America's Children and the Environment, Third Edition

DRAFT Indicators

Special Features: Birth Defects

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 birth defects topic in the Special Features 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/.

Birth Defects

The term "birth defects" covers a range of structural defects of the limbs or mouth; defects that affect development of the spinal cord; and defects of reproductive organs and internal organs, such as the heart; all of which occur while the baby is developing in the mother's body.[1,2] A birth defect may affect how the body looks, works, or both. Some birth defects can be detected before birth, others can be detected when the baby is born, and others may not be detected until some time has passed after birth.

Birth defects are the leading cause of infant death in the first year of life, accounting for about 20% of infant deaths in 2005.[3] Infants who do survive with a birth defect often have lifelong disabilities, such as intellectual disability, heart problems, or difficulty in performing everyday activities such as walking.

Some birth defects are inherited. Other risk factors for birth defects include prenatal exposure of the fetus to certain pharmaceuticals (such as Accutane® or Thalidomide), exposure to alcohol, and insufficient folate in a woman's diet.[3,4] The causes of a significant portion (about 60–70%) of birth defects are unknown, but research suggests that defects could be influenced by environmental factors.[3,5-7] Several environmental contaminants cause birth defects when pregnant women are exposed to high concentrations. Mercury poisoning in Minamata, Japan resulted in birth defects such as deafness and blindness.[8] Prenatal exposures to high concentrations of polychlorinated biphenyls (PCBs) and related chemicals have resulted in stained and acned skin and deformed nails in children.[9] However, the relationship between exposure to lower concentrations of environmental contaminants and birth defects is less clear.

A number of epidemiological studies have evaluated the relationship between environmental and occupational exposures to chemicals and birth defects. A scientific review that evaluated multiple studies of women's occupational exposure to organic solvents found an increased risk for birth defects such as heart defects and oral cleft defects in children born to exposed women.[10] In a recent study conducted in Massachusetts, women who were exposed to drinking water contaminated with the solvent tetrachloroethylene around the time of conception were found to have an increased risk of giving birth to a child with a birth defect.[11]

Studies have found associations between children's birth defects and employment of their parents in certain job categories, such as vehicle mechanic, sawmill worker, welder, janitor, electronic equipment operator, and pesticide applicator.[12-15] An extensive review of the literature concluded that the evidence linking neural tube defects to paternal exposures to dioxins and solvents was suggestive of an association, although not strong enough to draw a solid conclusion regarding causality. The same review concluded that there is not enough evidence to determine if there are associations between other types of birth defects and paternal exposures to dioxin, solvents, pesticides, and outdoor air pollutants.[7]

Multiple studies have suggested an association between maternal and paternal exposure to pesticides (both before and after conception) and increased risk of offspring having or dying

from birth defects.[12-14,16-29] A subsequent review study that evaluated many of these individual studies together, however, concluded that the data are inadequate at this time to confirm an association between pesticide exposure and the risk of birth defects.[7]

Disinfection byproducts in drinking water have also been linked to birth defects in some epidemiological studies. Disinfection byproducts are formed when organic material found in source water reacts with chemicals (primarily chlorine) used in treatment of drinking water to control microbial contaminants. Some individual epidemiological studies have found an association between the presence of disinfection byproducts in drinking water and increased risk of birth defects, especially neural tube defects and oral clefts.[30-32] Recent reviews of published studies, however, found that due to inconsistent findings among multiple studies, there was not enough evidence to conclude that there is an association between exposure to disinfection byproducts and birth defects.[7,33]

A limited number of studies and a review article have found an association between cardiac birth defects and exposure to air pollutants, specifically carbon monoxide, ozone, particulate matter, and sulfur dioxide.[34-36] EPA air pollution documents have made similar conclusions regarding sulfur dioxide and ozone.[37,38]

Some studies have also found that exposure to endocrine disrupting chemicals may cause urogenital malformations in newborn boys, such as cryptorchidism (undescended testes) and hypospadias (abnormally placed urinary opening).[13,21,39-47] An analysis of a large national database showed a significant increase in the incidence of congenital penile anomalies, particularly hypospadias, from 1988–2000.[48] According to studies by the Centers for Disease Control and Prevention, the prevalence of hypospadias in the United States has doubled in recent decades.[49] This considerable increase, combined with evidence of an association between endocrine-disrupting contaminants and urogenital birth defects in animal studies, has led to the hypothesis that environmental exposures are a contributing factor.[50] However, a review study recently concluded that there is inadequate evidence at this time of associations between male genital birth defects and exposure to environmental contaminants such as pesticides, PCBs, wood preservatives, and phthalates.[7]

The process of fetal development is intensely complicated, requiring the precise coordination of cell division, growth, and movement. During the process of fetal development there are critical periods of susceptibility or vulnerability, at which point exposure to environmental contaminants may be especially damaging.[51] For example, two air pollution epidemiology studies found that the first two months of gestation are a particularly vulnerable period, during which exposure to air pollutants may cause birth defects of the heart and oral clefts.[35,52] Similarly, studies have found that being conceived during the spring, when pesticide use is at its highest and drinking water contamination may occur, is a risk factor for birth defects.[14,27,53] These types of studies are useful for generating hypotheses about the relationship between environmental exposures and the development of birth defects.

There is currently no unified national monitoring system for birth defects, although many birth defects can be observed shortly after delivery and are recorded on birth certificates. A national-scale indicator could be constructed using birth certificate data, but would miss any birth defect

that is not immediately recognized at birth. Most states have some type of birth defects monitoring program, although the type of tracking varies widely among the states. As of 2008, 45 states, the U.S. Department of Defense, and Puerto Rico had some type of existing birth defects monitoring program.[54] A small portion of these states have the most complete type of tracking system, which includes actively researching medical records for birth defects and following children through the first year of life. The remaining states have some type of monitoring program, but do not have all the aspects of a complete surveillance system.

The Texas monitoring program, which has monitored birth defects since 1995, is considered one of the most complete in the nation.[55] Data from the Texas registry for several major defects are presented in this section, as an example.

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Indicator S5: Birth defects in Texas, 1999–2007

Overview

Indicator S5 presents information about the number of infants born with birth defects in Texas. The data come from a registry of birth defects for the state of Texas, which compiles data on any birth defects identified in the first year after each child is born. The Texas Registry staff routinely review medical records at all hospitals and birthing centers where babies are delivered or treated to identify birth defects. Indicator S5 shows how the rates of different types of birth defects have changed over time.

The Texas Birth Defects Registry

The data for this indicator come from the Texas Birth Defects Epidemiology and Surveillance Branch. The Texas monitoring program began monitoring the Houston/Galveston and South Texas areas in 1995 and expanded in 1999 to cover the entire state. The Texas monitoring program covers approximately 380,000 births each year, which represents almost 10% of all births in the United States. The Texas monitoring program reports a wide array of birth defects.

Although most states have a birth defects monitoring program in place, the comprehensiveness of these programs varies. Texas's birth defects monitoring program is one of the most complete in the nation, using high-quality surveillance methods to examine a wide range of birth defects throughout a child's first year of life.[55] The Texas Registry staff routinely visit all hospitals and birthing centers where babies are delivered or treated and review logs to find potential cases, and medical records to identify birth defects.[56] The rates of birth defects in Texas are not necessarily representative of those in other states or the nation as a whole.

Comparing the Texas Birth Defects Registry with Other Data Sources

To examine whether the rate of birth defects in Texas is similar to the rate for the country as a whole, it is useful to compare birth defect rates from birth certificates. Birth certificates record only those birth defects apparent at birth, and do not represent defects that become apparent after some time. Unlike the individual state surveillance systems, whose methods vary greatly from state to state, the procedures for recording birth defects on birth certificates are similar for all states. The birth certificate reported rates of birth defects for Texas are generally similar to the nationwide rates.[57]

Comparing the Texas Birth Defects Registry data to the birth certificate data for Texas reveals that the active surveillance strategies detect a far greater number of birth defects than can be detected at an infant's birth. For specific birth defects that could be directly compared, the Texas surveillance program typically detects two to three times the number of birth defects reported on birth certificates, demonstrating the importance of tracking birth defects that are not observed at the time of delivery.[56,57] Texas birth certificates list potential birth defects for clinicians to choose from when recording the details of an infant's birth. An analysis by the Texas Birth

Defects Registry found that birth certificates identify these listed birth defects only 15% of the time that they occur. Furthermore, of those birth defects listed on Texas birth certificates, the most obvious birth defects, such as missing limbs, are only identified 43% of the time.[58]

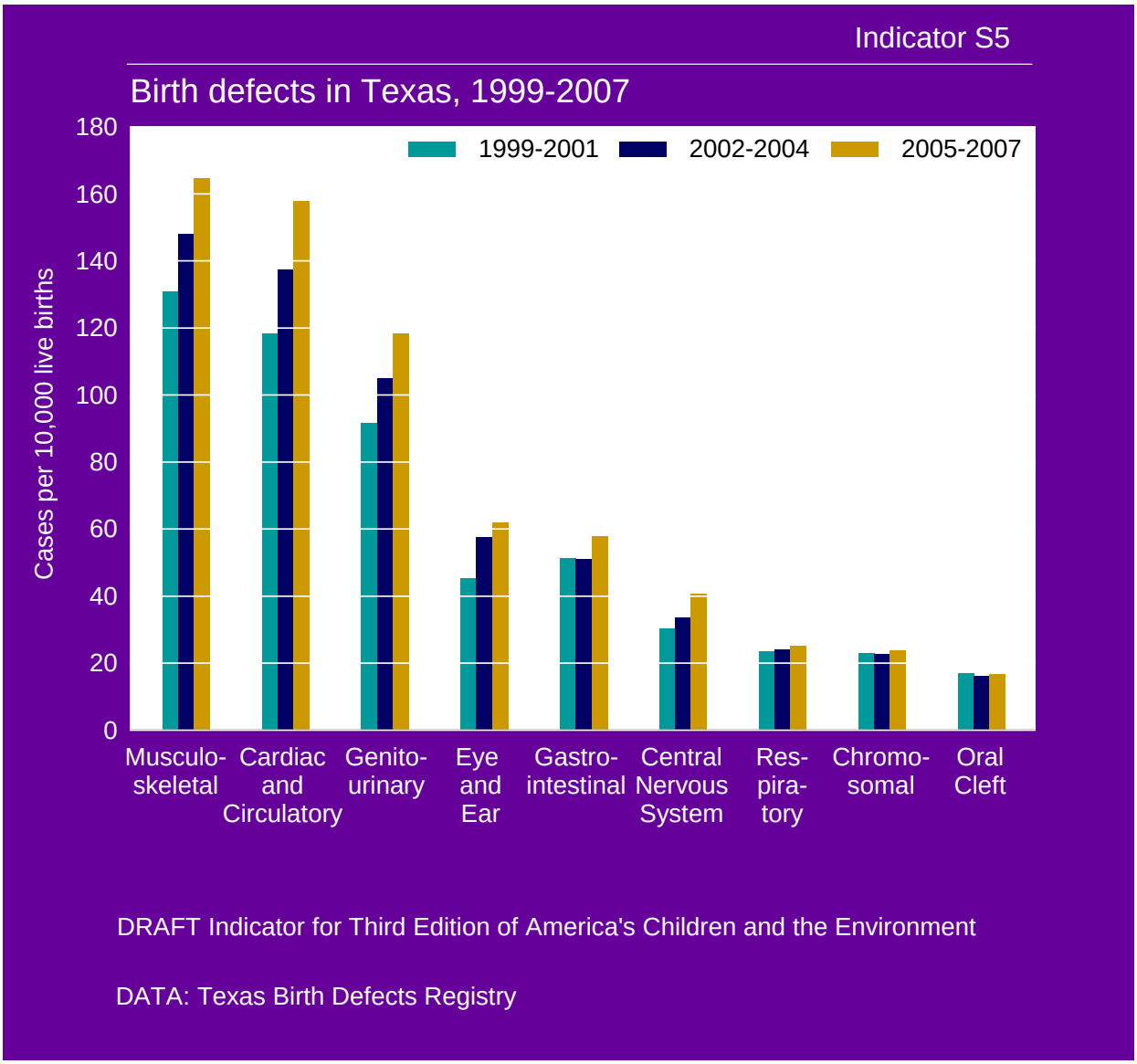
Data Presented in the Indicator

Indicator S5 displays the number of birth defects per 10,000 live births for the state of Texas. Indicator S5 shows data for 1999–2007 and groups birth defects by structural categories. A supplemental data table for this indicator provides information showing how birth defect rates vary by race/ethnicity.

Statistical Testing

Statistical analysis has been applied to this indicator to determine whether any changes in prevalence over time 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 occurred randomly. It should be noted that when statistical testing is conducted for multiple differences (e.g., for multiple structural categories), the large number of comparisons involved increases the probability that some differences identified as statistically significant may actually have occurred randomly.

A finding of statistical significance for a health indicator depends not only on the numerical differences in the annual values, but also on the annual number of observations and the variability of those values. For example, the statistical test is more likely to detect a trend when data have been obtained over a longer period. A finding that there is or is not a statistically significant difference in prevalence over time is not the only information that should be considered when determining the public health implications of those differences.



- Musculoskeletal defects are the most common type of birth defect in Texas, with 165 cases per 10,000 live births for the years 2005–2007. The second most common type of birth defect in Texas is cardiac and circulatory, with 158 cases per 10,000 live births for the years 2005–2007.

- The rates for all categories of birth defects in Texas have increased or remained stable for the period of 1999–2007. Some of the biggest increases were seen for musculoskeletal defects, cardiac and circulatory defects, genitourinary defects, eye and ear defects, and central nervous system defects.
    - Statistical Note: The increases were statistically significant for musculoskeletal defects, cardiac and circulatory defects, genitourinary defects, eye and ear defects, gastrointestinal defects, central nervous system defects, and respiratory defects.

Data Tables

Table S5: Birth defects in Texas, 1999–2007

	Cases per 10,000 live births		
	1999–2001	2002–2004	2005–2007
Musculoskeletal	131.1	148.1	164.8
Cardiac and Circulatory	118.4	137.4	157.9
Genitourinary	91.7	105.1	118.4
Eye and Ear	45.2	57.5	62.1
Gastrointestinal	51.5	51.0	57.8
Central Nervous System	30.5	33.6	40.7
Respiratory	23.5	24.1	25.3
Chromosomal	23.0	22.8	23.9
Oral Cleft	17.0	16.2	16.9

DATA: Texas Birth Defects Registry

Table S5a: Birth defects in Texas, 2005–2007, by race/ethnicity

	Cases per 10,000 live births			
	White Non-Hispanic	Black Non-Hispanic	Hispanic	Other Non-Hispanic
Musculoskeletal	171.6	163.2	162.1	142.6
Cardiac and Circulatory	154.6	151.1	164.5	125.8
Genitourinary	132.2	115.1	109.6	120.2
Eye and Ear	60.1	48.0	67.3	52.4
Gastrointestinal	60.2	46.1	60.2	39.5
Central Nervous System	41.8	43.7	39.5	35.8
Respiratory	23.1	23.4	27.6	20.5
Chromosomal	23.5	19.9	25.3	18.2
Oral Cleft	18.1	11.1	17.5	15.7

DATA: Texas Birth Defects Registry

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Metadata

Metadata for	Texas Birth Defects Registry
Brief description of the data set	Since 1994, the Texas Birth Defects Epidemiology and Surveillance Branch has maintained the Texas Birth Defects Registry, a population-based birth defects surveillance system. Through multiple sources of information, the Registry monitors all births in Texas (approximately 380,000 each year) and identifies cases of birth defects. Registry staff routinely visit all hospitals and birthing centers where affected children are delivered or treated up through the first year of life. Staff review logs to find potential cases, and medical records to identify those indicating one or more birth defects. They then abstract relevant information onto a form designed for this purpose.
Who provides the data set?	Texas Department of State Health Services
How are the data gathered?	The Texas Birth Defects Registry uses active surveillance: o Does not require reporting by hospitals or medical professionals. o Trained program staff regularly visit medical facilities. • Have authority to review log books, hospital discharge lists, and other records. o Program staff use medical charts for each potential birth defect identified. Records in the birth defect registry were matched to birth certificates and fetal death certificates filed with the Vital Statistics Unit of Texas DSHS to gather demographic data.
What documentation is available describing data collection procedures?	Methods report available at: http://www.dshs.state.tx.us/birthdefects/Data/99-04_Methods.pdf.
What types of data relevant for children's environmental health indicators are available from this database?	Birth defects: o central nervous system defects; o ear and eye defects; o cardiac and circulatory defects; o respiratory defects; o oral clefts; o gastrointestinal defects; o genitourinary defects, including hypospadias; o musculoskeletal defects; and o chromosomal defects.
What is the spatial representation of the database (national or	Statewide (Texas) as well as: o public health region; o county; and

Metadata for	**Texas Birth Defects Registry**
other)?	o border residence status.
Are raw data (individual measurements or survey responses) available?	Raw data for 1996–2007 are available through special request. Data are stratified by: statewide, public health regions, county, and border residence status. Results are available by: o specific birth defect category; o mother's race/ethnicity; o gender; and o mother's age group at delivery.
How are database files obtained?	Annual report database files for 1999–2004 can be found at the following website: http://soupfin.tdh.state.tx.us/bdefdoc.htm. Raw data are also available through 2007, by written request. Published reports for 1995–2007 can be accessed at: http://www.dshs.state.tx.us/birthdefects/Data/reports.shtm.
Are there any known data quality or data analysis concerns?	Registry only includes birth defects diagnosed within one year of delivery (with the exception of fetal alcohol syndrome). Secondly, diagnoses made outside Texas or in Texas facilities that staff members do not have access to are excluded. Data collected from medical records and such are subject to differences in clinical practice. Due to flooding during June 2001, several hospitals in Houston lost medical records. An estimated 50 fetuses and infants were born during this time with diagnosed birth defects at the affected hospitals.
What documentation is available describing QA procedures?	An article in *Birth Defects Research Part A: Clinical and Molecular Teratology* highlights quality issues: Miller, E. 2006. Evaluation of the Texas Birth Defects Registry: An active surveillance system. *Birth Defects Research Part A: Clinical and Molecular Teratology*. 76(11): 787-792. See: http://www3.interscience.wiley.com/journal/113455770/abstract.
For what years are data available?	1996–2007.
What is the frequency of data collection?	Ongoing.
What is the frequency of data release?	Annual.
Are the data comparable across	Yes, generally. However, data from different locations may not be comparable due to differences in clinical practice. Note that prior

Metadata for	**Texas Birth Defects Registry**
time and space?	to 1999, only certain regions were included in the registry.
Can the data be stratified by race/ethnicity, income, and location (region, state, county or other geographic unit)?	Using the interactive data query system (http://soupfin.tdh.state.tx.us/bdefdoc.htm) data can be stratified by: o mother's race/ethnicity; and o geographical unit: • statewide; • public health region; • county; and • border residence status.

1

Methods

Indicator

S5. Birth Defects in Texas, 1999-2007.

Summary

Since 1994, the Texas Birth Defects Epidemiology and Surveillance Branch has maintained the Texas Birth Defects Registry, a population-based birth defects surveillance system. The Texas monitoring program began monitoring the Houston/Galveston and South Texas areas in 1995 and expanded in 1999 to cover the entire state. Since 1999, the Registry has monitored all births in Texas (approximately 380,000 each year) and has identified cases of birth defects using multiple sources of information. Indicator S5 uses Texas Birth Defects Registry data to calculate the rates of different types of birth defects in Texas by the structural category and three-year period. Table S5a gives the rates of different types of birth defects in Texas by the structural category and mother's race/ethnicity, for the period 2005-2007.

Data Summary

Indicator	S5. Birth defects in Texas, 1999-2007.		
Time Period	1999-2007		
Data	Texas Birth Defects Registry		
Years (1999-2007)	1999-2001	2002-2004	2005-2007
Live births	1,077,574	1,131,584	1,192,367
Missing or unknown race/ethnicity	1,728	1,963	1,120

Overview of Data Files

Summary data were compiled by the Texas Department of State Health Services. These data gave the numbers of cases, total numbers of live births, and rates of birth defects per 10,000 live births for each combination of structural category, mother's race/ethnicity (All, White non-Hispanic, Black non-Hispanic, Hispanic, and Other non-Hispanic).

Calculation of Indicator

For each structural category and three-year period, the rate of birth defects was calculated as the number of live births with any of those birth defects divided by the total number of live births:

Rate of birth defects per 10,000 live births =
Number of live births with birth defects in structural category and time period / Number of live births in structural category and time period × 10000

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 rates of birth defects in Texas were used to determine whether the trends were statistically significant. Using a logistic regression model, the logarithm of the odds that a given child has a particular type of birth defect is assumed to be the sum of explanatory terms for the three-year period and the mother's race/ethnicity. The odds that a given child has this type of birth defect is the probability that the child has this birth defect divided by the probability that the child does not have this birth defect. Thus if two three-year periods have similar (or equal) rates of birth defects, then they will also have similar (or equal) values for the logarithm of the odds. The explanatory term for the three-year period was the middle year of that period, treated as a numerical value rather than a categorical value. Using this model, the trend in the rates for a given type of birth defect is statistically significant if the regression coefficient for the middle year is statistically significantly different from zero. The uncertainties of the regression coefficients were calculated using the SAS® (SAS Institute, Cary, North Carolina) statistical software GENMOD procedure and a binomial logistic model, treating the births for each race/ethnicity and three-year period as a random sample of births. A p-value at or below 0.05 implies that the trend is statistically significant at the 5% significance level. Each structural category is analyzed separately. No adjustment is made for multiple comparisons.

For these statistical analyses we used five race/ethnicity groups: White non-Hispanic; Black non-Hispanic; Hispanic; Other non-Hispanic; Unknown. The numbers and cases for the Unknown category were calculated by subtracting the totals for the other four race/ethnicity groups from the totals for all births. The Unknown race/ethnicity category includes births where the mother's race/ethnicity is unknown or there was a refusal to answer.

For each comparison, we present unadjusted and adjusted analyses. The unadjusted analyses directly compare the rates for different three-year periods. The adjusted analyses add race/ethnicity terms to the statistical model and compare the rates between different three-year periods after accounting for the effects of the race/ethnicity group. For example, if births to White non-Hispanic mothers tend to have much higher probabilities of a birth defect in a given structural category, compared with Black non-Hispanics, and if the number of births to White non-Hispanic mothers is increasing much more rapidly than the number of births to Black non-Hispanic mothers, then the unadjusted trend would be significant but the adjusted trend (taking into account race/ethnicity) would not be significant.

Comparisons of the trends in the rates of birth defects in Texas from 1999 to 2007 are shown in Table 1. For the unadjusted comparisons, the only explanatory variables are the intercept and a term for the middle year of the three-year period. For the adjusted comparisons ("Adjusted for race/ethnicity"), the explanatory variables are the intercept and a term for the middle year of the three-year period together with terms for each race/ethnicity group. For these adjusted comparisons, the statistical test compares the three-year rates after accounting for any differences in the race/ethnicity distributions between the three-year periods.

For more details on these statistical analyses, see the description of the similar methods used for the National Vital Statistics System (NVSS) birth outcomes indicator in the memorandum by Cohen (2010).[1]

Table 1. Statistical significance tests for the trends of birth defects in Texas, from 1999-2007.

				P-Values	
Structural Category	**From**	**To**	**Against**	**Unadjusted**	**Adjusted for race/ethnicity**
Musculoskeletal	1999	2007	year	< 0.0005	< 0.0005
Cardiac and Circulatory	1999	2007	year	< 0.0005	< 0.0005
Genitourinary	1999	2007	year	< 0.0005	< 0.0005
Eye and Ear	1999	2007	year	< 0.0005	< 0.0005
Gastrointestinal	1999	2007	year	< 0.0005	< 0.0005
Central Nervous System	1999	2007	year	< 0.0005	< 0.0005
Respiratory	1999	2007	year	0.005	0.011
Chromosomal	1999	2007	year	0.148	0.152
Oral Cleft	1999	2007	year	0.862	0.885

[1] Cohen, J. 2010. *Selected statistical methods for testing for trends and comparing years or demographic groups in other ACE health-based indicators.* Memorandum submitted by Jonathan Cohen ICF, to Dan Axelrad, EPA, 15 November, 2010.