America's Children and the Environment, Third Edition

DRAFT Indicators

Health: Childhood Cancer

EPA is preparing the third edition of *America's Children and the Environment* (ACE3), following the previous editions published in December 2000 and February 2003. ACE is EPA's compilation of children's environmental health indicators and related information, drawing on the best national data sources available for characterizing important aspects of the relationship between environmental contaminants and children's health. ACE includes four sections: Environments and Contaminants, Biomonitoring, Health, and Special Features.

EPA has prepared draft indicator documents for ACE3 representing 23 children's environmental health topics and presenting a total of 42 proposed children's environmental health indicators. This document presents the draft text, indicators, and documentation for the childhood cancer topic in the Health section.

For more information on America's Children and the Environment, please visit www.epa.gov/ace. For instructions on how to submit comments on the draft ACE3 indicators, please visit www.epa.gov/ace/ace3drafts/.

Childhood Cancer

Childhood cancer is not a single disease, but includes a variety of malignancies in which abnormal cells divide in an uncontrolled manner. These cancer cells can invade nearby tissues and can migrate by way of the blood or lymph systems to other parts of the body.[1] The forms of cancer that are most common vary according to age. The most common childhood cancers are leukemias (cancer of the white blood cells) and cancers of the brain or central nervous system, which together account for more than half of childhood cancers.[2]

Cancer in childhood is quite rare compared with cancer in adults, but it still causes more deaths than any factor, other than injuries, among children from infancy to age 15 years.[2] The annual incidence of childhood cancer has increased slightly over the last 30 years; however, mortality has declined significantly for many cancers due largely to improvements in treatments.[2] The causes of the increased incidence are not fully understood, but the changes have been too rapid to be explained by genetics and too steady to be explained by the introduction of better diagnostic techniques, which would be expected to cause a one-time spike in rates. The proportion of this increase caused by environmental factors has yet to be determined.[3]

The causes of cancer in children are poorly understood, though in general it is thought that different forms of cancer have different causes. According to scientists at the National Cancer Institute, established risk factors for the development of childhood cancer include family history, specific genetic syndromes (such as Down syndrome), radiation, and certain pharmaceutical agents used in chemotherapy.[3] Ionizing radiation, from sources such as x-rays, is a known cause of leukemia and brain tumors.[4-6] A recent review found that there is an approximately 40% increased risk of childhood leukemia and other cancers after maternal exposure to ionizing radiation during pregnancy.[7] A number of studies suggest that other environmental contaminants may play a role in the development of childhood cancers. The majority of these studies have focused on pesticides and solvents, such as benzene. According to the President's Cancer Panel, "the true burden of environmentally induced cancer has been grossly underestimated."[8] Newer research is also suggesting that childhood cancer may be caused by a combination of genetic predisposition and environmental exposure.[9-11]

Leukemia is the most common form of cancer in children. According to the Centers for Disease Control and Prevention (CDC), adults and children who undergo chemotherapy and radiation therapy for cancer treatment, take immune suppressing drugs, or have certain genetic conditions, such as Down syndrome, are at a higher risk of developing acute leukemia.[12] Ionizing radiation from sources such as x-rays is a known cause of leukemia.[4-6] Confirmed causal factors explain less than 10% of the incidence of childhood leukemia, meaning that the cause is unknown in at least 90% of leukemia cases.[7] A review of the literature concludes that there is strong evidence for an association between paternal exposure to solvents—including benzene, carbon tetrachloride, and trichloroethylene—and childhood leukemias.[13-16] A wealth of evidence suggests a link between parental, prenatal, and childhood exposures to pesticides and childhood leukemia, including a meta-analysis of 31 studies, which found a significant association between childhood leukemia and prenatal maternal occupational pesticide exposure.[14,17-26] Finally,

growing literature has suggested an association between childhood exposures to hazardous air pollutants and leukemia.[27-29] A recent study exploring the relationship between childhood leukemia and hazardous air pollutants (HAPs) found an increased risk for childhood leukemia in census tracts where children were exposed to a group of 25 potentially carcinogenic HAPs, as well as in census tracts ranked highest for point-source HAP exposure.[28] Several other studies have found associations between leukemia and surrogate measures of exposure to motor vehicle exhaust, including traffic density and vehicle density.[7,30-32] However, other studies conducted in California and Denmark did not find an association between these proxy measures of motor vehicle exhaust and childhood leukemia,[33-36] and review studies have concluded that the overall evidence of possible relationship is inconclusive.[7,37] According to the U.S. Surgeon General, there is suggestive evidence that prenatal and postnatal exposure to environmental tobacco smoke can lead to leukemia in children.[38]

Cancers of the nervous system, including brain tumors, are also one of the relatively common cancers in children. Known risk factors for childhood brain tumors include radiation therapy and certain genetic syndromes, although these factors explain only a small portion of cases.[3] As with childhood leukemias, prenatal exposure to ionizing radiation is a known cause of brain tumors.[5,6] Research also suggests that parental, prenatal, and childhood exposure to pesticides may lead to brain tumors in children.[14,25,26] The U.S. Surgeon General has concluded that there is suggestive evidence linking prenatal and postnatal exposure to environmental tobacco smoke and childhood brain tumors.[38]

Lymphomas, which affect a child's lymph system, are another relatively common form of childhood cancer. The cause of most cases of childhood lymphoma is unknown; however, it is clear that children with compromised immune systems are at a greater risk of developing lymphomas.[3] Extensive review studies have found suggestive associations between parental, prenatal, and childhood exposure to pesticides and childhood lymphomas.[14,26] According to the U.S. Surgeon General, there is suggestive evidence that prenatal and postnatal exposure to environmental tobacco smoke can lead to childhood lymphomas.[38]

Other childhood cancers with identified associations to environmental contaminants include thyroid cancer, Wilms' tumor (a type of kidney cancer), and Ewing's sarcoma (a cancer of the bone or soft tissue). An increased risk of thyroid cancer in children has been linked to ionizing radiation exposure.[39-41] Much of the evidence for this association comes from studies of individuals in areas with high ionizing radiation exposure due to the Chernobyl accident in eastern Europe. There is limited research indicating that exposure to pesticides may be a causal factor in the development of Wilms' tumor and Ewing's sarcoma in children.[19,26,42] The only known causal factors for Wilms' tumor and Ewing's sarcoma are certain birth defects and genetic conditions.

The development of cancer, or carcinogenesis, is a multistep process leading to the uncontrolled growth and division of cells. This process can begin when an individual's DNA is damaged. Ionizing radiation can initiate carcinogenesis directly by causing damage to DNA, or indirectly by forming DNA-damaging free radicals—highly reactive atoms or molecules with unpaired electrons.[40] Pesticides can similarly damage DNA, but they may also lead to childhood cancer by

affecting immune system regulation, or by mimicking estrogen or disrupting hormone activity in other ways.[19] Pesticides, solvents, and other chemicals may cause mutations in parents' reproductive cells that increase the risk of their children developing certain cancers, or parental exposure may affect the child directly while in utero.[15,42]

This section presents indicators of cancer incidence and mortality for children ages 0 to 19 years for the period of 1992–2007 (Indicator D5) and the cancer incidence, by cancer type, for children ages 0 to 19 years for the period of 1992–2007 (Indicator D6). Changes in childhood cancer mortality are most likely reflective of changes in treatment options, rather than environmental exposures. However, showing childhood cancer mortality rates in conjunction with childhood cancer incidence rates highlights the severity of childhood cancer and provides information on the proportion of children that survive.

Indicator D5 provides an indication of broad trends in childhood cancer over time, while Indicator D6 provides more detailed information about the incidence of specific types of cancer in children.

Indicator D5: Cancer incidence and mortality for children ages 0 to 19 years, 1992–2007

Indicator D6: Cancer incidence for children ages 0 to 19 years by type, 1992–2006

Overview

Indicators D5 and D6 present information about the number of new childhood cancer cases and the number of deaths caused by childhood cancer. The data come from a national registry that collects information from tumor registries located in specific geographic regions around the country. Indicator D5 shows how the rates of all new childhood cancers and all childhood cancer deaths have changed over time, and Indicator D6 shows how the rates of specific types of childhood cancers have changed over time.

SEER

The National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) Program collects information on cancer incidence, survival, and prevalence from tumor registries located in specific geographic areas. These tumor registries collect information for all tumors within their geographic region. The sample population covered by the SEER tumor registries is comparable to the general U.S. population in terms of poverty and education. However, the population covered by the SEER tumor registries tends to be more urban and has a higher proportion of foreign-born persons compared with the general U.S. population.[43]

Over the years, the SEER program has expanded to include a greater number of tumor registries. Currently, the SEER program includes data from 17 tumor registries, but complete data from all 17 registries exist only for the years 2000–2007. Indicators D5 and D6 were developed using SEER data from 13 different tumor registries that provide data starting in 1992 and sample geographic areas containing 13.8% of the total U.S. population.[44] The SEER data for the 13 longer-established registries, instead of all 17, were used to develop the D5 and D6 indicators because this allowed for more comprehensive trend analysis while still covering a substantial portion of the population.

SEER reports the incidence data by single year of age, but reports mortality data in five age groups for children under the age of 20: under 1 year, 1–4, 5–9, 10–14, and 15–19 years. For this reason, both indicators use SEER data for all children 0 to 19 years of age, in contrast to the other indicators in this report that define children as younger than age 18 years. The indicators begin with data from the year 1992.

Data Presented in the Indicators

Childhood cancer incidence refers to the number of new childhood cancer cases reported for a specified period of time. Childhood cancer incidence is shown in Indicator D5 and Indicator D6

as the number of childhood cancer cases reported per million children for one year. The incidence rate is age-adjusted, meaning that each year's incidence calculation uses the age distribution of children from the year 2000. For example, 25.3% of all U.S. children were between the ages of 5 and 9 years in 2000, and this percentage is assumed to be the same for each year from 1992 to 2007. This age adjustment ensures that differences in cancer rates over time are not simply due to changes in the age composition of the population. Indicator D5 also shows childhood cancer mortality as the number of deaths per million children for each year.

Trends in the total incidence of childhood cancer, as shown by Indicator D5, are useful for assessing the overall burden of cancer among children. However, broad trends mask changes in the frequency of specific types of cancers that often have patterns that diverge from the overall trend. Moreover, environmental factors may be more likely to contribute to some childhood cancers than to others. Indicator D6 highlights patterns for specific types of childhood cancers.

Some types of childhood cancers are very rare, and as such the yearly incidence is particularly low and variable. Due to this fact, Indicator D6 shows the incidence of individual childhood cancers in groupings of three years. Each bar in the graph represents the annual number of cases of that specific cancer diagnosed per million children, calculated as the average number of cases per year divided by the average population of children (in millions) per year for each three-year period.

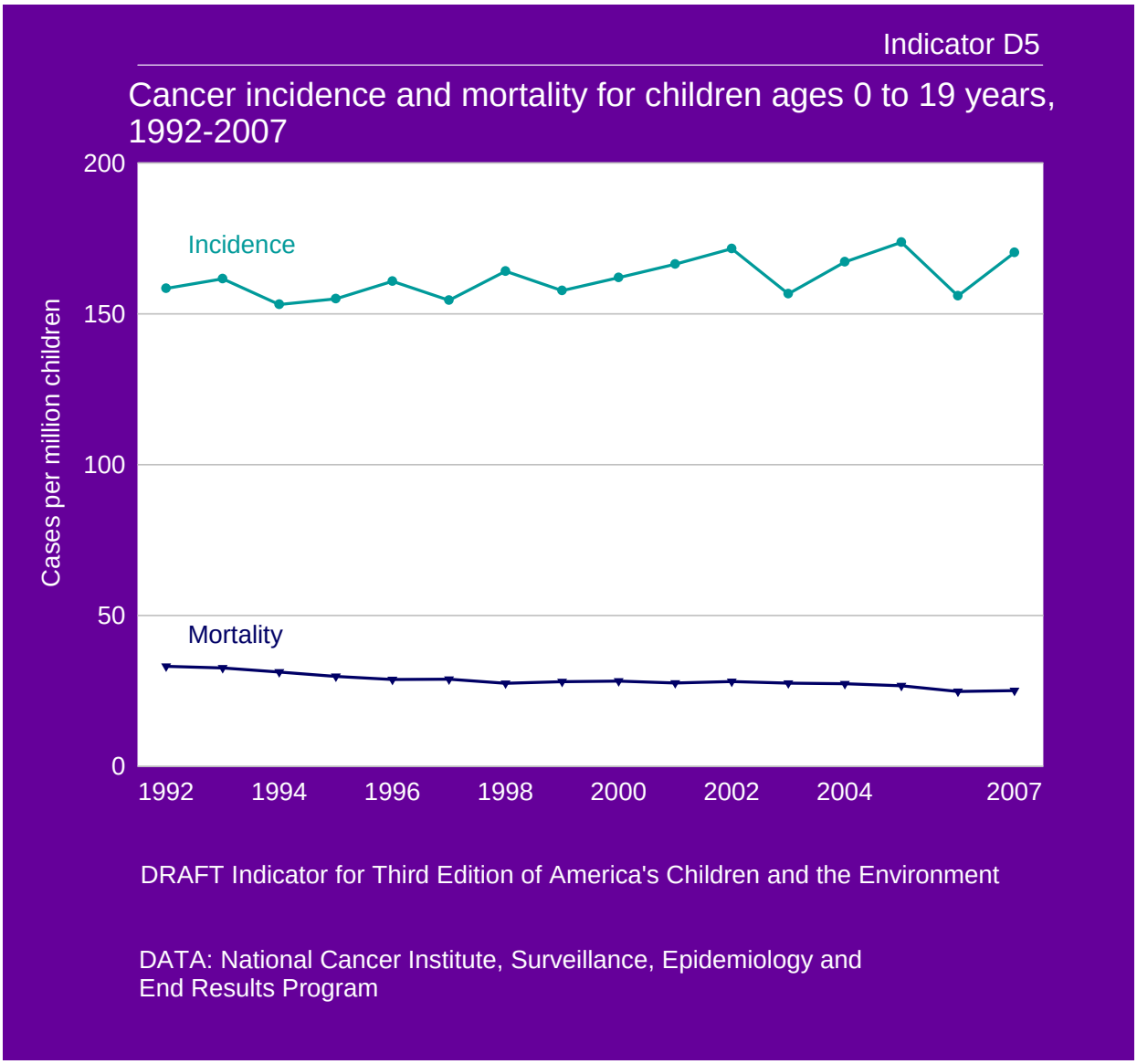
In addition to the data shown in the Indicator D5 graph, supplemental tables show childhood cancer incidence and mortality by race/ethnicity and sex, as well as childhood cancer incidence by age. In addition to the data shown in the Indicator D6 graph, a supplemental table shows childhood cancer incidence by cancer type and age group.

Statistical Testing

Statistical analysis has been applied to the indicators to determine whether any changes in prevalence over time, or any differences in prevalence between demographic groups, are statistically significant. These analyses use a 5% significance level ($p \leq 0.05$), meaning that a conclusion of statistical significance is made only when there is no more than a 5% chance that the observed change over time or difference between demographic groups occurred randomly. It should be noted that when statistical testing is conducted for differences among multiple demographic groups (e.g., considering both race/ethnicity and income level), the large number of comparisons involved increases the probability that some differences identified as statistically significant may actually have occurred randomly. For Indicator D6, the statistical analysis of changes over time for incidence of specific types of cancer uses annual incidence data for each year 1992–2006, rather than the three-year groupings of data shown in the figure.

A finding of statistical significance for a health indicator depends not only on the numerical difference in the value of a reported statistic between two groups, but also on the number of observations in the survey and various aspects of the survey design. For example, if the prevalence of a health effect is different between two groups, the statistical test is more likely to detect a difference when data have been obtained from a larger number of people in those groups. A finding that there is or is not a statistically significant difference in prevalence between

two groups or in prevalence over time is not the only information that should be considered when determining the public health implications of those differences.



- There has been a statistically significant increase in the age-adjusted annual incidence of cancer in children from 158 cases per million children in 1992 to 170 cases per million children in 2007. There has been a statistically significant decrease in cancer mortality from 33 deaths per million children in 1992 to 25 deaths per million children in 2007.

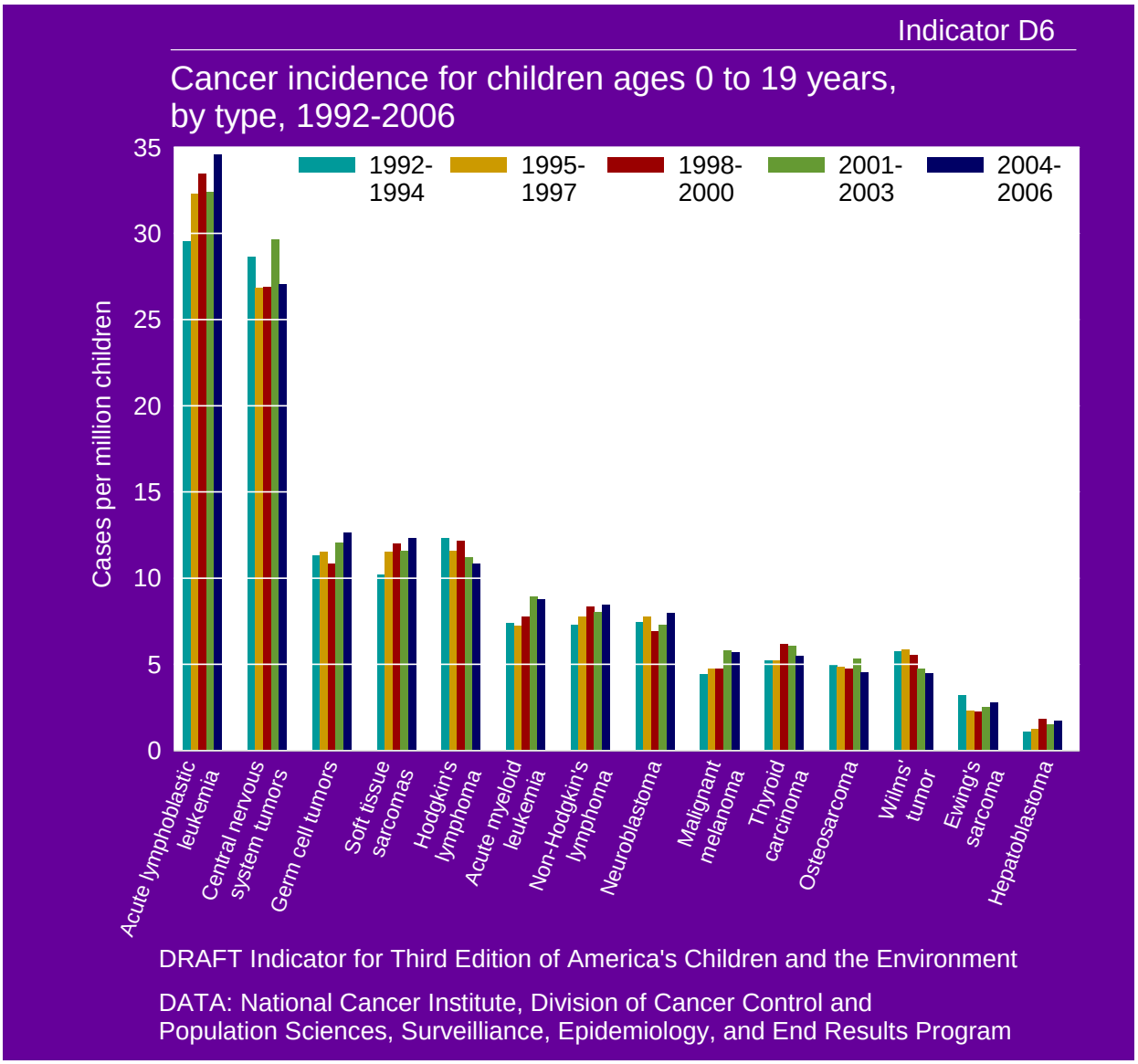
- Childhood cancer incidence and mortality rates vary by sex. In 2005–2007, rates of cancer incidence and mortality for boys were 177 cases per million and 28 deaths per million, compared with 156 cases per million and 23 deaths per million for girls. These sex differences were statistically significant. (See Table D5b.)

- In 2005–2007, childhood cancer incidence was highest among White non-Hispanic children at 188 cases per million. Hispanic children had an incidence rate of 153 cases per million, Asian and Pacific Islander non-Hispanic children had an incidence rate of 145 cases per

million, American Indian and Alaska Native non-Hispanic children had an incidence rate of 134 cases per million, and Black non-Hispanic children had an incidence rate of 127 cases per million. (See Table D5b.)

- Statistical note: The cancer incidence rate for White non-Hispanic children was statistically significantly higher than the rates of each of the other race/ethnicity categories. The cancer incidence rate for Black non-Hispanic children was also statistically significantly lower than the rates for Asian and Pacific Islander non-Hispanic children and Hispanic children. The remaining differences between race/ethnicity groups were not statistically significant.

- Childhood cancer incidence rates vary by age. Rates are highest among infants, decline until age 9, and then rise again with increasing age. In 2005–2007, children under 5 and those of ages 15 to 19 years experienced the highest incidence rates of cancer at approximately 207 and 215 cases per million, respectively. Children ages 5 to 9 years and 10 to 14 years had lower incidence rates at 114 and 134 cases per million, respectively. These differences among age groups were statistically significant. (See Table D5c.)



- Leukemia, which includes acute lymphoblastic leukemia and acute myeloid leukemia, was the most common cancer diagnosis for children from 2004–2006, representing about 27% of total cancer cases. Incidence of acute lymphoblastic (lymphocytic) leukemia was 30 cases per million in 1992–1994 and 35 cases per million in 2004–2006. Rates of acute myeloid (myelogenous) leukemia were 7 cases per million in 1992–1994 and 8 cases per million in 2004–2006. These increases were not statistically significant.

- Central nervous system tumors represented about 16% of childhood cancers in 2004–2006. The incidence of central nervous system tumors was 29 cases per million in 1992–1994 and 27 per million in 2004–2006. This change was not statistically significant.

- Lymphomas, which include Hodgkin's lymphoma and non-Hodgkin's lymphoma, represented approximately 14% of childhood cancers in 2004–2006. Incidence of

Hodgkin's lymphoma was 12 cases per million in 1992–1994 and 11 per million in 2004–2006. There were approximately 7 cases of non-Hodgkin's lymphomas per million children in 1992–1994 and 9 per million in 2004–2006. The increase in the incidence rate of non-Hodgkin's lymphoma was statistically significant, while there was no statistically significant change to the incidence rate of Hodgkin's lymphoma.

- Between the years 1992 and 2006, increases in the incidence of germ cell tumors, soft tissue sarcomas, malignant melanomas, and hepatoblastomas were statistically significant, as was the decrease in the incidence of Wilms' tumor (tumors of the kidney). However, the increase in germ cell tumor incidence was not significant after accounting for the influence of differences in age, sex, and race/ethnicity.

- Different types of cancer affect children at different ages. Neuroblastomas and Wilms' tumor (tumors of the kidney) are usually found only in young children (ages 0 to 9 years). Central nervous system tumors and leukemias are most common through age 14 years (leukemias being highest among 0- to 4-year-olds); lymphomas, carcinomas (thyroid carcinoma and other carcinomas), and germ cell tumors are more common in those 15 to 19 years old. These age group differences were statistically significant. (See Table D6a.)

Data Tables

Table D5: Cancer incidence and mortality for children ages 0 to 19 years, 1992-2007

1992–1997						
	Rate per million children					
	1992	1993	1994	1995	1996	1997
Incidence	158.4	161.6	153.1	154.9	160.8	154.5
Mortality	33.1	32.6	31.2	29.8	28.7	28.8
1998–2003						
	Rate per million children					
	1998	1999	2000	2001	2002	2003
Incidence	164.1	157.7	162.0	166.4	171.6	156.6
Mortality	27.5	28.0	28.2	27.6	28.1	27.5
2004–2007						
	Rate per million children					
	2004	2005	2006	2007		
Incidence	167.2	173.7	155.9	170.3		
Mortality	27.3	26.7	24.8	25.1		
DATA: National Cancer Institute, Surveillance, Epidemiology, and End Results (SEER) Program.						

Table D5a: Cancer incidence for children ages 0 to 19 years by race/ethnicity and sex, 2005–2007

	Rate per million children		
	Male	Female	All
All Races/Ethnicities	177.0	155.8	166.7
White non-Hispanic	198.0	176.8	187.7
Black non-Hispanic	127.4	126.3	126.9
American Indian/Alaska Native non-Hispanic	118.0	150.7	134.3
Asian or Pacific Islander non-Hispanic	151.0	138.1	144.8
Hispanic	171.5	132.9	152.6
DATA: National Cancer Institute, Surveillance, Epidemiology, and End Results (SEER) Program.			

Table D5b: Cancer mortality for children ages 0 to 19 years by race/ethnicity and sex, 2005–2007

	Rate per million children		
	Male	Female	All
All Races/Ethnicities	28.2	22.8	25.5
White non-Hispanic	28.1	22.7	25.5

Black non-Hispanic	28.3	22.2	25.3
American Indian/Alaska Native non-Hispanic	22.3	12.7	17.6
Asian or Pacific Islander non-Hispanic	26.0	20.8	23.4
Hispanic	29.2	24.5	26.9

DATA: National Cancer Institute, Surveillance, Epidemiology, and End Results (SEER) Program.

Following the recommendations of the National Cancer Institute, the mortality rates for all the groups except for "All races/ethnicities" excluded data from the following regions, which had large numbers with unknown ethnicity: Washington DC and ND. See http://seer.cancer.gov/seerstat/variables/mort/origin_recode_1990+/yr1969_2007.

Table D5c: Cancer incidence for children 0 to 19 years by age, 2005–2007

	Rate per million children
0–4 years	206.7
5–9 years	113.7
10–14 years	133.9
15–19 years	214.8
0–19 years	166.7

DATA: National Cancer Institute, Surveillance, Epidemiology, and End Results (SEER) Program.

Table D6: Cancer incidence for children ages 0 to 19 years, by type, 1992-2006

	Rate per million children				
	1992-1994	**1995-1997**	**1998-2000**	**2001-2003**	**2004-2006**
Acute lymphoblastic leukemia	29.5	32.3	33.4	32.4	34.5
Acute myeloid leukemia	7.3	7.7	8.3	8.0	8.5
Central nervous system tumors	28.7	26.8	26.9	29.6	27.0
Hodgkin's lymphoma	12.3	11.6	12.2	11.2	10.8
Non-Hodgkin's lymphoma	7.4	7.2	7.7	9.0	8.8
Burkitt's lymphoma	2.0	1.9	2.3	2.4	2.2
Thyroid carcinoma	5.2	5.2	6.2	6.1	5.5
Malignant melanoma	4.4	4.7	4.7	5.8	5.7
Other and unspecified carcinomas†	3.8	3.9	3.9	3.6	3.3
Germ cell tumors	11.3	11.5	10.8	12.0	12.6
Soft tissue sarcomas	10.2	11.5	12.0	11.5	12.3
Osteosarcoma	4.9	4.8	4.8	5.3	4.5
Ewing's sarcoma	3.2	2.3	2.2	2.5	2.8

Neuroblastoma	7.4	7.7	6.9	7.3	8.0
Wilms' tumor	5.7	5.8	5.5	4.7	4.4
Hepatoblastoma	1.1	1.2	1.8	1.5	1.7

DATA: National Cancer Institute, Surveillance, Epidemiology, and End Results (SEER) Program.

† "Other and unspecified carcinomas" represents all carcinomas and other malignant epithelial neoplasms other than thyroid carcinoma and malignant melanoma.

Table D6a: Cancer incidence rates per million children for malignant cancers by age and type, 2004–2006

	Rate per million children				
	Ages 0-4	**Ages 5-9**	**Ages 10-14**	**Ages 15-19**	**Ages 0-19**
Acute lymphoblastic leukemia	66.3	33.6	22.8	17.0	34.5
Acute myeloid leukemia	13.2	4.6	7.3	9.0	8.5
Central nervous system tumors	35.1	30.4	23.2	19.7	27.0
Hodgkin's lymphoma	NA**	4.1	12.0	26.0	10.8
Non-Hodgkin's lymphoma	3.2	5.2	10.5	15.9	8.8
Burkitt's lymphoma	1.5	2.6	2.4	2.2	2.2
Thyroid carcinoma	NA**	1.6	4.6	15.5	5.5
Malignant melanoma	0.95*	1.7	4.3	15.5	5.7
Other and unspecified carcinomas†	NA**	NA**	3.5	9.0	3.3
Germ cell tumors	7.5	2.9	9.2	30.8	12.6
Soft-tissue sarcomas	11.1	7.1	12.8	18.3	12.3
Osteosarcoma	NA**	2.6	7.3	7.9	4.5
Ewing's sarcoma	NA**	1.6	3.5	5.1	2.8
Neuroblastoma	28.5	2.8	1.4	NA**	8.0
Wilms' tumor	13.4	3.8	NA**	NA**	4.4
Hepatoblastoma	6.9	NA**	NA**	NA**	1.7

DATA: National Cancer Institute, Surveillance, Epidemiology, and End Results (SEER) Program.

† "Other and unspecified carcinomas" is a subset of the ICCC group "XI Carcinomas and other malignant epithelial neoplasms."

* The estimate should be interpreted with caution because the standard error of the estimate is relatively large: the relative standard error, RSE, is at least 30% but is less than 40% (RSE = standard error divided by the estimate).

** The estimate is not reported because it has large uncertainty: the relative standard error, RSE, is at least 40% (RSE = standard error divided by the estimate).

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Metadata

Metadata for	Surveillance, Epidemiology, and End Results (SEER)
Brief description of the data set	The Surveillance, Epidemiology, and End Results (SEER) program is an authoritative source of information on cancer incidence and mortality in the United States. SEER collects and publishes cancer data from a set of 17 population-based regional cancer registries located throughout the country.
Who provides the data set?	National Cancer Institute.
How are the data gathered?	Data on all diagnosed cancer cases in the geographical area for a cancer registry are compiled each year and submitted to SEER. Mortality data are collected by the National Center for Health Statistics. Population data are provided by the Census Bureau.
What documentation is available describing data collection procedures?	See http://seer.cancer.gov/index.html for detailed description of SEER organization and data collection practices.
What types of data relevant for children's environmental health indicators are available from this database?	Cancer incidence and mortality including cancer type, tumor site, tumor morphology, and stage at diagnosis, first course of treatment, and follow-up for vital status. Demographic information. State and county.
What is the spatial representation of the database (national or other)?	The most recent SEER database has 17 population-based cancer registries in 14 states and covers 26% of the U.S. population. A subset of the current SEER includes 13 population-based cancer registries in 10 states and covers 14% of the U.S. population. The registries include: the Alaska Native, Atlanta, Connecticut, Detroit, Hawaii, Iowa, Los Angeles, New Mexico, Rural Georgia, San Francisco-Oakland, San Jose-Monterey, Seattle-Puget Sound, and Utah tumor registries. These data are taken to represent cancer incidence for the entire United States. See below for further discussion.
Are raw data (individual measurements or survey responses) available?	Yes.
How are database files obtained?	http://seer.cancer.gov/data/access.html includes various methods of accessing SEER data. Raw data for each person can be obtained. For ACE, annual summary cancer incidence and mortality rate data were obtained using SEER*Stat software available from the same website.

Metadata for	**Surveillance, Epidemiology, and End Results (SEER)**
Are there any known data quality or data analysis concerns?	The population covered by SEER is comparable to the general U.S. population with regard to measures of poverty and education. The SEER population tends to be somewhat more urban and has a higher proportion of foreign-born persons than the general U.S. population. Cancer mortality data has significant percentages of persons with unknown ethnicity in a few states.
What documentation is available describing QA procedures?	http://seer.cancer.gov/qi/index.html provides information on SEER quality improvement.
For what years are data available?	Data are available from the original 9 SEER registries from1973–present, but over time the coverage of SEER has increased to cover more individuals and geographic regions. See below for further discussion.
What is the frequency of data collection?	Annually.
What is the frequency of data release?	Annually.
Are the data comparable across time and space?	The national coverage has increased over time from 9 to 17 cancer registries. Time comparisons should be between the same set of registries. Thus, long-term trend comparisons use SEER 9 (the original 9 registries) beginning with 1973 and cover the smallest percentage (9.5% in 2000) of the U.S. population. The full set of registries (SEER 17) has the broadest coverage (26%), but provides data only from the year 2000 forward. SEER 13 covers 14% of the population and provides data from 1992 forward. Population coverage varies by state. Over time the cancer classifications used by SEER have changed. As scientific knowledge has improved, some cancers that were once more generally classified are now given a more exact definition. However, with each annual update SEER updates the current and previous years' data to reflect the latest classification scheme. The one exception would be for conditions that are now classified as malignant cancers but were not previously and were therefore not registered by the SEER cancer registries for earlier years. This applies only to a limited number of rare tumor types, so it is not expected to contribute to changes in cancer incidence over time.
Can the data be stratified by race/ethnicity, income, and location (region, state, county or	The data can be stratified by race and ethnicity, as well as median county income. Incidence data within the given SEER registry can be geographically stratified by state and county Mortality data can be geographically stratified by state and county.

Metadata for	**Surveillance, Epidemiology, and End Results (SEER)**
other geographic unit)?	

Methods

Indicator

D5. Cancer incidence and mortality for children ages 0 to 19 years, 1992-2007.

Summary

Since 1973, the Surveillance, Epidemiology, and End Results (SEER) Program of the National Cancer Institute (NCI) has been collecting and publishing cancer incidence data from population-based cancer registries that currently cover a total of 17 geographical areas in the United States and one quarter of the population. Since the coverage area has expanded over time, the trend analyses for indicator D5 were based on the SEER 13 registries that cover 13.8% of the U.S. population for the years 1992 and later. Data include the type of cancer, age at diagnosis, year of diagnosis, sex, race, and ethnicity. For indicator D5, cancer incidence rates for malignant cancers in children ages 0 to 19 years were calculated using the SEER*Stat software provided by the NCI. SEER*Stat calculates incidence rates for each age group by dividing the number of new cancer cases by the total population for that age group in the cancer registry geographical area. SEER*Stat then calculates age-adjusted incidence rates as a weighted average of the rates for each five-year age group, where the weights are the proportions of persons in each age group in the selected standard population; for these analyses the incidence rates were age-adjusted to the 2000 U.S. Standard Population. National cancer mortality rates were also obtained from SEER, which uses data from the National Vital Statistics System, administered by the National Center for Health Statistics. Data include the type of cancer, age at death, year of death, sex, race, and ethnicity. For indicator D5, cancer mortality rates for malignant cancers in children ages 0 to 19 years were calculated using the SEER*Stat software provided by the NCI. The mortality rates were age-adjusted to the 2000 U.S. Standard Population. Tables D5a, D5b, and D5c provide the age-adjusted cancer incidence and mortality rates for children 19 and under, stratified by race/ethnicity, sex, and age for the period 2005–2007.

Data Summary

Indicator	D5. Cancer incidence and mortality for children under 20					
Time Period	1992-2007					
Data	Cancer incidence of malignant cancers in SEER 13 registries for children ages 0 to 19 years. U.S. mortality from malignant cancers in children ages 0 to 19 years.					
Years	1992	1993	1994	1995	1996	1997
Cancer incidence	1,649	1,724	1,644	1,680	1,765	1,708
Cancer mortality	2,417	2,419	2,354	2,275	2,224	2,261
Years	1998	1999	2000	2001	2002	2003

Indicator	D5. Cancer incidence and mortality for children under 20					
Cancer incidence	1,831	1,769	1,825	1,884	1,943	1,775
Cancer mortality	2,176	2,243	2,271	2,226	2,271	2,233
Years	2004	2005	2006	2007		
Cancer incidence	1,907	1,987	1,788	1,959		
Cancer mortality	2,223	2,183	2,035	2,068		

Overview of Data Files

The following files are needed to calculate this indicator. All these files together with the SEER*Stat software used to calculate the incidence and mortality rates are available from the SEER website: http://seer.cancer.gov/data/access.html. The data and analyses used for this indicator were obtained using version 6.6.2 of SEER*Stat.

- SEER 13 Regs Research Data, Nov 2009 Sub (1992–2007) <Katrina/Rita Population Adjustment> - Linked To County Attributes - Total U.S., 1969–2007 Counties. Incidence data from the SEER 13 registries: Connecticut; Hawaii; Iowa; New Mexico; Utah; Atlanta, Georgia; Detroit, Michigan; San Francisco-Oakland, California; Seattle-Puget Sound, Washington; Los Angeles, California; San Jose-Monterey, California; Rural Georgia; and the Alaska Native Tumor Registry.

- Mortality - All COD, Aggregated With State, Total U.S. (1969–2007) <Katrina/Rita Population Adjustment>. Mortality data from the entire United States for all causes of death. Mortality from All Malignant Cancers was selected.

The databases incorporated into the SEER*Stat software include census population data used to compute the incidence and mortality rates and to age-adjust the rates to the 2000 U.S. Standard Population. These population data are obtained by NCI from the Census Bureau. Age-adjustment is explained below.

Calculation of Indicator

All the calculations for this indicator were carried out using SEER*Stat software, version 6.6.2. In this section we detail the menu options required for carrying out these analyses.

Note that any User-Defined variable previously created using the File and Dictionary menus in the same or any earlier session will not need to be recreated.

Incidence

Click the Rate Session button "Σ".

Data tab. Select "Incidence – SEER 13 Regs Research Data, Nov 2009 Sub (1992–2007) <Katrina/Rita Population Adjustment>"

Statistic tab. Check "Rates (Age – Adjusted)" and "Show Standard Errors and Confidence Intervals." For "Standard Population" select "2000 US Std Population (19 age groups – census P25-1130)." For "Age Variable" select "Age recode with <1 year olds."

Selection tab. Check "Malignant Behavior." For "Age at Diagnosis" click the Edit button and then select the age group 0–19 using "Age recode with <1 year olds" = 00, 01-04, 05-09, 10-14, and 15-19. This restricts the data to malignant cancers in children ages 0 to 19 years.

Table tab. From the "Available Variables" panel, expand "Race, Sex, Year Dx, Registry, County" and select "Year of diagnosis." Click the Row button. This tabulates the rates by calendar year.

Output tab. For "Display Rates as Cases Per" select "1,000,000."

Click the Execute button to run the analyses and create the output Rate Matrix.

Use the Matrix and Export menus to output the data to a text file.

Mortality

Click the Rate Session button "Σ".

Data tab. Select "Mortality - All COD, Aggregated With State, Total U.S. (1969–2007) <Katrina/Rita Population Adjustment>."

Statistic tab. Check "Rates (Age – Adjusted)" and "Show Standard Errors and Confidence Intervals." For "Standard Population" select "2000 US Std Population (19 age groups – census P25-1130)." For "Age Variable" select "Age recode with <1 year olds."

Selection tab. For "Age at Death" click the Edit button and then select the age group 0–19 using "Age recode with <1 year olds" = 00, 01-04, 05-09, 10-14, and 15-19. For "Other (Case Files)" click the Edit button and then follow the menus to select "Site and Morphology," "Cause of death recode," and "All Malignant Cancers." This restricts the data to malignant cancers in children ages 0 to 19 years.

Table tab. From the "Available Variables" panel, expand "Race, Sex, Year Dth, State, Registry" and select "Year of Death." Click the Row button. This tabulates the rates by calendar year.

Output tab. For "Display Rates as Cases Per" select "1,000,000."

Click the Execute button to run the analyses and create the output Rate Matrix.

Use the Matrix and Export menus to output the data to a text file.

Age adjustment

For measure D5, all cancer incidence and mortality rates were age-adjusted to the 2000 U.S. Standard Population using 5 age groups for children.. The calculations were carried out automatically by the SEER*Stat software. The age-adjusted rates are often preferred when comparing different populations (such as for different calendar years or different race groups) since differences in the age-adjusted cancer rates are mainly attributable to factors other than age. In general, very young children and adolescents will tend to have a higher crude (unadjusted) cancer rate than children ages 5 to 14. The age adjustment replaces the distribution of ages in each given population by the same standard age distribution, in this case the age distribution of the U.S. population in 2000.

The calculation is shown by the following example which gives the age-adjusted cancer incidence rate for the year 2007 for children under 20.

Age-adjusted Cancer Incidence for 2007.

Age Group [1]	***Cases [2]***	***SEER 13 Population [3]***	***Crude Rate (Cases per Million)[4] = [2]/[3] ×1,000,000***	***U.S. 2000 Standard Population [5]***	***U.S. 2000 Proportion of Age Group 0-19 [6]***	***Adjusted Rate (Cases per Million) = [4] × [6]***
00 years	137	597,549	229.270	3,794,901	0.048	11.044
01-04 years	446	2,301,679	193.772	15,191,619	0.193	37.365
05-09 years	321	2,735,716	117.337	19,919,840	0.253	29.668
10-14 years	373	2,815,403	132.485	20,056,779	0.255	33.729
15-19 years	682	2,933,583	232.480	19,819,518	0.252	58.486
00-19 years	**1,959**	**11,383,930**	**172.085**	**78,782,657**	**1.000**	**170.291**

The first three columns give the number of new malignant cancer cases in 2007 and the total population for each children's age group within the counties included in the SEER 13 cancer registries. The number of cases divided by the SEER 13 population and multiplied by 1 million gives the crude rate shown in the fourth column. For example, for the age group 00 years, there were 137 cases in a population of 597,549 giving a crude rate of (137/597549) × 1000000 = 193.772 cases per million. The crude rate for all children under 20 is 172.085 (bottom row).

The U.S. 2000 Standard Population for children is shown in the fifth column. This is the age distribution of children for the entire United States in 2000, in five age groups (0, 1–4, 5–9, 10–14, and 15–19). The standard age distribution for children ages 0 to 19 years is shown in the

sixth column. The U.S. 2000 Standard Population in each age group is divided by the total U.S. 2000 Standard Population for children under 20 years, i.e., 78,782,657.

The age-adjusted population is a weighted average of the crude rates (column 4) weighted by the U.S. 2000 Standard Population proportions (column 6). Thus, the first five rows of column 7 contain the products of columns 4 and 6, and the age-adjusted rate is given by the total for column 7, shown in the bottom row as 170.291.

For this example, the crude rate for ages 0 to 19 years, 172.085, is very close to the age-adjusted rate, 170.291, reflecting the fact that in 2007 the age distribution for children 0 to 19 years in the SEER 13 regions closely matches the 2000 U.S. population age distribution. For other years or for different race/ethnicity/sex groups crude and age-adjusted rates can differ by a much greater percentage.

Relative Standard Error

The uncertainties of the incidence and mortality rates were computed by the SEER*Stat software under the assumption that the counts have Poisson distributions. The relative standard error is the standard error of the rate divided by the estimated rate:

$$\text{Relative Error (\%)} = [\text{Standard Error (Rate)} / \text{Rate}] \times 100\%$$

Rates with a relative error less than 30% were treated as being reliable and were tabulated. For indicator D5, all the relative standard errors were at most 30% and so all values were tabulated.

Rates by Race, Ethnicity, Sex, and Age

For the Tables D5a, D5b, and D5c, cancer incidence and mortality rates are tabulated by race, ethnicity, sex, and age.

The following SEER*Stat data files were used for the Addendum analyses:

- SEER 13 Regs Research Data, Nov 2009 Sub (1992–2007) <Katrina/Rita Population Adjustment> - Linked To County Attributes - Total U.S., 1969–2007 Counties. Incidence data from the SEER 13 registries: Connecticut; Hawaii; Iowa; New Mexico; Utah; Atlanta, Georgia; Detroit, Michigan; San Francisco-Oakland, California; Seattle-Puget Sound, Washington; Los Angeles, California; San Jose-Monterey, California; Rural Georgia; and the Alaska Native Tumor Registry.

- Mortality - All COD, Aggregated With State, Total U.S. (1990–2007) <Katrina/Rita Population Adjustment>. Mortality data from the entire United States for all causes of death. Mortality from All Malignant Cancers was selected.

The supplementary tables by race, ethnicity, sex, and age for incidence in 2005-2007 and mortality in 2004-2006 were calculated as follows:

Incidence by Race/Ethnicity and Sex

Click the Rate Session button "Σ".

Data tab. Select "Incidence – SEER 13 Regs Research Data, Nov 2009 Sub (1992–2006) <Katrina/Rita Population Adjustment."

Statistic tab. Check "Rates (Age – Adjusted)" and "Show Standard Errors and Confidence Intervals." For "Standard Population" select "2000 US Std Population (19 age groups – census P25-1130)." For "Age Variable" select "Age recode with <1 year olds."

Selection tab. Check "Malignant Behavior." For "Age at Diagnosis" click the Edit button and then select the age group 0–19 using "Age recode with <1 year olds" = 00, 01-04, 05-09, 10-14, and 15-19. For "Race, Sex, Year Dx, Registry, County" click the Edit button and select the years 2005-2007 using "Year of Diagnosis" = 2005, 2006, and 2007. This restricts the data to malignant cancers in children ages 0 to 19 years diagnosed in 2005-2007.

Table tab. From the "Available Variables" panel, expand "Race, Sex, Year Dx, Registry, County" and select "Sex." Click the Row button. Use the menus "File," "Dictionary," and "Merge" to create a User-Defined Merged variable Raceeth from the Race recode (W, B, AI, API) and Origin recode NHIA (Hispanic, Non-Hisp) variables in the database:

- Raceeth = All if Race recode = White, Black, American Indian/Alaskan Native, Asian or Pacific Islander, Other Unspecified (1991+) or Unknown
- Raceeth = WhiteNH if Race recode = White and Origin recode NHIA = Non-Spanish-Hispanic-Latino
- Raceeth = BlackNH if Race recode = Black and Origin recode NHIA = Non-Spanish-Hispanic-Latino
- Raceeth = AIANNH if Race recode = American Indian/Alaskan Native and Origin recode NHIA = Non-Spanish-Hispanic-Latino
- Raceeth = APINH if Race recode = Asian or Pacific Islander and Origin recode NHIA = Non-Spanish-Hispanic-Latino
- Raceeth = Hispanic if Origin recode NHIA = Spanish-Hispanic-Latino

In the Table tab, from the "Available Variables" panel, expand "Merged" and select "Raceeth." Click the Column button. These options tabulate the rates by sex and race/ethnicity.

Output tab. For "Display Rates as Cases Per" select "1,000,000."

Click the Execute button to run the analyses and create the output Rate Matrix.

Use the Matrix and Export menus to output the race/ethnicity/sex data to a text file.

Incidence by Age

Assuming you are in the same session as above, modify the selections as follows:

Table tab. In the Table tab, from the "Display Variables" panel, select the Row variable "Sex" and click Remove. Also select the Column variable "Raceeth" and click Remove. Use the menus "File" and "Dictionary" to create a User-Defined variable AgesD5 that takes the values 0-4, 5-9, 10-14, 15-19, and 0-19 if the "Age at Diagnosis" is in the selected age group. Age at Diagnosis is defined by the values of "Age recode with <1 year olds." In the Table tab, from the "Available Variables" panel, expand "User-Defined" and select "AgesD5." Click the Row button. This tabulates the rates by the selected age groups.

Click the Execute button to run the analyses and create the output Rate Matrix.

Use the Matrix and Export menus to output the data to a text file. Tabulate the rates for selected age groups.

Mortality by Race/Ethnicity and Sex

Click the Rate Session button "Σ".

Data tab. Select "Mortality - All COD, Aggregated With State, Total U.S. (1990–2007) <Katrina/Rita Population Adjustment>."

Statistic tab. Check "Rates (Age – Adjusted)" and "Show Standard Errors and Confidence Intervals." For "Standard Population" select "2000 US Std Population (19 age groups – census P25-1130)." For "Age Variable" select "Age recode with <1 year olds."

Selection tab. For "Age at Death" click the Edit button and then select the age group 0 to 19 years using "Age recode with <1 year olds" = 00, 01-04, 05-09, 10-14, and 15-19. For "Race, Sex, Year Dth, State, Registry" click the Edit button and select the years 2005–2007 using "Year of Death" = 2005, 2006 and 2007. For "Other (Case Files)" click the Edit button and then follow the menus to select "Site and Morphology," "Cause of death recode," and "All Malignant Cancers." These options restrict the data to malignant cancers in children ages 0 to 19 years who died in 2005–2007.

Table tab. From the "Available Variables" panel, expand "Race, Sex, Year Dth, State, Registry" and select "Sex." Click the Row button. Use the menus "File," "Dictionary," and "Merge" to create a User-Defined Merged variable Raceeth2 from the Race recode (W, B, AI, API), Origin recode 1990+ (Hispanic, Non-Hisp), and State variables in the database. As explained below, the mortality rates for Hispanic and Non-Hispanic subgroups excluded data from two regions with insufficiently complete ethnicity data:

- Raceeth2 = All if Race recode = White, Black, American Indian/Alaskan Native, or Asian or Pacific Islander

- Raceeth2 = WhiteNH if Race recode = White, Origin recode 1990+ (Hispanic, Non-Hisp) = Non-Spanish-Hispanic-Latino or Unknown, and State ≠ Washington DC or North Dakota
- Raceeth2 = BlackNH if Race recode = Black, Origin recode 1990+ (Hispanic, Non-Hisp) = Non-Spanish-Hispanic-Latino or Unknown, and State ≠ Washington DC or North Dakota
- Raceeth2 = AIANNH if Race recode = American Indian/Alaskan Native, Origin recode 1990+ (Hispanic, Non-Hisp) = Non-Spanish-Hispanic-Latino or Unknown, and State ≠ Washington DC or North Dakota
- Raceeth2 = APINH if Race recode = Asian or Pacific Islander, Origin recode 1990+ (Hispanic, Non-Hisp) = Non-Spanish-Hispanic-Latino or Unknown, and State ≠ Washington DC or North Dakota
- Raceeth2 = Hispanic if Origin recode 1990+ (Hispanic, Non-Hisp) = Spanish-Hispanic-Latino, and State ≠ Washington DC or North Dakota

Hispanic Index. Following the recommendations of the National Cancer Institute (NCI), the mortality rates for all the groups except for "All" excluded data from two regions that had large numbers with unknown ethnicity: Washington DC and North Dakota. As explained at the url

http://seer.cancer.gov/seerstat/variables/mort/origin_recode_1990+/yr1969_2007,

NCI defined a Hispanic Index to measure the reliability of the Hispanic origin data for the mortality data from each year and state. The Hispanic Index is defined as

Hispanic Index = ([Hispanic Population / Total Population] × Unknown Origin Count / Hispanic Count) × 100%

When this index gives a value >= 10.00, data on Hispanic and non-Hispanic mortality are deemed unreliable. The Excel file of Hispanic Indexes, available at the same url, shows that for the years 2005 to 2007, Washington DC and North Dakota had Hispanic Index values >= 10.00 for one or more of those years. We therefore defined Raceeth2 to exclude those regions from the 2005–2007 mortality rate calculations for groups that included Hispanics and non-Hispanics in their definitions.

In the Table tab, from the "Available Variables" panel, expand "Merged" and select "Raceeth2." Click the Column button. These options tabulate the rates by sex and race/ethnicity.

Output tab. For "Display Rates as Cases Per" select "1,000,000."

Click the Execute button to run the analyses and create the output Rate Matrix.

Use the Matrix and Export menus to output the race/ethnicity/sex data to a text file.

Questions and Comments

Questions regarding these methods, and suggestions to improve the description of the methods, are welcome. Please use the "Contact Us" link at the bottom of any page in the America's Children and the Environment website.

Statistical Comparisons

Statistical analyses of the cancer incidence and mortality rates were used to determine whether the differences between rates for different demographic groups were statistically significant. For these analyses, the incidence counts and populations for each combination of calendar year, age group, sex, and race/ethnicity were obtained from the SEER database using the same age and race/ethnicity groups described above. Incidence data for malignant cancers in the years 1992 to 2007 were obtained from the SEER data set "SEER 13 Regs Research Data, Nov 2009 Sub (1992–2007) <Katrina/Rita Population Adjustment> - Linked To County Attributes - Total U.S., 1969–2007 Counties." U.S. mortality data for 1992 to 2007 were obtained from the SEER data set "Mortality - All COD, Aggregated With State, Total U.S. (1990–2007) <Katrina/Rita Population Adjustment>." For the US mortality data, the analysis excluded data from two regions which had large numbers with unknown ethnicity in 2005-2007: Washington DC and North Dakota.[i]

Using a Poisson regression model, the number of cases for each demographic subgroup was assumed to have a Poisson distribution with a mean equal to the population of that demographic subgroup multiplied by the rate. The logarithm of the rate was assumed to be the sum of explanatory terms for age, sex, and race/ethnicity. Using this model, the difference in the value of a rate between different demographic groups is statistically significant if the difference between the corresponding sums of explanatory terms is statistically significantly different from zero. A p-value at or below 0.05 implies that the difference is statistically significant at the 5% significance level. No adjustment is made for multiple comparisons.

For each type of comparison, we present unadjusted and adjusted analyses. The unadjusted analyses compare a rate between different demographic groups. The adjusted analyses add other demographic explanatory variables to the statistical model and use the statistical model to account for the possible confounding effects of these other demographic variables. For example, the unadjusted race/ethnicity comparisons compare the rates between different race/ethnicity pairs. The adjusted analyses add age and sex terms to the statistical model and compare the rates between different race/ethnicity pairs after accounting for the effects of the other demographic variables. For example, if Hispanic children tend to be younger than White non-Hispanics, and if the rate strongly depends on age only, then the unadjusted differences between these two race/ethnicity groups would be significant but the adjusted difference (taking into account age) would not be significant.

[i] NCI provides a Hispanic Index for each state and calendar year at the url: http://seer.cancer.gov/seerstat/variables/mort/origin_recode_1990+/yr1969_2007.
NCI recommends excluding mortality data from all states with a Hispanic Index at or above 10.0. Applying this rule to individual years would introduce a bias by excluding different states in different years. Excluding all states if they had a Hispanic Index at or above 10 in any calendar year would be too data restrictive. Thus we decided to only exclude data from Washington DC and North Dakota, which had high Hispanic Indexes in 2005-2007.

Comparisons of incidence rates between pairs of race/ethnicity groups are shown in Table 1. Comparisons of mortality rates between pairs of race/ethnicity groups are shown in Table 2. In Tables 1 and 2, for the "Unadjusted" comparisons, the only explanatory variables are terms for each race/ethnicity group. For these unadjusted comparisons, the statistical tests compare the rates for each pair of race/ethnicity groups. For the "Adjusted for age, sex" comparisons, the explanatory variables are terms for each race/ethnicity together with terms for each age group and sex. For these adjusted comparisons, the statistical test compares the pair of race/ethnicity groups after accounting for any differences in the age and sex distributions between the race/ethnicity groups.

Additional comparisons are shown in Table 3 for incidence rates and in Table 4 for mortality rates. The AGAINST = "age" unadjusted p-value compares the rates between all the age groups. The adjusted p-value includes adjustment terms for sex and race/ethnicity in the model. The AGAINST = "sex" unadjusted p-value compares the rates between the two sexes. The adjusted p-value includes adjustment terms for age and race/ethnicity in the model. The AGAINST = "year" unadjusted p-value compares the trends in the rates by regressing against the calendar year. The adjusted p-value includes adjustment terms for age, sex, and race/ethnicity in the model.

For more details on these statistical analyses, see the memorandum by Cohen (2010).[ii]

Table 1. Statistical significance tests comparing cancer incidence rates for children ages 0 to 19, between pairs of race/ethnicity groups, for 2005-2007.

		P-VALUES		
Variable	**RACE1**	**RACE2**	**Unadjusted**	**Adjusted for age, sex**
Cancer incidence	White non-Hispanic	Black non-Hispanic	< 0.0005	< 0.0005
Cancer incidence	White non-Hispanic	API non-Hispanic	< 0.0005	< 0.0005
Cancer incidence	White non-Hispanic	AIAN non-Hispanic	0.003	0.002
Cancer incidence	White non-Hispanic	Hispanic	< 0.0005	< 0.0005
Cancer incidence	Black non-Hispanic	API non-Hispanic	0.020	0.030
Cancer incidence	Black non-Hispanic	AIAN non-Hispanic	0.665	0.744
Cancer incidence	Black non-Hispanic	Hispanic	< 0.0005	< 0.0005
Cancer incidence	API non-Hispanic	AIAN non-Hispanic	0.499	0.476
Cancer incidence	API non-Hispanic	Hispanic	0.430	0.369
Cancer incidence	AIAN non-Hispanic	Hispanic	0.298	0.261

Table 2. Statistical significance tests comparing cancer mortality rates for children ages 0 to 19, between pairs of race/ethnicity groups, for 2005-2007.

		P-VALUES		
Variable	**RACE1**	**RACE2**	**Unadjusted**	**Adjusted for age, sex**
Cancer mortality	White non-Hispanic	Black non-Hispanic	0.757	0.842

[ii] Cohen, J. 2010. *Selected statistical methods for testing for trends and comparing years or demographic groups in other ACE health-based indicators.* Memorandum submitted to Dan Axelrad, EPA, 26 August, 2010.

		P-VALUES		
Variable	**RACE1**	**RACE2**	**Unadjusted**	**Adjusted for age, sex**
Cancer mortality	White non-Hispanic	API non-Hispanic	0.136	0.198
Cancer mortality	White non-Hispanic	AIAN non-Hispanic	< 0.0005	< 0.0005
Cancer mortality	White non-Hispanic	Hispanic	0.591	0.200
Cancer mortality	Black non-Hispanic	API non-Hispanic	0.231	0.284
Cancer mortality	Black non-Hispanic	AIAN non-Hispanic	< 0.0005	< 0.0005
Cancer mortality	Black non-Hispanic	Hispanic	0.503	0.254
Cancer mortality	API non-Hispanic	AIAN non-Hispanic	< 0.0005	< 0.0005
Cancer mortality	API non-Hispanic	Hispanic	0.096	0.066
Cancer mortality	AIAN non-Hispanic	Hispanic	< 0.0005	< 0.0005

Table 3. Other statistical significance tests comparing cancer incidence rates for children ages 0 to 19 for 2005 to 2007 (trends for 1992-2007).

				P-VALUES	
Variable	**From**	**To**	**Against**	**Unadjusted**	**Adjusted***
Cancer incidence	2005	2007	age	< 0.0005	< 0.0005
Cancer incidence	2005	2007	sex	< 0.0005	< 0.0005
Cancer incidence	2005	2007	race	< 0.0005	< 0.0005
Cancer incidence	1992	2007	year	< 0.0005	< 0.0005

*For AGAINST = "age," the p-values are adjusted for sex and race/ethnicity.
For AGAINST = "sex," the p-values are adjusted for age and race/ethnicity.
For AGAINST = "year," the p-values are adjusted for age, sex, and race/ethnicity.

Table 4. Other statistical significance tests comparing cancer mortality rates for children ages 0 to 19 for 2005 to 2007 (trends for 1992-2007).

				P-VALUES	
Variable	**From**	**To**	**Against**	**Unadjusted**	**Adjusted***
Cancer mortality	2005	2007	age	< 0.0005	< 0.0005
Cancer mortality	2005	2007	sex	< 0.0005	< 0.0005
Cancer mortality	2005	2007	race	< 0.0005	< 0.0005
Cancer mortality	1992	2007	year	< 0.0005	< 0.0005

*For AGAINST = "age," the p-values are adjusted for sex and race/ethnicity.
For AGAINST = "sex," the p-values are adjusted for age and race/ethnicity.
For AGAINST = "year," the p-values are adjusted for age, sex, and race/ethnicity.

Methods (D6)

Indicator

D6. Cancer incidence for children ages 0 to 19 years, by type, 1992-2006.

Summary

Since 1973, the Surveillance, Epidemiology, and End Results (SEER) Program of the National Cancer Institute (NCI) has been collecting and publishing cancer incidence data from population-based cancer registries that currently cover a total of 17 geographical areas in the United States and one quarter of the population. Since the coverage area has expanded over time, the trend analyses for indicator D6 were based on the SEER 13 registries that cover 13.8% of the U.S. population for the years 1992 and later. Data include the type of cancer (cancer site), age at diagnosis, and year of diagnosis. For indicator D6, cancer incidence rates for specific malignant cancers in children ages 0 to 19 years for three-year periods 1992-1994 to 2004-2006 were calculated using the SEER*Stat software provided by the NCI. SEER*Stat calculates incidence rates for each age group by dividing the number of new cancer cases by the total population for that age group in the cancer registry geographical area. SEER*Stat then calculates age-adjusted incidence rates as a weighted average of the rates for each five-year age group, where the weights are the proportions of persons in each age group in the selected standard population; for these analyses the incidence rates were age-adjusted to the 2000 U.S. Standard Population. Table D6a provides the age-adjusted cancer incidence rates for children ages 19 years and under, stratified by age group and cancer type, for the period 2004–2006.

Data Summary

Indicator	D6. Cancer incidence for children under 20 by type, 1992-2006.					
Time Period	1992-2006					
Data	Cancer incidence of malignant cancers in SEER 13 registries for children ages 0 to 19 years.					
Years	1992	1993	1994	1995	1996	1997
Cancer incidence	1, 646	1,723	1,644	1,679	1,764	1,708
Years	1998	1999	2000	2001	2002	2003
Cancer incidence	1,829	1,768	1,822	1,882	1,942	1,771
Years	2004	2005	2006			
Cancer incidence	1,901	1,983	1,773			

Overview of Data Files

The following files are needed to calculate this indicator. All these files together with the SEER*Stat software used to calculate the incidence rates are available from the SEER website: http://seer.cancer.gov/data/access.html. The data and analyses used for this measure were obtained using version 6.6.2 of SEER*Stat.

- SEER 13 Regs Research Data, Nov 2008 Sub (1992–2006) <Katrina/Rita Population Adjustment> - Linked To County Attributes - Total U.S., 1969–2006 Counties. Incidence data from the SEER 13 registries: Connecticut; Hawaii; Iowa; New Mexico; Utah; Atlanta, Georgia; Detroit, Michigan; San Francisco-Oakland, California; Seattle-Puget Sound, Washington; Los Angeles, California; San Jose-Monterey, California; Rural Georgia; and the Alaska Native Tumor Registry.

The databases incorporated into the SEER*Stat software include census population data used to compute the incidence rates and to age-adjust the rates to the 2000 U.S. Standard Population. These population data are obtained by NCI from the Census Bureau. Age-adjustment is explained below.

Calculation of Indicator

All the calculations for this indicator were carried out using SEER*Stat software, version 6.6.2. In this section we detail the menu options required for carrying out these analyses.

Note that any User-Defined variable previously created using the File and Dictionary menus in the same or any earlier session will not need to be recreated.

ICCC site recode ICD-O-3.

Click the Rate Session button "Σ".

Data tab. Select "SEER 13 Regs Research Data, Nov 2008 Sub (1992–2006) <Katrina/Rita Population Adjustment>."

Statistic tab. Check "Rates (Age – Adjusted)" and "Show Standard Errors and Confidence Intervals." For "Standard Population" select "2000 US Std Population (19 age groups – census P25-1130)." For "Age Variable" select "Age recode with <1 year olds."

Selection tab. Check "Malignant Behavior." For "Age at Diagnosis" click the Edit button and then select the age group 0 to 19 years using "Age recode with <1 year olds" = 00, 01-04, 05-09, 10-14, and 15-19. This restricts the data to malignant cancers in children ages 0 to 19 years.

Table tab. Use the menus "File" and "Dictionary" to create a User-Defined variable YearsD6 that takes the values 1992–1994, 1995–1997, 1998–2000, 2001–2003 and 2004–2006 if the "Year of Diagnosis" is in the selected year group. In the Table tab, from the "Available Variables" panel, expand "User-Defined" and select "YearsD6." Click the Row button. From the

"Available Variables" panel, expand "Site and Morphology" and select "ICCC site recode ICD-O-3." Click the Column button. This tabulates the rates by the selected calendar year groups and cancer types.

Output tab. For "Display Rates as Cases Per" select "1,000,000."

Click the Execute button to run the analyses and create the output Rate Matrix.

Use the Matrix and Export menus to output the data to a text file. Tabulate the rates for selected cancer types and year groups.

AYA Site Recode.

The cancer types acute lymphocytic leukemia and Wilms' tumor are not specifically included in the ICCC site recode ICD-O-3 categories. Thus the incidence rate for these two cancers is calculated separately using the "AYA site recode," which codes cancer types for adolescents and young adults.

Modify the above selections as follows:

Table tab. In the Table tab, from the "Display Variables" panel, select the Column variable "ICCC site recode ICD-O-3" and click Remove. From the "Available Variables" panel, expand "Site and Morphology" and select "AYA site recode." Click the Column button. This tabulates the rates by the selected calendar year groups for the cancer types coded in the AYA site recode.

Click the Execute button to run the analyses and create the output Rate Matrix.

Use the Matrix and Export menus to output the AYA site recode data to a text file. Tabulate the rates for selected cancer types and year groups.

Age-adjustment

For measure D6, all cancer incidence and mortality rates were age-adjusted to the 2000 U.S. Standard Population using 19 age groups. The calculations were carried out automatically by the SEER*Stat software. The age-adjusted rates are often preferred when comparing different populations (such as for different calendar years or different race groups) since differences in the age-adjusted cancer rates are mainly attributable to factors other than age. In general, a younger population will tend to have a lower crude (unadjusted) cancer rate. The age-adjustment replaces the distribution of ages in each given population by the same standard age distribution, in this case the age distribution of the U.S. population in 2000.

The calculation is shown by the following example which gives the age-adjusted cancer incidence rate for the years 2004–2006 for acute myeloid leukemia in children under 20.

Age-adjusted Acute Myeloid Leukemia Incidence for 2004-2006.

Age Group [1]	*Cases [2]*	*SEER 13 Population [3]*	*Crude Rate (Cases per Million)[4] = [2]/[3]*	*U.S. 2000 Standard Population [5]*	*U.S. 2000 Proportion of Age Group 0-19 [6]*	*Adjusted Rate (Cases per Million) = [4] × [6]*
00 years	37	1,753,659	21.099	3,794,901	0.048	1.016
01-04 years	76	6,769,698	11.226	15,191,619	0.193	2.165
05-09 years	38	8,220,990	4.622	19,919,840	0.253	1.169
10-14 years	64	8,760,297	7.306	20,056,779	0.255	1.860
15-19 years	77	8,577,973	8.976	19,819,518	0.252	2.258
00-19 years	**292**	**34,082,617**	**8.567**	**78,782,657**	1.000	**8.468**

The first three columns give the number of new malignant acute myeloid leukemia cases in 2004–2006 and the total population for each children's age group within the counties included in the SEER 13 cancer registries. The number of cases divided by the SEER 13 population and multiplied by 1 million gives the crude rate shown in the fourth column. For example, for the age group 00 years, there were 37 cases in a population of 1,753,659 giving a crude rate of (37/1753659) × 1000000 = 21.099 cases per million. The crude rate for all children under 20 is 8.567 (bottom row).

The U.S. 2000 Standard Population for children is shown in the fifth column. This is the age distribution for the entire United States in 2000. For analyzing children's populations only five age groups are needed (0, 1–4, 5–9, 10–14, and 15–19). However, for analyzing children and adults the U.S. 2000 Standard Population has 19 age groups, since the U.S. 2000 Standard Population also includes five-year age groups up to 80–84 and the 85+ age group.

The standard age distribution for children 0 to 19 years is shown in the sixth column. The U.S. 2000 Standard Population in each age group is divided by the total U.S. 2000 Standard Population for children under 20, i.e., 78,782,657.

The age-adjusted population is a weighted average of the crude rates (column 4) weighted by the U.S. 2000 Standard Population proportions (column 6). Thus, the first five rows of column 7 contain the products of columns 4 and 6, and the age-adjusted rate is given by the total for column 7, shown in the bottom row as 8.468.

For this example, the crude rate for ages 0 to 19 years, 8.567, is very close to the age-adjusted rate, 8.468, reflecting the fact that the age distribution for children 0 to 19 years in the SEER 13 regions closely matches the 2000 U.S. population age distribution. For other years or for different cancer types, crude and age-adjusted rates can differ by a much greater percentage.

Relative Standard Error

The uncertainties of the incidence and mortality rates were computed by the SEER*Stat software under the assumption that the counts have Poisson distributions. The relative standard error is the standard error of the rate divided by the estimated rate:

Relative Error (%) = [Standard Error (Rate) / Rate] × 100%

Rates with a relative error less than 30% were treated as being reliable and were tabulated. For indicator D6, all the relative standard errors in Table D6 were at most 30% and so all values were tabulated. For Table D6a (see below), some relative standard errors were greater than 30% and less than 40% and those rates were tabulated but flagged as to be interpreted with caution. Rates with a relative standard error greater than or equal to 40%, or without an estimated relative standard error, were treated as being unreliable; these values were not tabulated and were flagged as having a large uncertainty.

Rates by Age Group

For Table D6a, cancer incidence for 2004–2006 is tabulated by cancer type and age group.

The Table D6a was calculated as follows using SEER*Stat:

ICCC site recode ICD-O-3.

Click the Rate Session button "Σ".

Data tab. Select "SEER 13 Regs Research Data, Nov 2008 Sub (1992–2006) <Katrina/Rita Population Adjustment>."

Statistic tab. Check "Rates (Age – Adjusted)" and "Show Standard Errors and Confidence Intervals." For "Standard Population" select "2000 US Std Population (19 age groups – census P25-1130)." For "Age Variable" select "Age recode with <1 year olds."

Selection tab. Check "Malignant Behavior." For "Age at Diagnosis" click the Edit button and then select the age group 0 to 19 years using "Age recode with <1 year olds" = 00, 01-04, 05-09, 10-14, and 15-19. For "Race, Sex, Year Dx, Registry, County" click the Edit button and select the years 2004–2006 using "Year of Diagnosis" = 2004, 2005 and 2006. This restricts the data to malignant cancers in children ages 0 to 19 years diagnosed in 2004–2006.

Table tab. Use the menus "File" and "Dictionary" to create a User-Defined variable AgesD6 that takes the values 0-4, 5-9, 10-14, 15-19, and 0-19 if the "Age at Diagnosis" is in the selected age group. Age at Diagnosis is defined by the values of "Age recode with <1 year olds." In the Table tab, from the "Available Variables" panel, expand "User-Defined" and select "AgesD6." Click the Row button. From the "Available Variables" panel, expand "Site and Morphology" and select "ICCC site recode ICD-O-3." Click the Column button. This tabulates the rates by the selected age groups and cancer types.

Output tab. For "Display Rates as Cases Per" select "1,000,000."

Click the Execute button to run the analyses and create the output Rate Matrix.

Use the Matrix and Export menus to output the data to a text file. Tabulate the rates for selected cancer types and age groups.

AYA Site Recode.

The cancer types acute lymphocytic leukemia and Wilms' tumor are not specifically included in the ICCC site recode ICD-O-3 categories. Thus the incidence rate for these two cancers is calculated separately using the "AYA site recode," which codes cancer types for adolescents and young adults.

Modify the above selections as follows:

Table tab. In the Table tab, from the "Display Variables" panel, select the Column variable "ICCC site recode ICD-O-3" and click Remove. From the "Available Variables" panel, expand "Site and Morphology" and select "AYA site recode." Click the Column button. This tabulates the rates by the selected age groups for the cancer types coded in the AYA site recode.

Click the Execute button to run the analyses and create the output Rate Matrix.

Use the Matrix and Export menus to output the AYA site recode data to a text file. Tabulate the rates for selected cancer types and age groups.

Questions and Comments

Questions regarding these methods, and suggestions to improve the description of the methods, are welcome. Please use the "Contact Us" link at the bottom of any page in the America's Children and the Environment website.

Statistical Comparisons

Statistical analyses of the cancer incidence rates for each cancer type were used to determine whether the differences between rates for different demographic groups were statistically significant. Each cancer type was analyzed separately. For these analyses, the incidence counts and populations for each combination of calendar year, age group, sex, and race/ethnicity were obtained from the SEER database using the same age and race/ethnicity groups described above. Incidence data for malignant cancers in the years 1992 to 2007 were obtained from the SEER data set "SEER 13 Regs Research Data, Nov 2009 Sub (1992–2007) <Katrina/Rita Population Adjustment> - Linked To County Attributes - Total U.S., 1969–2007 Counties."

Using a Poisson regression model, the number of cases for each demographic subgroup was assumed to have a Poisson distribution with a mean equal to the population of that demographic subgroup multiplied by the rate. The logarithm of the rate was assumed to be the sum of explanatory terms for age, sex, and race/ethnicity. Using this model, the difference in the value of a rate between different demographic groups is statistically significant if the difference between the corresponding sums of explanatory terms is statistically significantly different from

zero. A p-value at or below 0.05 implies that the difference is statistically significant at the 5% significance level. No adjustment is made for multiple comparisons.

For each type of comparison, we present unadjusted and adjusted analyses. The unadjusted analyses compare a rate between different demographic groups. The adjusted analyses add other demographic explanatory variables to the statistical model and use the statistical model to account for the possible confounding effects of these other demographic variables. For example, the unadjusted age comparisons compare the rates between the different age groups. The adjusted analyses add sex and race/ethnicity terms to the statistical model and compare the rates between different age groups after accounting for the effects of the other demographic variables. For example, if Hispanic children tend to be younger than White non-Hispanics, and if the cancer incidence rate strongly depends on race/ethnicity only, then the unadjusted differences between age groups would be significant because of their different race/ethnicity breakdowns but the adjusted difference (taking into account race/ethnicity) would not be significant.

The statistical comparisons for each cancer type are shown in Table 1. The AGAINST = "age" unadjusted p-value compares the rates between all the age groups for the years 2004-2006. The adjusted p-value includes adjustment terms for sex and race/ethnicity in the model. The AGAINST = "year" unadjusted p-value compares the trends in the rates for the period 1992 to 2006 by regressing against the calendar year. Instead of using the three-year rates given in the tables and graphs, the statistical trend analysis used the annual rates to improve the precision of the trend estimates and p-values. The adjusted p-value includes adjustment terms for age, sex, and race/ethnicity in the model.

For more details on these statistical analyses, see the memorandum by Cohen (2010).[iii]

Table 1. Statistical significance tests comparing cancer incidence rates for children ages 0 to 19 between age groups for 2004 to 2006 and analyzing trends for 1992-2006.

				P-VALUES	
Type of Cancer	**From**	**To**	**Against**	**Unadjusted**	**Adjusted***
Acute lymphoblastic leukemia	2004	2006	age	< 0.0005	< 0.0005
Acute lymphoblastic leukemia	1992	2006	year	0.132	0.019
Acute myeloid leukemia	2004	2006	age	< 0.0005	< 0.0005
Acute myeloid leukemia	1992	2006	year	0.132	0.154
Central nervous system tumors	2004	2006	age	< 0.0005	< 0.0005
Central nervous system tumors	1992	2006	year	0.381	0.816
Hodgkin's lymphoma	2004	2006	age	< 0.0005	< 0.0005
Hodgkin's lymphoma	1992	2006	year	0.362	0.090
Non-Hodgkin's lymphoma	2004	2006	age	< 0.0005	< 0.0005
Non-Hodgkin's lymphoma	1992	2006	year	< 0.0005	0.001
Burkitt's lymphoma	2004	2006	age	0.472	0.488

[iii] Cohen, J. 2010. *Selected statistical methods for testing for trends and comparing years or demographic groups in other ACE health-based indicators.* Memorandum submitted to Dan Axelrad, EPA, 26 August, 2010.

				P-VALUES	
Type of Cancer	**From**	**To**	**Against**	**Unadjusted**	**Adjusted***
Burkitt's lymphoma	1992	2006	year	0.243	0.172
Thyroid carcinoma	2004	2006	age	0**	0**
Thyroid carcinoma	1992	2006	year	0.175	0.520
Malignant melanoma	2004	2006	age	< 0.0005	< 0.0005
Malignant melanoma	1992	2006	year	< 0.0005	< 0.0005
Other and unspecified carcinomas†	2004	2006	age	< 0.0005	< 0.0005
Other and unspecified carcinomas†	1992	2006	year	0.641	0.277
Germ cell tumors	2004	2006	age	< 0.0005	< 0.0005
Germ cell tumors	1992	2006	year	0.035	0.176
Soft tissue sarcomas	2004	2006	age	< 0.0005	< 0.0005
Soft tissue sarcomas	1992	2006	year	0.008	0.009
Osteosarcoma	2004	2006	age	< 0.0005	
Osteosarcoma	1992	2006	year	0.820	0.608
Ewing's sarcoma	2004	2006	age	< 0.0005	< 0.0005
Ewing's sarcoma	1992	2006	year	0.985	0.970
Neuroblastoma	2004	2006	age	< 0.0005	< 0.0005
Neuroblastoma	1992	2006	year	0.152	0.763
Wilms' tumor	2004	2006	age	< 0.0005	< 0.0005
Wilms' tumor	1992	2006	year	< 0.0005	0.016
Hepatoblastoma	2004	2006	age	0*	0*
Hepatoblastoma	1992	2006	year	0.031	0.005

*For AGAINST = "age," the p-values are adjusted for sex and race/ethnicity.
For AGAINST = "year," the p-values are adjusted for age, sex, and race/ethnicity.
* * P-value = zero because one age group has exactly zero cases.
†"Other and unspecified carcinomas" is a subset of the ICCC group "XI Carcinomas and other malignant epithelial neoplasms."