DSHS Grand Rounds

October 26

Recent Findings from Epidemiologic Research on Birth Defects in Texas and Beyond

Presenters:
Mark Canfield, PhD and Peter Langlois, PhD
Birth Defects Epidemiology and Surveillance, DSHS

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Peer-reviewed Literature

Hoyt AT, Canfield MA, Romitti PA, Botto LD , Anderka MT, Krikov SV, Tarpey MK, Feldkamp ML. Associations between maternal periconceptional exposure to secondhand tobacco smoke and major birth defects. Am J Obstet Gynecol. 2016 Jul 18. pii: S0002-9378(16)30456-2. doi:0.1016/j.ajog.2016.07.022.

Van Horne BS, Moffitt KB, Canfield MA, Case AP, Greeley CS, Morgan R, Mitchell LE. Maltreatment of children under age 2 with specific birth defects: a population-based study. Pediatrics. 2015 Dec;136(6):e1504-12.

Langlois PH, Scheuerle AE. Descriptive epidemiology of birth defects thought to arise by new mutation. Birth Defects Res A Clin Mol Teratol. 2015 Nov;103(11):913-27.

Lee LJ, Symanski E, Lupo PJ, Hoyt AT, Canfield MA, et al. Data linkage between the national birth defects prevention study and the occupational information network (O*NET) to assess workplace physical activity, sedentary behaviors, and emotional stressors during pregnancy. Am J Ind Med. 2015 Dec 17. doi: 10.1002/ajim.22548.

Mai CT, Isenburg J, Langlois PH, et al. Population-based birth defects data in the United States, 2008 to 2012: Presentation of state-specific data and descriptive brief on variability of prevalence. Birth Defects Res A Clin Mol Teratol. 2015 Nov;103(11):972-93.

Reefhuis J, Gilboa SM, Anderka M, et al.. The National Birth Defects Prevention Study: A review of the methods. Birth Defects Res A Clin Mol Teratol. 2015 Aug;103(8):656-69.

Dolk H. Preventing birth defects: The value of the NBDPS case-control approach. Birth Defects Res A Clin Mol Teratol. 2015 Aug;103(8):670-9.

John Hellerstedt, MD
DSHS Commissioner

Introductions

John Hellerstedt, MD
DSHS Commissioner is pleased to
introduce our DSHS Grand Rounds speakers

Recent Findings from Epidemiologic Research on Birth Defects in Texas and Beyond

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Birth Defects Epidemiology
and Surveillance, DSHS

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DSHS Grand Rounds: Recent Findings from Epidemiologic Research on Birth Defects in Texas

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October 26, 2016

*Disclosure

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Topics to be Covered:

1. Program History and Overview
2. Birth Defects Prevalence and Differences across Subgroups
3. Birth Defects Mortality/Survival
4. Linkage Studies
5. Critical Congenital Heart Defects
6. Microcephaly and Zika in Texas
7. Birth Defects Risk Factors
8. Program Resources

1. Program History and Overview

Program History

"Baby tragedy has no bounds/Woodlands, like the Valley, sees infants missing brains."

1991 Headlines

Early Program Milestones

- 1993: Legislation enacted
- 1994: Registry established
- 1996: Center established
- 1999: Registry became statewide

Birth Defects Epidemiology & Surveillance Branch, Texas DSHS: 2 Components

Texas Birth Defects Registry (TBDR)

- One of largest birth defects surveillance systems globally
- Funded by State of Texas and Title V Office, DSHS and CDC
- Monitor and describe the occurrence of birth defects in TX
- Conduct cluster investigations
- Collaborative population-based research and prevention
- Family outreach

Texas Center for Birth Defects Research and Prevention

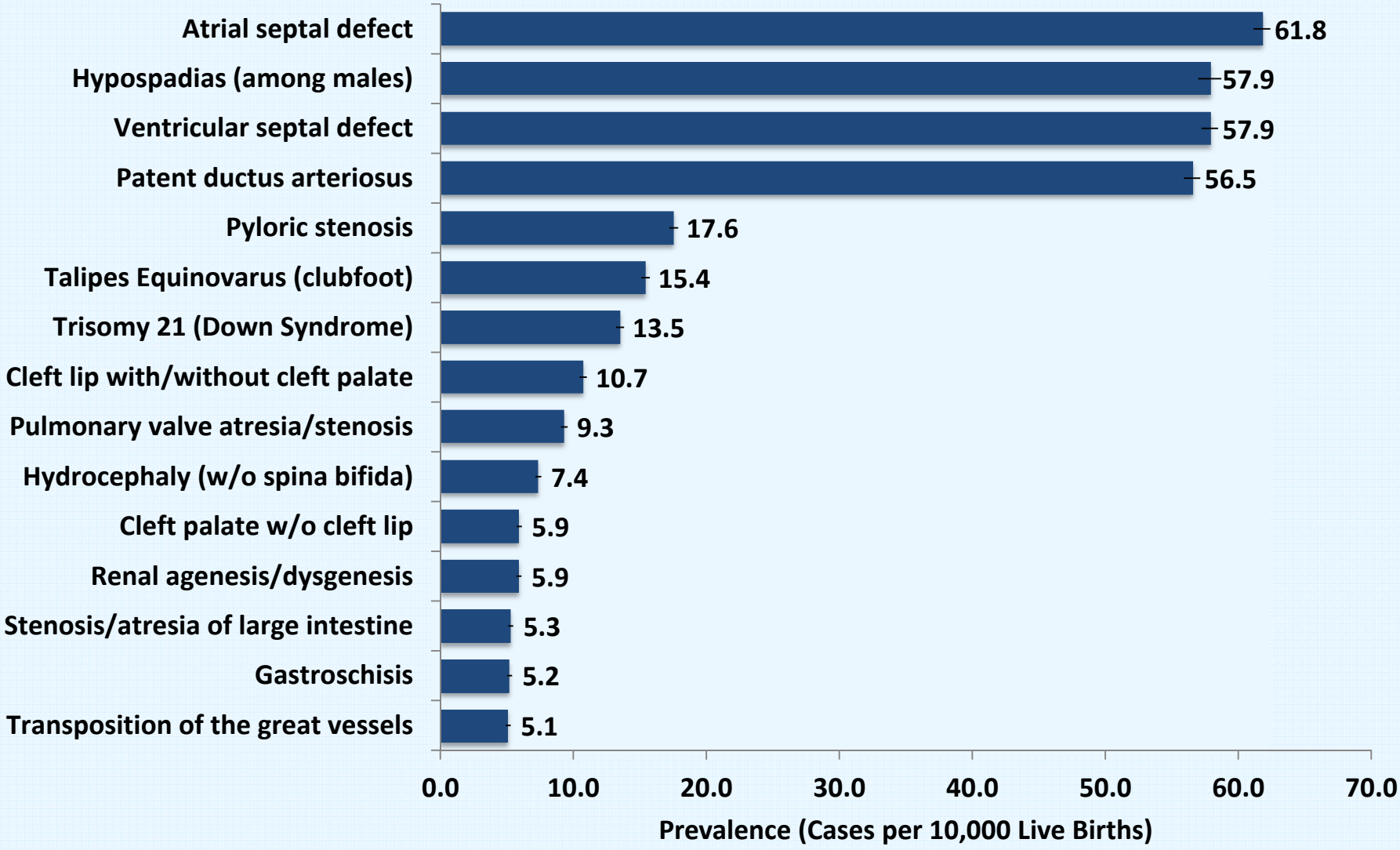
- One of 10 in U.S. – funded by CDC from 1996 to 2014
- Collaborate in the National Birth Defects Prevention Study: largest of its kind to date
- Establish collaborative epidemiologic-genetic research - TX

Features of the Texas Birth Defects Registry

- Computerized database of infants and pregnancies affected by birth defects
- Active surveillance--trained staff visit facilities to identify cases and collect info
- Structural/chromosomal malformations
- Collect diagnoses through infancy
- Emphasis on QA and diagnostic accuracy
- Emphasis on hospitals/related clinics
- Includes all pregnancy outcomes

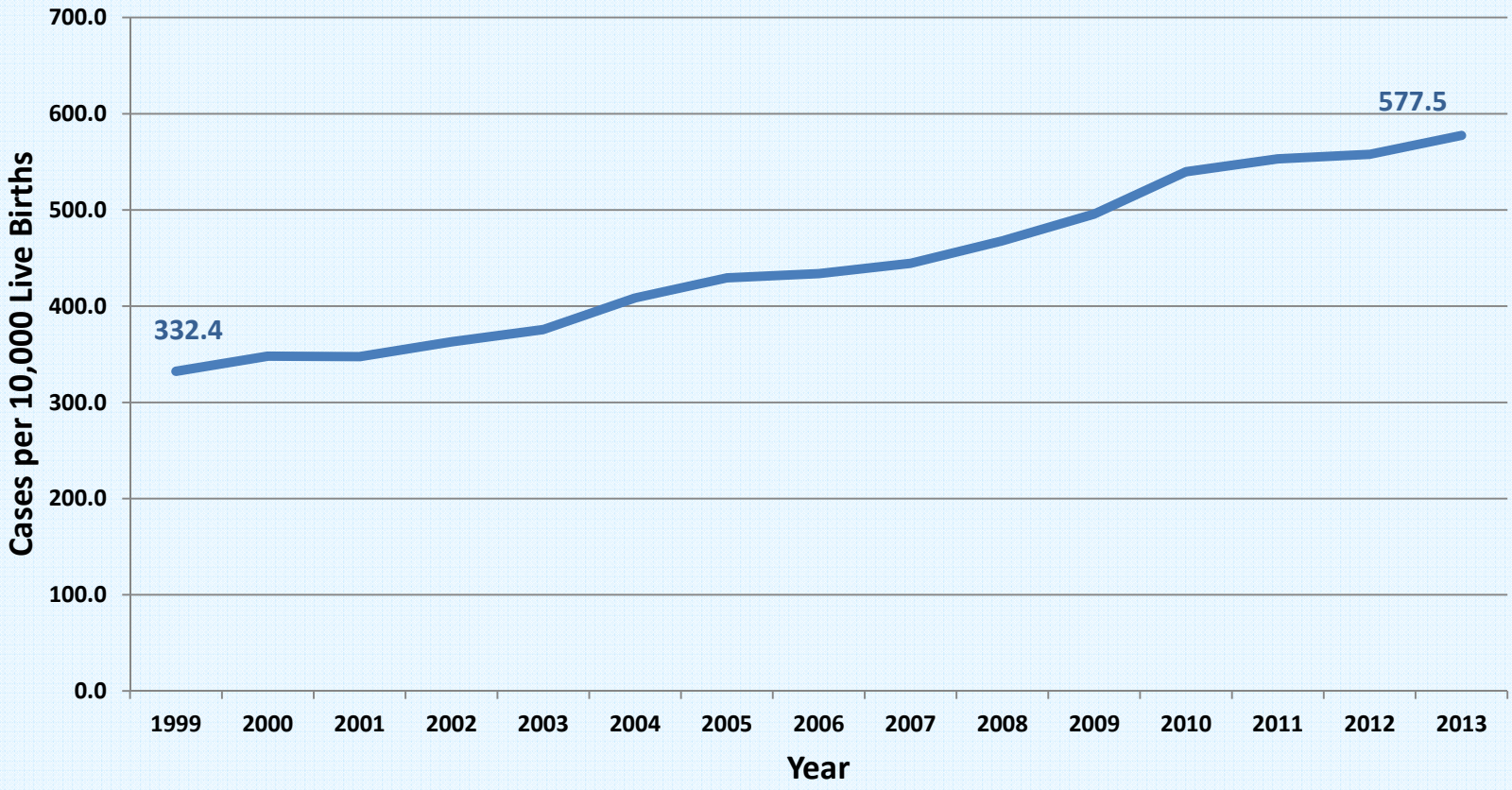
2. Birth Defects Prevalence and Differences across Subgroups

The 15 Most Common Birth Defects in Texas, 1999-2013 (represents >250,000 infants/fetuses)

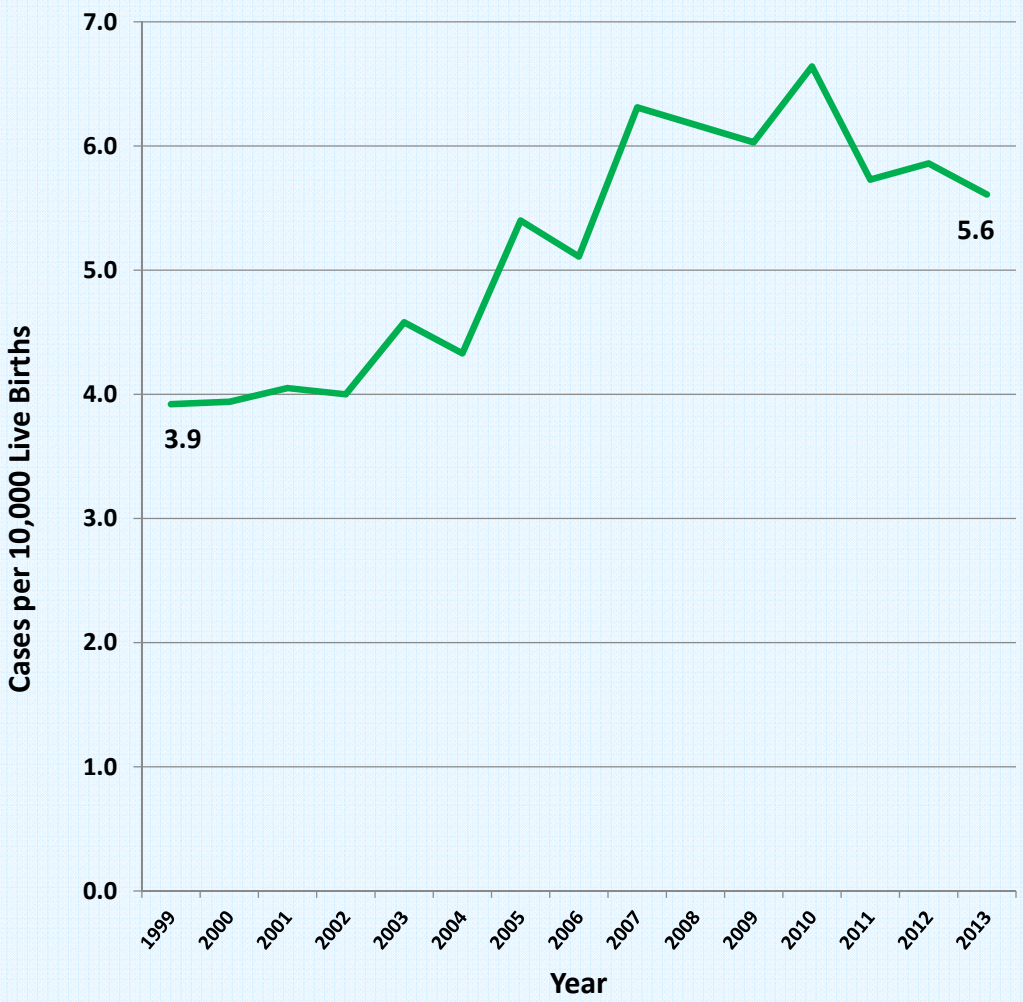


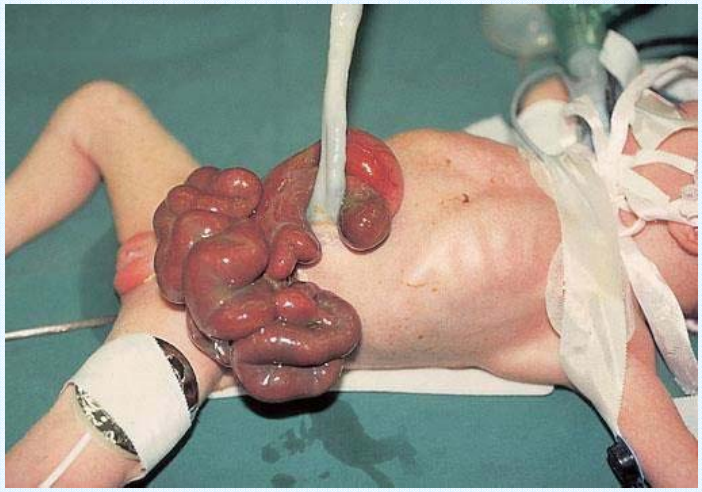
Birth Defects Differences Across Time

Birth Prevalence of Children with Any Monitored Birth Defect, by Delivery Year, Texas, 1999-2013

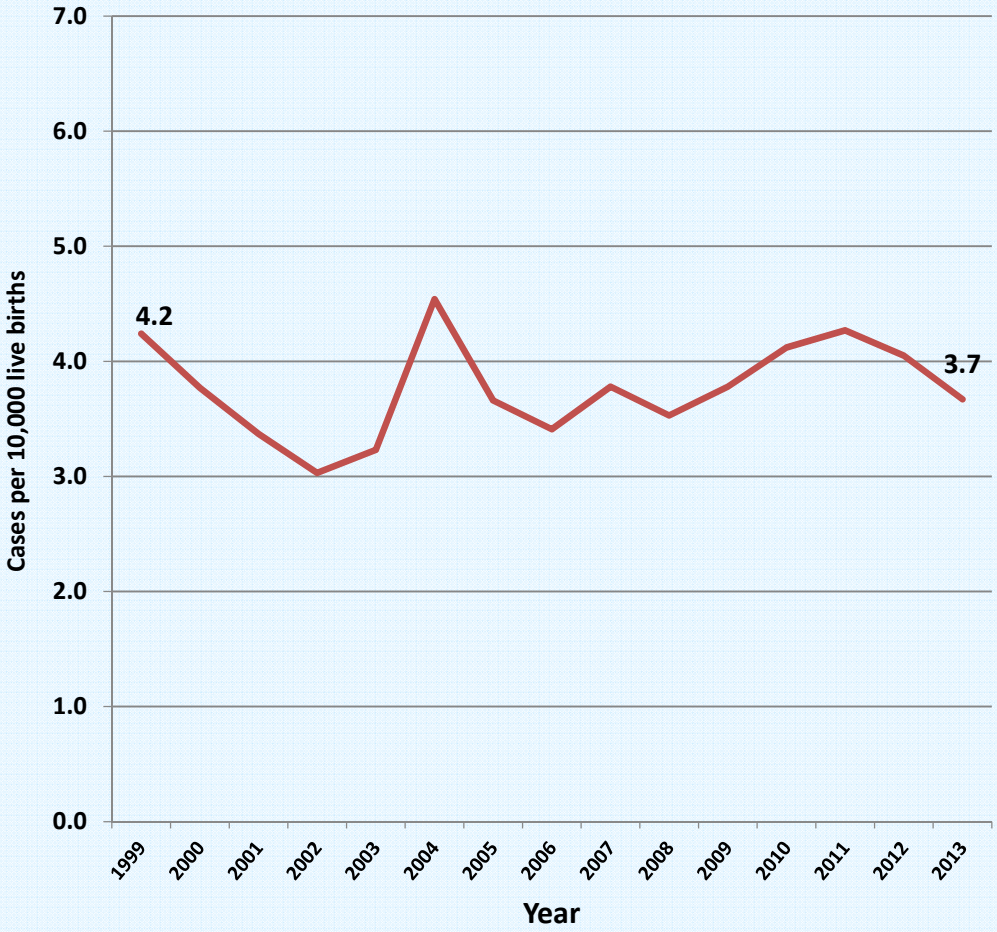


Prevalence of Gastroschisis Over Time, Texas, 1999-2013

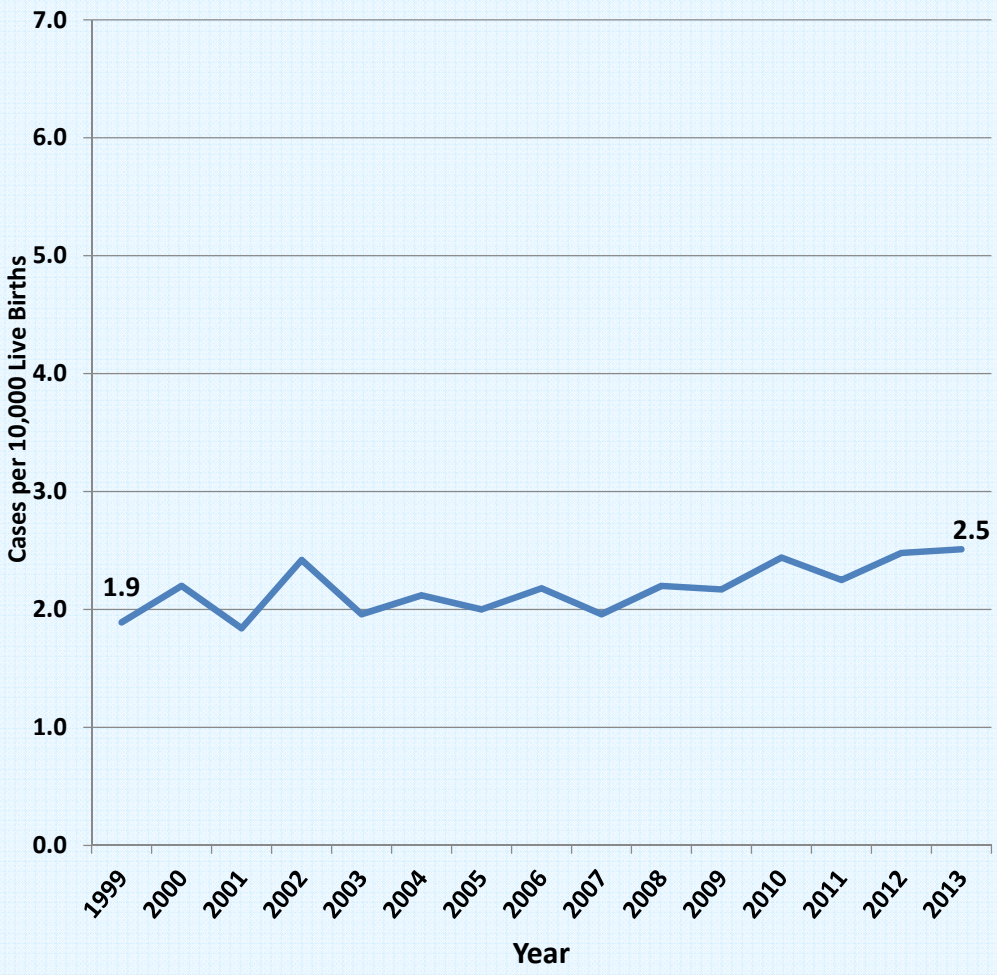




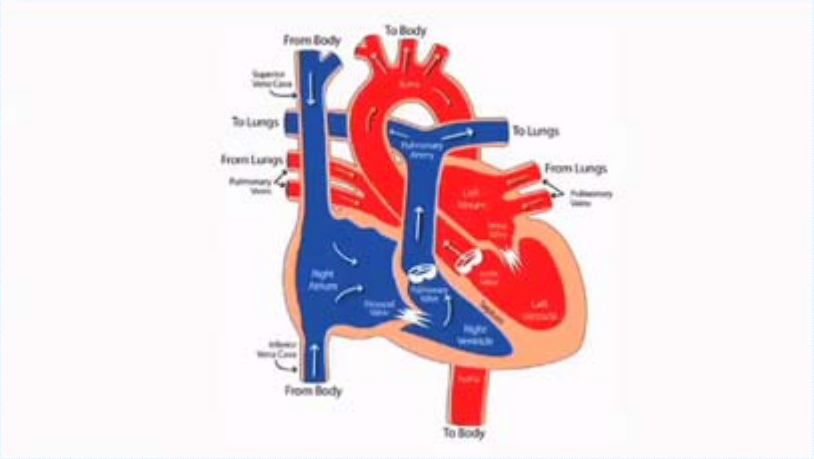
Prevalence of Spina bifida Over Time, Texas, 1999-2013



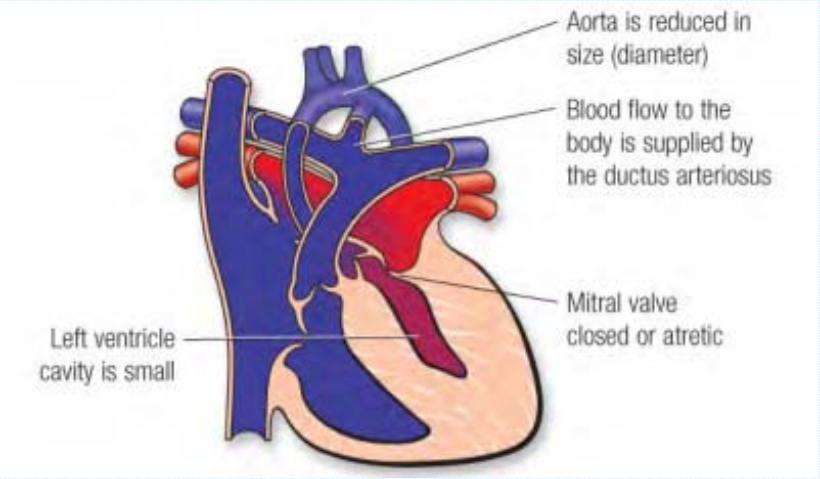
Prevalence of Hypoplastic Left Heart Syndrome Over Time, Texas, 1999-2013



Normal Heart

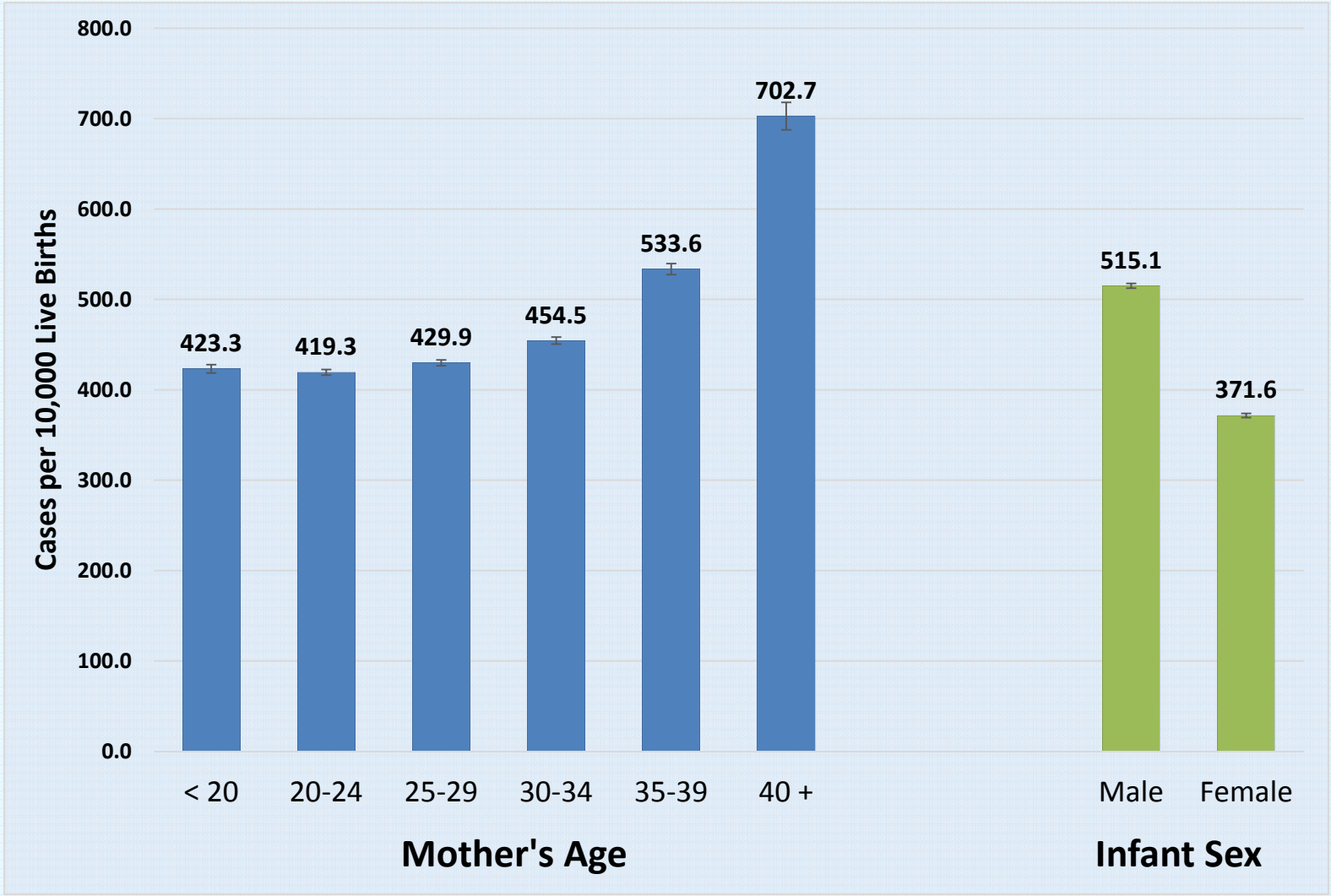


Heart with HLHS

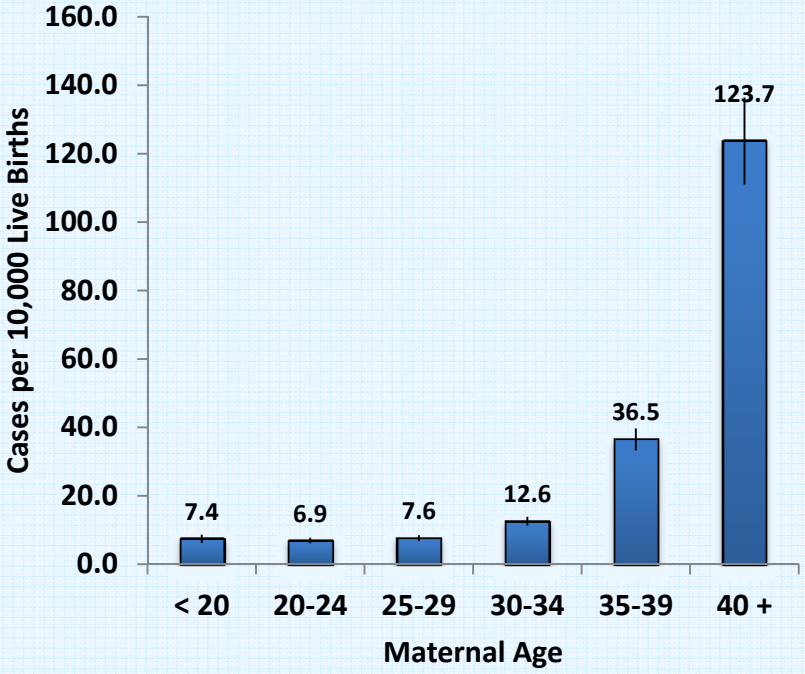


Birth Defects Difference Across Demographic Groups

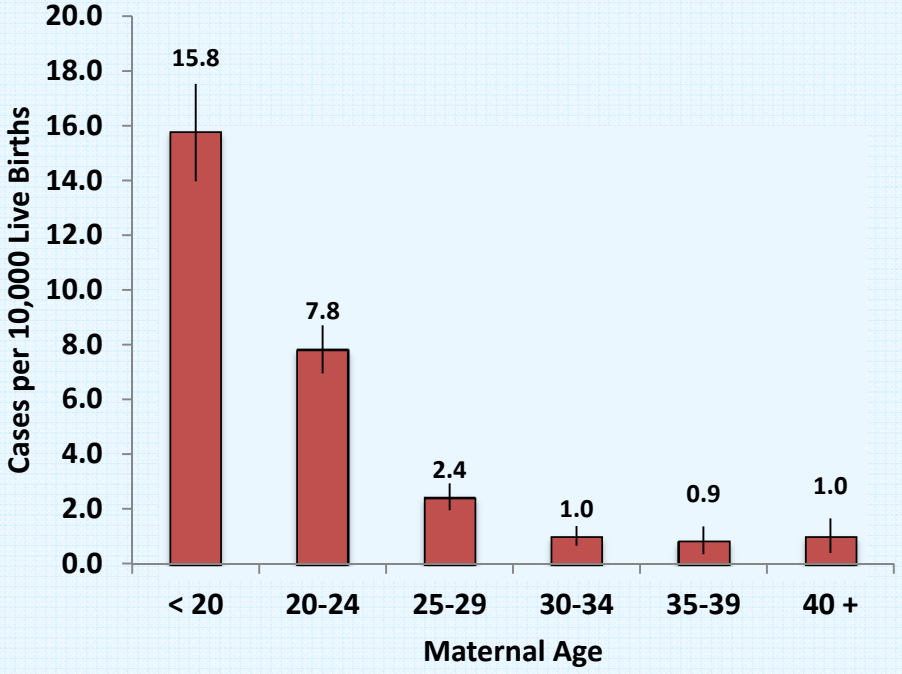
Any Monitored Defect
by Maternal Age and Infant Sex, Texas, 1999-2013



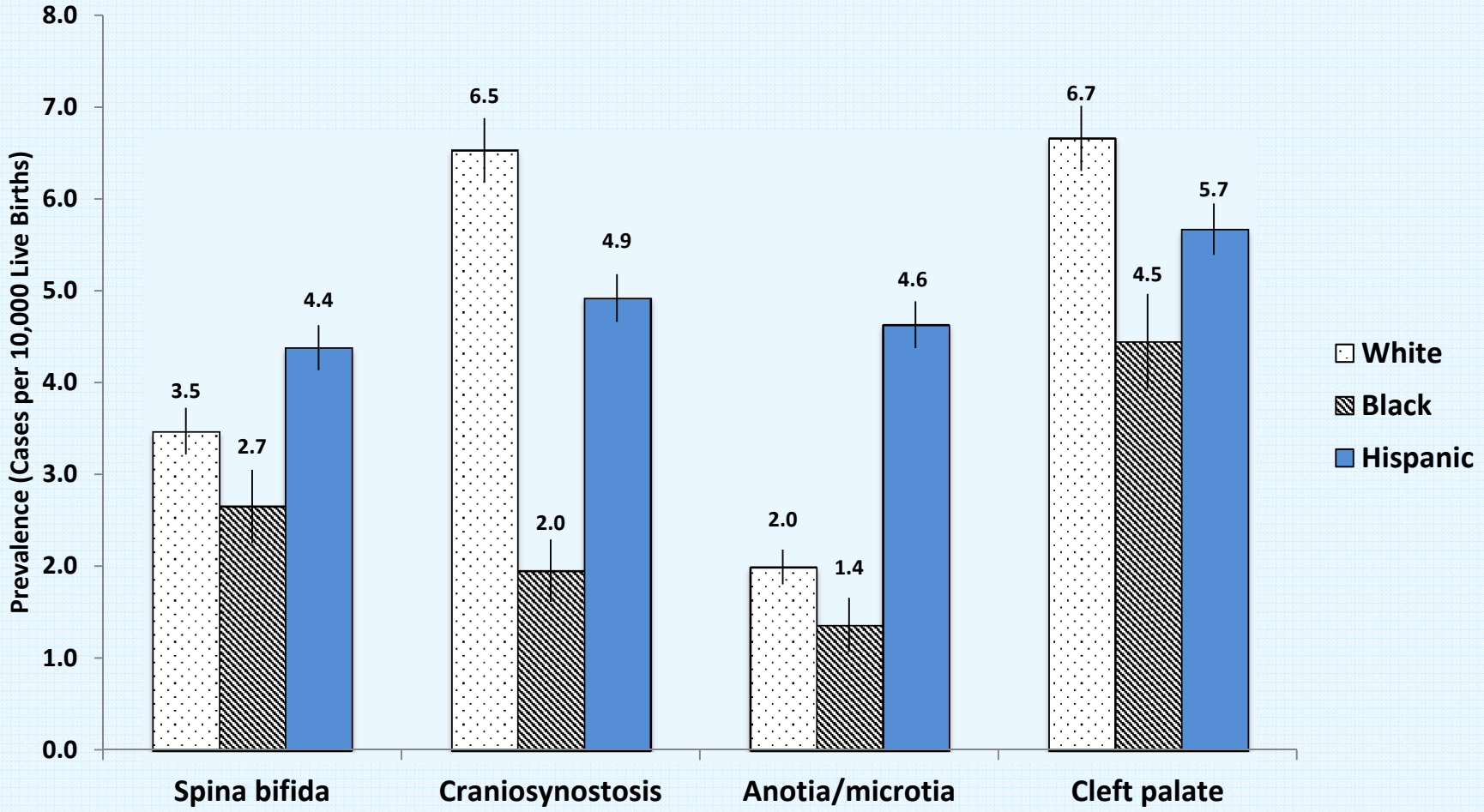
Prevalence of Down syndrome by Maternal Age, Texas, 1999-2013



Prevalence of Gastroschisis by Maternal Age, Texas, 1999-2013

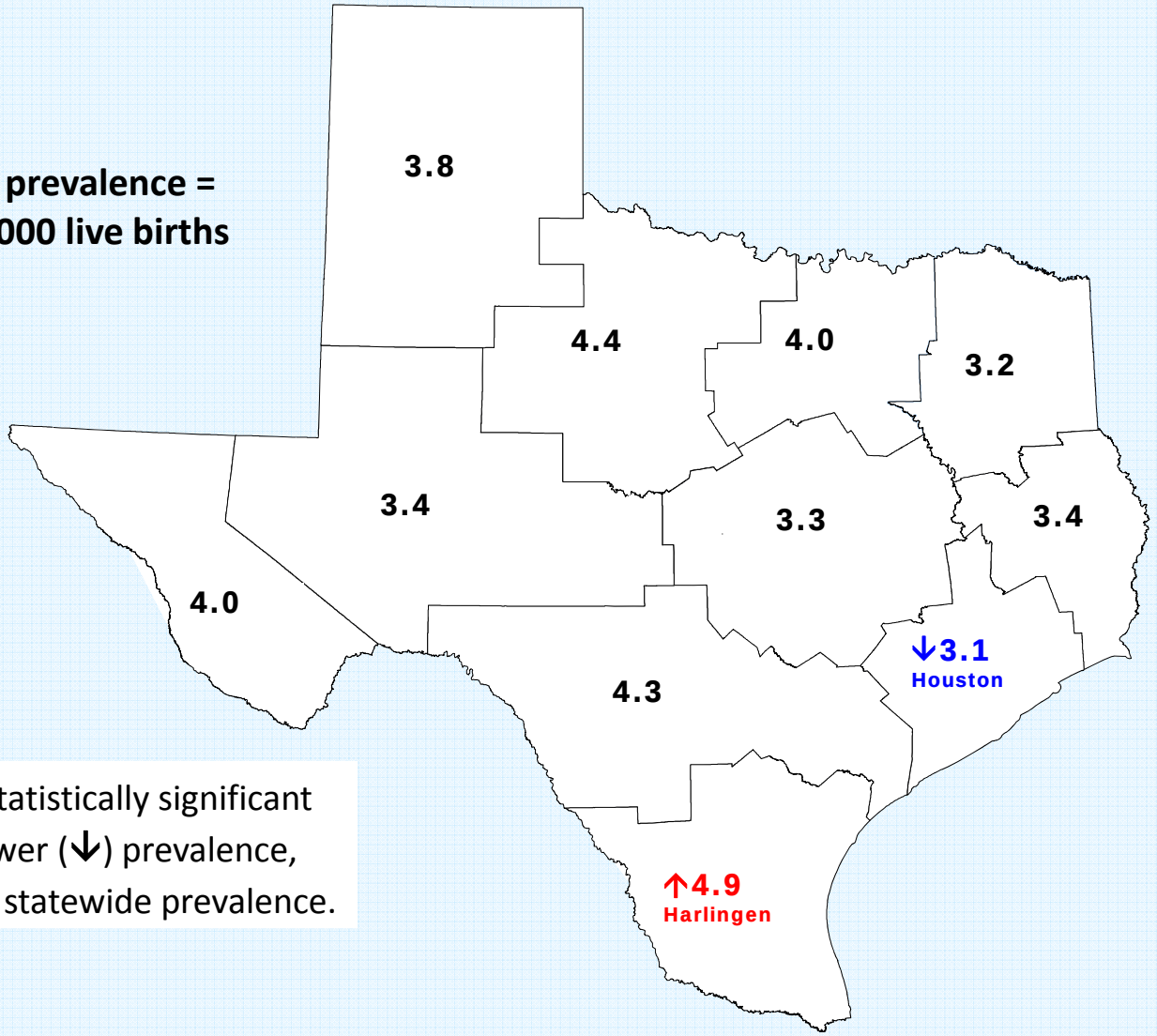


Selected Defects by Race/Ethnicity, Texas, 1999-2013



Spina bifida Prevalence, Texas, 1999-2013

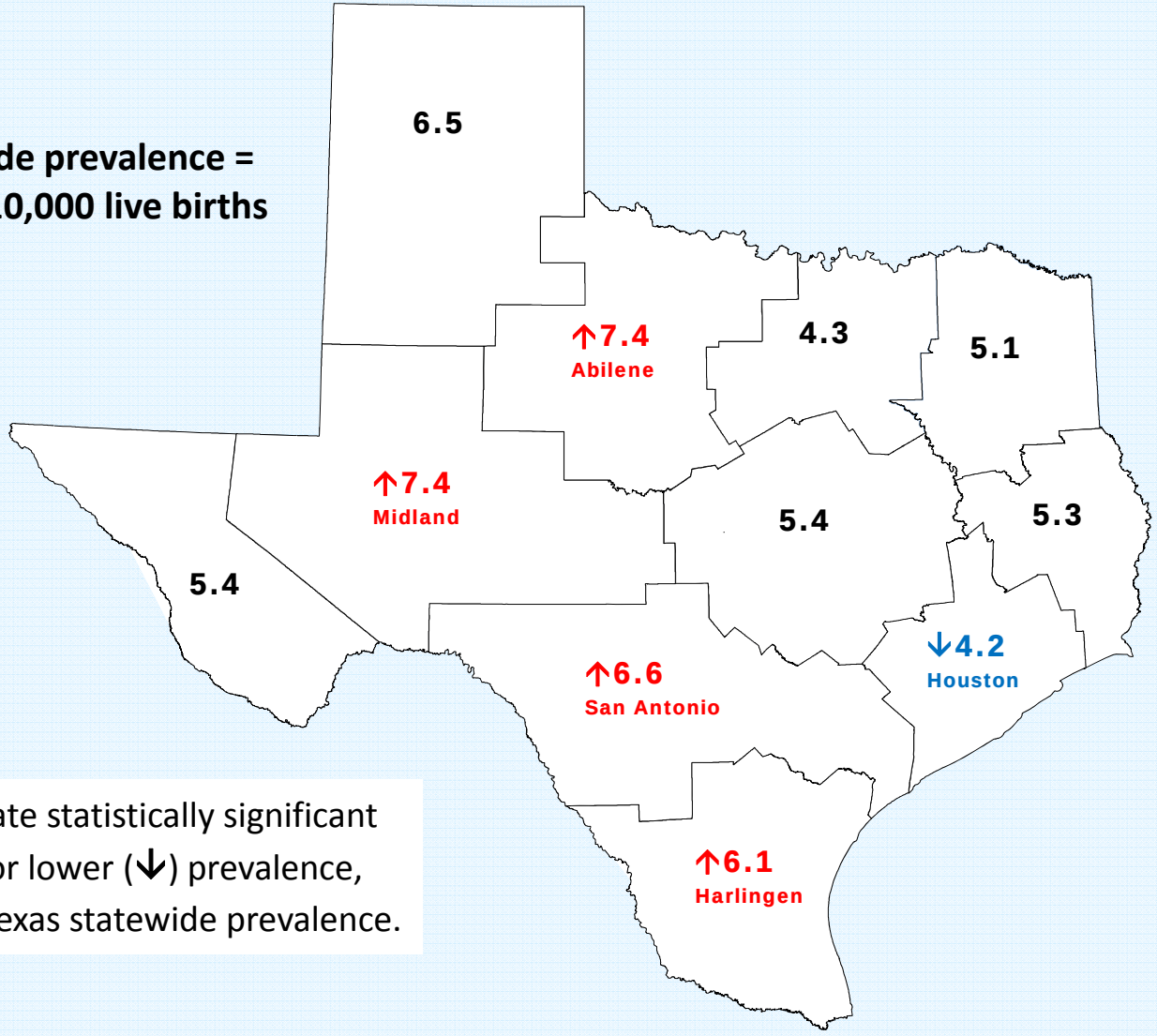
Texas statewide prevalence = 3.8 cases per 10,000 live births



Arrows indicate statistically significant higher (↑) or lower (↓) prevalence, compared to Texas statewide prevalence.

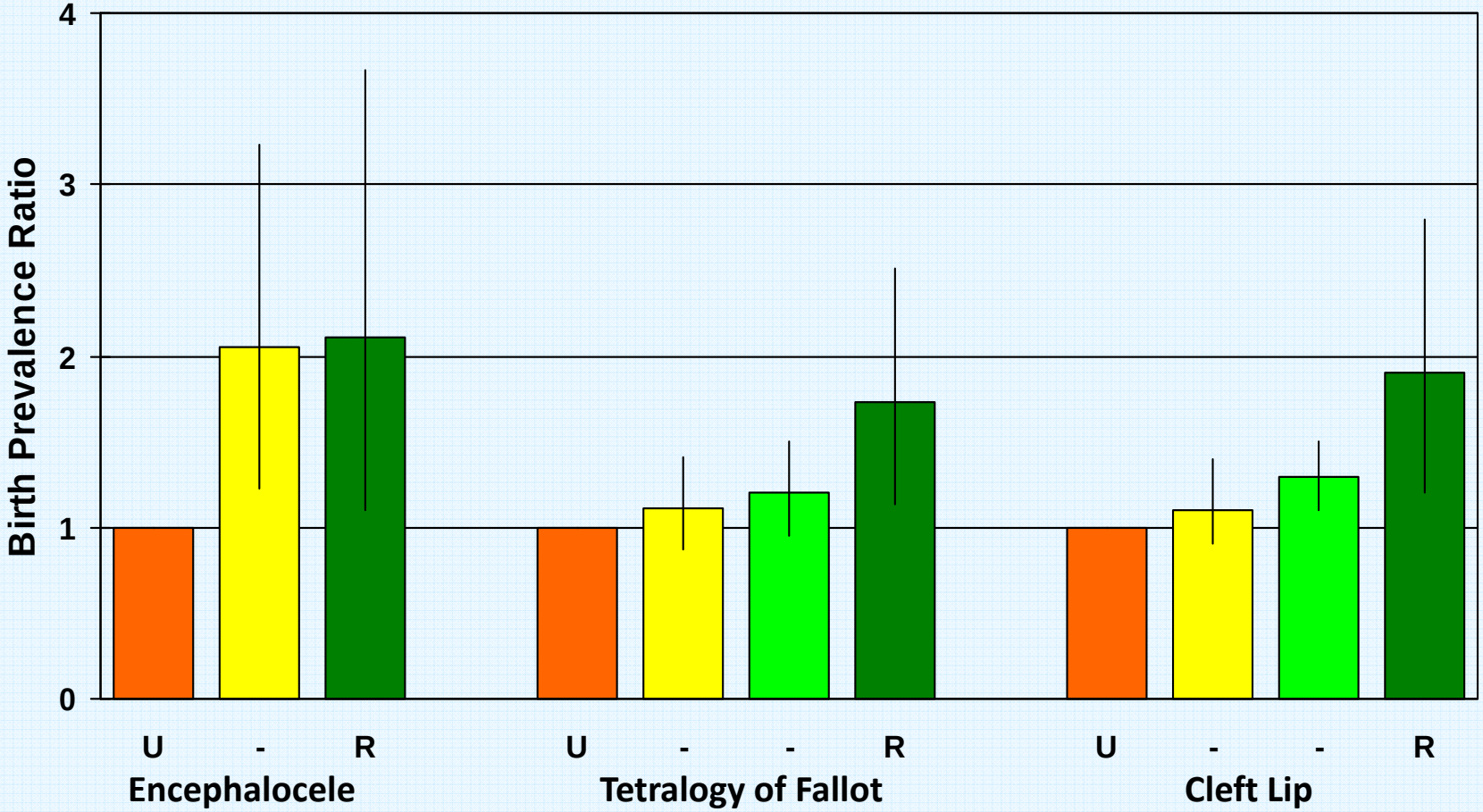
Gastroschisis Prevalence, Texas, 1999-2013

Texas statewide prevalence = 5.2 cases per 10,000 live births



Arrows indicate statistically significant higher (↑) or lower (↓) prevalence, compared to Texas statewide prevalence.

Urban vs. Rural Prevalence of Selected Birth Defects in Texas



References:
Luben TJ et al. Urban-rural residence and the occurrence of neural tube defects in Texas. *Health and Place* 2009.
Langlois PH et al. Occurrence of conotruncal heart defects in Texas: A comparison of urban/rural classifications. *J Rural Health* 2009.
Messer LC et al. Urban-rural residence and the occurrence of cleft lip and palate in Texas. *Ann Epid* 2010.

3. Birth Defects Mortality and Survival

10 Most Common Causes of Death, by Age Group, Texas, 2013

	<1	1-4	5-14	15-24	25-34*
Rank					
1	**Birth Defects 525**	Unintentional Injuries 148	Unintentional Injuries 141	Unintentional Injuries 1,134	Unintentional Injuries 1,303
2	Short Gestation/Low Birth Weight 340	Malignant Neoplasms 49	Malignant Neoplasms 109	Suicide 419	Suicide 543
3	SIDS 153	**Birth Defects 43**	**Birth Defects 33**	Homicide 310	Malignant Neoplasms 357
4	Maternal Pregnancy Complications 145	Homicide 28	Suicide 27	Malignant Neoplasms 141	Homicide 347
5	Unintentional Injury 83	Heart Disease 22	Chronic, Low Respiratory Disease 20	Heart Disease 72	Heart Disease 284
6	Placenta, Cord, Membranes Complications 80	Perinatal Period 9	Homicide 19	**Birth Defects 29**	HIV 69
7	Bacterial Sepsis 55	Chronic, Low Respiratory Disease 9	Heart Disease 14	Cerebrovascular 20	Diabetes 66
8	Respiratory Distress of Newborn 53	Influenza/Pneumonia 8	Cerebrovascular 12	Septicemia 18	Cerebrovascular 51
9	Neonatal Hemorrhage 51	Septicemia 4	Influenza/Pneumonia 10	HIV 18	Chronic Liver Disease/Cirrhosis 46
10	Assault (Homicide) 42	3 conditions 3/Ea	Septicemia 5	Influenza/Pneumonia 18	Influenza/Pneumonia 44

*For the 25-34 age group, there were 38 deaths due to birth defects in 2013.

Neonatal and Postneonatal Adjusted Hazard Ratios for Selected Birth Defects, by Maternal Race/Ethnicity: 12 State Birth Defects Surveillance Programs, National Birth Defects Prevention Network, 1999-2007

Birth Defects	Non-Hispanic Black		Hispanic	
	Neonatal (<28 days)	Postneonatal (28-364 days)	Neonatal (<28 days)	Postneonatal (28-364 days)
Congenital heart defects				
• Transposition of great arteries	1.0	2.1*	0.9	1.5*
• Tetralogy of Fallot	1.0	1.8*	1.1	1.7*
• Atrioventricular septal defects (AVSD)	1.2	1.6*	1.2	1.7*
• AVSD (without Down syndrome)	1.0	1.3*	1.0	1.6*
• Hypoplastic left heart syndrome	0.9	1.3*	1.0	1.3*
• Coarctation of aorta	1.3	1.8*	0.9	1.2
Gastrointestinal defects				
• Esophageal atresia/ tracheoosophageal fistula	1.9*	2.8*	1.6*	1.5
• Rectal and large intestinal atresia/stenosis	1.1	1.6*	1.3*	1.5*
Musculoskeletal defects				
• Upper limb deficiencies	1.0	2.1*	1.1	1.7*
• Diaphragmatic hernia	1.2	1.7*	0.8*	1.4*
Chromosomal defects				
• Trisomy 21 (Down syndrome)	1.0	1.9*	0.8	1.2

Wang Y *et al*, *Journal of Pediatrics* 2015.

4. Linkage Studies

Maltreatment and Birth Defects: Methods

- **Study population:** > 3 million Texas children born 2002-2009, without any birth defect ("unexposed") or with target birth defects ("exposed")
  - Down syndrome (cognitive realm) n=3,743
  - Spina bifida (physical realm) n=971
  - Cleft lip (CLP) (communication realm) n=2,943
- **Primary outcome** - confirmed maltreatment (reported at CPS/Texas DFPS):
  - Physical
  - Sexual
  - Emotional abuse
  - Neglectful supervision
  - Medical or physical neglect
  - Refusal to assume parental responsibility
  - Abandonment
- **Data linkage:**
  - Birth defect cases in Texas Registry linked to birth certificates (routine)
  - Child Protective Services (CPS) client list linked to Texas birth certificates
- **Analysis:** Cox regression to calculate hazard ratios, adjusted for SES, etc.

Van Horne BS et al. *Pediatrics* 2015.

Results: Maltreatment among Children with Specific Birth Defects (compared to kids w/o birth defects)

- Risk of confirmed maltreatment varied by birth defect, age, and type of maltreatment.
- Adjusted relative risk of maltreatment **(<2 yrs.)**
  - **Spina bifida:** 1.68 (95% CI=1.12-2.24)
  - **CLP:** 1.40 (95% CI=1.35-1.98)
  - **Down syndrome:** 1.08 (0.85-1.37) *(no difference)*
- Among maltreated, risk of **medical neglect** 3-6 times higher in children in this age group with these birth defects (failure to provide adequate medical care).

Van Horne BS *et al. Pediatrics* 2015.

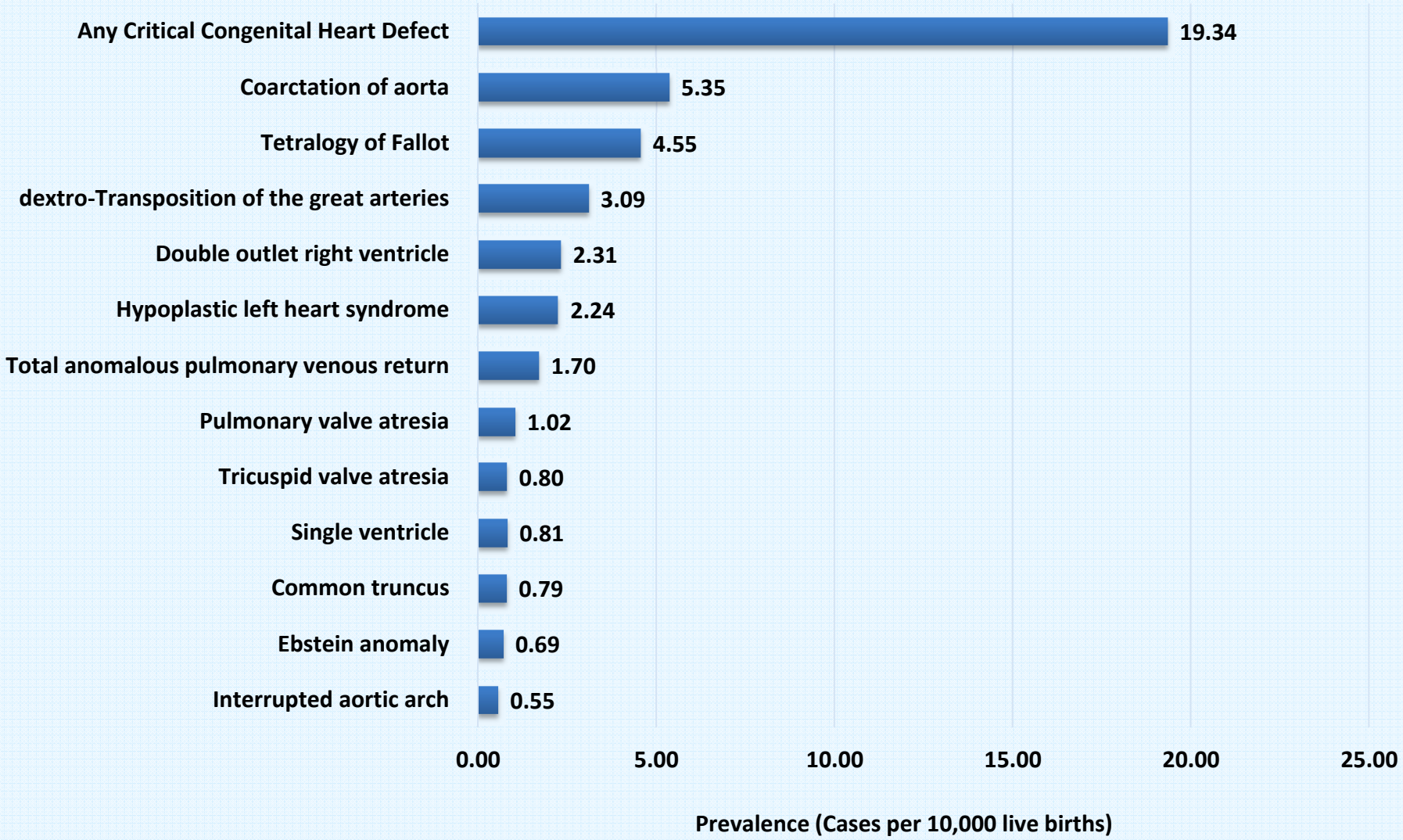
Other Linkage Studies

- Birth Defects and Childhood Cancer
- Birth Defects and Newborn Screening Analytes
- Birth Defects and HIV

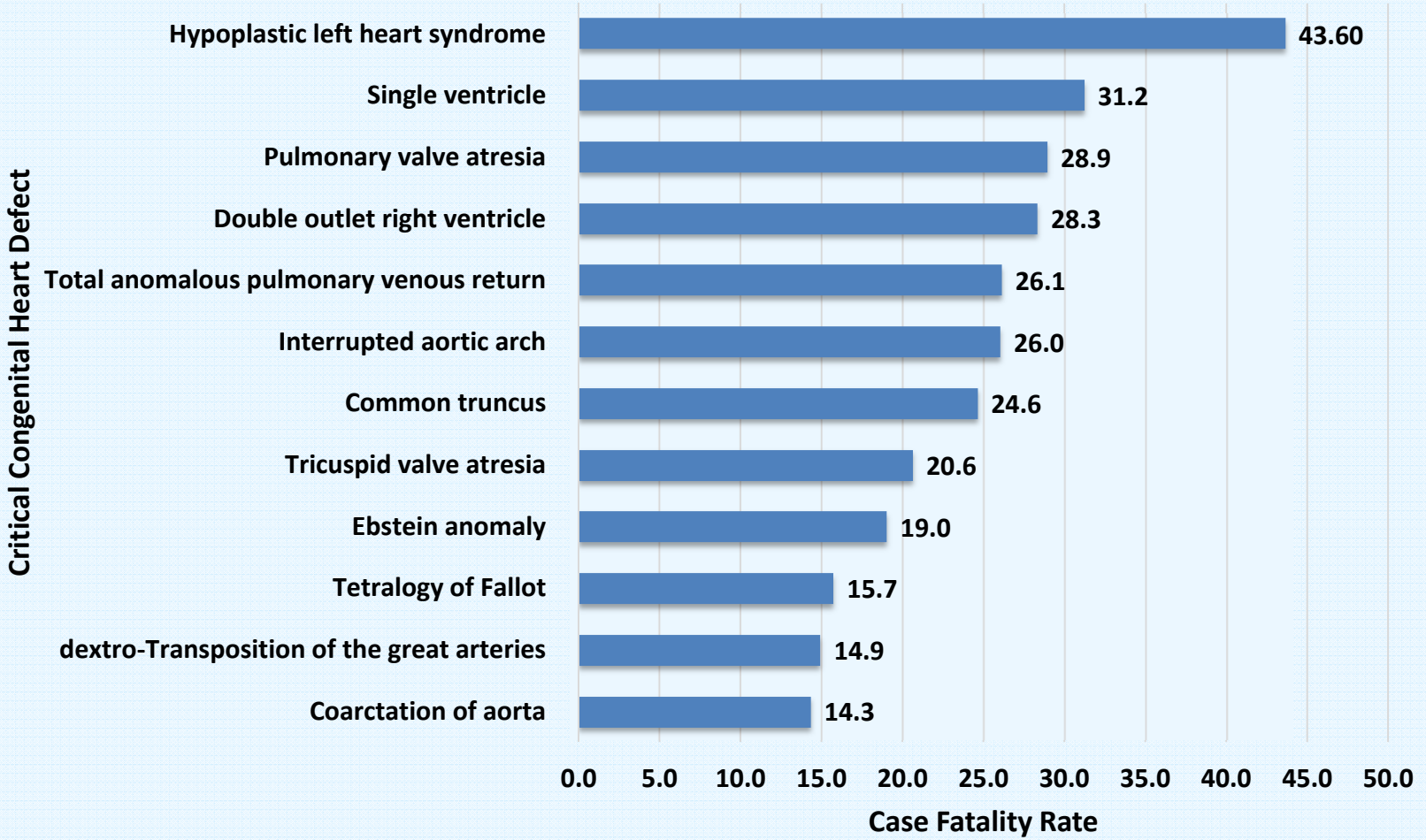
5. Critical Congenital Heart Defects

Pulse Oximeter

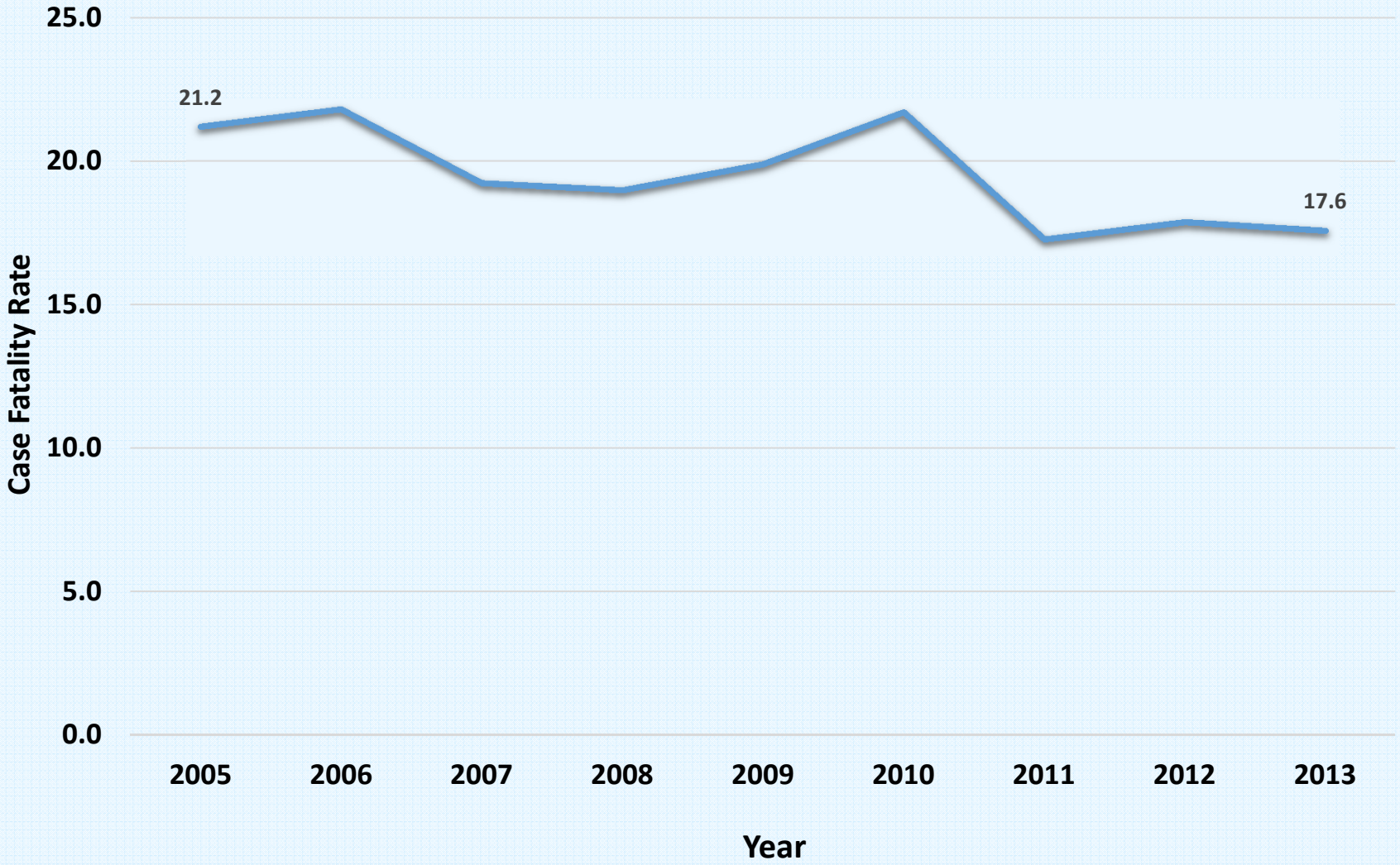
Prevalence of Critical Congenital Heart Defects (CCHDs) Targeted for Pulse Oximetry Screening, Texas, 2005-2013



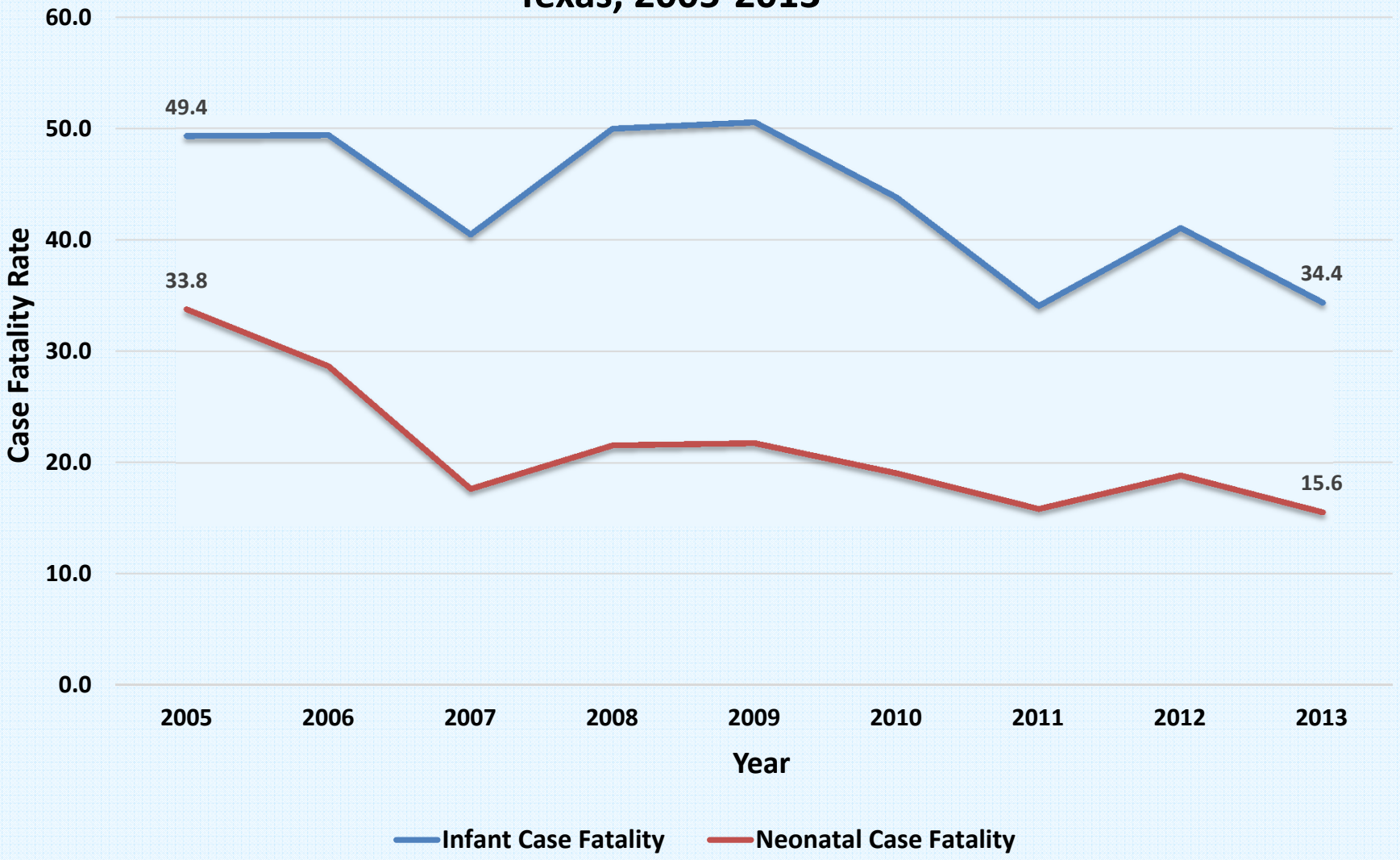
Infant Case Fatality of Critical Congenital Heart Defects Targeted for Pulse Oximetry Screening, Texas, 2005-2013



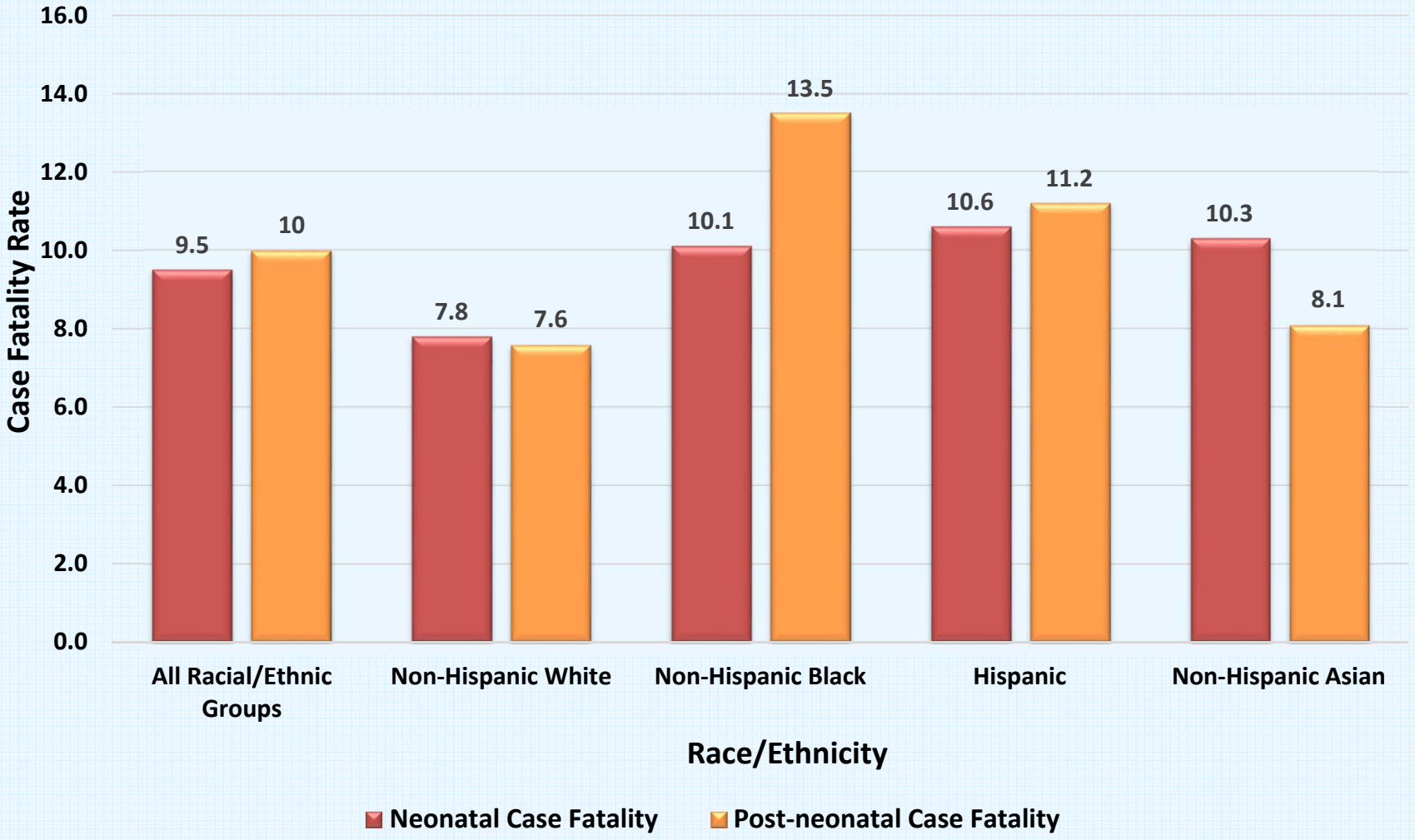
Infant Case Fatality (%) of Any Critical Congenital Heart Defect Targeted for Pulse Oximetry Screening, Texas, 2005-2013



Infant and Neonatal Case Fatality of Hypoplastic Left Heart Syndrome, Texas, 2005-2013



Neonatal and Post-neonatal Case Fatality from Any Critical Congenital Heart Defect Targeted for Pulse Oximetry Screening, by Maternal Race/Ethnicity, Texas, 2005-2013



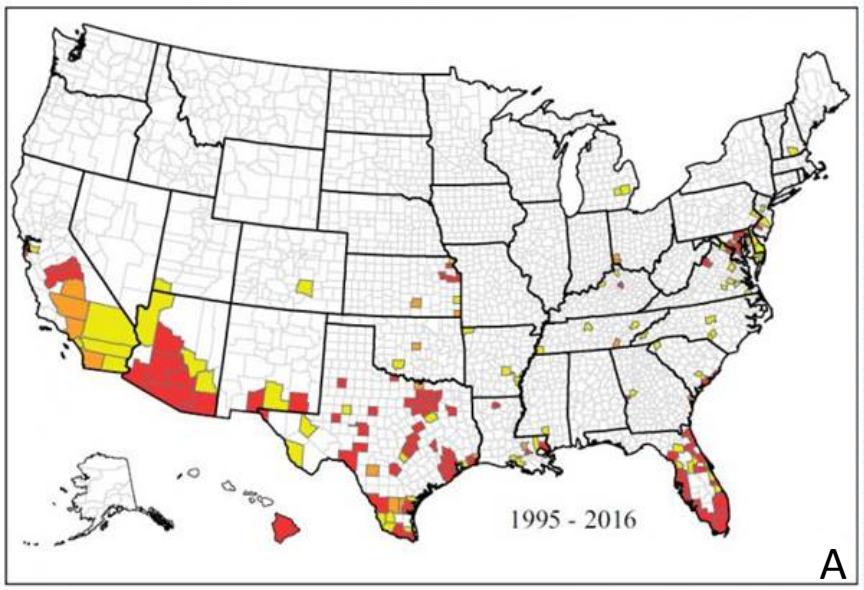
6. Microcephaly and Zika in Texas

Zika Virus

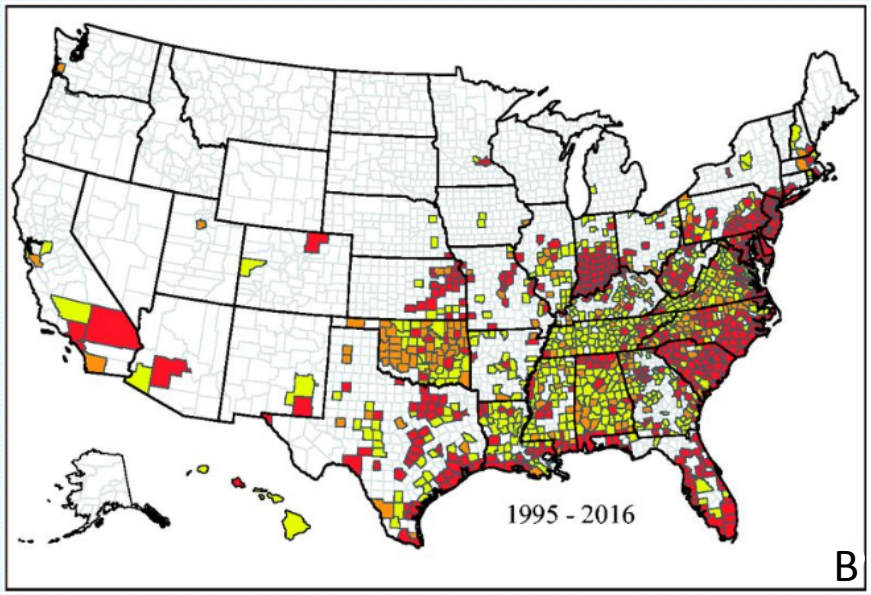
- Fall 2015: NE Brazil reported a twenty-fold microcephaly increase that coincided with an outbreak of Zika virus
- 12/1/2015: Pan-American Health Organization Epi Alert about Zika and microcephaly
- 2/1/2016: World Health Organization declares Zika to be a global Emergency

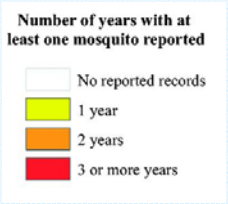
The reported occurrence of Ae. aegypti & albopictus by county between 1 January 1995 - March 2016 in the United States

Ae. aegypti (A)



Ae. albopictus (B)





Micah B. Hahn et al. *J Med Entomol* 2016;jme.tjw072

Zika in Texas (as of 10/17/2016)

- **Biggest concern:** adverse birth outcomes among pregnant women with Zika (risk of microcephaly and other birth defects = 1 to 30%)

- Texas has had 231 reported, confirmed cases of Zika virus disease
  - 2 sexually transmitted
  - All others travel-related (mostly from Central America, Caribbean)
  - Focusing on pregnancy and birth outcomes:
    - 14 Zika+ cases among pregnant women
    - 2 Zika+ neonates with microcephaly
- Additionally, people with asymptomatic Zika virus infection or unspecified flavivirus infection:
    - 59 pregnant women
    - 3 neonates

Microcephaly

Head Circumference

- Used to measure “severity”
- Severe: < 3rd percentile for age and sex
- Also called occipital-frontal circumference (OFC)

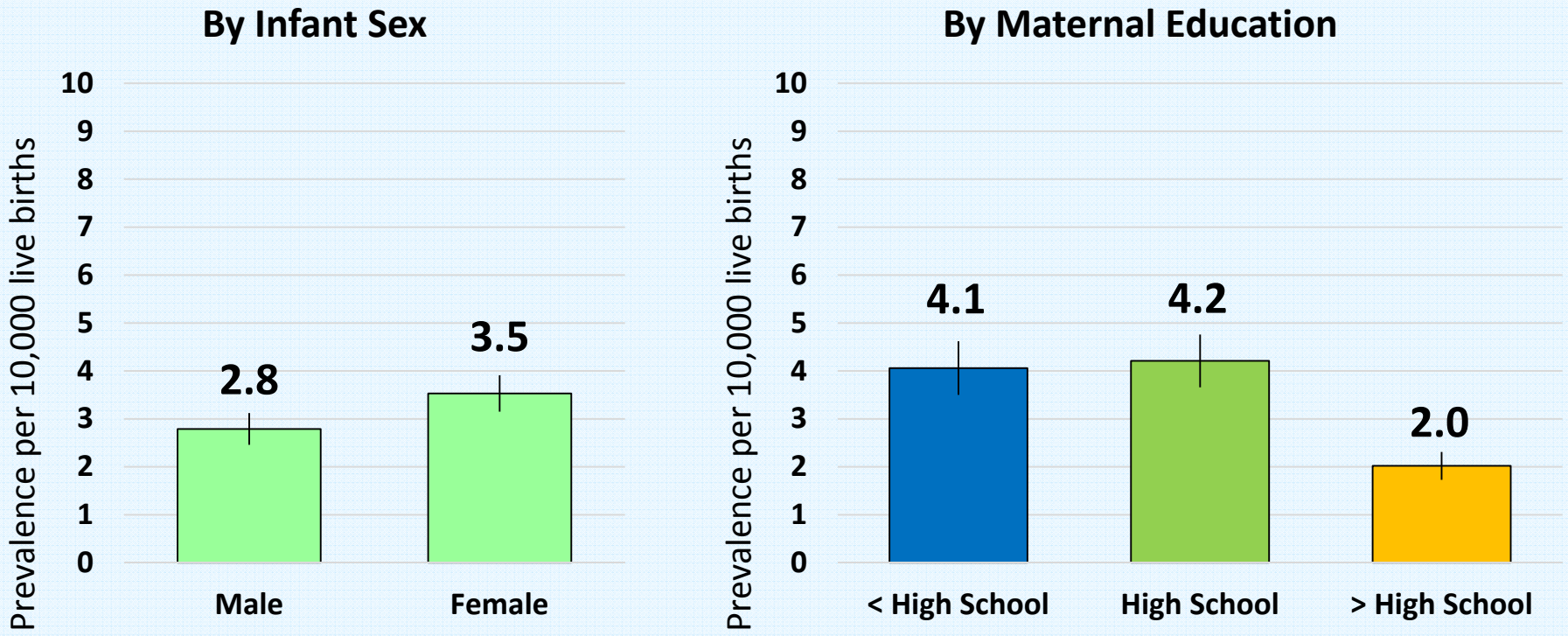
Explained Microcephaly Cases

- **Part of co-occurring malformations**
  - Neural tube defects
  - Holoprosencephaly
  - Craniosynostosis
  - Other brain reduction defects
- **Documented causes**
  - Chromosomal anomalies
  - Infection (cytomegalovirus, toxoplasmosis)
  - Genetic/syndromic
  - Prenatal alcohol exposure

Breakdown of Microcephaly Cases in Texas, 2008-2012

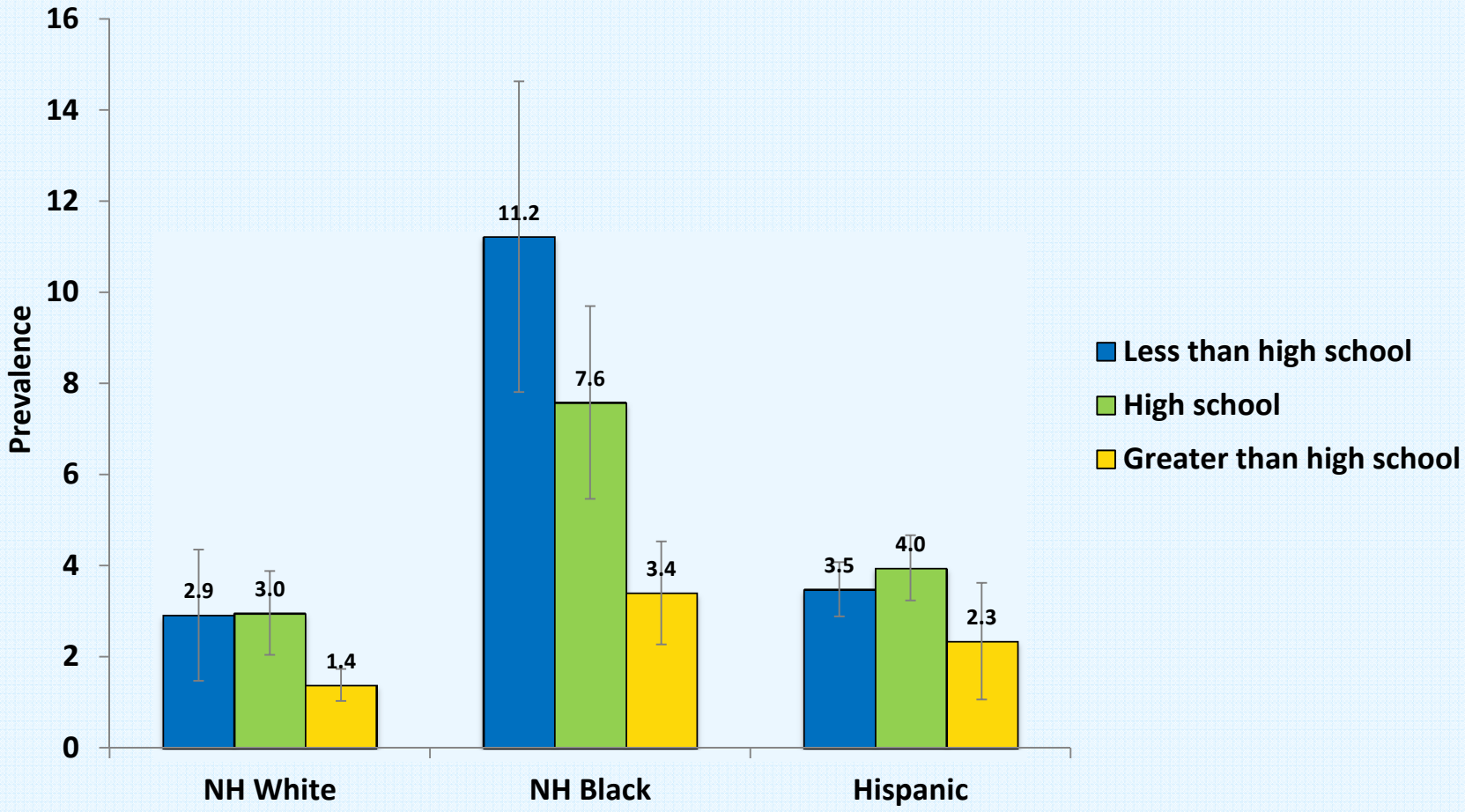
CATEGORY	CASES	% OF TOTAL CASES	BIRTH PREVALENCE (CASES/10,000 LIVE BIRTHS)
Explained Cases	856	30%	4.4
Unexplained Cases	2,013	--	10.3
Unexplained Severe Cases	615	21%	3.2
Unexplained Less Severe Cases	1,398	49%	7.2
Total Cases	2,869	100%	14.7

Prevalence of Unexplained Severe Microcephaly*, by Infant Sex and Maternal Education, Texas, 2008-2012



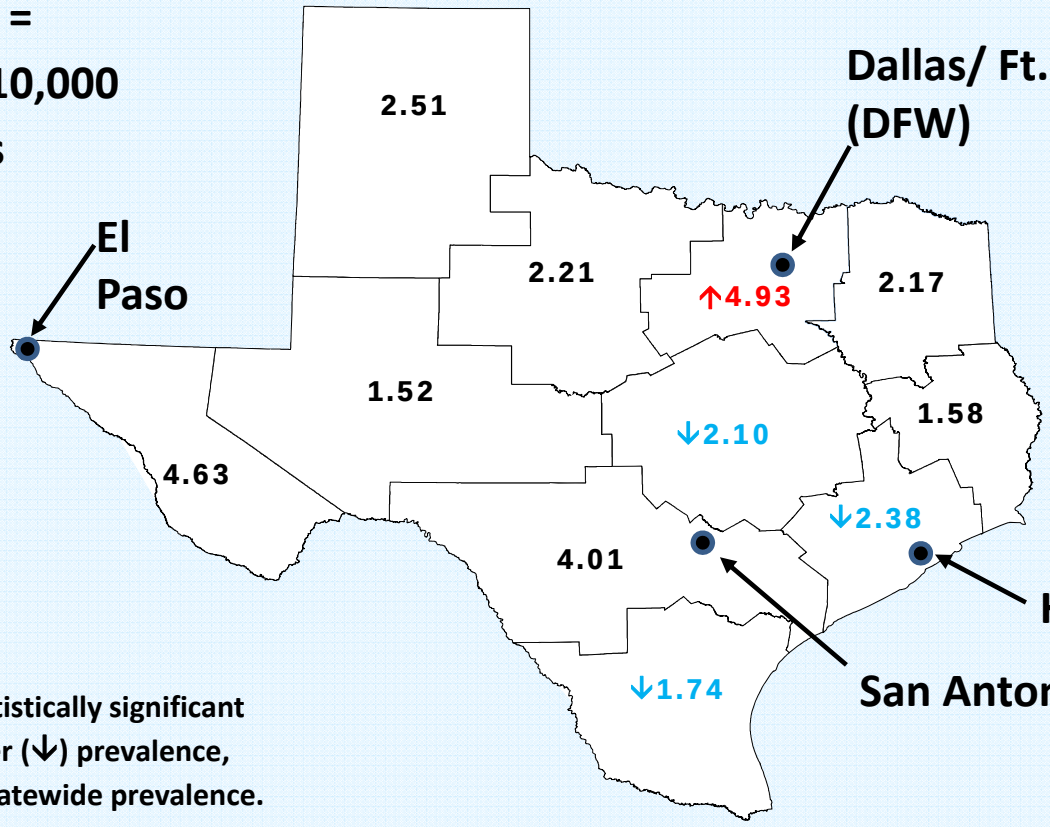
*Head circumference at delivery <3rd percentile for infant sex and gestational age

Unexplained Severe Microcephaly Cases, by Maternal Race and Education, Texas, 2008-2012



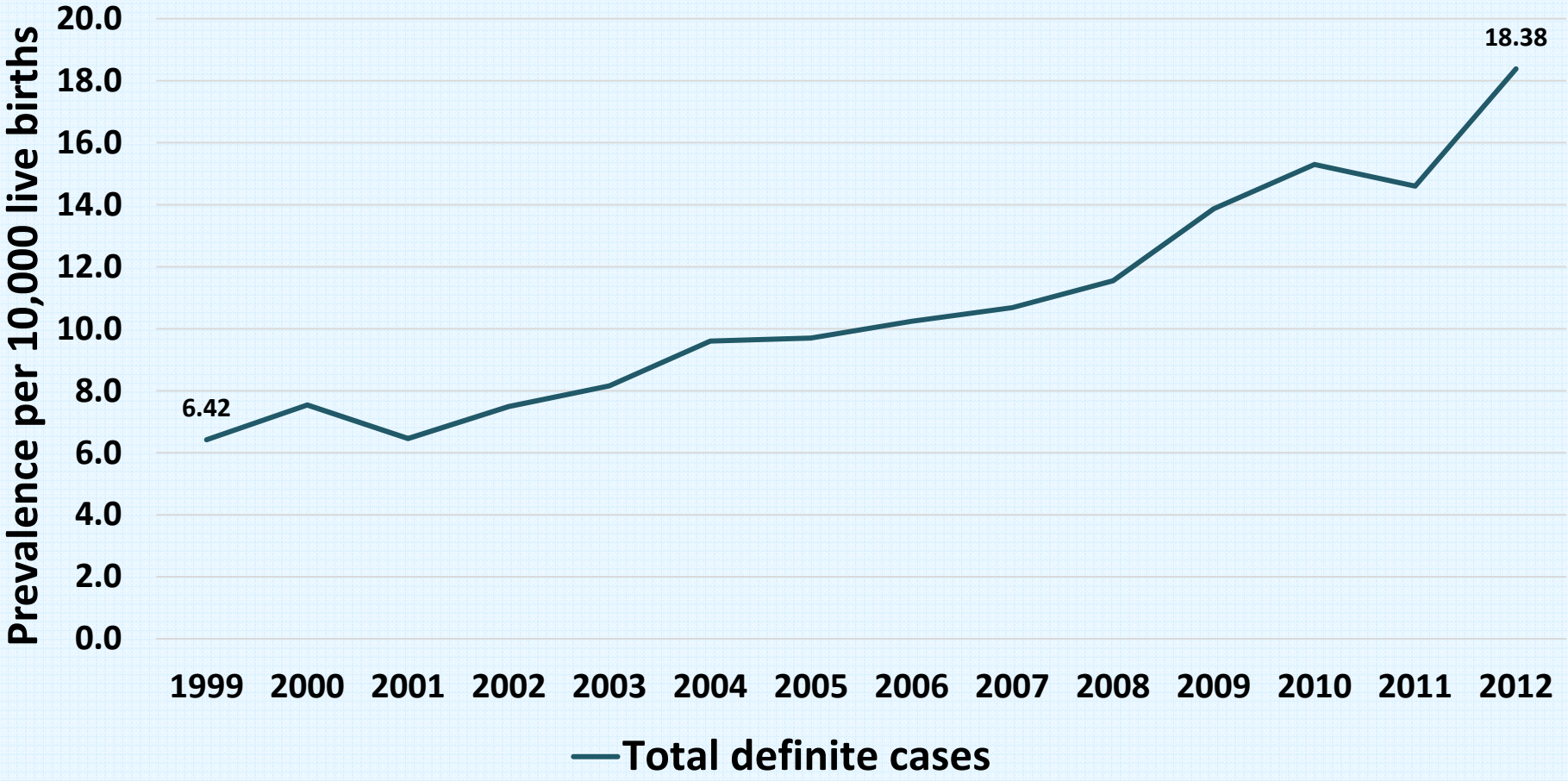
Prevalence of Unexplained Severe Cases of Microcephaly (Head Circumference < 3rd percentile), by Texas Region, 2008-2012

Texas statewide prevalence = 3.15 cases per 10,000 live births



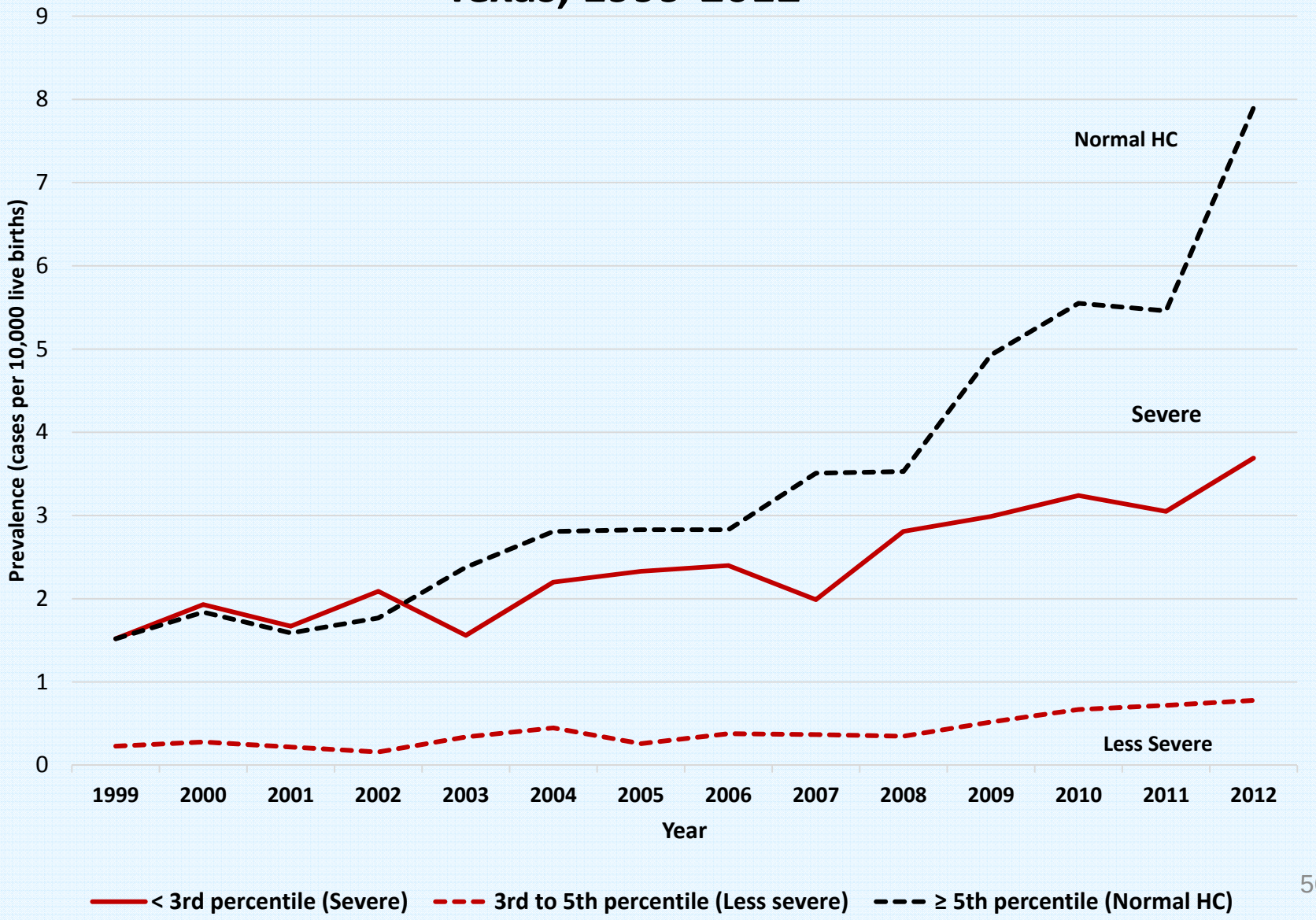
Arrows indicate statistically significant higher (↑) or lower (↓) prevalence, compared to Texas statewide prevalence.

Microcephaly*: Total Definite Cases, Texas, 1999-2012 (n=5,774)



*The Texas Birth Defects Registry used a case definition that included any clinical mention in a medical record of “microcephaly” or “small head” before the first birthday.

Unexplained Cases of Definite Microcephaly, by Percentile of Head Circumference (HC), Texas, 1999-2012



Birth Defects Associated with Congenital Zika Virus Infection

BIRTH DEFECT	# CASES/YR
MICROCEPHALY	819
OTHER BRAIN AND SKULL ANOMALIES Abnormal brain cortex, corpus callosum Fetal brain disruption sequence	2438
NEURAL TUBE DEFECTS + HOLOPROSENCEPHALY Anencephaly, spina bifida, encephalocele Holoprosencephaly	337
OTHERS Eye abnormalities Congenital contractures (e.g. arthrogryposis) Congenital deafness	591
TOTAL	3550

7. Exploring Birth Defects Risk Factors in the National Birth Defects Prevention Study

Texas Center for Birth Defects Research and Prevention, 1996-2013

- Cooperative agreement grant with CDC
- One of 10 centers in the nation
- National Birth Defects Prevention Study
  - Largest population-based case-control study on birth defects
  - Study includes 30 specific birth defects
  - Additional clinical review and classification of cases
  - Computer-assisted maternal phone interview
  - Cheek cell samples (DNA): mom, dad, infant

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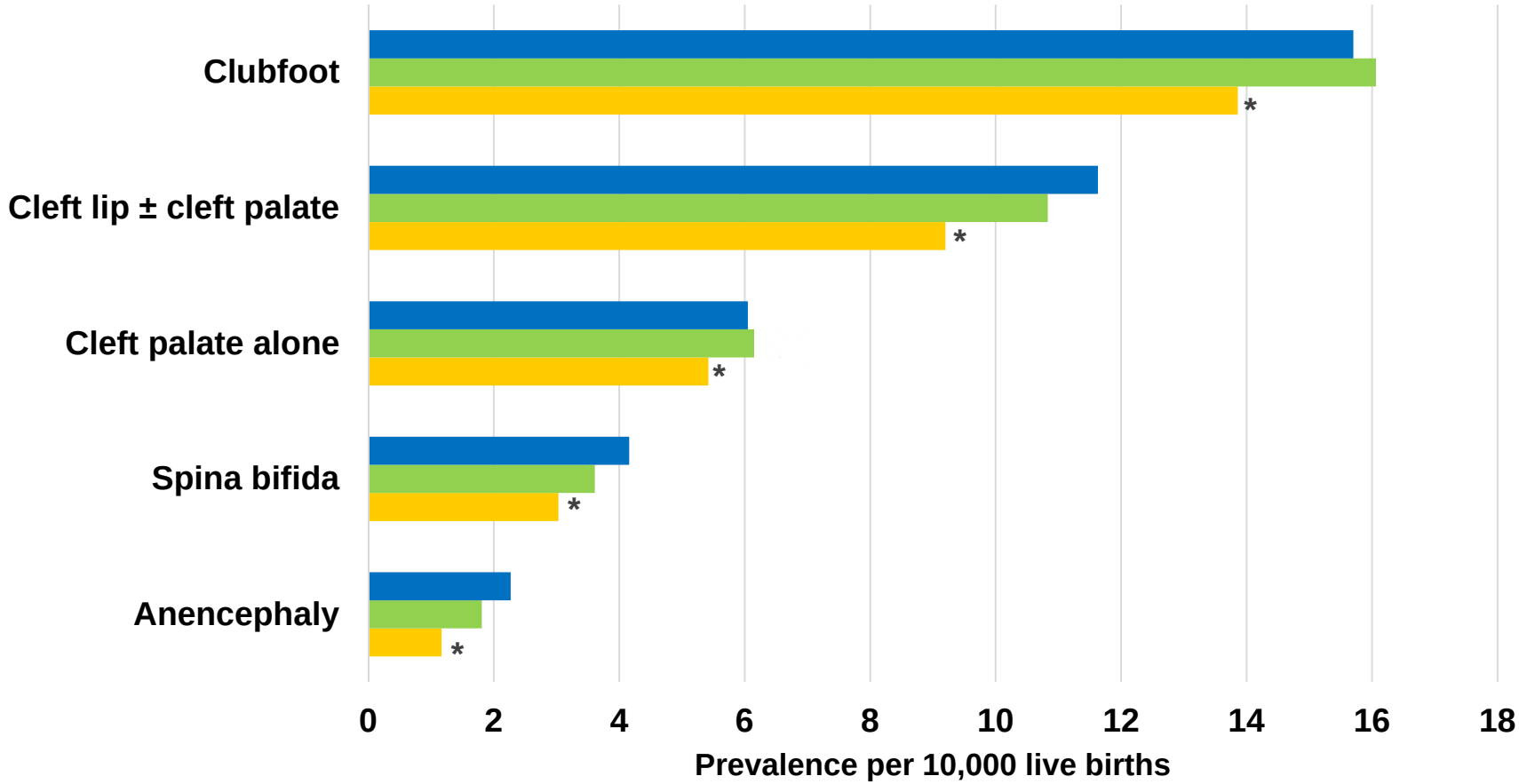
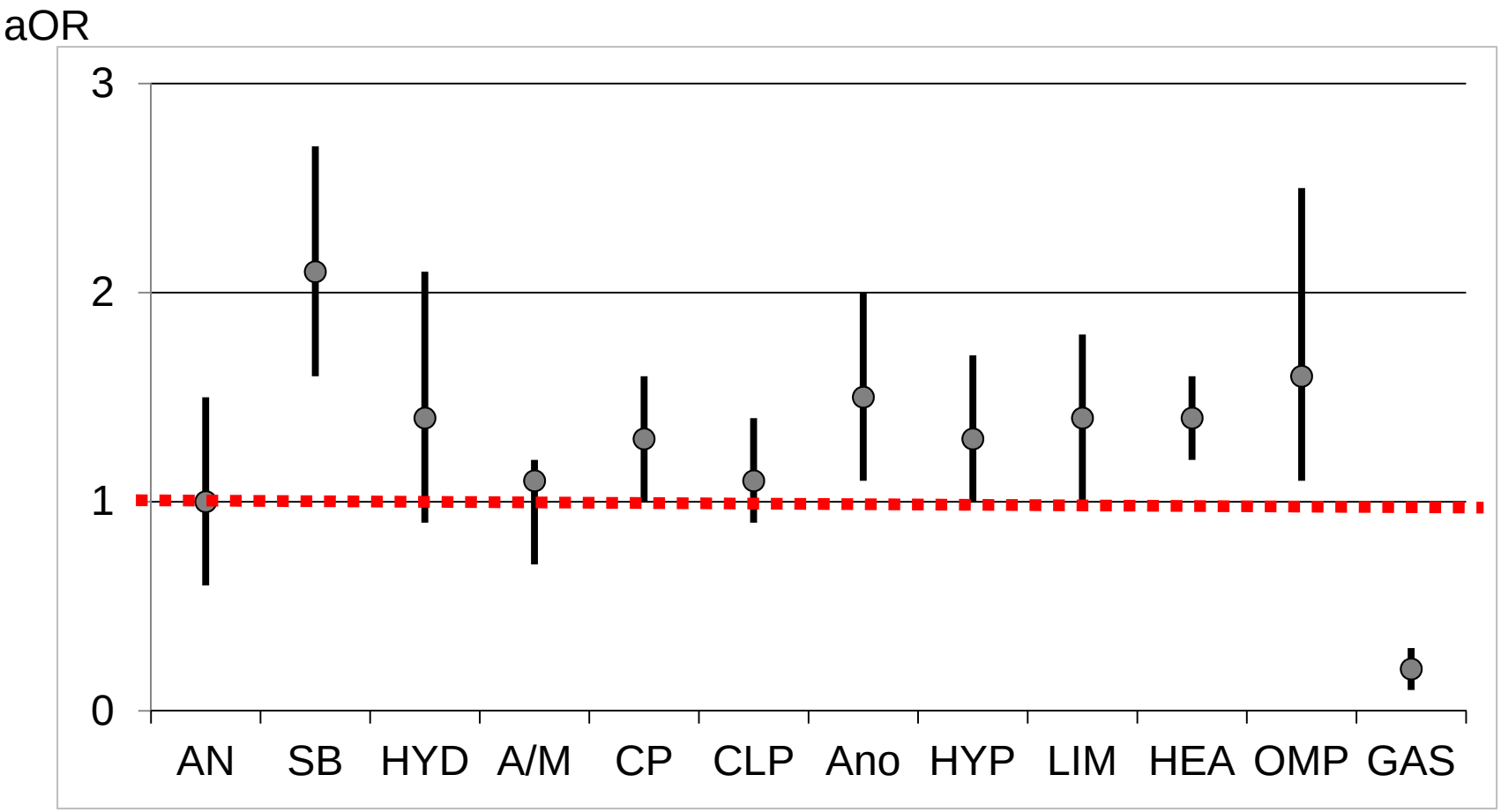
Prevalence of Selected Birth Defects by Mother's Education, NBDPS, 1999-2013



* Indicates statistically significant difference at 95% level

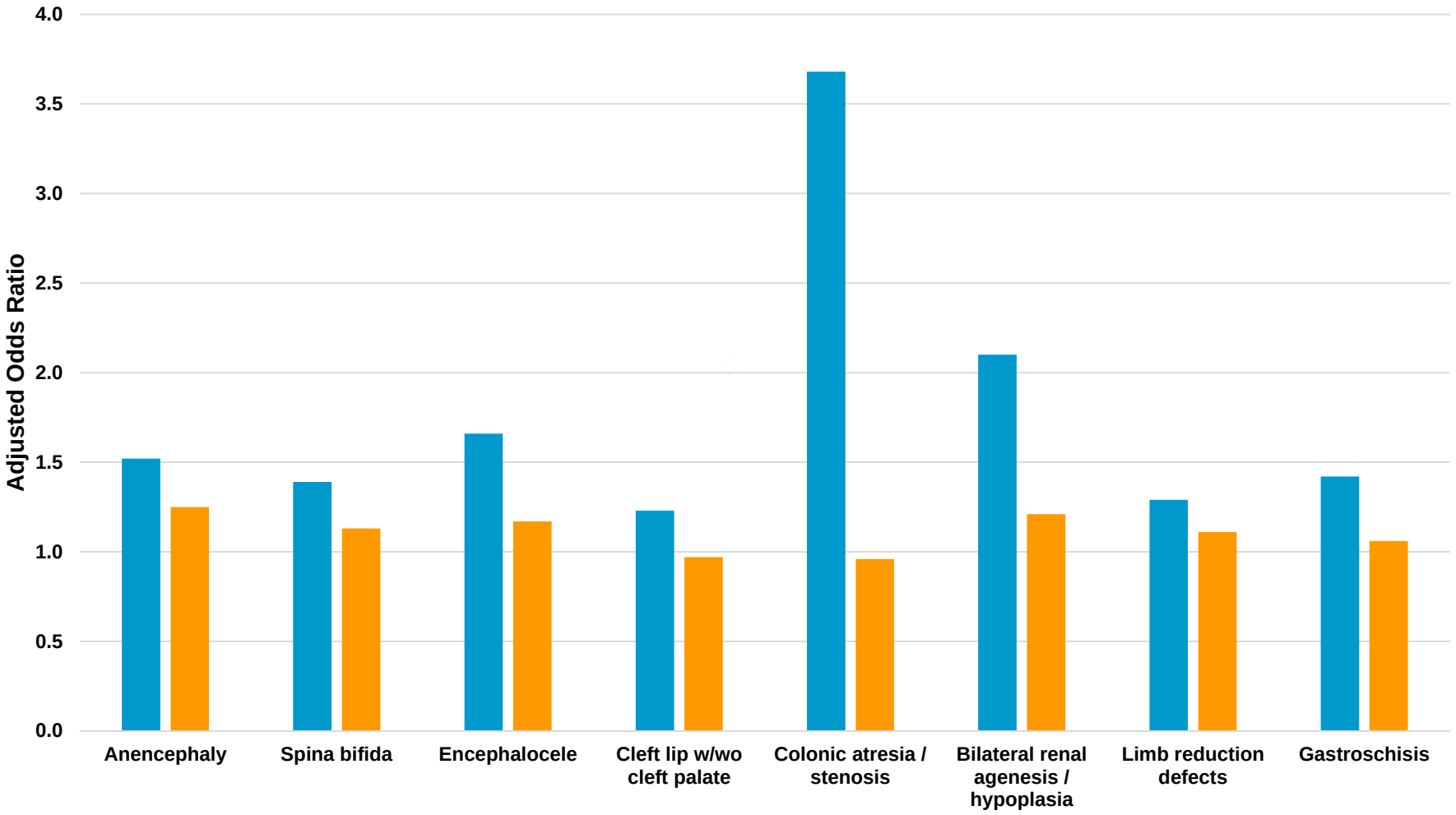
Yang J et al. *Am J Epidemiol* 2008.

Adjusted Odds Ratios for Pre-pregnancy Obesity and Selected Isolated Birth Defects, 1997–2002



Waller DK et al. *Archives Pediatr & Adolesc Med* 2007.

Periconceptional* Fever and Major Birth Defects, 1997-2011



* 1 month before to 2 months after conception.

Waller DK et al. Provisional Unpublished Data, 2016.

Fever, Antipyretics, and Oral Clefts, 1997-2004: Adjusted Odds Ratios

national • birth • defects • prevention • study

Phenotype	Fever		No antipyretic use	Antipyretic use
	no ill	febrile ill	aOR (CI)	aOR (CI)
Controls	4074	73		
CL+/-P	1089	37	**2.04 (1.36-3.07)**	1.07 (0.82-1.40)
CL+/-P_I	950	29	**1.81 (1.17-2.82)**	1.14 (0.87-1.50)
CLP_I	604	21	**2.06 (1.25-3.40)**	1.01 (0.72-1.44)
CL_I	346	8	1.39 (0.66-2.94)	1.35 (0.91-2.00)
CL+/-P_M	139	8	**3.87 (1.80-8.32)**	0.52 (0.19-1.42)
CLP_M	113	6	**3.77 (1.57-9.01)**	0.33 (0.08-1.33)
CL_M	26	2	**4.48 (1.02-19.76)**	1.26 (0.29-5.42)
CP_I	433	11	1.45 (0.76-2.77)	1.01 (0.68-1.50)
CP_M	116	6	**3.00 (1.26-7.12)**	1.02 (0.49-2.13)

_I: Isolated defects; _M: Multiple defects

Hashmi S et al. *Birth Defects Res A Clin Mol Teratol* 2008.

Mothers Exposed to Secondhand Smoke Exposure (B1P3) & Selected Isolated Defects

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Adjusted OR (95%CI)Ψ
Secondhand Smoke Exposure (B1P3)

Birth Defect	n	No Exposure (Referent)	n	Any Exposure in the Workplace/School or Household
Controls Controls (clefts)	5468 5363		1012 1005	
Amniotic band syndrome-limb body wall complex (ABS-LBWC)	104	1.00	40	**1.66 (1.10-2.51)**
Neural tube defects	823	1.00	219	**1.55 (1.29-1.85)**
Anencephaly and craniorachischisis	247	1.00	66	**1.66 (1.22-2.25)**
Cleft palate	570	1.00	125	**1.31 (1.06-1.63)**
Cleft lip +/- cleft palate	1147	1.00	245	**1.24 (1.05-1.46)**
Cleft lip without cleft palate	440	1.00	94	**1.41 (1.10-1.81)**
Bilateral renal agenesis or hypoplasia	45	1.00	15	**1.99 (1.05-3.75)**

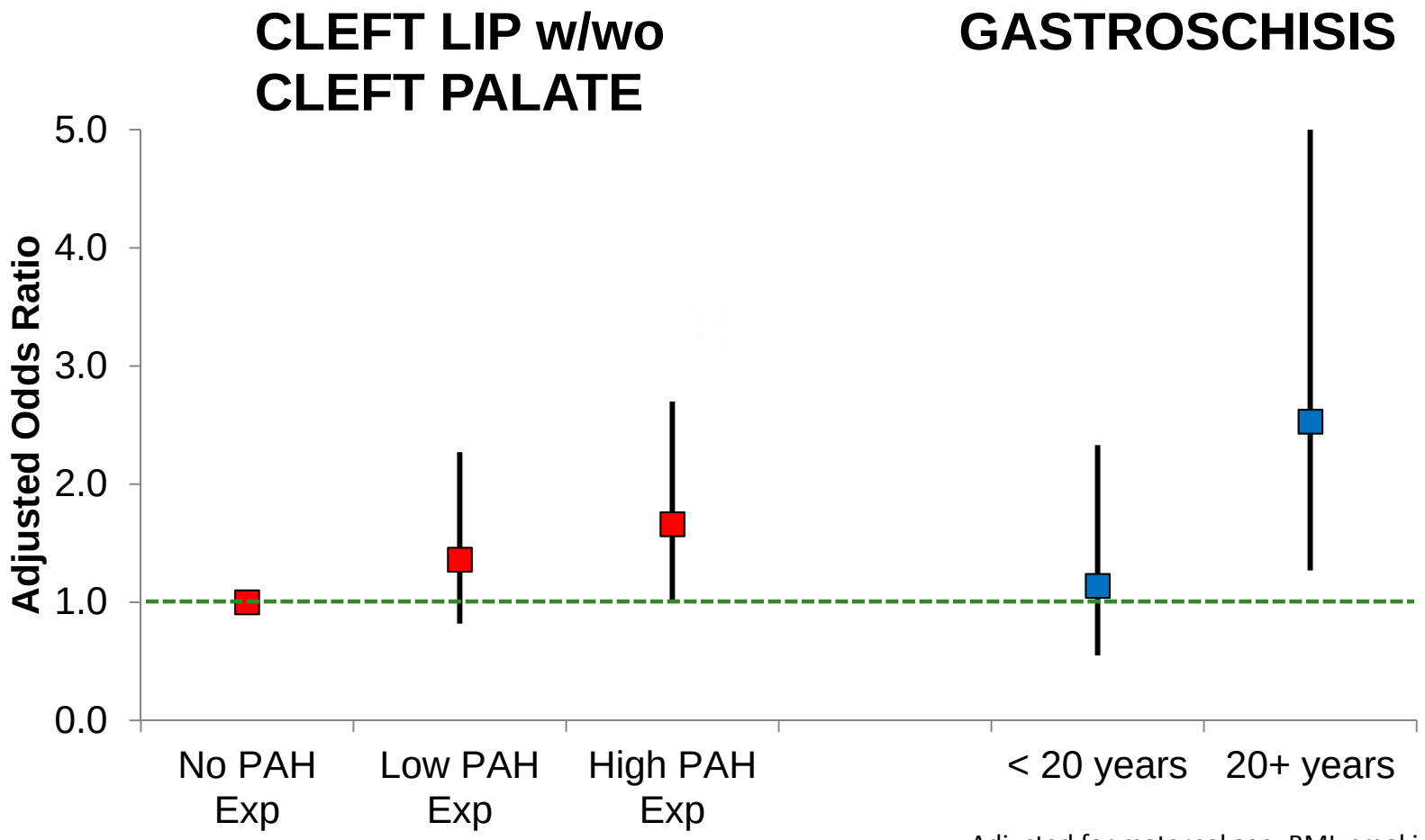
Ψ Adjusted for: Maternal age, race, BMI, nativity, folic acid intake in multivitamins or alone, dietary folate equivalent, parity, pregnancy intention, household income, study center, and time to interview.

Hoyt AT et al. *Am J Obstet Gynecol*, 2016.

Occupational Exposure to Polycyclic Aromatic Hydrocarbons

- Formed from incomplete burning of coal, tobacco
- Human exposure common, through:
  - Tobacco smoke
  - Other smoke
  - Air pollution
  - Occupation (coke ovens, foundries, coal tar use, asphalt manufacturing and use)
  - Eating charbroiled foods

Occupational Exposure to Polycyclic Aromatic Hydrocarbons: Some Results



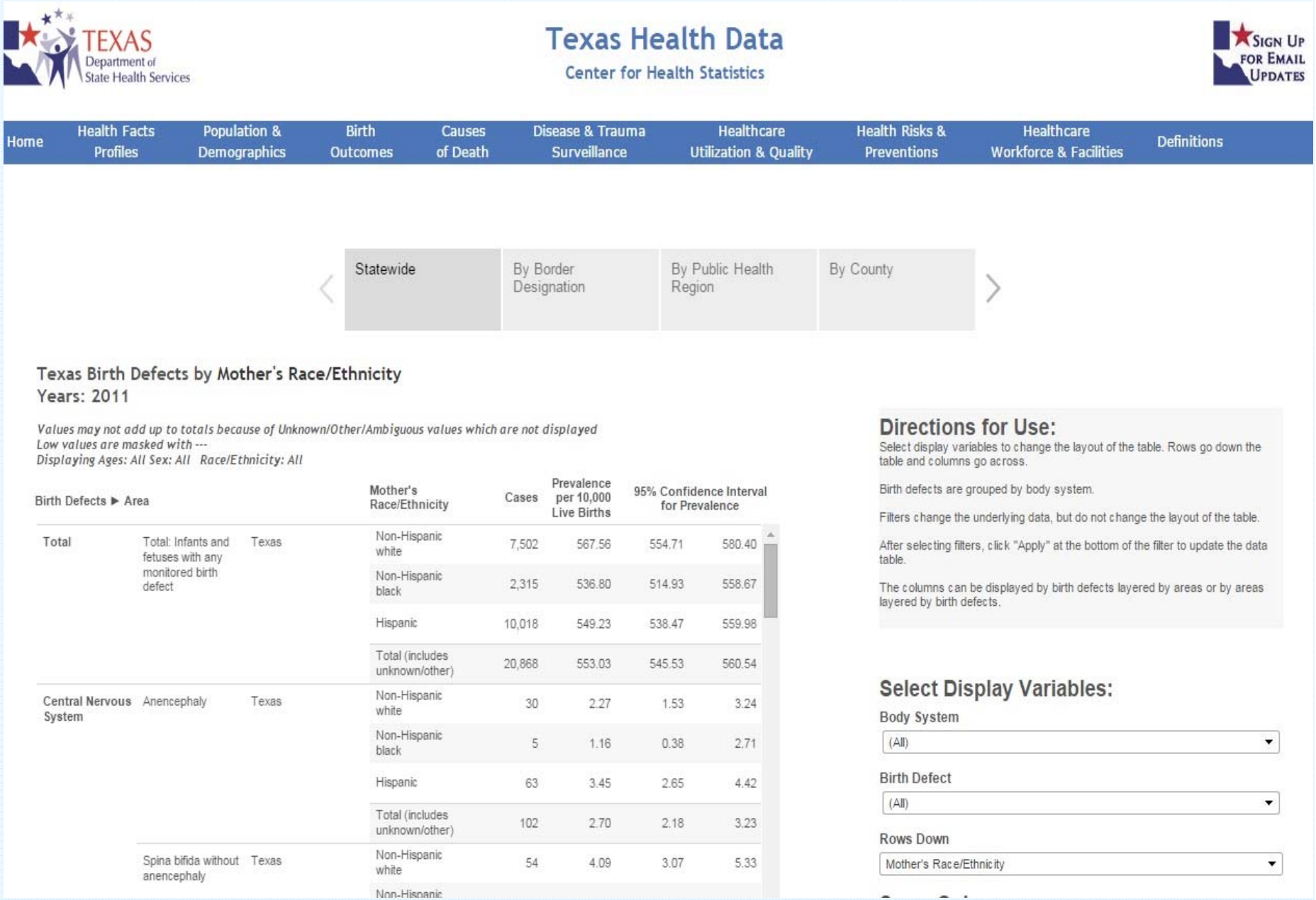
Adjusted for maternal education.

Langlois et al. *The Cleft Palate-Craniofacial Journal* 2013.

Adjusted for maternal age, BMI, smoking, education, gestational diabetes, study center.

Lupo et al. *Environmental Health Perspectives* 2012.

8. Program Resources



Available at: http://healthdata.dshs.texas.gov/Registries/BirthDefects

The Texas Birth Defects

MONITOR

TEXAS
Department of State Health Services
Birth Defects Epidemiology and Surveillance

A Semi-Annual Data
and Research Update

Volume 20 December 2014

Down Syndrome

Information about Down Syndrome for New and Expecting Parents

Your baby has or may have Down syndrome. It is natural for you to have questions, concerns or fears. You are not alone in your feelings or on the journey ahead of you. Know that the outlook for people with Down syndrome has improved over time because of advances in medical care, education and public attitudes. This brochure has facts about Down syndrome and a list of places where you can go to find more information and support.

About Down Syndrome

Each cell in the human body has 23 pairs of chromosomes; babies get half of each pair from their mom and the other half from their dad. Down syndrome is a genetic condition that is usually caused by an extra copy of the twenty-first chromosome. It is not caused by anything either parent did or did not do.

About 250,000 people in the United States have Down syndrome. Down syndrome does not usually run in families.

Children with Down syndrome will grow and develop like other babies, but may meet milestones later than a typical child. The mental, behavioral and developmental progress of people with Down syndrome varies widely and cannot be predicted before a person is born. Currently, the average life expectancy for people with Down syndrome is about 60 years.

Your Child with Down Syndrome

You can help your child fulfill his or her potential by having high expectations. Nurture and relate to your child like any other, and create a supportive and caring environment to help your child thrive.

People with Down syndrome are active and valued members of their community. This includes children who are involved in social and school programs, and adults who have jobs and live independently or with some support.

- Children with Down syndrome are more like other children than they are different.
- Babies with Down syndrome usually have developmental delays. Early intervention like occupational and speech therapy helps babies meet their milestones.
- Most babies with Down syndrome have low muscle tone at birth. This usually improves with time, and physical therapy can help.
- Half of babies with Down syndrome will have health issues. This could include heart or gastrointestinal conditions that may require surgery. Babies with Down syndrome have higher chances for feeding and digestive issues, hearing loss, vision impairments, and respiratory infections. Most of these conditions can be treated with good health care.
- People with Down syndrome can do all the things a typical person can do, including participate in sports and have a job.
- People with Down syndrome usually have a mild to moderate range of intellectual disability.
- Children with Down syndrome often attend regular schools in regular education classes with differing levels of support. There are now many college programs for people with intellectual delays.
- People with Down syndrome can have regular jobs or ones with support.
- People with Down syndrome can live independently or in a group home, and have friends and intimate relationships.

Available at:

https://www.dshs.texas.gov/birthdefects/downsyndrome/

THANK YOU

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http://www.dshs.state.tx.us/birthdefects/

Questions and Answers

Q & A Moderator

Janna Zumbrun, MSSW
Associate Commissioner of Disease Control and Prevention

Remote sites can send in questions by typing in the *GoToWebinar* chat box or email GrandRounds@dshs.state.tx.us.

For those in the auditorium, please come to the microphone to ask your question.

November 2

Caring for our Most Vulnerable: Levels of Neonatal Care

Presenter:
Eugene C. Toy, MD
Assistant Dean for Educational Programs, and Professor and Vice Chair of Medical Education, Department of Obstetrics and Gynecology, University of Texas Medical School at Houston