and Environmental Medicine 41(12):1128-1133.
Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	AST, ALT, GGT, Hepatitis B virus surface antigen (HBsAg), and anti-hepatitis C virus antibody (anti-HCV).
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	200266

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	A total of 251 male workers were included from 4 vinyl chloride monomer manufacturing plants. Other details on recruitment strategy, eligibility criteria, year of enrollment, and participation rates were not provided.
	Metric 2:	Attrition	Low	There was no indication of attrition and details on the number of eligible participants throughout the study was limited. Attrition could not be adequately assessed due to a lack of information regarding recruitment and selection.
	Metric 3:	Comparison Group	Medium	The low-EDC-low-VCM group (187 participants) was used as the comparison group, and there is indirect evidence groups are similar. Limited details were provided for setting, inclusion and exclusion criteria, and methods of participant selection.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	NIOSH recommended methods 1003 and 1007 were used for personal and area sampling, respectively. Air samples were collected, stored at 4 deg. C, and analyzed within 2 weeks of the sampling event. However, historical job changes, changes in exposure levels over time, and timing (year or days during work week) or duration of area or personal sampling were not reported.
	Metric 5:	Exposure Levels	Medium	EDC and VCM levels were reported for the different categories of jobs, which were classified into low-EDC-low-VCM, mod-EDC-low-VCM, and low-EDC-mod-VCM groups.
	Metric 6:	Temporality	High	The age of participants (mean age 33.7-40.1 years) and employment duration (mean 7.5-14.3 years) were reported, and the temporality between the exposure and outcome appears to be appropriate.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	AST, ALT, and GGT "were analyzed with a Hitachi 7050 autoanalyzer". A basis for the cutoff values used in Table 4 to determine "abnormal" AST, ALT, and GGT levels was not provided.
	Metric 8:	Reporting Bias	High	Odds ratios for abnormal liver function were provided with 95% confidence intervals, the number per exposure level, and significance when applicable.
Domain 4: Potential Confounding / Variability Control				

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Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	AST, ALT, GGT, Hepatitis B virus surface antigen (HBsAg), and anti-hepatitis C virus antibody (anti-HCV).
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	200266

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Medium	The study reports information on potential confounders (age, hepatitis, BMI, alcohol use, and employment duration), and controls for hepatitis, BMI and alcohol consumption in the multiple logistic regression analyses. There is indirect evidence that appropriate adjustments were made.
	Metric 10:	Covariate Characterization	Medium	An interviewer administered the questionnaires to collect information about potential confounders and occupational history.
	Metric 11:	Co-exposure Counfounding	Low	Exposure to ethylene dichloride was evaluated in a vinyl chloride monomer (VCM) manufacturing facility, and VCM was also subsequently analyzed using personal and area sampling. Results for VCM exposure concentrations were provided. VCM is also suspected to cause liver damage.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design (cohort) was appropriate to assess the outcome of interest (”markers of liver damage”). Chi-squared (X2) test and multiple logistic regression were used for statistical analyses.
	Metric 13:	Statistical Power	Medium	The number of participants was adequate to detect an effect in the exposed populations, although power calculations were not provided. There were >20 participants in each group.
	Metric 14:	Reproducibility of Analyses	Low	A description of the logistic regression analysis was provided, however, study authors do not provide information on categorization of abnormal liver function.
	Metric 15:	Statistical Analysis	High	There were no identifiable logistic regression model assumption violations.
Domain 6: Other (if applicable) Considerations for Biomarker Selection and Measurement (Lakind et al. 2014)				
	Metric 16:	Use of Biomarker of Exposure	N/A	Biomarker of exposures were not assessed.
	Metric 17:	Effect Biomarker	High	This study uses aspartate aminotransferase, alanine aminotransferase, and y-glutamyltransferase as biomarkers of effect. While these no works cited to explain their connection to liver function, all three are well-known marker of liver function. Similarly, Hepatitis B virus surface antigen and antihepatitis C virus anitbody are also well-known measures of liver function and health.
	Metric 18:	Method Sensitivity	Low	No limit of detection information is provided for any of the effect biomarkers.
	Metric 19:	Biomarker Stability	Medium	While the study does not provide a lot of information regarding biomarker storage or stability, the authors do mention that venous blood used to detect biomarkers was stored at 4 degrees C.
	Metric 20:	Sample Contamination	Medium	No specific information regarding potential sample contamination was provided.
	Metric 21:	Method Requirements	Medium	Aspartate aminotransferase, alanine aminotransferase, and y-glutamyltransferase were analyzed using a Hitachi 7050 autoanalyzer. Hepatitis B virus surface antibody and antihepatitis C virus antibody were assessed with radioimmunoassay and enzyme-linked immunosorbent assay.

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Health Outcome(s):	Hepatic/Liver
Reported Health Effect(s):	AST, ALT, GGT, Hepatitis B virus surface antigen (HBsAg), and anti-hepatitis C virus antibody (anti-HCV).
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	200266

Domain	Metric	Rating	Comments
	Metric 22: Matrix Adjustment	N/A	No information on matrix adjustment was provided/available.

Additional Comments: A group of 251 male workers from 4 vinyl chloride monomer (VCM) manufacturing plants were included in this assessment to examine if occupational exposure to VCM and ethylene dichloride (EDC) "resulted in increased risk of liver damage" by examining AST, ALT, and GGT levels in the blood. Increased ORs for abnormal AST (>37 IU/L) and ALT (>41 IU/L) in the mod-EDC-low-VCM group (0.17-333.7 ppm EDC, 0.18-0.34 ppm VCM), compared with the low-EDC-low-VCM group, was reported. Exposure levels were measured using area and personal sampling, but the timing and duration of the sampling events were not reported.

Overall Quality Determination Medium

Study Citation:	Dosemeci, M., Cocco, P., Chow, W.H. (1999). Gender differences in risk of renal cell carcinoma and occupational exposures to chlorinated aliphatic hydrocarbons. American Journal of Industrial Medicine 36(1):54-59.
Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	renal cell carcinoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	4697224

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	The details of the study design were reported elsewhere (Chow et al. 1994, HERO ID 701514). Brief details about the setting, date, number of eligible participants, and control matching were reported. Reasons for exclusions/non-participation were described with details by Chow et al. (1994).
	Metric 2:	Attrition	High	For the details of the study design and attrition of study subjects, the study authors referred to another publication by Chow et al., 1994. Chow et al. (1994) mentioned that at the end of the personal interview, the respondents were given a self-administered food-frequency questionnaire. Of the subjects interviewed for the study, 632 patients (79% of 796 eligible patients) and 653 control subjects (79% of 707 eligible control subjects) returned the diet questionnaire. A number of subjects, whose responses were considered unreliable, were excluded from the analysis, including 48 patients and three control subjects who had seven or more skipped food items or had questionable data and 50 patients whose next-of-kin respondent was not a spouse. Also excluded were two patients with unknown smoking status, since smoking is a risk factor.
	Metric 3:	Comparison Group	Medium	The cases were pulled from the Minnesota Cancer Surveillance System. Controls were selected from the general population of Minnesota; controls age 20-64 years were selected through random digital dialing and controls age 65-85 years were collected from files through the Health Care Financing Administration. Controls were age- and gender-stratified and were of the same race. Characteristics of cases and controls were not provided in the text or a table.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	High	Occupational histories including the most recent and usual occupation and industry, job activities, started-year and ended-year, and part-time/full-time status were collected. Occupations and industries were coded according to the standard occupational classification (SOC) and standard industrial classification (SIC) schemes. The National Cancer Institute developed job exposure matrices (JEM) for nine individual chlorinated aliphatic hydrocarbons (CAHCs), all CAHCs-combined, and all organic solvents-combined. These JEMs were merged with assigned SOC and SIC to determine the exposure status to these chemicals for each study subject. Application of the JEM was described elsewhere (Dosemeci et al. 1994, HERO ID 632334; Gomez et al. 1994, HERO ID 702154).
	Metric 5:	Exposure Levels	Medium	Details of the application of the JEM were described elsewhere (Dosemeci et al. 1994, HERO ID 632334; Gomez et al. 1994, HERO ID 702154). Dosemeci et al. (1994) described more details about that this study assigned three levels of probability (low, medium, high) to industries and occupations for chemical exposure levels.

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Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	renal cell carcinoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	4697224

Domain	Metric		Rating	Comments
	Metric 6:	Temporality	Medium	Occupational questionnaires identified prior exposures based on reported recent and usual occupations as well as duration of employment. Outcome status was determined from registry data. The authors note that some occupational history was incomplete which may result in some uncertainty in regard to temporality.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Cases were identified as newly diagnosed and histologically confirmed renal cell carcinoma through the Minnesota Cancer Surveillance System and information about each participant was collected using a questionnaire. Validation was not specified.
	Metric 8:	Reporting Bias	Medium	A description of measured outcomes is reported and ORs were stratified by sex. Effect estimates are reported with a confidence interval. One table showed the total numbers of men and women respectively for each chemical, but numbers of cases/controls were not reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Appropriate adjustments were made in the final analysis, including age, gender, smoking, hypertension and the use of diuretics and/or anti-hypertension drugs, and BMI. Results were stratified by sex.
	Metric 10:	Covariate Characterization	Medium	Information about participants was collected using a questionnaire, and it includes potential confounders, e.g., smoking habits. Validation was not specified.
	Metric 11:	Co-exposure Counfounding	Medium	Co-exposures were identified through the job exposure matrices. Chemicals were evaluated individually and as a group.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen (case-control) was appropriate for the research question (renal cell carcinoma risk from occupational organic solvent exposure). Logistic regression models were used to estimate the relative risk and 95% CI.
	Metric 13:	Statistical Power	Low	Statistical power calculations were not provided. No significant effects were observed with 1,2-dichloroethane. The number of participated women to calculate odds ratio was inadequate to detect an effect in the participants for other chemicals or the combined risk, because it was very low.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis was brief, but is sufficient to understand precisely what has been done and to be conceptually reproducible with access to the analytic data.
	Metric 15:	Statistical Analysis	High	Model assumptions for logistic regression were met. The odds ratios were adjusted for age, smoking, hypertension status and/or use of diuretic and/or anti-hypertension drugs, and body mass index for men and women separately.

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Health Outcome(s):	Renal/Kidney
Reported Health Effect(s):	renal cell carcinoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	4697224

Domain	Metric	Rating	Comments
Additional Comments:	A group of 438 cases (273 men and 165 women) were selected from the Minnesota Cancer Surveillance System that had been newly diagnosed with renal cell carcinoma. Controls included 687 participants (462 men and 225 women) age- and gender- stratified that were selected from either the general population of Minnesota (age 20-64 years) or from the Health Care Financing Administration files (age 65-85). No significant increase in the risk of renal cell carcinoma was observed with exposure to 1,2-dichloroethane among men or women separately, or for all participants exposed.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Dosemeci, M., Cocco, P., Chow, W.H. (1999). Gender differences in risk of renal cell carcinoma and occupational exposures to chlorinated aliphatic hydrocarbons. American Journal of Industrial Medicine 36(1):54-59.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	renal cell carcinoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	4697224

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	The details of the study design were reported elsewhere (Chow et al. 1994, HERO ID 701514). Brief details about the setting, date, number of eligible participants, and control matching were reported. Reasons for exclusions/non-participation were described with details by Chow et al. (1994).
	Metric 2:	Attrition	Medium	For the details of the study design and attrition of study subjects, the study authors referred to another publication by Chow et al., 1994. Chow et al. (1994) mentioned that at the end of the personal interview, the respondents were given a self-administered food-frequency questionnaire. Of the subjects interviewed for the study, 632 patients (79% of 796 eligible patients) and 653 control subjects (79% of 707 eligible control subjects) returned the diet questionnaire. A number of subjects, whose responses were considered unreliable, were excluded from the analysis, including 48 patients and three control subjects who had seven or more skipped food items or had questionable data and 50 patients whose next-of-kin respondent was not a spouse. Also excluded were two patients with unknown smoking status, since smoking is a risk factor.
	Metric 3:	Comparison Group	Medium	The cases were pulled from the Minnesota Cancer Surveillance System. Controls were selected from the general population of Minnesota; controls age 20-64 years were selected through random digital dialing and controls age 65-85 years were collected from files through the Health Care Financing Administration. Controls were age- and gender-stratified and were of the same race. Characteristics of cases and controls were not provided in the text or a table.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	High	Occupational histories including the most recent and usual occupation and industry, job activities, started-year and ended-year, and part-time/full-time status were collected. Occupations and industries were coded according to the standard occupational classification (SOC) and standard industrial classification (SIC) schemes. The National Cancer Institute developed job exposure matrices (JEM) for nine individual chlorinated aliphatic hydrocarbons (CAHCs), all CAHCs-combined, and all organic solvents-combined. These JEMs were merged with assigned SOC and SIC to determine the exposure status to these chemicals for each study subject. Application of the JEM was described elsewhere (Dosemeci et al. 1994, HERO ID 632334; Gomez et al. 1994, HERO ID 702154).
	Metric 5:	Exposure Levels	Medium	Details of the application of the JEM were described elsewhere (Dosemeci et al. 1994, HERO ID 632334; Gomez et al. 1994, HERO ID 702154). Dosemeci et al. (1994) described more details about that this study assigned three levels of probability (low, medium, high) to industries and occupations for chemical exposure levels.

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Study Citation:	Dosemeci, M., Cocco, P., Chow, W.H. (1999). Gender differences in risk of renal cell carcinoma and occupational exposures to chlorinated aliphatic hydrocarbons. American Journal of Industrial Medicine 36(1):54-59.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	renal cell carcinoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	4697224

Domain	Metric		Rating	Comments
	Metric 6:	Temporality	Medium	Occupational questionnaires identified prior exposures based on reported recent and usual occupations as well as duration of employment. Outcome status was determined from registry data. The authors note that some occupational history was incomplete which may result in some uncertainty in regard to temporality.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Cases were identified as newly diagnosed and histologically confirmed renal cell carcinoma through the Minnesota Cancer Surveillance System and information about each participant was collected using a questionnaire. Validation was not specified.
	Metric 8:	Reporting Bias	Medium	A description of measured outcomes is reported and ORs were stratified by sex. Effect estimates are reported with a confidence interval. One table showed the total numbers of men and women respectively for each chemical, but numbers of cases/controls were not reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Appropriate adjustments were made in the final analysis, including age, gender, smoking, hypertension and the use of diuretics and/or anti-hypertension drugs, and BMI. Results were stratified by sex.
	Metric 10:	Covariate Characterization	Medium	Information about participants was collected using a questionnaire, and it includes potential confounders, e.g., smoking habits. Validation was not specified.
	Metric 11:	Co-exposure Counfounding	Medium	Co-exposures were identified through the job exposure matrices. Chemicals were evaluated individually and as a group.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen (case-control) was appropriate for the research question (renal cell carcinoma risk from occupational organic solvent exposure). Logistic regression models were used to estimate the relative risk and 95% CI.
	Metric 13:	Statistical Power	Low	Statistical power calculations were not provided. No significant effects were observed with 1,2-dichloroethane. The number of participated women to calculate odds ratio was inadequate to detect an effect in the participants for other chemicals or the combined risk, because it was very low.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis was brief, but is sufficient to understand precisely what has been done and to be conceptually reproducible with access to the analytic data.
	Metric 15:	Statistical Analysis	High	Model assumptions for logistic regression were met. The odds ratios were adjusted for age, smoking, hypertension status and/or use of diuretic and/or anti-hypertension drugs, and body mass index for men and women separately.

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Study Citation:	Dosemeci, M., Cocco, P., Chow, W.H. (1999). Gender differences in risk of renal cell carcinoma and occupational exposures to chlorinated aliphatic hydrocarbons. American Journal of Industrial Medicine 36(1):54-59.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	renal cell carcinoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	4697224

Domain	Metric	Rating	Comments
Additional Comments:	A group of 438 cases (273 men and 165 women) were selected from the Minnesota Cancer Surveillance System that had been newly diagnosed with renal cell carcinoma. Controls included 687 participants (462 men and 225 women) age- and gender- stratified that were selected from either the general population of Minnesota (age 20-64 years) or from the Health Care Financing Administration files (age 65-85). No significant increase in the risk of renal cell carcinoma was observed with exposure to 1,2-dichloroethane among men or women separately, or for all participants exposed.		

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Garcia, E., Hurley, S., Nelson, D.O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health: A Global Access Science Source 14(1):14.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	breast cancer in females
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	3014082

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	A total of 112,378 women were included in this study out of 133,479 eligible female participants from the California Teacher Study cohort. A full description of the cohort is provided in Bernstein et al. 2002 (HERO ID 808446). Reasons for exclusion were provided. The reported information indicates that participant selection in or out of the study and participation was not likely to be biased.
	Metric 2:	Attrition	High	112,378/133,479 participants were included in the study. Exclusions were for the purpose of the study and analysis. Exclusion criteria were documented. Included participants had completed questionnaires. The California Cancer Registry is estimated to be 99% complete.
	Metric 3:	Comparison Group	Medium	There is only indirect evidence that groups are similar. Participants were recruited from the same eligible population with the same method of ascertainment. Comparisons were provided for participants with and without breast cancer. Characteristics between these two groups were generally similar. 5 Quintiles of exposure were used, and Q2-5 were compared with Q1.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	High	The Assessment System for Population Exposure Nationwide and the Human Exposure Model are used as part of the National-Scale Air Toxics Assessment produced by the EPA and was used to estimate ambient HAP concentrations for geographic locations. Methods are described online through the US EPA Assessment Methods.
	Metric 5:	Exposure Levels	Medium	The distribution of the NATA annual ambient concentration for each compound was plotted in Figure 1 using a box plot, and 5 Quintiles were used in the analyses.
	Metric 6:	Temporality	Medium	The follow-up period was from 1995-2011, and the NATA estimates were made in 2002 because it was approximately half way between the start and end of the follow-up period. However, it is unclear whether exposures fall within relevant exposure windows for the outcome of interest.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Annual linkage between the CTS cohort and the California Cancer Registry (CCR) was used to identify cases of invasive breast cancer. The CCR is estimated to be 99% complete. The case of invasive breast cancer was defined by ICD codes.

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Study Citation:	Garcia, E., Hurley, S., Nelson, D.O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health: A Global Access Science Source 14(1):14.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	breast cancer in females
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	3014082

Domain	Metric		Rating	Comments
	Metric 8:	Reporting Bias	Medium	A description of measured outcome is reported for adjustments by age and race, and effect estimates are reported with a 95% confidence interval. The measured outcomes using multiple comparisons were generally described in the text, but non-significant results were excluded from Table 3.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	The models were stratified by age and race. Additionally, adjustments were made for multiple comparisons among subsets of the participants (significant results reported in Table 3). Socioeconomic status (SES) of each participant was not evaluated, however, cohort SES characteristics were thought to be similar by study authors.
	Metric 10:	Covariate Characterization	Medium	Information about baseline characteristics for each participant was collected through a questionnaire. It is unknown if the questionnaire was validated.
	Metric 11:	Co-exposure Counfounding	Medium	A total of 37 compounds were identified as mammary gland carcinogens, but 13 were not included in this analysis. Thirteen compounds were excluded from the analysis due to insufficient variability (nine because they had the same value for all census tracts in the state of California; and four because they had less than 25% non-zero values). Ethylene dichloride (1,2-dichloroethane) was among the 24 compounds evaluated in this assessment, and evaluations for breast cancer were conducted for each of these 24 individual compounds.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen (prospective cohort) was appropriate for the research question (incidence of breast cancer). Cox proportional hazard models and SAS 9.3 were used in this assessment. Data analysis was described.
	Metric 13:	Statistical Power	Medium	Statistical power calculations were not provided. No significant effects were observed with ethylene dichloride (1,2-dichloroethane), however, this study utilized a large cohort, approximately 112,000 individuals. Distributions of chemicals of interest suggest there were sufficient numbers of participants in exposure subgroups.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to understand precisely what has been done and to be conceptually reproducible with access to the analytic data.
	Metric 15:	Statistical Analysis	High	The statistical models that were used were identified and described. ”No apparent violation of the underlying assumption of proportional hazards was detected”.

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Study Citation:	Garcia, E., Hurley, S., Nelson, D.O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health: A Global Access Science Source 14(1):14.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	breast cancer in females
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	3014082

Domain	Metric	Rating	Comments
Additional Comments:	A group of 112,378 female participants from the California Teacher Study cohort were assessed for their estimated exposure to ambient air pollutants, including ethylene dichloride (1,2-dichloroethane), and the incidence of invasive breast cancer. Air contaminant concentrations were estimated using the US EPA NATA and the ASPEN and HEM models. The approximate median concentration of 1,2-dichloroethane is between 1E-4 and 1E-2 (estimated from Figure 1). Exposures were categorized into 5 Quintiles, and compared against Quintile 1. No significant increase in the estimated hazard rate ratio for invasive breast cancer was observed with Quintile 2-5 exposure estimates for 1,2-dichloroethane, adjusted for age and race, when compared against Quintile 1, or when further adjusted using multiple comparisons.		

Overall Quality Determination High

* No biomarkers were identified for this evaluation.

Study Citation:	Garcia, E., Hurley, S., Nelson, D.O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health: A Global Access Science Source 14(1):14.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	breast cancer in females
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	3014082

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	A total of 112,378 women were included in this study out of 133,479 eligible female participants from the California Teacher Study cohort. A full description of the cohort is provided in Bernstein et al. 2002 (HERO ID 808446). Reasons for exclusion were provided. The reported information indicates that participant selection in or out of the study and participation was not likely to be biased.
	Metric 2:	Attrition	High	112,378/133,479 participants were included in the study. Exclusions were for the purpose of the study and analysis. Exclusion criteria were documented. Included participants had completed questionnaires. The California Cancer Registry is estimated to be 99% complete.
	Metric 3:	Comparison Group	Medium	There is only indirect evidence that groups are similar. Participants were recruited from the same eligible population with the same method of ascertainment. Comparisons were provided for participants with and without breast cancer. Characteristics between these two groups were generally similar. 5 Quintiles of exposure were used, and Q2-5 were compared with Q1.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	High	The Assessment System for Population Exposure Nationwide and the Human Exposure Model are used as part of the National-Scale Air Toxics Assessment produced by the EPA and was used to estimate ambient HAP concentrations for geographic locations. Methods are described online through the US EPA Assessment Methods.
	Metric 5:	Exposure Levels	Medium	The distribution of the NATA annual ambient concentration for each compound was plotted in Figure 1 using a box plot, and 5 Quintiles were used in the analyses.
	Metric 6:	Temporality	Medium	The follow-up period was from 1995-2011, and the NATA estimates were made in 2002 because it was approximately half way between the start and end of the follow-up period. However, it is unclear whether exposures fall within relevant exposure windows for the outcome of interest.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Annual linkage between the CTS cohort and the California Cancer Registry (CCR) was used to identify cases of invasive breast cancer. The CCR is estimated to be 99% complete. The case of invasive breast cancer was defined by ICD codes.
	Metric 8:	Reporting Bias	Medium	A description of measured outcome is reported for adjustments by age and race, and effect estimates are reported with a 95% confidence interval. The measured outcomes using multiple comparisons were generally described in the text, but non-significant results were excluded from Table 3.

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Study Citation:	Garcia, E., Hurley, S., Nelson, D.O., Hertz, A., Reynolds, P. (2015). Hazardous air pollutants and breast cancer risk in California teachers: A cohort study. Environmental Health: A Global Access Science Source 14(1):14.
Health Outcome(s):	Reproductive/Developmental
Reported Health Effect(s):	breast cancer in females
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	3014082

Domain	Metric		Rating	Comments
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	The models were stratified by age and race. Additionally, adjustments were made for multiple comparisons among subsets of the participants (significant results reported in Table 3). Socioeconomic status (SES) of each participant was not evaluated, however, cohort SES characteristics were thought to be similar by study authors.
	Metric 10:	Covariate Characterization	Medium	Information about baseline characteristics for each participant was collected through a questionnaire. It is unknown if the questionnaire was validated.
	Metric 11:	Co-exposure Counfounding	Medium	A total of 37 compounds were identified as mammary gland carcinogens, but 13 were not included in this analysis. Thirteen compounds were excluded from the analysis due to insufficient variability (nine because they had the same value for all census tracts in the state of California; and four because they had less than 25% non-zero values). Ethylene dichloride (1,2-dichloroethane) was among the 24 compounds evaluated in this assessment, and evaluations for breast cancer were conducted for each of these 24 individual compounds.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design chosen (prospective cohort) was appropriate for the research question (incidence of breast cancer). Cox proportional hazard models and SAS 9.3 were used in this assessment. Data analysis was described.
	Metric 13:	Statistical Power	Medium	Statistical power calculations were not provided. No significant effects were observed with ethylene dichloride (1,2-dichloroethane), however, this study utilized a large cohort, approximately 112,000 individuals. Distributions of chemicals of interest suggest there were sufficient numbers of participants in exposure subgroups.
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to understand precisely what has been done and to be conceptually reproducible with access to the analytic data.
	Metric 15:	Statistical Analysis	High	The statistical models that were used were identified and described. ”No apparent violation of the underlying assumption of proportional hazards was detected”.

Additional Comments: A group of 112,378 female participants from the California Teacher Study cohort were assessed for their estimated exposure to ambient air pollutants, including ethylene dichloride (1,2-dichloroethane), and the incidence of invasive breast cancer. Air contaminant concentrations were estimated using the US EPA NATA and the ASPEN and HEM models. The approximate median concentration of 1,2-dichloroethane is between 1E-4 and 1E-2 (estimated from Figure 1). Exposures were categorized into 5 Quintiles, and compared against Quintile 1. No significant increase in the estimated hazard rate ratio for invasive breast cancer was observed with Quintile 2-5 exposure estimates for 1,2-dichloroethane, adjusted for age and race, when compared against Quintile 1, or when further adjusted using multiple comparisons.

Overall Quality Determination High

* No biomarkers were identified for this evaluation.

Study Citation:	Guo, P., Yokoyama, K., Piao, F., Sakai, K., Khalequzzaman, M., Kamijima, M., Nakajima, T., Kitamura, F. (2013). Sick building syndrome by indoor air pollution in Dalian, China. International Journal of Environmental Research and Public Health 10(4):1489-1504.
Health Outcome(s):	sick building syndrome
Reported Health Effect(s):	The statistical analysis considers all subjective self-reported symptoms together (not segregated by health outcome) as a group health outcome –sick building syndrome. The study compared two conditions for each studied chemical: combined self-reported symptoms to no symptoms. Therefore, only one form 3 was completed.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1938385

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Low	Residents of a housing estate of 3000 homes were invited to a community meeting to explain the purpose of the study and volunteers were invited to participate. It was not reported whether these volunteers were different from the overall eligible population.
	Metric 2:	Attrition	Low	Of the 70 families that agreed to participate, questionnaires were provided by 59. Reasons of uncompleted questionnaires were not fully provided, and there was no comparison between those who participated and those who did not.
	Metric 3:	Comparison Group	Low	The overall description of the analysis sample indicated a wide range of ages and lengths of stay at the current residence. Thus it is hard to know that subjects in all exposure groups were similar. In addition, the methods of selecting participants in all exposure groups were not fully reported. The numbers of male and female smokers were reported, respectively, but the smoking status and age were not controlled in the statistical analysis.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure concentrations for each home were obtained by diffusion sampling over 24 hrs in the bedroom, kitchen, and outdoors; temperature, the vertical height of samplers, and ventilation (hours windows left open) were reported. Samples were analyzed by GC/MS. The number of samples per home is unclear. The frequency of measurements for each house was not reported.
	Metric 5:	Exposure Levels	Low	The frequency of detection was not reported, so it is difficult to ascertain the actual exposure range. In addition, the reported exposure levels were median, geometric mean, and 95% CI, so they are inadequate to develop an exposure-response estimate.
	Metric 6:	Temporality	Uninformative	For 1,2-dichloroethane, the study evaluated self-reported symptoms in the past (”since they moved into their flats”) and their association with sampling conducted during the study; thus, exposure was measured after the outcome.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Low	Participants provided self-reported symptoms using a questionnaire. Study authors cited a previous study, Kamijima et al., 2005 (in Japanese, HERO ID 1598645) for further details on the questionnaire. It was not clear whether the questionnaire was validated.

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Study Citation:	Guo, P., Yokoyama, K., Piao, F., Sakai, K., Khalequzzaman, M., Kamijima, M., Nakajima, T., Kitamura, F. (2013). Sick building syndrome by indoor air pollution in Dalian, China. International Journal of Environmental Research and Public Health 10(4):1489-1504.
Health Outcome(s):	sick building syndrome
Reported Health Effect(s):	The statistical analysis considers all subjective self-reported symptoms together (not segregated by health outcome) as a group health outcome –sick building syndrome. The study compared two conditions for each studied chemical: combined self-reported symptoms to no symptoms. Therefore, only one form 3 was completed.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1938385

Domain	Metric		Rating	Comments
	Metric 8:	Reporting Bias	Low	The study only mentioned subjective symptoms in the abstract or methods. The abstract and method sections did not report the specific symptoms included in the questionnaire or whether the questionnaire was open-ended for symptoms. The questionnaire was cited to Kamijima et al. 2005 (in Japanese).
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	Comparisons were made separately by sex. The distribution of age and time spent living in residence differed greatly between those reporting symptoms and those not reporting symptoms. Smoking was indicated but not controlled for in the analysis. In short, the statistical analysis did not consider these three potential confounders, age, time spent living in residence, and smoking.
	Metric 10:	Covariate Characterization	Low	Covariates were presumably evaluated via a questionnaire that was cited to Kamijima et al. 2005 (in Japanese).
	Metric 11:	Co-exposure Counfounding	Low	The analysis did not account for other exposures. A number of other VOCs, HCHO, and NO2 were measured in the homes. The concentrations of several other VOCs and HCHO were much higher (5-30x) than 1,2-dichloroethane and may also be associated with these symptoms.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Low	The study design is best characterized as cross-sectional. Only one analysis to compare exposure concentrations between those with and without symptoms was adjusted for a confounder, sex, via stratification. Other potential confounders were not adjusted for. Study authors combine responses for symptoms reported before and during the sampling period in one statistical analysis, which may not reflect the relationship between symptoms and contaminants' exposure at each period.
	Metric 13:	Statistical Power	Medium	Statistical power was not reported. The number of participants was sufficient to detect a difference in median concentration between those with and without symptoms.
	Metric 14:	Reproducibility of Analyses	Medium	Study presents sufficient description of analysis (statistical methods) to be conceptually reproducible with access to the raw data.
	Metric 15:	Statistical Analysis	Low	Study uses a Wilcoxon's rank sum test to compare exposure concentrations in persons with and without symptoms; test for equal variance is not reported.

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Study Citation:	Guo, P., Yokoyama, K., Piao, F., Sakai, K., Khalequzzaman, M., Kamijima, M., Nakajima, T., Kitamura, F. (2013). Sick building syndrome by indoor air pollution in Dalian, China. International Journal of Environmental Research and Public Health 10(4):1489-1504.
Health Outcome(s):	sick building syndrome
Reported Health Effect(s):	The statistical analysis considers all subjective self-reported symptoms together (not segregated by health outcome) as a group health outcome –sick building syndrome. The study compared two conditions for each studied chemical: combined self-reported symptoms to no symptoms. Therefore, only one form 3 was completed.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1938385

Domain	Metric	Rating	Comments
Additional Comments:	Concentrations of VOCs (including 1,2-dichloroethane), HCHO, and NO2 were measured in the 59 homes of families that agreed to participate after being informed of the nature of the study. Participants completed questionnaires asking about symptoms since they moved into the homes and the concentrations of selected compounds were compared among men and women reporting any symptoms vs no symptoms. Concentrations of 1,2-dichloroethane in homes of people with symptoms were higher than in homes without. p-Dichlorobenzene was measured in the homes as well, but median concentration was <DL and no further analysis was made. Unacceptable due to selection bias, lack of confounding control, inadequate outcome characterization, and lack of temporality.		

Overall Quality Determination — Uninformative

* No biomarkers were identified for this evaluation.

Study Citation:	Kernan, G.J., Ji, B.T., Dosemeci, M., Silverman, D.T., Balbus, J., Zahm, S.H. (1999). Occupational risk factors for pancreatic cancer: A case-control study based on death certificates from 24 U.S. states. American Journal of Industrial Medicine 36(2):260-270.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Death from pancreatic cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	194820

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	The National Cancer Institute, National Institute of Occupational Safety and Health, and the National Center for Health Statistics reviewed death certificates from 24 states to select cases from those that had died from pancreatic cancer and matched controls. Controls with cause of death related to the outcome of interest (i.e. pancreatic diseases) were excluded from the study. All key elements of the study design were reported.
	Metric 2:	Attrition	Medium	There was no direct evidence of subject loss or exclusion of subgroups from analyses. The authors provide the total number of cases and controls in the analysis. Case and control data were taken from a registry. It can be assumed that the data are complete for each subject.
	Metric 3:	Comparison Group	High	Controls were selected from the same pool of death certificates from 24 states that cases were selected from. Controls with cause of death related to the outcome of interest were eliminated. Differences in baseline characteristics were controlled for via matching, stratification, and adjustment.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure was assessed via occupation and industry data on death certificates. A job matrix was further applied to assess the likely levels of exposure. Probability and intensity of exposure were estimated across four levels for each occupation. Only employment captured on the death certificate could be considered. The exposure assessment needs exposure information before the job listed on the death certificates.
	Metric 5:	Exposure Levels	Medium	The study offers 4 levels of estimated probability and intensity of exposure (referent, low, medium, high).
	Metric 6:	Temporality	Medium	Exposure was determined by occupational and industry codes on death certificates and indicate that exposure would precede disease, however, the timing and latency period is less clear.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Causes of mortality were determined from death certificates for both cases and controls. Death certificates were drawn from death registries of participating states (n=24). Causes of death were coded using ICD-9 codes, and pancreatic cancer was identified as ICD 157.
	Metric 8:	Reporting Bias	Medium	Measured outcomes, effect estimates and confidence intervals are reported. Number of exposed cases is reported for each analysis, however the number of controls (exposed and unexposed) are not reported for analyses.

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Study Citation:	Kernan, G.J., Ji, B.T., Dosemeci, M., Silverman, D.T., Balbus, J., Zahm, S.H. (1999). Occupational risk factors for pancreatic cancer: A case-control study based on death certificates from 24 U.S. states. American Journal of Industrial Medicine 36(2):260-270.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Death from pancreatic cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	194820

Domain	Metric		Rating	Comments
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Medium	Potential confounders were accounted for in the following ways: matching (five year age group, state, race, and gender); adjustment in models (age, marital status, metropolitan, and residential status); and stratification (race and gender). Smoking was not included as a confounder.
	Metric 10:	Covariate Characterization	Medium	Data used to assess potential confounders was derived from death certificates, an adequate measure. However, no information about cigarette smoking and other lifestyle factors were available for adjustment in the analysis.
	Metric 11:	Co-exposure Counfounding	Medium	The variety of industries considered in the analysis diminishes concerns about co-exposures.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The case-control study design and statistical analysis methods were appropriate to assess the exposures/outcome of interest.
	Metric 13:	Statistical Power	Medium	This study had an adequate sample size to detect an effect (n for cases = 63,097; n for controls = 252,386).
	Metric 14:	Reproducibility of Analyses	Medium	The description of analysis was sufficient and would be reproducible.
	Metric 15:	Statistical Analysis	High	The model to calculate risk estimates was transparent.

Additional Comments: This case-control study examined the risk of death from pancreatic cancer in different occupational settings. Exposure was solely assessed using occupation/industry at time of death (reported on death certificate) and the application of a job matrix assessing likely levels of exposure for different positions. This means of estimating exposure may not fully represent a participant's exposure history. Additionally, the number of impacted participants (exposed cases) was inadequate to perform quality analyses for some exposure levels.

Overall Quality Determination High

* No biomarkers were identified for this evaluation.

Study Citation:	Kernan, G.J., Ji, B.T., Dosemeci, M., Silverman, D.T., Balbus, J., Zahm, S.H. (1999). Occupational risk factors for pancreatic cancer: A case-control study based on death certificates from 24 U.S. states. American Journal of Industrial Medicine 36(2):260-270.
Health Outcome(s):	Endocrine
Reported Health Effect(s):	Death from pancreatic cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	194820

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	The National Cancer Institute, National Institute of Occupational Safety and Health, and the National Center for Health Statistics reviewed death certificates from 24 states to select cases from those that had died from pancreatic cancer and matched controls. Controls with cause of death related to the outcome of interest (i.e. pancreatic diseases) were excluded from the study. All key elements of the study design were reported.
	Metric 2:	Attrition	Medium	There was no direct evidence of subject loss or exclusion of subgroups from analyses. The authors provide the total number of cases and controls in the analysis. Case and control data were taken from a registry. It can be assumed that the data are complete for each subject.
	Metric 3:	Comparison Group	High	Controls were selected from the same pool of death certificates from 24 states that cases were selected from. Controls with cause of death related to the outcome of interest were eliminated. Differences in baseline characteristics were controlled for via matching, stratification, and adjustment.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Exposure was assessed via occupation and industry data on death certificates. A job matrix was further applied to assess the likely levels of exposure. Probability and intensity of exposure were estimated across four levels for each occupation. Only employment captured on the death certificate could be considered. The exposure assessment needs exposure information before the job listed on the death certificates.
	Metric 5:	Exposure Levels	Medium	The study offers 4 levels of estimated probability and intensity of exposure (referent, low, medium, high).
	Metric 6:	Temporality	Medium	Exposure was determined by occupational and industry codes on death certificates and indicate that exposure would precede disease, however, the timing and latency period is less clear.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Causes of mortality were determined from death certificates for both cases and controls. Death certificates were drawn from death registries of participating states (n=24). Causes of death were coded using ICD-9 codes, and pancreatic cancer was identified as ICD 157.
	Metric 8:	Reporting Bias	Medium	Measured outcomes, effect estimates and confidence intervals are reported. Number of exposed cases is reported for each analysis, however the number of controls (exposed and unexposed) are not reported for analyses.
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Kernan, G.J., Ji, B.T., Dosemeci, M., Silverman, D.T., Balbus, J., Zahm, S.H. (1999). Occupational risk factors for pancreatic cancer: A case-control study based on death certificates from 24 U.S. states. American Journal of Industrial Medicine 36(2):260-270.
Health Outcome(s):	Endocrine
Reported Health Effect(s):	Death from pancreatic cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	194820

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Medium	Potential confounders were accounted for in the following ways: matching (five year age group, state, race, and gender); adjustment in models (age, marital status, metropolitan, and residential status); and stratification (race and gender). Smoking was not included as a confounder.
	Metric 10:	Covariate Characterization	Medium	Data used to assess potential confounders was derived from death certificates, an adequate measure. However, no information about cigarette smoking and other lifestyle factors were available for adjustment in the analysis.
	Metric 11:	Co-exposure Counfounding	Medium	The variety of industries considered in the analysis diminishes concerns about co-exposures.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The case-control study design and statistical analysis methods were appropriate to assess the exposures/outcome of interest.
	Metric 13:	Statistical Power	Medium	This study had an adequate sample size to detect an effect (n for cases = 63,097; n for controls = 252,386).
	Metric 14:	Reproducibility of Analyses	Medium	The description of analysis was sufficient and would be reproducible.
	Metric 15:	Statistical Analysis	High	The model to calculate risk estimates was transparent.

Additional Comments: This case-control study examined the risk of death from pancreatic cancer in different occupational settings. Exposure was solely assessed using occupation/industry at time of death (reported on death certificate) and the application of a job matrix assessing likely levels of exposure for different positions. This means of estimating exposure may not fully represent a participant's exposure history. Additionally, the number of impacted participants (exposed cases) was inadequate to perform quality analyses for some exposure levels.

Overall Quality Determination High

* No biomarkers were identified for this evaluation.

Study Citation:	Niehoff, N.M., Gammon, M.D., Keil, A.P., Nichols, H.B., Engel, L.S., Sandler, D.P., White, A.J. (2019). Airborne mammary carcinogens and breast cancer risk in the Sister Study. Environment International 130:104897.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Breast cancer diagnosis (overall), tumor characteristics, and estrogen receptor positive (ER+) invasive breast cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5440630

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	Data from the Sister Study were used. The Sister Study is "a prospective cohort of 50,884 women from across the US who were ages 35–74 at enrollment (Sandler et al., 2017). Participants were recruited from 2003 to 2009 using a national advertising campaign in English and Spanish. Women were eligible for the Sister Study if they had a sister who had been diagnosed with breast cancer, but no prior breast cancer themselves."Exclusions from the study occurred for the following reasons:-breast cancer diagnosed before enrollment was complete, or did not have follow-up information (n = 163)-Residential address couldn't be geocoded (n = 1003, < 2%) - This is a small perecentage, but all of those who were excluded for this reason were from Puerto Rico, West Virginia, Missouri, or Oklahoma.Key elements of the study design are reported. There is some potential for selection bias, but based on the small percentage of those eligible who were excluded, participation was not likely to be substantially biased.
	Metric 2:	Attrition	High	Response rates in the overall Sister study remained over 91% over follow-up. Reasons for non-response were not reported, and characteristics of those lost to follow up were not reported or compared with those included, but 9% loss to follow-up is minimal.
	Metric 3:	Comparison Group	High	Differences in baseline characteristics of groups were considered as potential confounding variables.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	The EPA NATA database of census-tract level modeled air toxics data was used. The study authors note the potential for exposure misclassification: "Concentrations at the census tract level do not fully account for variation in an individual's daily activities that could lead to higher or lower exposure, and all women within a census tract are assigned the same concentration."
	Metric 5:	Exposure Levels	Medium	There were five quintiles of exposure, so there was a sufficient range and distribution of exposure.
	Metric 6:	Temporality	Medium	This is a prospective cohort study.Exposure data from 2005 were chosen because they represented the middle of the enrollment period (2003-2009).The study reported that "94% of women enrolled in 2005 or later, and thus the exposure assessment primarily predated enrollment for the majority of Sister Study participants."The six percent of women who had the potential to have the outcome before exposure was measured in 2005 are a concern. But sensitivity analyses were used to assess whether the associations changed when restricted to those who enrolled in 2005 or later.The authors note that the study is making assumptions about the relevant exposure windows - therefore the exposure window is not certain.

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Study Citation:	Niehoff, N.M., Gammon, M.D., Keil, A.P., Nichols, H.B., Engel, L.S., Sandler, D.P., White, A.J. (2019). Airborne mammary carcinogens and breast cancer risk in the Sister Study. Environment International 130:104897.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Breast cancer diagnosis (overall), tumor characteristics, and estrogen receptor positive (ER+) invasive breast cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5440630

Domain	Metric		Rating	Comments
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	High	Women who reported a breast cancer diagnosis on the annual health updates or follow-up questionnaires were asked to provide additional diagnosis information, and to grant permission for the study to obtain medical records and pathology reports. Medical records were obtained for 81% of breast cancer diagnoses. Agreement between self-reported breast cancers and medical records was high (positive predictive value > 99%) (Sandler et al., 2017), so self-report was used when medical records were not available. Tumor characteristics (stage; histology; and estrogen receptor (ER) status) were abstracted from medical records, or self-reported.
	Metric 8:	Reporting Bias	High	A description of measured outcomes is reported. Effect estimates are reported with confidence intervals.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	Covariates considered included age, race, BMI, residence type, education, and smoking status. Potential confounders were identified using DAGs and literature review. Appropriate considerations were made for potential confounders.
	Metric 10:	Covariate Characterization	Medium	”Most covariates were assessed by self-report at the baseline interview.””At baseline, women completed a computer-assisted telephone interview and written questionnaires.”Previous publications might describe whether the questionnaires were validated, but validation was not specified in this publication.
	Metric 11:	Co-exposure Counfounding	Medium	Co-exposures to other air pollutants were assessed, but at the census tract level.Multipollutant classification trees were used, which might provide useful qualitative information.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	The study design (large prospective cohort) and analysis method (Cox proportional hazard single and multi-pollutant models accounting for potential confounders) were appropriate to assess the association between exposure and disease.
	Metric 13:	Statistical Power	Medium	The study had an adequate sample size (1975 cancer cases) and follow-up time (mean=8.4 years).
	Metric 14:	Reproducibility of Analyses	Medium	The description of the analysis is sufficient to be conceptually reproducible.

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Study Citation:	Niehoff, N.M., Gammon, M.D., Keil, A.P., Nichols, H.B., Engel, L.S., Sandler, D.P., White, A.J. (2019). Airborne mammary carcinogens and breast cancer risk in the Sister Study. Environment International 130:104897.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	Breast cancer diagnosis (overall), tumor characteristics, and estrogen receptor positive (ER+) invasive breast cancer
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	5440630

Domain	Metric	Rating	Comments
	Metric 15: Statistical Analysis	High	Hazard ratios and 95% confidence intervals (CIs) are reported "comparing index categories of exposure to exposures below the first quintile using Cox proportional hazards regression, with age as the time scale." The method of calculating the hazard ratios is transparent. The authors reported that "the proportional hazards assumption was evaluated by conducting a Wald test for an interaction between the continuous form of the air toxic measure and time." Censoring times and times at-risk are described.

Additional Comments: This was a well-conducted study of a large prospective cohort, but the measurement of exposure at the census-tract rather than the individual level is a limitation.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Sobel, W., Bond, G.G., Skowronski, B.J., Brownson, P.J., Cook, R.R. (1987). A soft tissue sarcoma case control study in a large multi-chemical manufacturing facility. Chemosphere 16(8-9):2095-2099.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	soft-tissue sarcoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1357737

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	From a pool of > 37,000 subjects who worked at least 1 year at chemical company between January 1940-December 1979, the study identified 14 people who died due to soft-cell sarcoma (via death certificate, medical records, or histopathology report). Referents were matched 9:1 with cases (126 matched controls).
	Metric 2:	Attrition	High	There was minimal subject exclusion from the analysis sample; one case could not be matched to controls and was excluded from analysis.
	Metric 3:	Comparison Group	High	Cases and controls were recruited from the same eligible population within the same time frame and matched on sex, race, year of birth and year of hire. Both cases and controls had to have worked ≥1 yr at the plant during the study period.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Work histories for cases and referents were coded to determine an individual's potential exposure to chemical of interest and reviewed by an industrial hygienist blinded to case status.
	Metric 5:	Exposure Levels	Low	Exposure was considered dichotomous, ever exposed or never exposed. There is no quantitative information on exposure levels or range of exposures.
	Metric 6:	Temporality	Low	Temporality of exposure and outcome is established. It is unclear if the interval between exposure and outcome is sufficient for soft tissue sarcoma outcomes.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	The soft-tissue sarcoma outcome was assessed by information provided by death certificates, medical records, and histopathology reports, but study authors did not report the proportions determined by each method.
	Metric 8:	Reporting Bias	High	All outcomes outlined were reported. Authors reported the number of cases and controls in the table. Maximum likelihood estimate ORs with respective 95 % confidence intervals were reported.
Domain 4: Potential Confounding / Variability Control				

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Study Citation:	Sobel, W., Bond, G.G., Skowronski, B.J., Brownson, P.J., Cook, R.R. (1987). A soft tissue sarcoma case control study in a large multi-chemical manufacturing facility. Chemosphere 16(8-9):2095-2099.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	soft-tissue sarcoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1357737

Domain	Metric		Rating	Comments
	Metric 9:	Covariate Adjustment	Low	Controls were matched with cases on age, sex, year of hire and survival information. There is indirect evidence that the considerations were made to identify potential confounders through evaluation of medical records of cases and controls (various heritable syndromes, family history of cancer, history of lymphedema, steroids, throrotrast, foreign body implants, chronic extensive scarring, radiation therapy, and immunological defects). Identified confounders between cases and controls were not reported and it is unclear if adjustments for these confounders were included in the final analyses.
	Metric 10:	Covariate Characterization	High	Potential covariates were assessed through evaluation of work histories and medical records.
	Metric 11:	Co-exposure Counfounding	Low	The study documented 13 chemicals, known to be associated with soft-tissue sarcoma (according to NTP, 1983) that were used at the manufacturing facility at some point since 1940. The authors note that some individuals were exposed to multiple chemicals during their employment history and were counted multiple times in the analysis for different chemical exposures. Co-exposures to chemicals to not appear to be adjusted for in analysis.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Low	The study design was adequate to assess the association between exposure and the outcome of interest (soft-tissue sarcoma). The study authors noted they used programs developed by Rothman and Boice to calculate odds ratios with CI intervals; the statistical methods are not further described. The page containing the Rothman and Boice reference appears to be missing from the PDF (or the citation is missing).
	Metric 13:	Statistical Power	Low	Statistical power was not calculated. For 1,2-dichloroethane, there was one case and 6 controls included in the analysis, which was not adequate to detect and effect.
	Metric 14:	Reproducibility of Analyses	Low	The study calculated odd ratios, and 95% CIs were calculated using point estimates and chi from hypothesis testing. The study authors noted they used programs developed by Rothman and Boice to calculate odds ratios with 95% CIs; the statistical methods are not further described and there was no reference for the programs cited.
	Metric 15:	Statistical Analysis	Low	A description of analyses/assumptions was not reported.

Additional Comments: A case-control study of workers at a chemical production facility who worked at least 1 year between January 1940-December 1979 (n=37,000) investigated the incidence of deaths due to soft-tissue sarcoma. The study identified 14 people who died due to soft-tissue sarcoma (through death certificate, medical records, or histopathology reports). Cases were matched to controls based on sex, race, year of birth and year of hire. 13 chemicals, including 1,2-dichloroethane, associated with soft-tissue sarcoma were used at the facility; it does not appear that co-exposures were adjusted for in the analysis. Odds ratios and corresponding CIs were calculated. No significant association was found between exposure to 1,2-DCE and soft-tissue sarcoma.

Overall Quality Determination Medium

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Study Citation:	Sobel, W., Bond, G.G., Skowronski, B.J., Brownson, P.J., Cook, R.R. (1987). A soft tissue sarcoma case control study in a large multi-chemical manufacturing facility. Chemosphere 16(8-9):2095-2099.
Health Outcome(s):	Cancer/Carcinogenesis
Reported Health Effect(s):	soft-tissue sarcoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1357737

Domain	Metric	Rating	Comments

* No biomarkers were identified for this evaluation.

Study Citation:	Sobel, W., Bond, G.G., Skowronski, B.J., Brownson, P.J., Cook, R.R. (1987). A soft tissue sarcoma case control study in a large multi-chemical manufacturing facility. Chemosphere 16(8-9):2095-2099.
Health Outcome(s):	Skin and Connective Tissue
Reported Health Effect(s):	soft-tissue sarcoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1357737

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	High	From a pool of > 37,000 subjects who worked at least 1 year at chemical company between January 1940-December 1979, the study identified 14 people who died due to soft-cell sarcoma (via death certificate, medical records, or histopathology report). Referents were matched 9:1 with cases (126 matched controls).
	Metric 2:	Attrition	High	There was minimal subject exclusion from the analysis sample; one case could not be matched to controls and was excluded from analysis.
	Metric 3:	Comparison Group	High	Cases and controls were recruited from the same eligible population within the same time frame and matched on sex, race, year of birth and year of hire. Both cases and controls had to have worked ≥1 yr at the plant during the study period.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Medium	Work histories for cases and referents were coded to determine an individual's potential exposure to chemical of interest and reviewed by an industrial hygienist blinded to case status.
	Metric 5:	Exposure Levels	Low	Exposure was considered dichotomous, ever exposed or never exposed. There is no quantitative information on exposure levels or range of exposures.
	Metric 6:	Temporality	Low	Temporality of exposure and outcome is established. It is unclear if the interval between exposure and outcome is sufficient for soft tissue sarcoma outcomes.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	The soft-tissue sarcoma outcome was assessed by information provided by death certificates, medical records, and histopathology reports, but study authors did not report the proportions determined by each method.
	Metric 8:	Reporting Bias	High	All outcomes outlined were reported. Authors reported the number of cases and controls in the table. Maximum likelihood estimate ORs with respective confidence intervals were reported.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	Low	Controls were matched with cases on age, sex, year of hire and survival information. There is indirect evidence that that considerations were made to identify potential confounders through evaluation of medical records of cases and controls (various heritable syndromes, family history of cancer, history of lymphedema, steroids, throrotrast, foreign body implants, chronic extensive scarring, radiation therapy, and immunological defects). Identified confounders between cases and controls were not reported and it is unclear if adjustments for these confounders were included in the final analyses.

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Study Citation:	Sobel, W., Bond, G.G., Skowronski, B.J., Brownson, P.J., Cook, R.R. (1987). A soft tissue sarcoma case control study in a large multi-chemical manufacturing facility. Chemosphere 16(8-9):2095-2099.
Health Outcome(s):	Skin and Connective Tissue
Reported Health Effect(s):	soft-tissue sarcoma
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	No linked references.
HERO ID:	1357737

Domain	Metric		Rating	Comments
	Metric 10:	Covariate Characterization	High	Potential covariates were assessed through evaluation of work histories and medical records.
	Metric 11:	Co-exposure Counfounding	Low	The study documented 13 chemicals, known to be associated with soft-tissue sarcoma (according to NTP, 1983) that were used at the manufacturing facility at some point since 1940. The authors note that some individuals were exposed to multiple chemicals during their employment history and were counted multiple times in the analysis for different chemical exposures. Co-exposures to chemicals to not appear to be adjusted for in analysis.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	Low	The study design was adequate to assess the association between exposure and the outcome of interest (soft-tissue sarcoma). The study authors noted they used programs developed by Rothman and Boice to calculate odds ratios with (95% CIs; the statistical methods are not further described. The page containing the Rothman and Boice reference appears to be missing from the PDF (or the citation is missing).
	Metric 13:	Statistical Power	Low	Statistical power was not calculated. For 1,2-dichloroethane, there was one case and 6 controls included in the analysis, which was not adequate to detect and effect.
	Metric 14:	Reproducibility of Analyses	Low	The study calculated odd ratios, and 95% CIs were calculated using point estimates and chi from hypothesis testing. The study authors noted they used programs developed by Rothman and Boice to calculate odds ratios with CI intervals; the statistical methods are not further described and there was no reference for the programs cited.
	Metric 15:	Statistical Analysis	Low	A description of analyses/assumptions was not reported.

Additional Comments: A case-control study of workers at a chemical production facility who worked at least 1 year between January 1940-December 1979 (n=37,000) investigated the incidence of deaths due to soft-tissue sarcoma. The study identified 14 people who died due to soft-tissue sarcoma (through death certificate, medical records, or histopathology reports). Cases were matched to controls based on sex, race, year of birth and year of hire. 13 chemicals, including 1,2-dichloroethane, associated with soft-tissue sarcoma were used at the facility; it does not appear that co-exposures were adjusted for in the analysis. Odds ratios and corresponding CIs were calculated. No significant association was found between exposure to 1,2-DCE and soft-tissue sarcoma.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.

Study Citation:	Teta, M. J., Ott, M. G., Schnatter, A. R. (1991). An update of mortality due to brain neoplasms and other causes among employees of a petrochemical facility. Journal of Occupational Medicine 33(1):45-51.
Health Outcome(s):	Mortality
Reported Health Effect(s):	all cause mortality, gastrointestinal cancer mortality, respiratory system cancer mortality, kidney and other urinary organ cancer mortality, skin cancer mortality, brain cancer mortality, lymphatic and hematopoietic tissue cancer mortality, benign neoplasm mortality, heart disease mortality, and liver cirrhosis mortality.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200633, 1629047
HERO ID:	200633

Domain	Metric		Rating	Comments
Domain 1: Study Participation				
	Metric 1:	Participant Selection	Medium	The facility was described in some detail. All male employees working for one day or more between 1941 and 1983 were included. There may be some healthy worker effect in this population.
	Metric 2:	Attrition	High	Study authors reported that vital status was complete for 99% of the population, and death certificates were obtained for 99% of decedents.
	Metric 3:	Comparison Group	High	SMRs were calculated using age-, race-, and calendar year-specific mortality rates of males in the United States. All included employees were male.
Domain 2: Exposure Characterization				
	Metric 4:	Measurement of Exposure	Low	All employees were treated as exposed. Table 4 indicates that relatively few employees were employed in areas designated as 1,2-DCA work areas. There is potential for substantial exposure misclassification.
	Metric 5:	Exposure Levels	Low	All employed individuals were categorized as exposed, and the reference population was described as unexposed. This represents two levels of exposure. The distribution of exposure within the employed population is unclear.
	Metric 6:	Temporality	Medium	Employees were followed from 1950 (or date of first hire) through 1983. The relevant timing of exposure is not entirely clear; however, this represents a sufficiently long period of follow-up.
Domain 3: Outcome Assessment				
	Metric 7:	Outcome Measurement or Characterization	Medium	Mortality was tracked using company records, Social Security Administration records, and the National Death Index. Specific ICD codes and use of a nosologist were not described, but there was no evidence to suggest the method had poor validity.
	Metric 8:	Reporting Bias	High	SMRs were provided with confidence intervals in addition to observed and expected cases. The authors state they did not carry out regional specific SMRs due to the higher prevalence of neoplasms in the surrounding area.
Domain 4: Potential Confounding / Variability Control				
	Metric 9:	Covariate Adjustment	High	SMRs were restricted to males. Rates were age-, race-, and calendar period-specific. No consideration was made for smoking.
	Metric 10:	Covariate Characterization	Medium	Demographic information was obtained from employment records. This was not a validated method, but there was no evidence to suggest it was an invalid method.

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Study Citation:	Teta, M. J., Ott, M. G., Schnatter, A. R. (1991). An update of mortality due to brain neoplasms and other causes among employees of a petrochemical facility. Journal of Occupational Medicine 33(1):45-51.
Health Outcome(s):	Mortality
Reported Health Effect(s):	all cause mortality, gastrointestinal cancer mortality, respiratory system cancer mortality, kidney and other urinary organ cancer mortality, skin cancer mortality, brain cancer mortality, lymphatic and hematopoietic tissue cancer mortality, benign neoplasm mortality, heart disease mortality, and liver cirrhosis mortality.
Chemical:	1,1-Dichloroethane- Isomer: 1,2-Dichloroethane
Linked HERO ID(s):	200633, 1629047
HERO ID:	200633

Domain	Metric		Rating	Comments
	Metric 11:	Co-exposure Counfounding	Low	Several other occupational exposures linked to cancer mortality were present, including vinyl chloride, butanol, and other petrochemicals.
Domain 5: Analysis				
	Metric 12:	Study Design and Methods	High	This study design was appropriate for the research question. Authors utilized retrospective occupational cohort data to determine standardized mortality rates for cancer-specific mortalities.
	Metric 13:	Statistical Power	Medium	While power was not calculated, there were over 1350 deaths from 7849 employees which was adequate to detect robust effect estimates.
	Metric 14:	Reproducibility of Analyses	Low	Most details were provided; however, ICD codes used to determine and group cancer mortality diagnoses were not provided.
	Metric 15:	Statistical Analysis	High	No issues identified.

Additional Comments: This study utilized an occupational cohort to retrospectively evaluate elevated rates of cancer mortality among petrochemical plant workers. There were numerous potentially hazardous chemicals mentioned in the plant description which may lead to co-exposure. Additionally, it appears that only a moderate portion of workers may have been exposed to 1,2-DCA or worked in 1,2-DCA areas which may lead to some exposure misclassification and limit the study's ability to inform hazard on 1,2-DCA.

Overall Quality Determination Medium

* No biomarkers were identified for this evaluation.