

The Texas Birth Defects MONITOR

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Changes in Spina Bifida Lesion Level After Folic Acid Fortification in the United States

Neural tube defects (NTDs) are serious birth defects of the brain and spine. NTDs occur when the neural tube does not close properly, early during a pregnancy, often before a woman knows she is pregnant. Folic acid, a B vitamin, can help prevent NTDs if taken before and during pregnancy. Folic acid can be obtained by taking a daily vitamin containing folic acid or by eating foods fortified with folic acid. In 1992, the U.S. Public Health Service recommended that all women capable of becoming pregnant consume 400 micrograms of folic acid daily to help prevent NTDs. In 1998, the U.S. Food and Drug Administration mandated folic acid be added to enriched grain products (such as bread, pasta, rice, and cereal) to increase folic acid consumption.

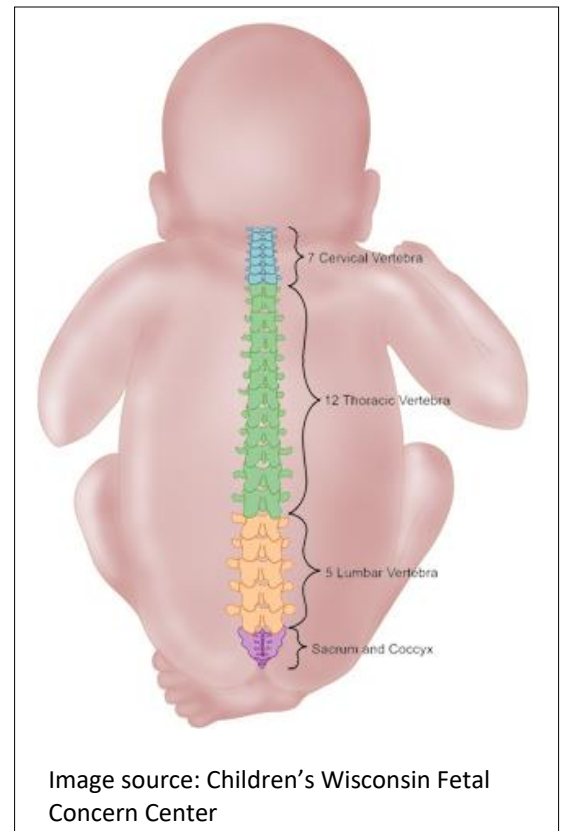
Spina bifida is a type of NTD that can happen anywhere along the spine when the neural tube does not close all the way. The location of the spina bifida lesion (an area of abnormal tissue change) is a major determinant of the long-term prognosis. The figure on the next page shows the names and locations of the vertebral column bones. Upper-level lesions, such as cervical or thoracic are associated with greater disability and mortality risk compared with lower-level lesions, such as sacral or lower lumbar lesions.

In this study, researchers looked at whether the severity of cases of spina bifida changed after the U.S. began mandated folic acid fortification of grain enriched products. This study showed that folic acid fortification has reduced the occurrence of spina bifida, and that much of the reduction was seen in the more severe types of spina bifida.

To assess whether folic acid fortification may have had an effect on the severity of spina bifida cases, the National Birth Defects Prevention Network issued a call for state birth defects programs' spina bifida lesion data before and after mandatory folic acid fortification for enriched cereal grains. Six active population-based birth defect programs provided data on cases of spina bifida from 1992-1996 (before mandatory fortification), and 1999-2016 (after mandatory fortification). Adjusted odds ratios, or relative risk, for case severity (upper-level lesions [cervical, thoracic] vs lower-level lesions [lumbar, sacral]) as well as prevalence ratios (PRs) were calculated.

In this study, researchers found:

- Overall spina bifida prevalence declined by 23%.
- Case severity (or the odds of upper-level to lower-level lesion cases) decreased by 70% between the pre- and post- fortification periods.
- The decrease was most pronounced for non-Hispanic White mothers.
- When examining the prevalence of just severe, upper-level lesion cases of spina bifida, a 72% decrease was seen after mandatory folic acid fortification.
- The prevalence of less severe, lower-level lesions remained relatively stable between the fortification periods.



Researchers determined that after mandatory folic acid fortification, the severity of cases of spina bifida decreased. For more information about this publication, please see:

Mai, C. T., Evans, J., Alverson, C. J., Yue, X., Flood, T., Arnold, K., Nestoridi, E., Denson, L., Adisa, O., Moore, C. A., Nance, A., Zielke, K., Rice, S., Shan, X., Dean, J. H., Ethen, M., Hansen, B., Isenburg, J., & Kirby, R. S. (2022). Changes in Spina Bifida Lesion Level After Folic Acid Fortification in the US. *The Journal of pediatrics*, S0022-3476(22)00597-2. doi.org/10.1016/j.jpeds.2022.06.023

Special thanks to Dr. Cara Mai for assistance with this article. Ms. Ethen, recently retired from the Texas Birth Defects Epidemiology and Surveillance Branch, also contributed to this paper.

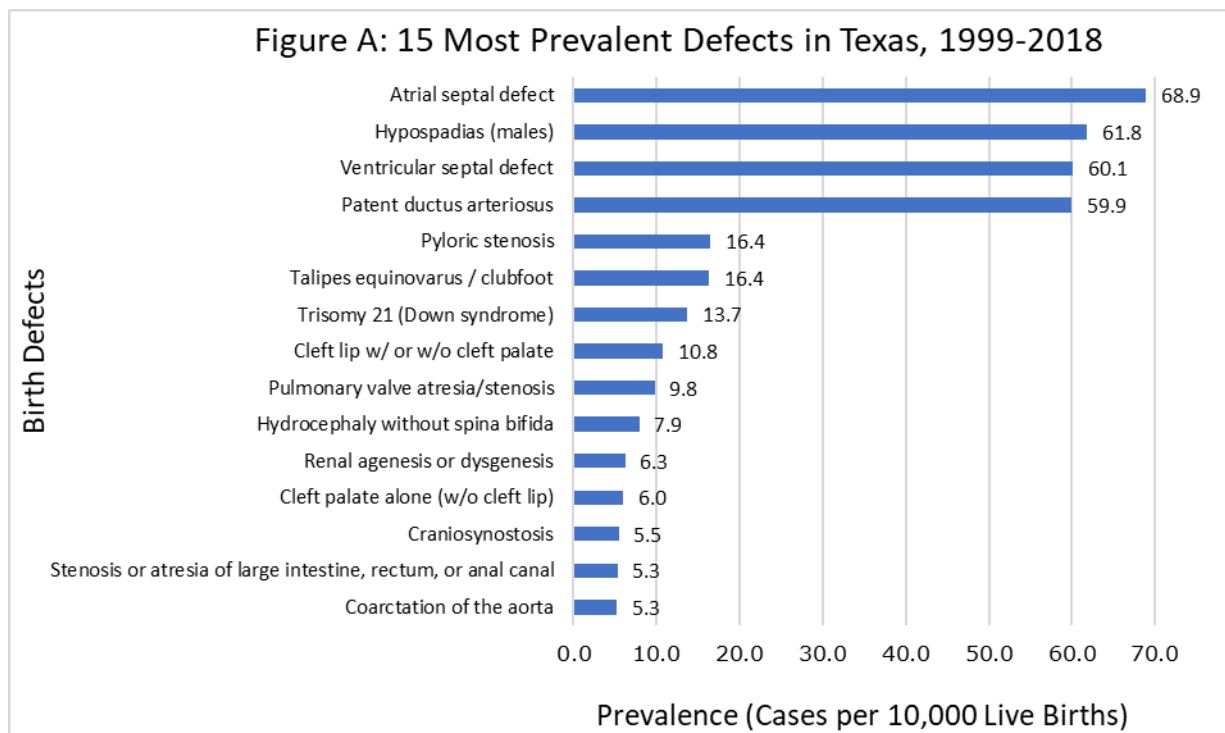
Folic Acid Awareness Week is September 10-16, 2023!

The 30-year anniversary of the U.S. Public Health Service's folic acid recommendation for prevention of neural tube defects (NTDs) was recognized in September 2022. Folic acid in foods helps prevent about 1,300 neural tube defects annually in the U.S. and saves more than \$600 million each year. Start a healthy habit today and get 400 micrograms (mcg) of folic acid every day. There are two easy ways to get the recommended amount: take a vitamin with 400 mcg folic acid daily or eat a bowl of cereal. Even if you're not trying to get pregnant, folic acid is for everyone because it helps your body make new cells.

Data from the Texas Birth Defects Registry, 1999-2018

The charts below show data from the most recently compiled annual report of the Texas Birth Defects Registry (TBDR), highlighting delivery years 1999 through 2018. During this 20-year period, about 5% of all births in Texas were affected by one or more major birth defects. In the most recent years, approximately 25,000 new case infants were added annually, which represents 6% of all births.

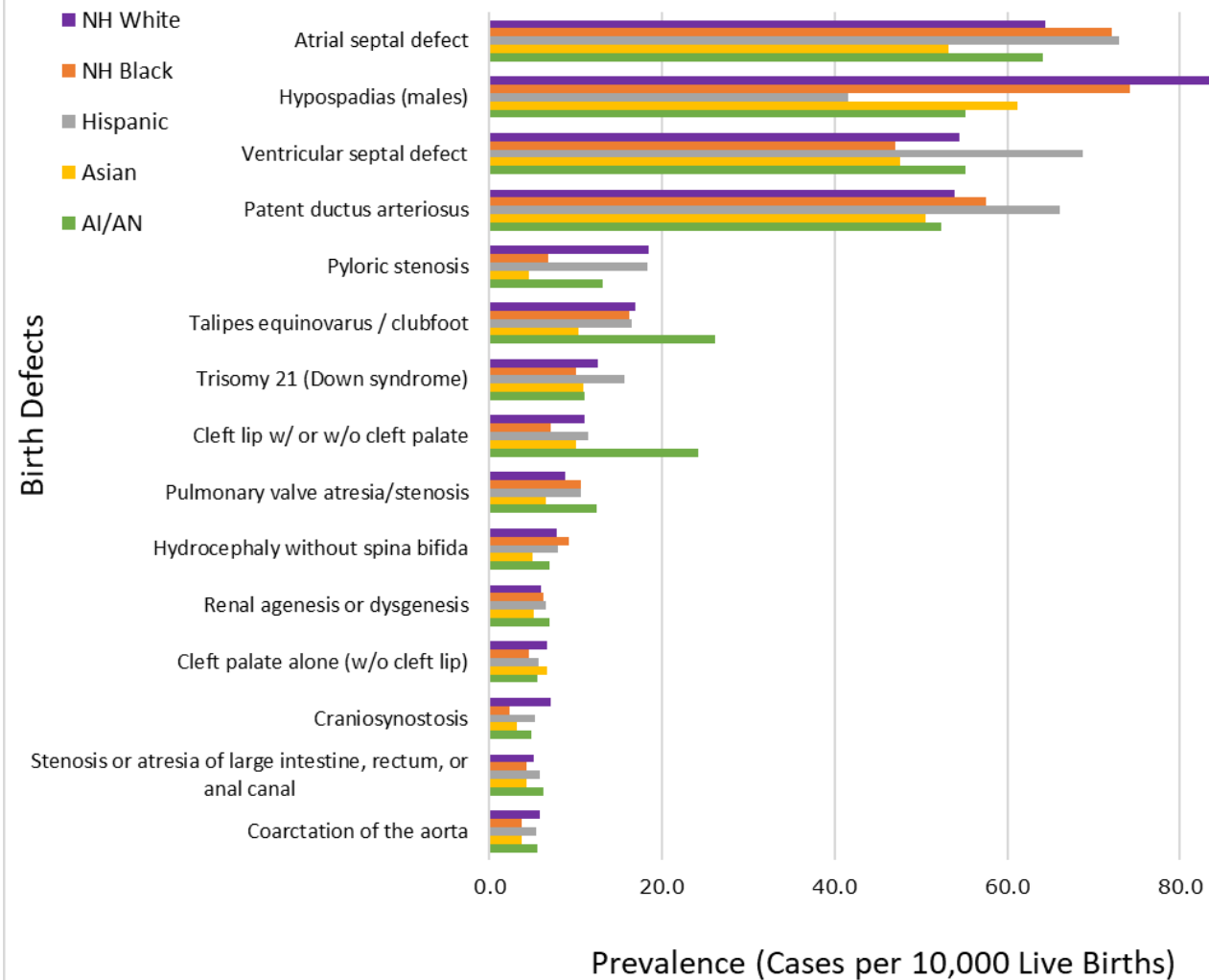
Figure A shows the 15 most prevalent birth defects from 1999 to 2018. Three of the top four most prevalent birth defects were heart defects (atrial septal defect, ventricular septal defect, and patent ductus arteriosus). Hypospadias, a condition in boys in which the urethral opening is misplaced, was the second most prevalent defect. Among more commonly known birth defects, Down syndrome was found to occur among 1 in 729 deliveries (or births), cleft lip 1 in 927 births, and cleft palate 1 in 1,678 births.



Birth Defect Prevalence by Maternal Race/Ethnicity

The prevalence of birth defects varies by race/ethnicity. Maternal race/ethnicity was categorized into the following categories: non-Hispanic (NH) White, NH Black, Hispanic, NH Asian/Pacific Islander (PI), NH American Indian/Alaska Native (AI/AN). Figure B on the next page shows the differences of the 15 most prevalent birth defects, by maternal race/ethnicity.

Figure B: 15 Most Prevalent Defects in Texas, 1999-2018 by Maternal Race/Ethnicity



Of the 15 most prevalent defects in Texas, the top three most prevalent defects differ within each racial/ethnic group:

- NH White: hypospadias in males, atrial septal defect, ventricular septal defect
- NH Black: hypospadias in males, atrial septal defect, patent ductus arteriosus
- Hispanic: atrial septal defect, ventricular septal defect, patent ductus arteriosus
- NH Asian/PI: hypospadias in males, atrial septal defect, patent ductus arteriosus
- NH AI/AN: atrial septal defect, ventricular septal defect, hypospadias in males

The Texas Birth Defects Registry Report of Birth Defects Among 1999-2018 Deliveries is available at dshs.texas.gov/birthdefects/Data/reports.shtm. For a glossary of birth defects terms, visit dshs.texas.gov/birthdefects/glossary.shtm.

Racial and Ethnic Differences in Survival Among Infants with Central Nervous System Defects — Texas, 1999–2017

In 2017, 6% of all live births in Texas were affected by one or more birth defects ⁽¹⁾. Birth defects are major contributors to infant mortality, accounting for approximately 20% of infant deaths ^(2,3). While national studies have provided infant survival rates for some central nervous system (CNS) defects ^(4,5,6), recent survival estimates for a range of CNS defects are not available for Texas infants. Additionally, little is known in Texas about the survival of infants with CNS defects by maternal race and ethnicity, which is relevant from a health disparities perspective.

Infants with CNS birth defects have negative outcomes across their life course, such as impaired mobility and quality of life; therefore, this group of defects remains a public health concern ^(2,3,4,5,6). In this project, survival estimates were calculated for infants born with various CNS defects in Texas and the impact of maternal race and ethnicity was examined.

We conducted a retrospective cohort analysis with data from the Texas Birth Defects Registry (TBDR) for delivery years 1999 to 2017. Cases of birth defects included in the analysis were spina bifida, encephalocele, microcephaly, holoprosencephaly, and hydrocephaly without spina bifida. Births with anencephaly were excluded because most cases do not result in a live birth. Infants with multiple CNS defects (e.g., having both spina bifida and microcephaly) were included in each relevant birth defect category. The time to death was calculated in days from the date of birth to the date of death.

Using the state vital records system, TBDR infant records were linked to their birth certificates to establish maternal residence in Texas. Additional elements such as maternal race, ethnicity and gestational age were supplemented by birth certificates as well. Maternal race and ethnicity were categorized as non-Hispanic White (NHW), non-Hispanic Black (NHB), and Hispanic. Other racial/ethnic groups were excluded, due to small numbers. Vital status (i.e., the occurrence of death) was derived from the medical record and from the linked death certificates.

The Kaplan-Meier method was used to calculate survival estimates for specific defects and by maternal race and ethnicity; differences were assessed by non-overlapping confidence intervals. Multivariable analyses using Cox proportional hazards models were conducted for each CNS defect to estimate the hazard ratio (HR), or the risk for death, for NHB (Black) and Hispanic infants, each relative to NHW (White) infants. HRs were adjusted for gestational age, a factor associated with infant mortality.

During 1999 to 2017, there were 7,322,262, registered live births among Texas residents, with 11,961 infants having one or more CNS defects. Infants with holoprosencephaly had the lowest survival probability (49%); in contrast, survival of infants with spina bifida was 92% (See Table 1 on the next page).

Table 1: Survival among infants with central nervous system defects, Texas, 1999-2017				
Birth Defect	Cases	Deaths	Survival	95% Confidence Interval (CI)
Holoprosencephaly	650	331	49%	45%–53%
Encephalocele	536	170	68%	64%–72%
Hydrocephaly without spina bifida	5449	965	82%	81%–83%
Microcephaly	3277	460	86%	85%–87%
Spina bifida	2492	208	92%	91%–93%

Note: ordered from lowest to highest % survival; some cases may have had co-occurring CNS defects, so the distribution of CNS defects will not total 100%.

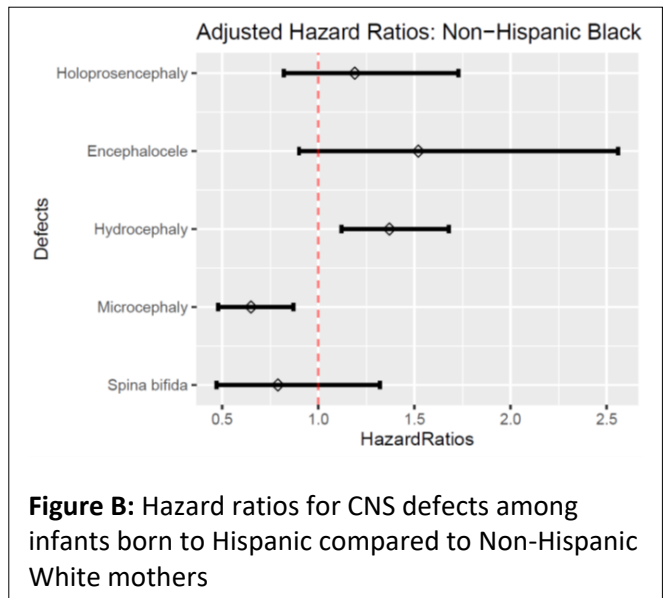
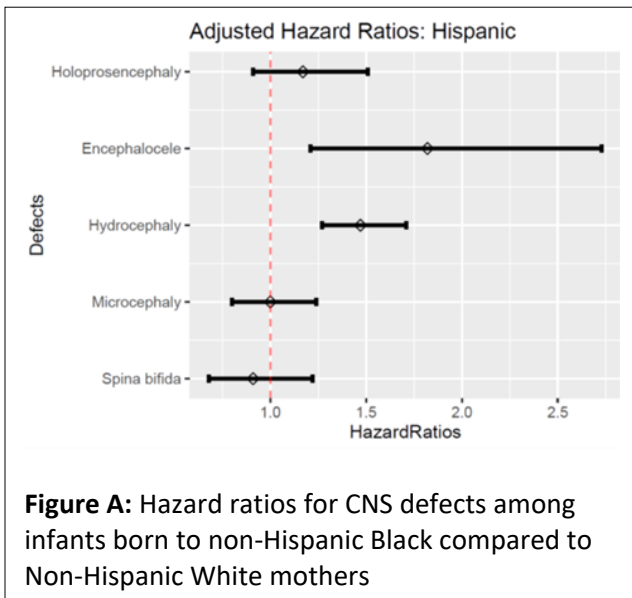
Meaningful differences in infant survival were observed for encephalocele, hydrocephaly without spina bifida, and microcephaly by maternal race/ethnicity. One observed difference in survival was for hydrocephaly without spina bifida, in which NHW (White) had the highest survival (86% [95% CI: 84%–88%]) followed by NHB (Black) (81% [95% CI: 78%–83%]) and Hispanic 80% [95% CI: 78%–81%]). No differences in survival among infants with spina bifida and holoprosencephaly were seen across maternal race and ethnicity groups.

The results from the multivariable analysis are shown in Table 2 and Figure A on the next page. Compared to NHW mothers, the mortality risk was significantly greater among infants born to NHB mothers for hydrocephaly without spina bifida (HR 1.37 or 37% higher) but significantly lower for microcephaly (HR 0.65 or 35% lower). The results also showed that compared to NHW mothers, the mortality risk was significantly greater among infants born to Hispanic mothers for encephalocele (HR 1.82 or 82% higher) and hydrocephaly without spina bifida (HR 1.47 or 47% higher) (Figure B on the next page).

Table 2: Adjusted hazard ratios (HRs)* for Non-Hispanic Black and Hispanic infants with CNS defects, compared to Non-Hispanic White infants, Texas, 1999-2017

Birth Defect	Non-Hispanic White	Non-Hispanic Black			Hispanic		
	HR	HR	95% CI	P-value	HR	95% CI	P-value
Holoprosencephaly	Ref	1.19	0.82-1.73	0.37	1.17	0.91-1.51	0.22
Encephalocele	Ref	1.52	0.90-2.56	0.12	1.82	1.21-2.73	0.004*
Hydrocephaly without spina bifida	Ref	1.37	1.12-1.68	0.003*	1.47	1.27-1.71	<.0001*
Microcephaly	Ref	0.65	0.48-0.87	0.004*	1.00	0.80-1.24	0.96
Spina bifida	Ref	0.79	0.47-1.32	0.36	0.91	0.68-1.22	0.52

*Adjusted hazard ratio (HR), or the relative risk of death, adjusted for gestational age, is statistically significant (P<0.05). Non-Hispanic White mothers served as the referent (ref) group. Infant race/ethnicity determined by mother’s race/ethnicity.



This study provides population-based infant survival estimates for a range of CNS defects in Texas. The survival estimates for Texas infants with spina bifida (>90%) is similar to those from other recent population-based studies conducted in the United States (4, 5, 6).

The lowest survival estimate was observed for infants with holoprosencephaly, and this could be due to co-occurring chromosomal conditions. Overall, racial, and ethnic differences in survival for infants with encephalocele, microcephaly and hydrocephaly without spina bifida were identified in Texas. This study identified differences in survival for infants with hydrocephaly without spina bifida whose mothers were non-white (Hispanic and NHB), compared to White (NHW). After adjusting for gestational age, infants born with this CNS defect to non-white (Hispanic and NHB) mothers had a higher risk for death compared to NHW. The cause of these differences could be attributed to factors such as maternal age, socio-economic status, and the pattern of co-occurring birth defects (e.g., syndromes or chromosomal anomalies) ^(4,5,6,7,8). Future analyses should account for these potential differences in birth defect survival patterns and assess the contribution of time trends.

This activity was reviewed by CDC (Centers for Disease Control and Prevention) and conducted consistent with applicable federal law and CDC policy. §

§ See e.g., 45 C.F.R. part 46.102(l)(2), 21 C.F.R. part 56; 42 U.S.C. §241(d); 5 U.S.C. §552a; 44 U.S.C. §3501 et seq.

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January is National Birth Defects Awareness Month

This is a time to raise awareness about birth defects and highlight efforts to improve the health of people living with these conditions across their lifespan. Join the nationwide effort to raise awareness of birth defects and their impact on individuals, parents, and families. For more information on National Birth Defects Awareness Month, visit cdc.gov/ncbddd/birthdefects/awareness-month/index.html.

- There are steps women can take to reduce the risk of birth defects before and during pregnancy. Taking at least 400 micrograms of folic acid every day, preventing infections, visiting the doctor regularly, avoiding harmful substances such as alcohol and tobacco, and managing conditions such as obesity and diabetes, are all some ways that help reduce birth defect risk.
- Birth defects are leading cause of death among infants in the United States. Improvements in care and screening are important during infancy. Newborn screening for congenital heart defects, for example, is an important tool to identify and provide treatment quickly.
- Some research shows that children born with certain birth defects have difficulty with learning or keeping up with developmental milestones. Access to resources such as Early Childhood Intervention and services such as physical therapy and special education can positively impact the development of a child born with birth defects.
- In adolescence, individuals with certain conditions face new challenges while transitioning from childhood to adulthood, such as changes in insurance and doctors. Some may begin making their own healthcare decisions. Recognizing and planning for these changes can improve the transition to adult health care.
- Birth defects affect individuals in adulthood in many ways. People living with birth defects should talk with their doctor about how pregnancy may affect them and their baby. Women who have had a previous pregnancy affected by a neural tube defect are increased risk for a subsequent NTD-affected pregnancy. To learn about genetic risks of having a baby with a birth defect, individuals can talk with a genetic counselor or clinical geneticist.

Content Source: Centers for Disease Control and Prevention



March 3 is World Birth Defects Day. Join us in our effort to raise awareness of birth defects, their causes, and their impact around the world!

Recent Publications from the Texas Birth Defects Epidemiology and Surveillance (BDES) Staff and Collaborators

Benavides, E., Lupo, P. J., Sosa, M., Whitworth, K. W., Canfield, M. A., Langlois, P. H., & Schraw, J. M. (2022). Correction: Urban-rural residence and birth defects prevalence in Texas: a phenome-wide association study. *Pediatric Research*, 91(6), 1625. doi.org/10.1038/s41390-021-01737-7

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Calendar 2023

January:

National Birth Defects
Prevention Month

February:

American Heart Month

February:

International Prenatal Infection
Prevention Month

February 14:

Congenital Heart Defect
Awareness Day

Spring 2023:

March of Dimes March for
Babies (check with MOD for
specific dates and locations)

March:

National Nutrition Month

March:

National Developmental
Disabilities Awareness Month

March 3:

World Birth Defects Day

April:

Alcohol Awareness Month

April:

National Autism
Awareness Month

April:

National Minority Health Month

April:

STD Awareness Month

April 3-9:

National Public Health Week

June:

National Congenital
Cytomegalovirus
Awareness Month

June 12-13:

36th Annual Meeting of the
Society for Pediatric and
Perinatal Epidemiologic
Research, Portland, Oregon

June 24-28:

63rd Annual Meeting for the
Society for Birth Defects
Research and Prevention,
Charleston, South Carolina

July:

National Cleft and
Craniofacial Awareness &
Prevention Month

July 30:

Gastroschisis Awareness Day

September:

Newborn Screening
Awareness Month

September:

National Infant Mortality
Awareness Month

September 10-16:

Folic Acid Awareness Week

October:

National Spina Bifida
Awareness Month

October:

National Down Syndrome
Awareness Month

November 5-8:

49th Annual Meeting of the
International Clearinghouse for
Birth Defects Surveillance and
Research, St. Julian's, Malta

November:

Prematurity Awareness Month
(March of Dimes)

About the Monitor

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Please visit the BDES website for updated information and to sign up for Branch updates:

dshs.texas.gov/birthdefects/.

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