CDC PUBLIC HEALTH GRAND ROUNDS

Understanding the Causes of Major Birth Defects: Steps to Prevention

Accessible version: https://youtu.be/vaoJePIMGvI

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U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

The Impact of Birth Defects and Current Understanding of their Causes

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Centers for Disease Control and Prevention

Acknowledgment and Disclaimer

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- **This content and conclusions are those of the author and should not be construed as the official position or policy of, nor should any endorsements be inferred by HRSA, the U.S. Government or the Utah Department of Health.**

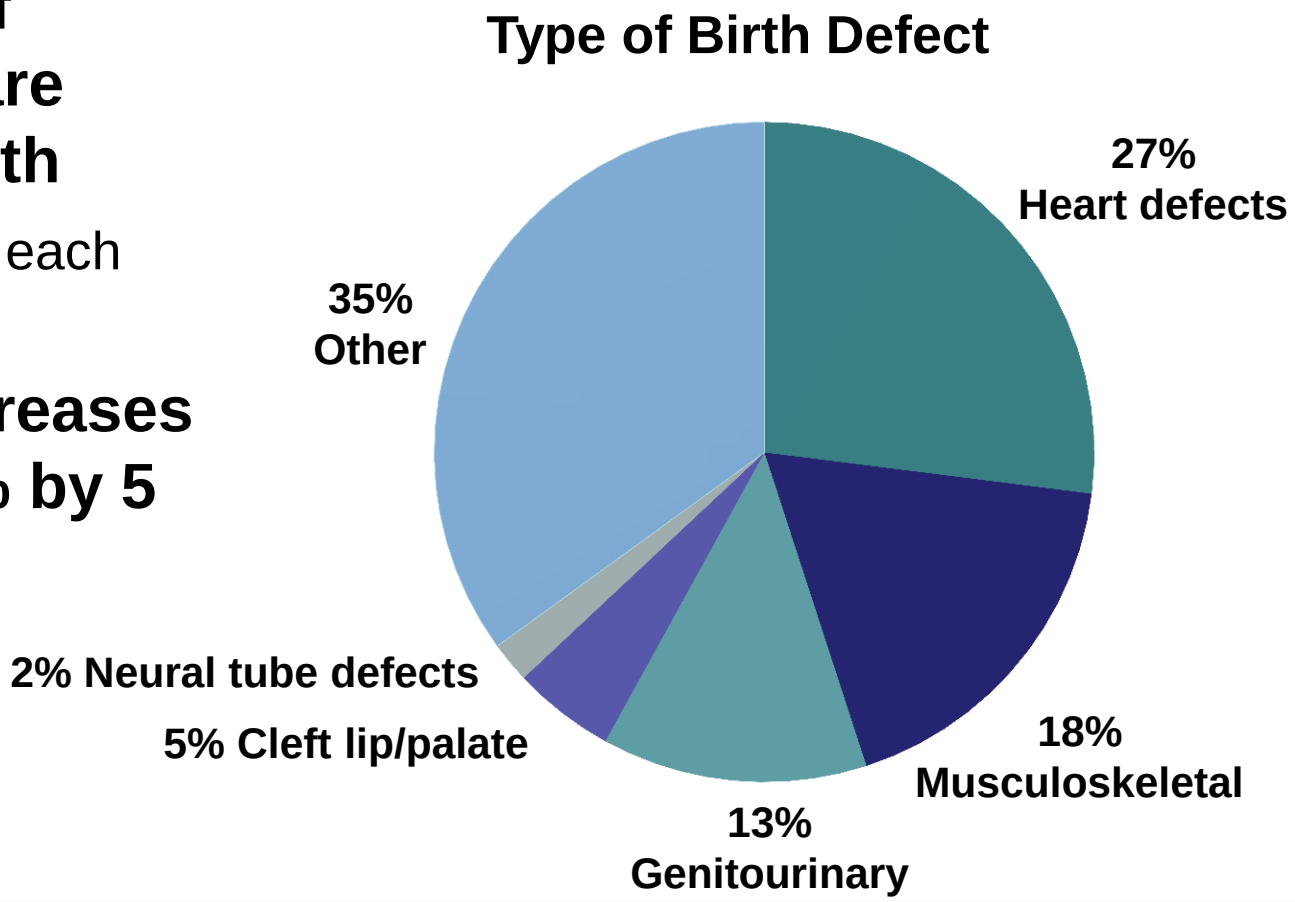
What Are Birth Defects?

- **An abnormality affecting body structure or function that is present at birth**
  - May be obvious at birth
  - May not be obvious at birth and diagnosed later in life
- **Functional defects include developmental disabilities (e.g., cerebral palsy or deafness)**
- **Structural defects include two types**
  - Major malformation
    - Surgical, medical or cosmetic importance
  - Minor malformation
    - Example of minor – single palmar crease

Single palmar crease

Major Birth Defects Are Common

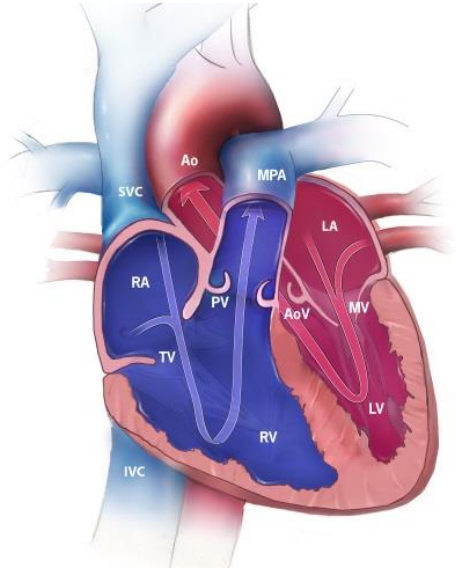
- **1 in 33 or 3% of children born are identified at birth**
  - 120,000 babies each year in the US
- **Prevalence increases to 1 in 20 or 5% by 5 years of age**



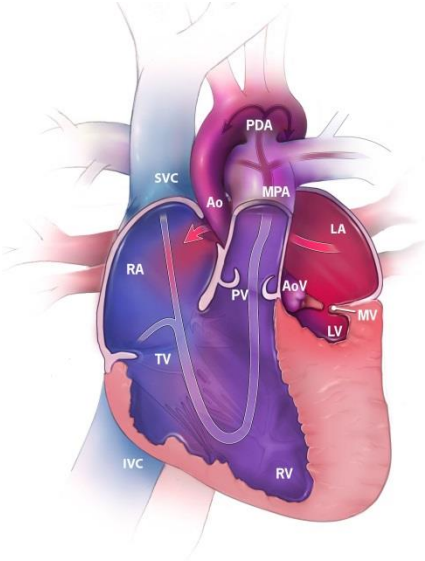
Kucik et al. Public Health Reports. 2012.

Heart Defects

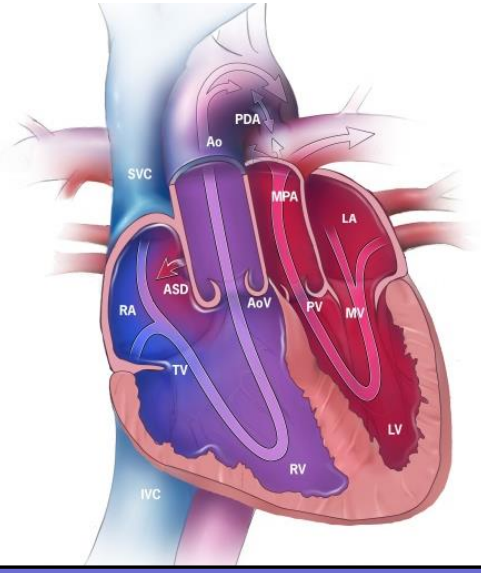
Normal Heart



Hypoplastic Left Heart Syndrome



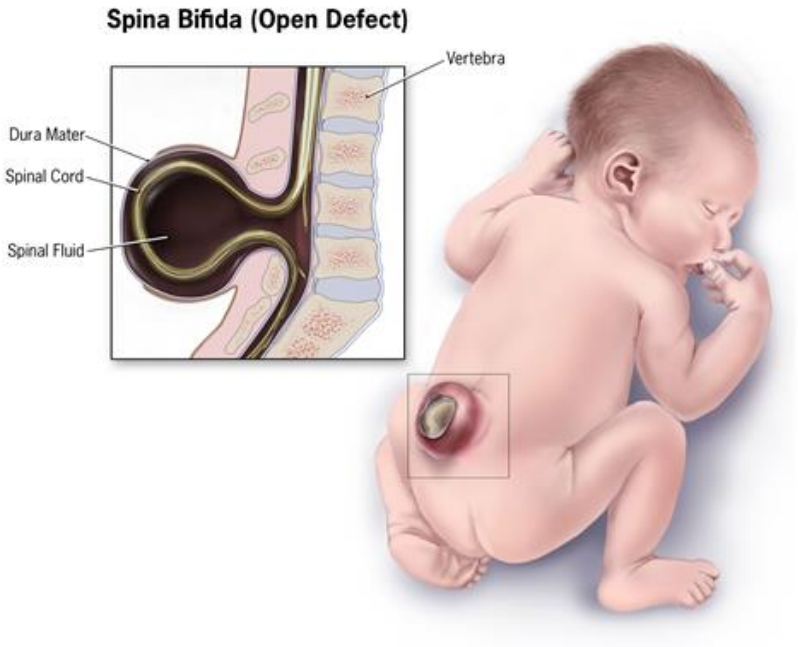
Transposition of the Great Arteries



These types of defects will require surgical repair

Neural Tube Defects

Spina bifida



Anencephaly

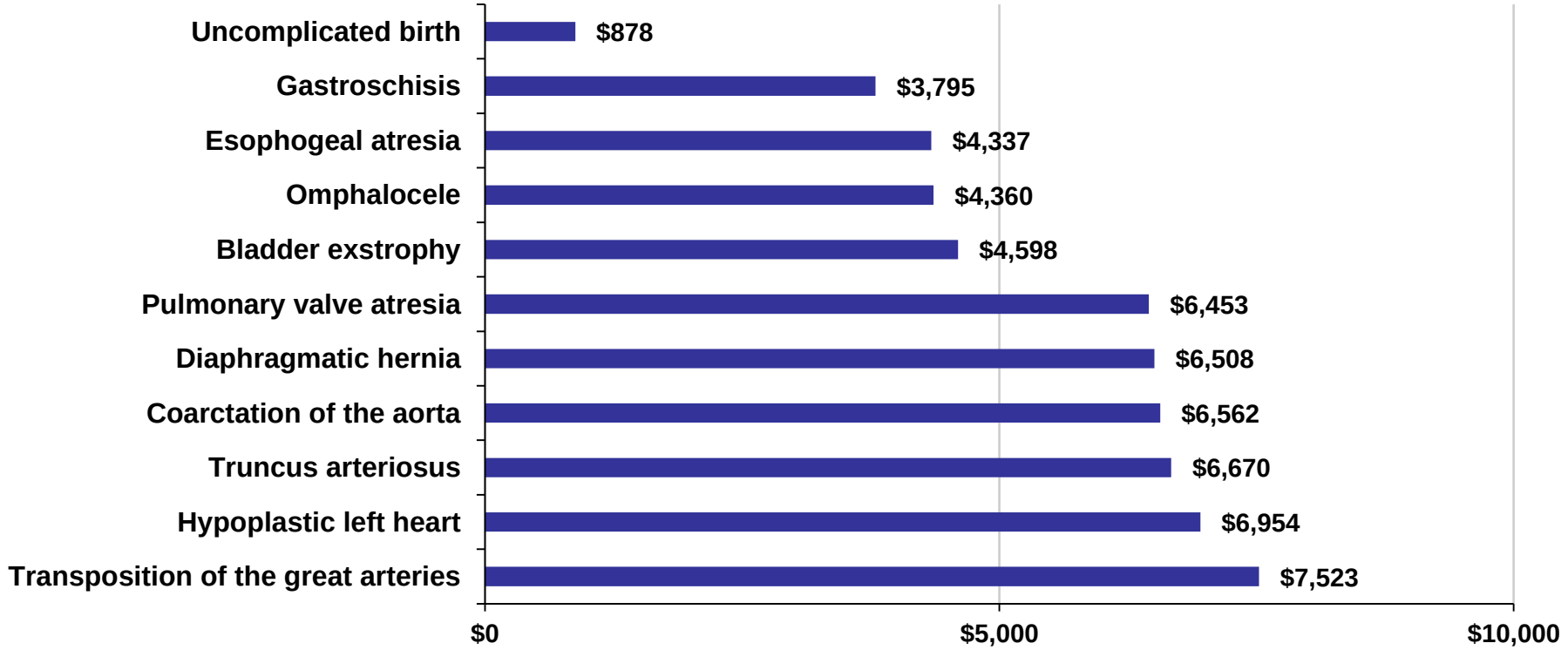
Abdominal Wall Defects

Gastroschisis

Omphalocele

Birth Defects Are Costly

Average daily hospital charges per newborn



CDC. *MMWR Morb Mortal Wkly Rep*. Jan 19, 2007

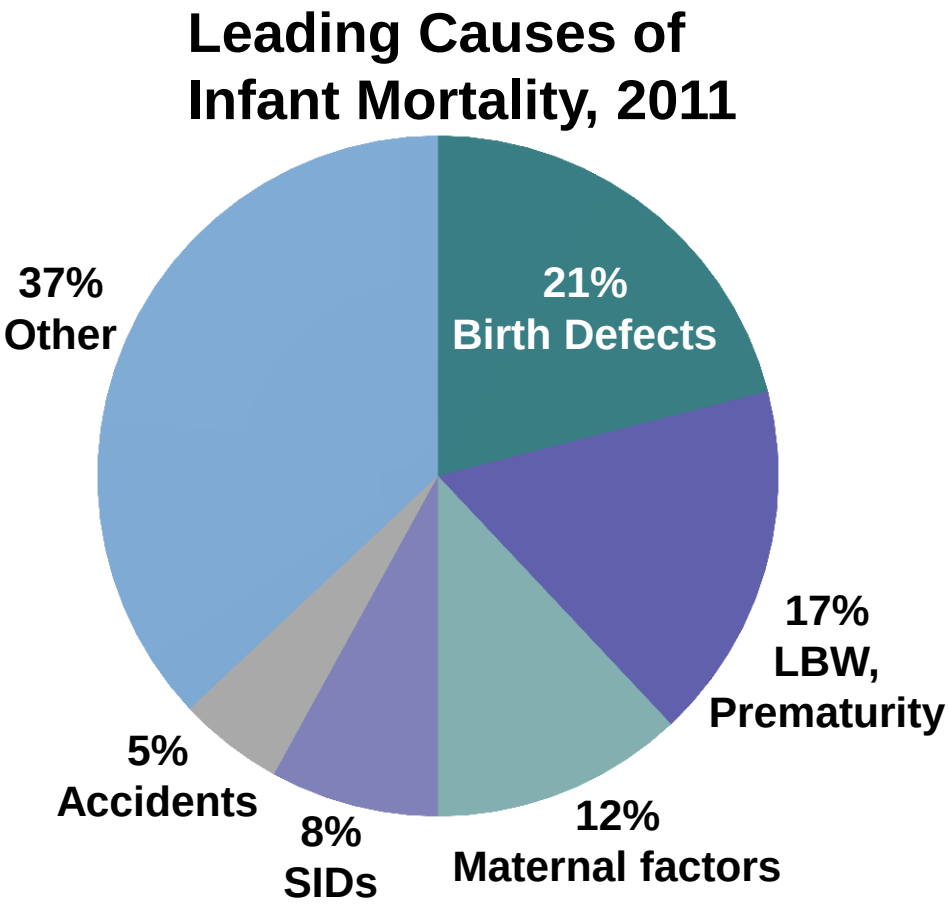
Birth Defects Are Costly

- In 2004, hospitalizations and medical charges cost $2.6 billion per year for all ages
- Medical care and advances in technology have improved long-term survival among children with birth defects

Russo CA, Elixhauser A. HCUP Statistical Briefs : Agency for Health Care Policy and Research (US); 2006-.2007 Jan.

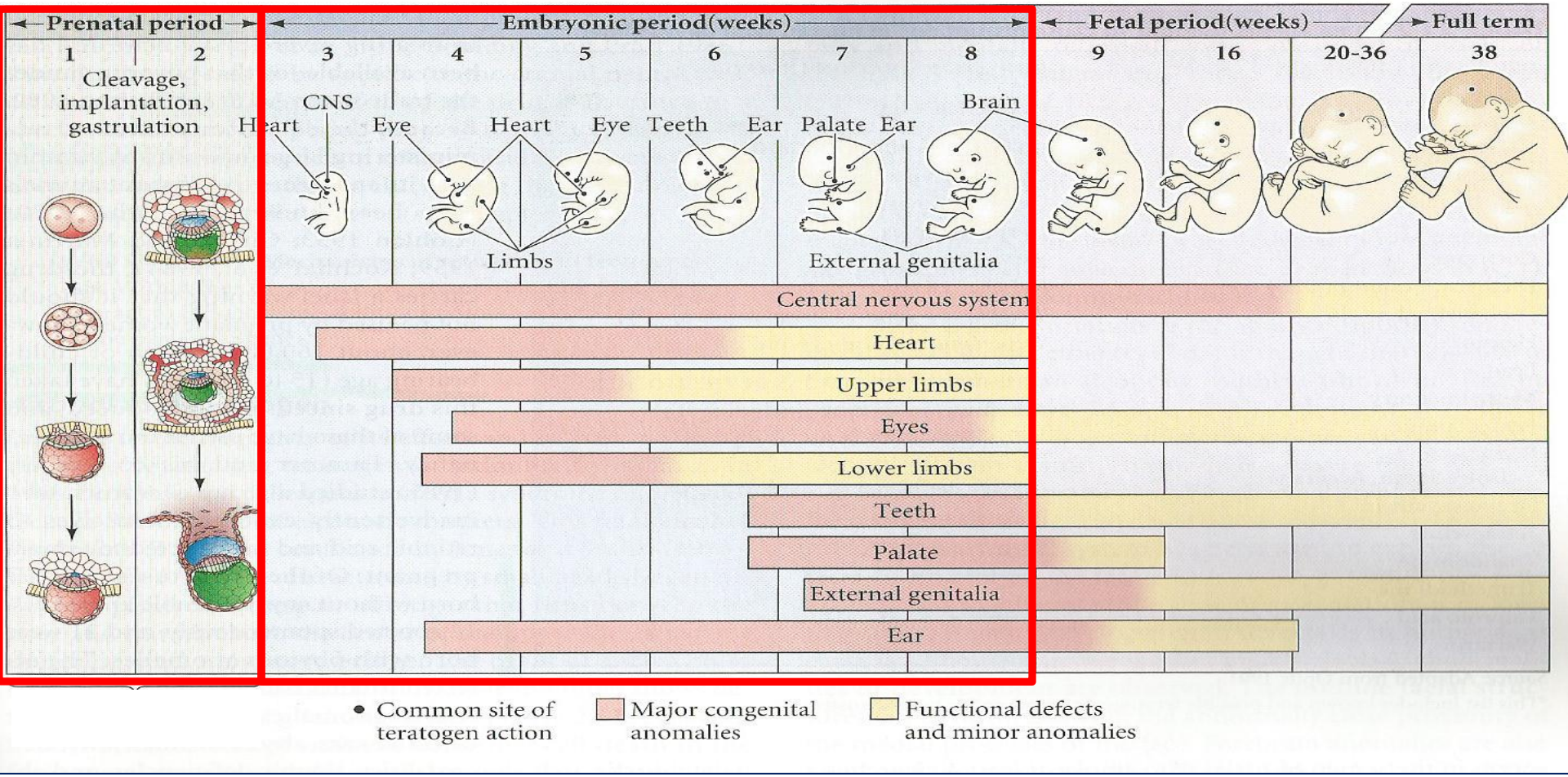
Birth Defects Are Critical

- **Infant mortality**
  - 6.7 deaths per 1,000 infants
  - 21% of deaths in the first year of life are due to birth defects
  - Congenital heart defects represent largest group



LBW: Low birth weight
2011 US National Vital Statistics Data, National Center for Health Statistics

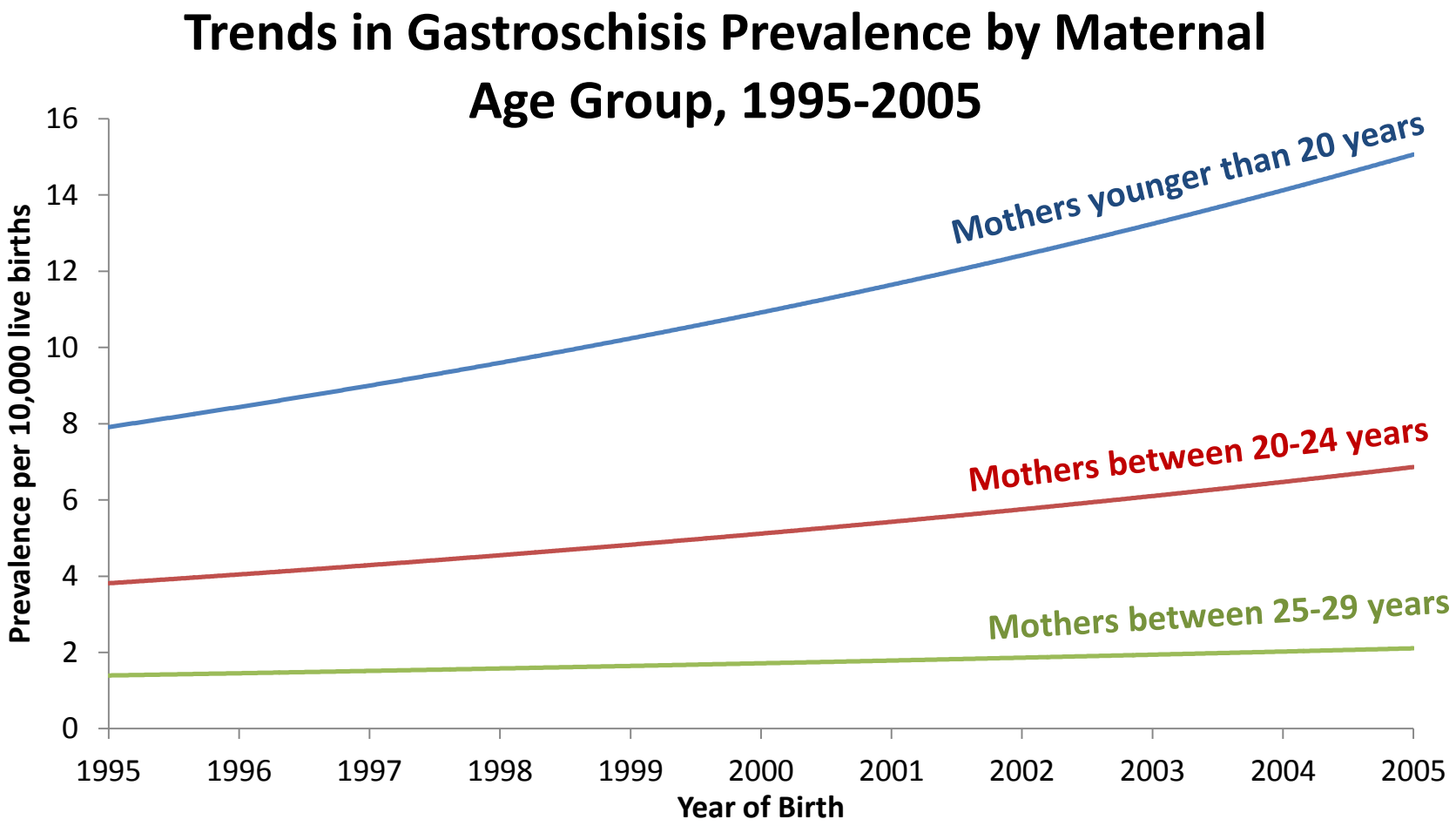
Most Major Birth Defects Occur Early in Pregnancy



Pregnancy Planning is Primary Prevention of Birth Defects

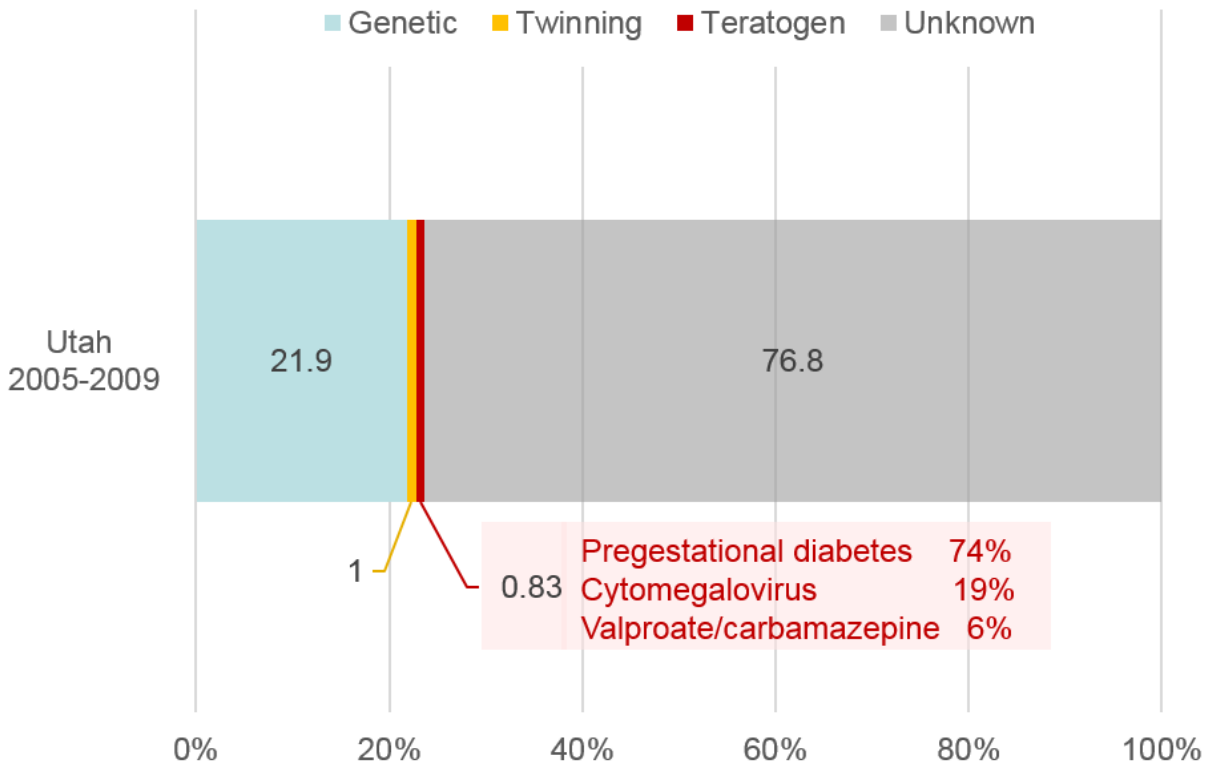
- The critical time period for all women to reduce their risk is before they become pregnant
- To reduce the risk of a neural tube defect, a woman must consume folic acid before conception
- Folic acid fortification of cereals and grains has been very effective because it increases folate levels among women in the US, whether planning a pregnancy or not

Increasing Prevalence of Gastroschisis Suggests Environmental Influence



Kirby et al. *Obstet Gynecol*. 2013

The Majority of Birth Defects Do Not Have an Identifiable Cause



Teratogen: an agent or factor that causes a malformation in an embryo

Utah Birth Defect Network, Utah Department of Health

Working to Identify the Unknown Causes

- Major birth defects should be systematically monitored in the population
- Environmental factors that women are exposed to should be investigated
- Major birth defects are common, costly and critical

Advancing Understanding of the Causes of Birth Defects

Jennita Reefhuis, PhD
Epidemiology Team Lead
Birth Defects Branch
Division of Birth Defects and Developmental Disabilities
National Center on Birth Defects and Developmental Disabilities

U.S. Department of Health and Human Services
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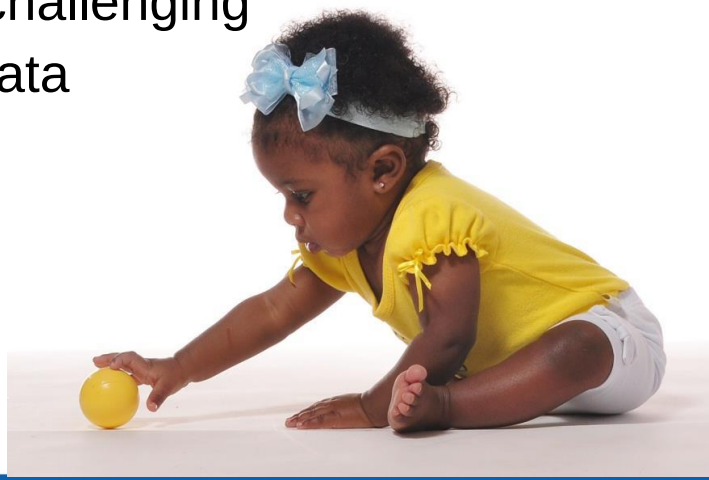
How To Study Rare Outcomes Such as Specific Birth Defects

- **Cohort studies**
  - Pro: Prospective exposure information
  - Con: Need a very large study to identify enough cases
- **Data-linkage studies**
  - Pro: Cost-efficient
  - Con: Methods for mother-baby linkage challenging
  - Con: Limited diagnostic and exposure data
- **Pregnancy registries**
  - Pro: Useful to identify major effects
  - Con: Not population based



Tinker, S. C., Gilboa, S., Reefhuis, J., Jenkins, M. M., Schaeffer, M., & Moore, C. A. (2014). *Current Epidemiology Reports*, 1-8.

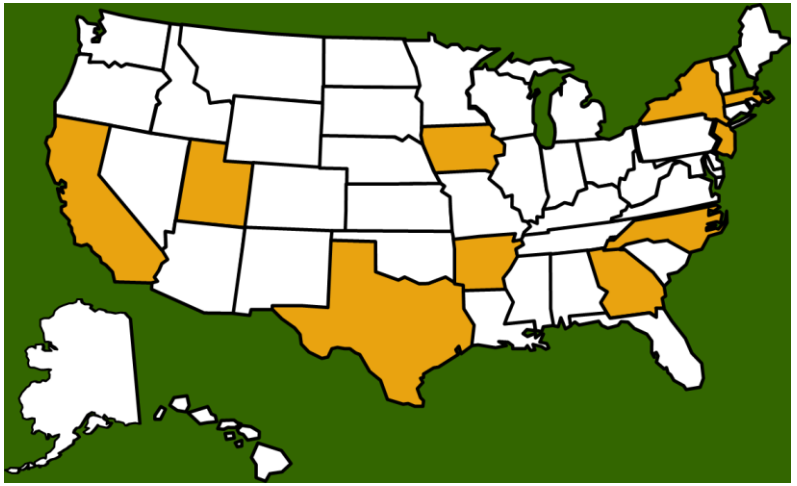
Studying Rare Birth Defects: The Best Option

- **Case-control studies**
  - Pro: Efficient
  - Pro: High-quality diagnostic data
  - Pro: Ability to look at specific birth defects
  - Con: Needs to be multi-center or many years to have sufficient data
  - Con: Potential recall bias

Case-control studies are used to identify factors that may contribute to a medical condition by comparing subjects who have that condition (the "cases") with similar patients who do not have the condition (the "controls“)

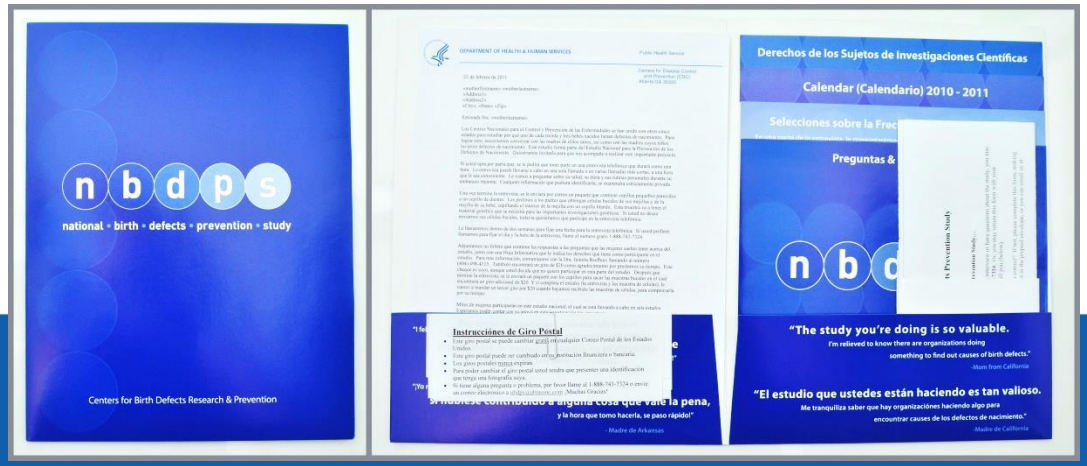
National Birth Defects Prevention Study

- **Population-based case control study**
- **Births October 1997-December 2011**
- **Cases from state-based birth defects surveillance systems**
- **Study cohort**
  - ~ 6 million total live births
  - 48,196 affected pregnancies



NBDPS Data Collection Methods

- **Over 30 defects studied**
- **Live-born control infants**
- **Telephone interview with mothers of cases and controls**
  - 32,209 case mothers interviewed (67.4%)
  - 11,805 control mothers interviewed (64.8%)
- **Buccal cell (cheek swab) requested from mother, father, and infant**



NBDPS: National Birth Defects Prevention Study

Selected NBDPS Results

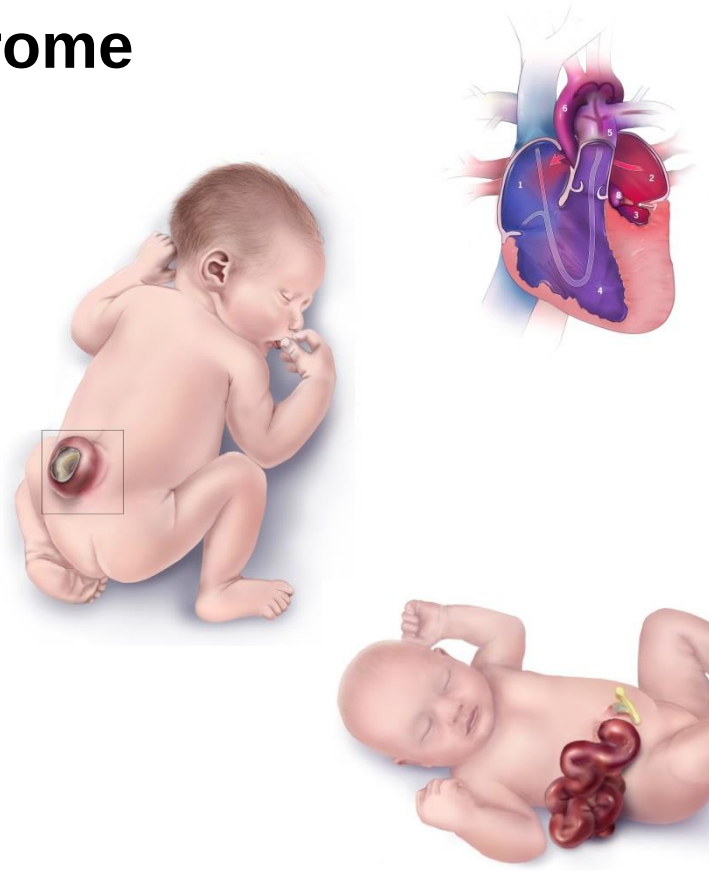
- **Over 200 peer-reviewed manuscripts**
- **Diabetes diagnosed before pregnancy**
  - Heart defects: odds ratio 4.6 (2.9 - 7.5)
  - Non-heart defects: odds ratio 2.3 (1.4 - 3.8)

- **Stress and neural tube defects**
  - 4 or more stressful life events in early pregnancy
    - Such as relative's death, financial or legal problems, violence
    - Odds ratio 1.5 (1.1 - 2.0)
  - Perception of social support
    - Emotional, financial, daily tasks
    - Odds ratio 0.8 (0.5 - 1.1)

Correa et al. *AJOG* 2008
Carmichael et al. Paediatr Perinat Epidemiol 2014
NBDPS: National Birth Defects Prevention Study

NBDPS Results: Exposure to Opioid Medications

- **Hypoplastic left heart syndrome**
  - 17 exposed cases
  - Odds ratio 2.4 (1.4 - 4.1)
- **Spina bifida**
  - 26 exposed cases
  - Odds ratio 2.0 (1.3 - 3.2)
- **Gastroschisis**
  - 26 exposed cases
  - Odds ratio 1.8 (1.1 - 2.9)



Broussard et al. *AJOG* 2011
NBDPS: National Birth Defects Prevention Study

Better Data to Help Inform Treatment Choices

- **Maternal disease in pregnancy may need treatment**
  - Disease can harm mother and baby (e.g., fever or diabetes)
- **Comparing risk-benefit of treatment compared with no treatment**
- **Comparing birth defect risk of different treatments–some options may be safer**
  - Choice of SSRIs for depression
  - Antibacterials in early pregnancy

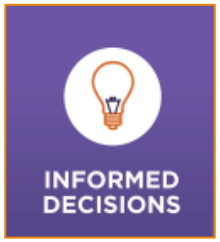
SSRIs: selective serotonin reuptake inhibitors
www.cdc.gov/pregnancy/meds/treatingfortwo/

Antibacterial Medication in Early Pregnancy

	Penicillin OR (95% CI)	Nitrofurantoins OR (95% CI)	Sulfonamides OR (95% CI)
Left ventricular outflow tract obstruction	1.0 (0.8 - 1.4)	1.6 (0.8 - 3.2)	2.9 (1.6 - 5.1)
Cleft lip with or without cleft palate	0.8 (0.6 - 1.1)	1.9 (1.1 - 3.3)	1.0 (0.5 - 1.9)
Neural tube defects	0.9 (0.6 - 1.2)	1.4 (0.7 - 3.0)	1.4 (0.7 - 2.9)

Crider et al. *JAMA Pediatrics* 2009

Treating for Two Initiative



- **Expand research to fill knowledge gaps**
  - Accelerate epidemiologic research into medication use and pregnancy outcomes
- **Evaluate evidence to develop reliable guidance**
  - Establish ongoing systematic review of evidence and expert body to translate into summary guidance
- **Deliver information to support decision-making**
  - Disseminate up-to-date, clinically relevant information to prescribers, pharmacists, patients, and consumers

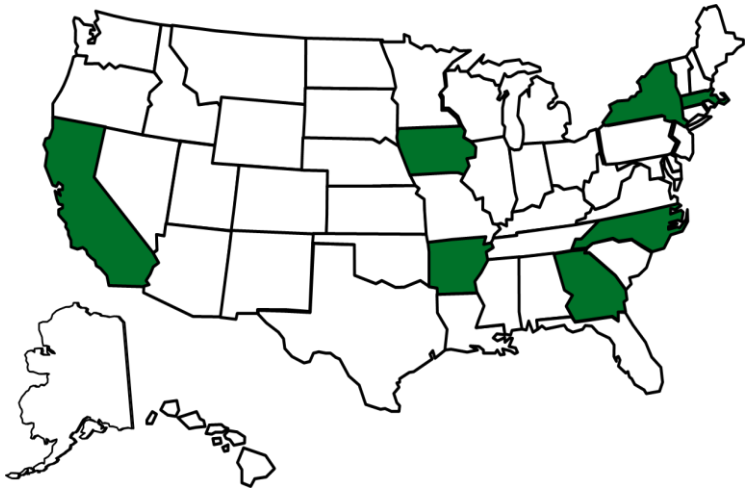
www.cdc.gov/pregnancy/meds/treatingfortwo/index.html

Exploring Modifiable Risk Factors – Medications with New and Expanded Uses

- **Pregnant women not included in clinical trials**
  - Excluded because of safety concerns
  - Often use medications after licensure
- **New medications constantly introduced**
- **Existing medications with new indications**
  - Antiepileptic topiramate used as weight-loss product
  - Antiepileptics used to treat migraines
- **Want to include questions about why person is taking medicine, and at what dosage**

Birth Defects Study To Evaluate Pregnancy Exposures

- **17 defects selected**
  - Severity
  - Prevalence
  - Consistent ascertainment
- **7 centers**
  - Arkansas, California, Georgia, Iowa, Massachusetts, New York, North Carolina
- **Births starting January 1, 2014**
- **Focus on first trimester exposures**



www.cdc.gov/ncbddd/birthdefects/bd-steps.html

Exploring Modifiable Risk Factors
Maternal Disease and Treatment with Medications

- **Increased survival among women with**
  - Cancer
  - Organ and tissue transplants
- **Increased prevalence**
  - Asthma
  - Attention-deficit hyperactivity disorder
- **Assess diagnostic and treatment details**
  - Diabetes
  - Mental health disorders

Going Beyond Case-Control Studies

- **To establish causation, confirmation of epidemiologic findings needed**
  - Surgeon General's 2014 report included a finding that smoking is causally related to orofacial clefts (such as cleft lip, cleft palate)
  - Isotretinoin and severe birth defects
  - Thalidomide and limb and other defects
- **Statistical modeling studies**
  - Assess the prevention impact of substituting "safer" medications

The health consequences of smoking: 50 years of progress. A Report of the Surgeon General, 2014.

Birth Defects Work Must Continue

- **Important to remember that 1 in 33 pregnancies are affected by birth defects**
  - Relatively common at the population level, but individual defects are rarer
- **CDC's Birth Defects Branch and its collaborators continue to contribute to:**
  - Identifying risk factors for birth defects among medicines, diseases, and environmental factors
  - Assessing risk-benefit of medications
  - Determining whether there are safer treatment options for certain diseases

Birth Defects Research and Emergency Preparedness: The Vaccines and Medications in Pregnancy Surveillance System

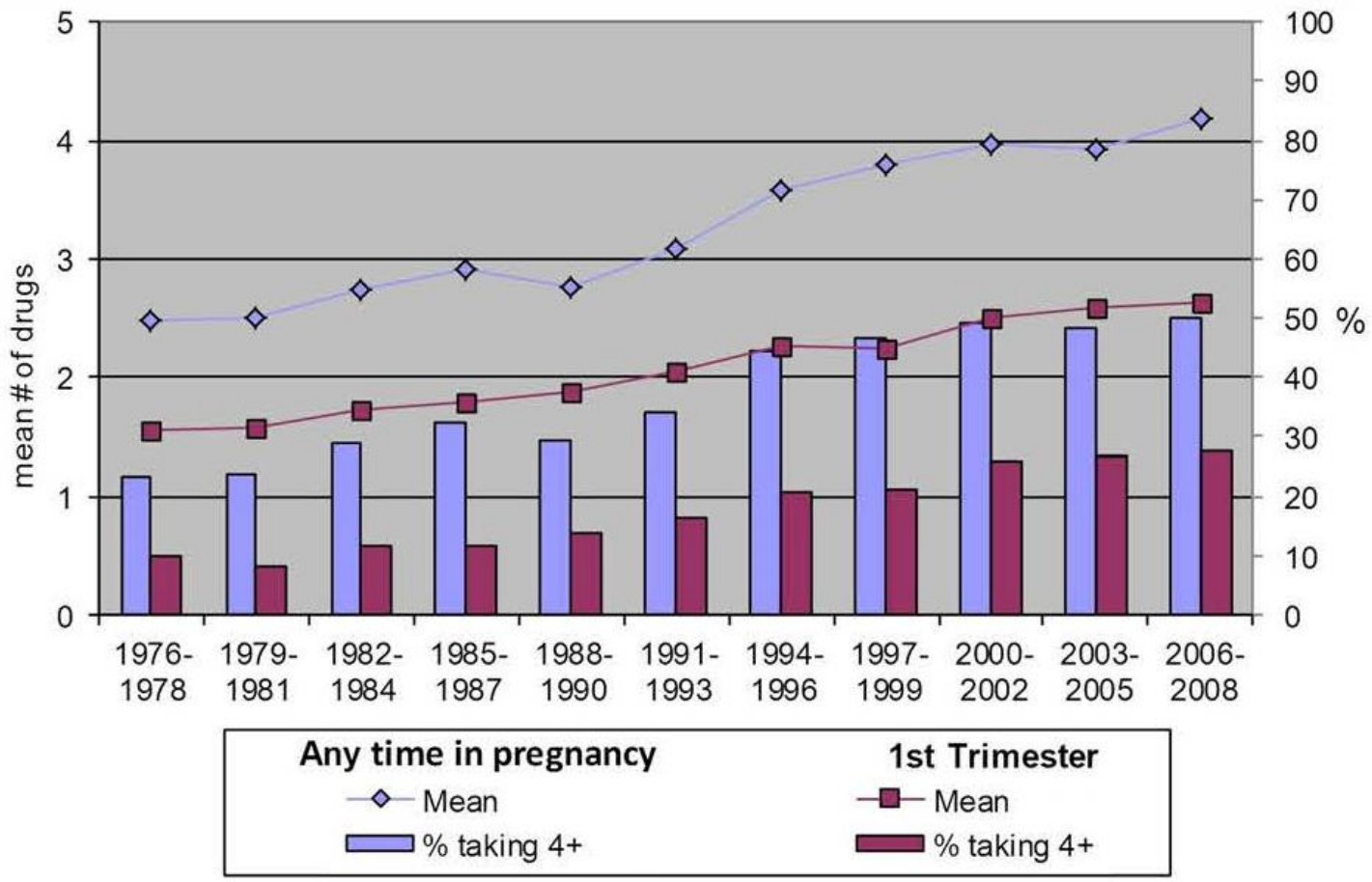
Allen A. Mitchell, MD

Director, Slone Epidemiology Center
Professor of Epidemiology and Pediatrics,
Boston University Schools of Public Health and Medicine

BOSTON UNIVERSITY

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

Trends in Medication Use During Pregnancy



Pregnancy Health Interview Study (Birth Defects Study), Slone Epidemiology Center, Boston University

Specific Examples

- **Medications whose exposure prevalence in pregnancy has increased in recent years include:**
  - Selective serotonin reuptake inhibitors (SSRIs)
  - Attention deficit hyperactivity disorder medications, primarily amphetamine mixed salts (e.g., Adderall®)

Mitchell, et al. *AJOG, 2015*.
Louik, et al. *Pharmacoepidemiol Drug Saf*, *in press*.

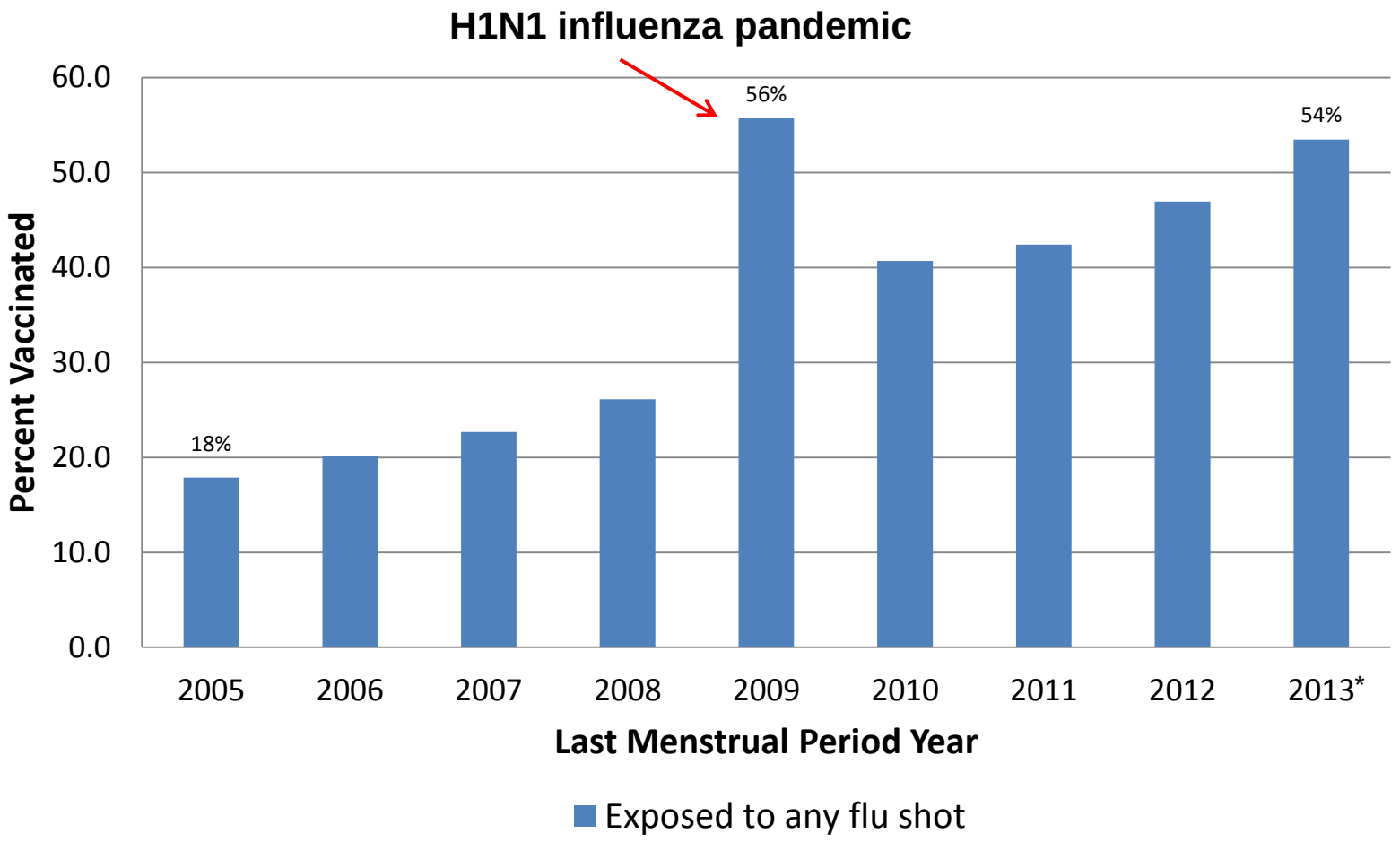
What Are the Implications of Greater Medication Use During Pregnancy?

- **For the purposes of birth defects prevention, we need to focus on medications and vaccines for which:**
  - Trends document increasing use in pregnant women

  and

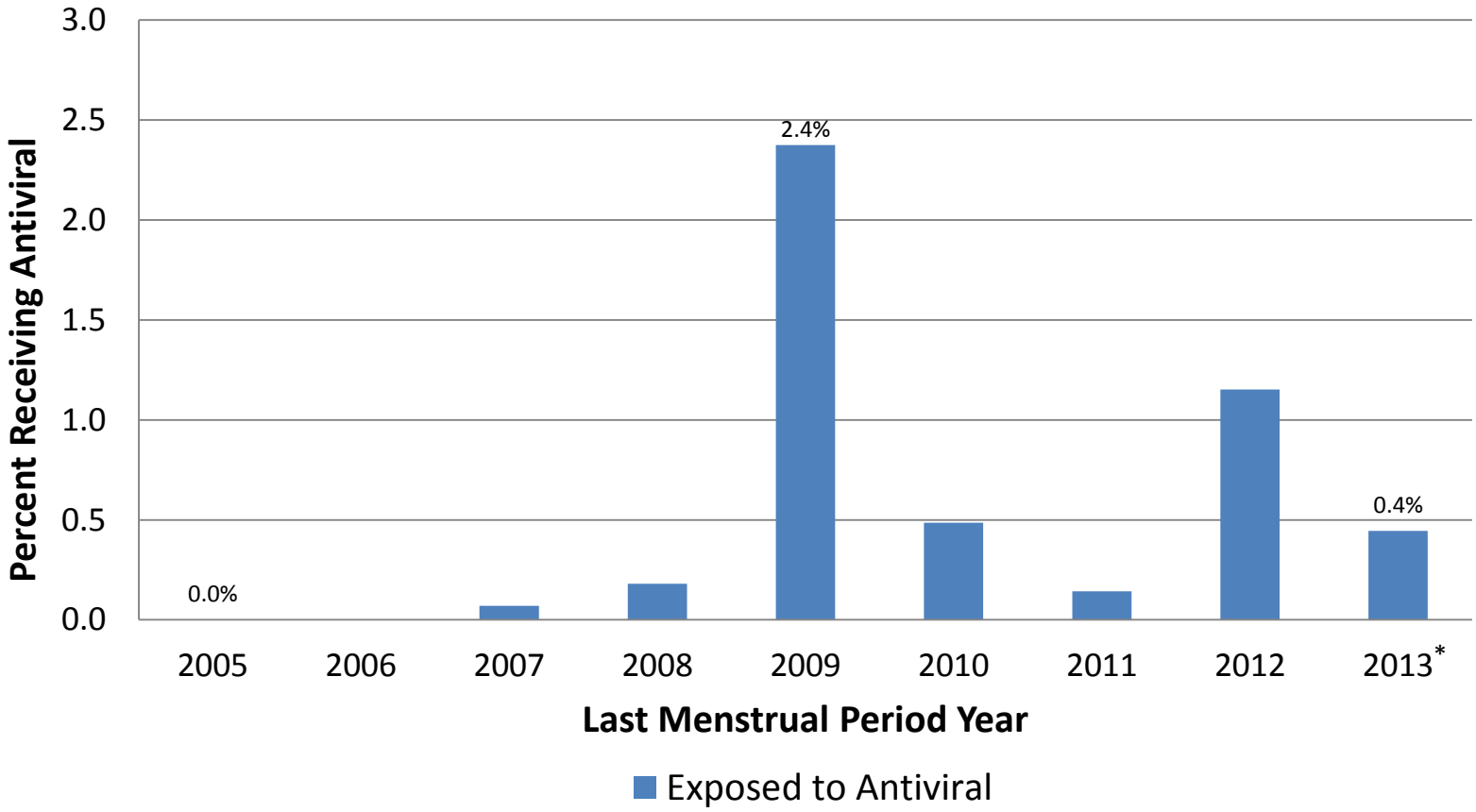
  - Pregnancy exposure is common but data on pregnancy risk and safety are insufficient

Proportion of Women Receiving Any Influenza Vaccine during Pregnancy



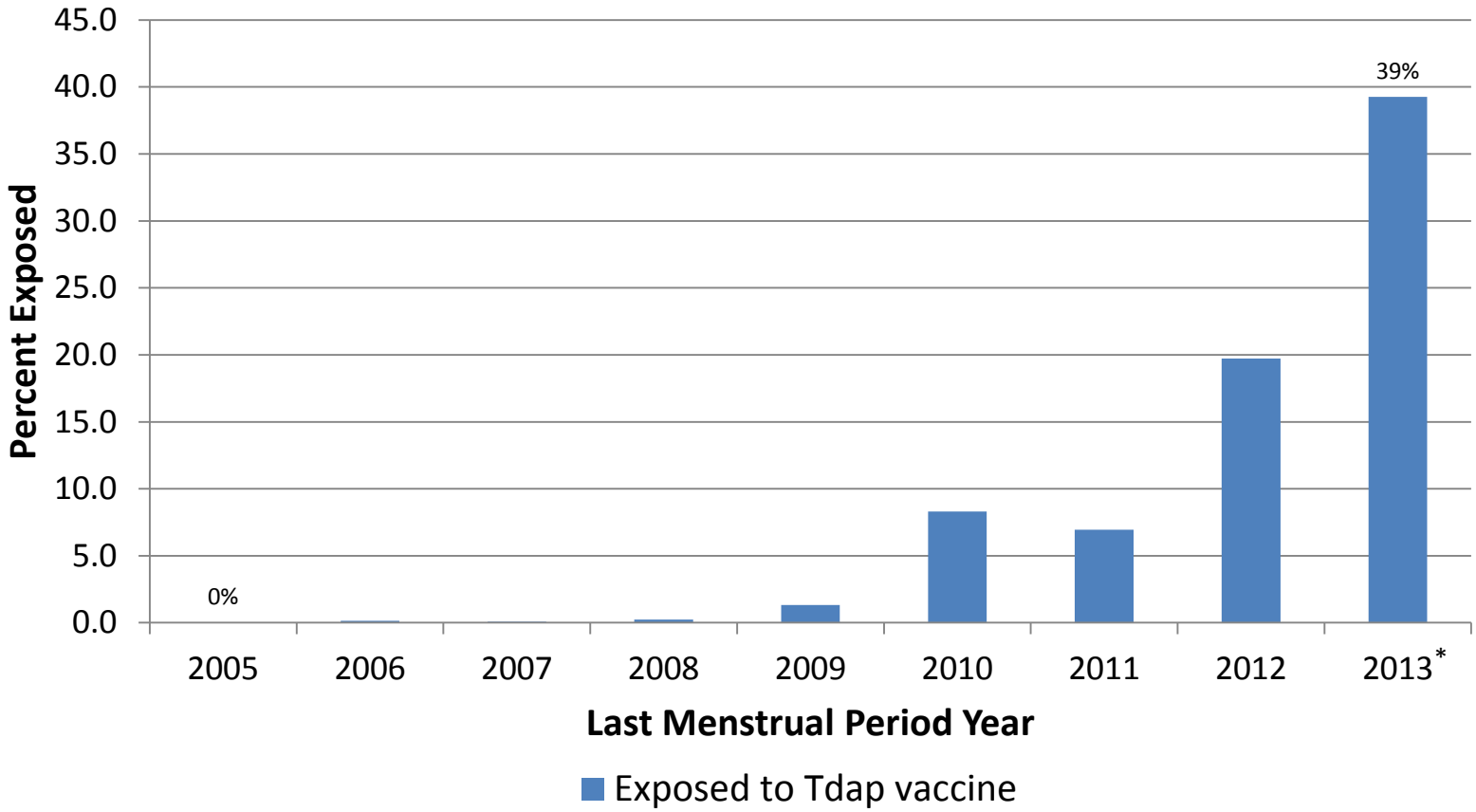
Unpublished data; Birth Defects Study, Slone Epidemiology Center, Boston University
* Incomplete year

Proportion of Women Receiving Influenza Antiviral Drugs during Pregnancy



Unpublished data; Birth Defects Study, Slone Epidemiology Center, Boston University
* Incomplete year

Proportion of Women Receiving Tdap Vaccine During Pregnancy



Unpublished data; Birth Defects Study, Slone Epidemiology Center, Boston University
Tdap: Tetanus Toxoid, Diphtheria Toxoid, and Acellular Pertussis Vaccine
* Incomplete year

How Do We Learn About Risks and Relative Safety for "New" Exposures in Pregnancy?

- Need to identify risks and relative safety of drugs, vaccines, and biologics (e.g., immune globulins) used by pregnant women
- Particularly important to have a system that is agile in its ability to identify and study new products

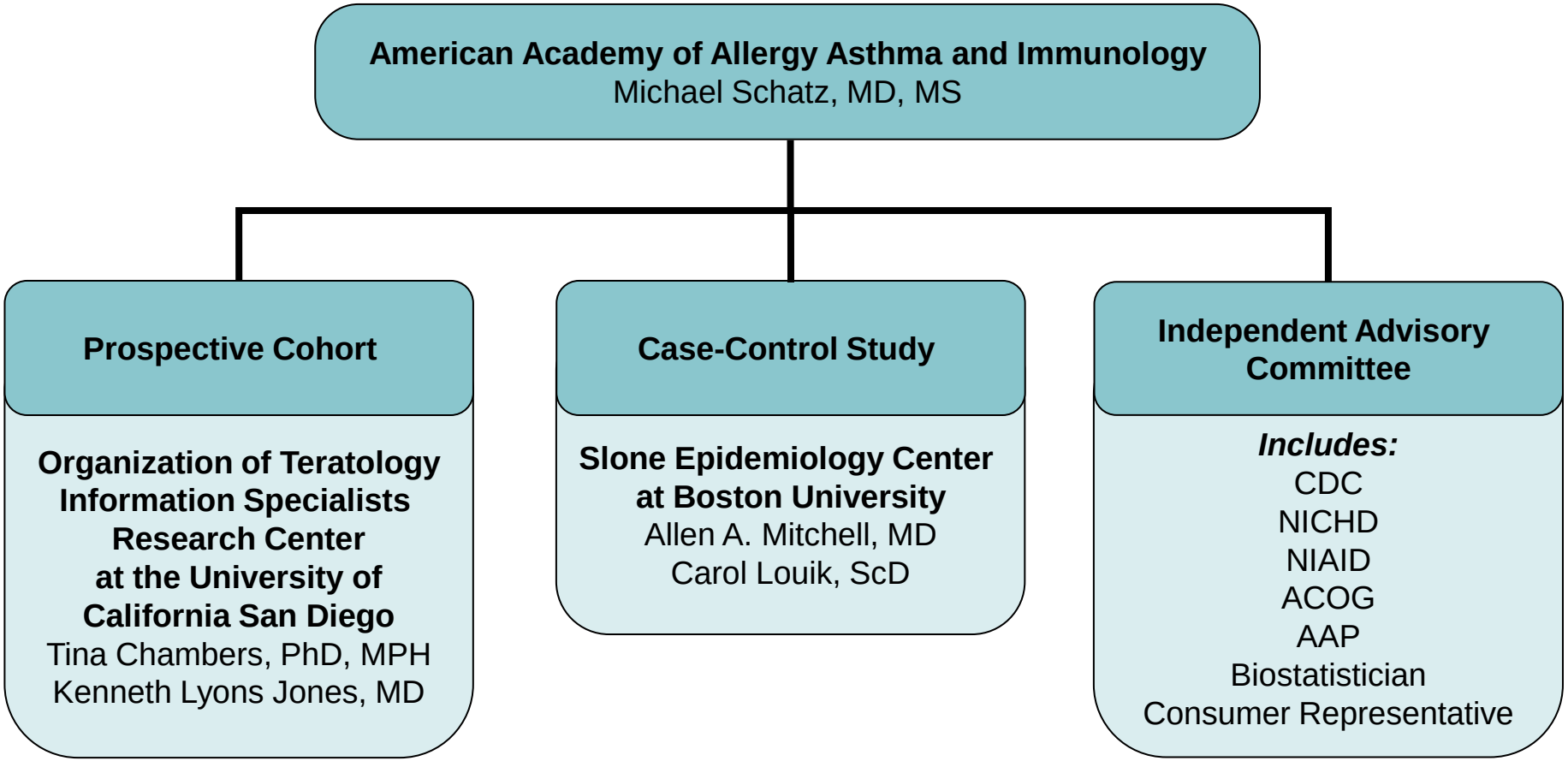
Vaccines and Medications in Pregnancy Surveillance System (VAMPSS)

- Specifically designed to assess the risks and safety of vaccines and medications used in pregnancy
- Funding model is public-private partnership
- Identifies wide range of relatively common adverse pregnancy outcomes, including birth defects overall
- Has statistical power to evaluate specific birth defects and their possible causal relation to drugs or vaccines

Objectives of VAMPSS

- **Targets new (and old) drugs and vaccines recommended for use or have come into use during pregnancy**
  - Current examples
    - Annual influenza, acellular pertussis vaccines
  - Future examples
    - Respiratory syncytial virus vaccines
    - Group B streptococcus vaccines
  - Emergent examples
    - Ebola vaccines, drugs, or biologics that might be licensed or approved for emergency use
- **Prospective cohort and case-control study arms can direct focus on new exposures within a few months' time**

Structure of VAMPSS



VAMPSS: Vaccines and Medications in Pregnancy Surveillance System
NICHD: National Institute of Child Health and Human Development
NIAID: National Institute of Allergy and Infectious Diseases

ACOG: American Congress of Obstetricians and Gynecologists
AAP: American Academy of Pediatrics

Prospective Cohort – Organization of Teratology Information Specialists

- **OTIS is a North American network of university or hospital-based services in existence since 1979**
- **Specialists provide risk counseling to 80 - 100,000 pregnant women and health care providers per year**
- **Network can screen callers from a geographically diverse area to identify those who received a vaccine or medication of interest, along with an unexposed comparison group**

OTIS: Organization of Teratology Information Specialists

Participants of Prospective Cohort–OTIS

- **OTIS sites refer potential participants to coordinating center**
  - An exposed cohort, a disease-matched cohort and a healthy unexposed cohort are concurrently recruited
  - Each cohort followed for birth defects overall, preterm birth, growth and spontaneous abortion
- **All groups receive**
  - A series of structured telephone interviews at standard time points during and after pregnancy, and an outcome interview
  - Medical records review

OTIS: Organization of Teratology Information Specialists

Data Collected from Prospective Cohort – OTIS

- **Maternal interviews and medical records review provide detailed information**
  - Dose, timing, duration of medication and vaccine exposure
  - Maternal disease or indication for medication
  - Pregnancy history, health history, demographics
  - Wide range of potential confounders including
    - Other prescription or over-the counter medications
    - Body mass index
    - Tobacco, alcohol and vitamin and mineral use

OTIS: Organization of Teratology Information Specialists

Case-Control–Birth Defects Study

- **BDS began in 1976 at Slone Epidemiology Center, Boston University**
- **Objectives**
  - Identify risks and safety of a wide range of medications and vaccines with respect to the wide range of specific birth defects
  - Establish ranges of risk for specific medications
  - Identify rates of exposure to specific agents

BDS: Birth Defects Study

Case-Control Study Participants–BDS

- **Study participants**
  - Infants with specific major congenital malformations (cases)
  - Infants without congenital malformations (controls)
- **Multi center design**
  - Hospital and clinic surveillance
    - Greater metropolitan Boston, Philadelphia, San Diego, Nashville
  - Birth defects registries
    - Massachusetts, New York

BDS: Birth Defects Study

Data Collected from Case-Control Study–BDS

- **Data obtained from mothers by computer-assisted telephone interview**
  - Interviewed by study nurses within six months of delivery
- **Interview data include**
  - Demographic and reproductive factors (e.g., age, education, number of previous pregnancies and births)
  - Medical history
  - Indications for use and use of prescription and OTC medications; including vaccines, vitamins and minerals, supplements
  - Wide range of potential confounders (e.g., smoking, alcohol, diet)

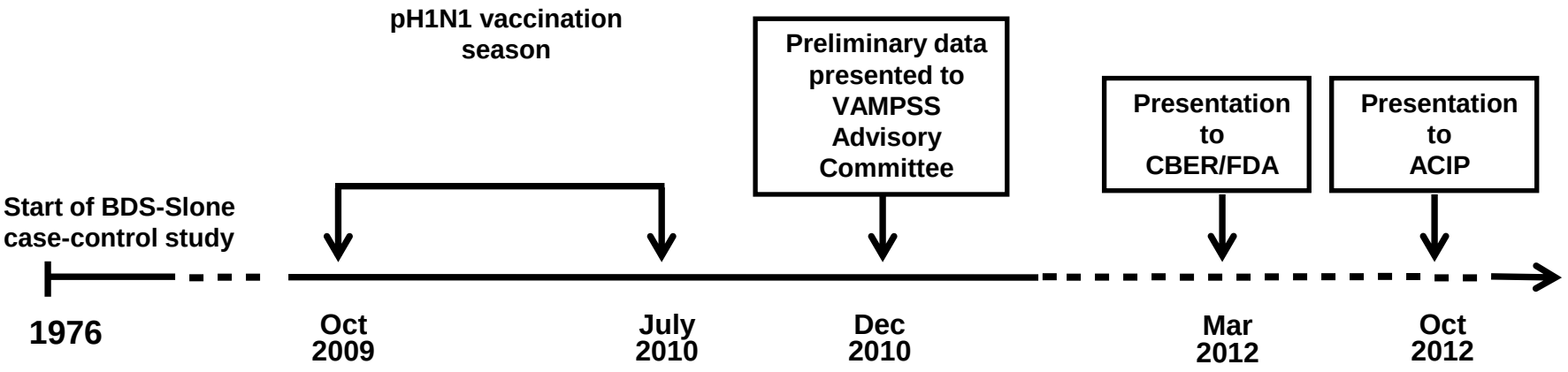
BDS: Birth Defects Study
OTC: Over-the-counter

VAMPSS and Pandemic H1N1 Influenza

- **Anticipating a pandemic caused by H1N1 influenza and the widespread use of the pH1N1 vaccine among pregnant women in 2009 - 2010**
- **BARDA requested VAMPSS to monitor the risks and relative safety of the pandemic H1N1 vaccine and influenza antiviral drugs**

BARDA: Biomedical Advanced Research and Development Authority
VAMPSS: Vaccines and medications in pregnancy surveillance system
pH1N1: pandemic H1N1 influenza virus

Timeline for VAMPSS pH1N1 Studies



- **VAMPSS was able to quickly modify data collection to meet the objectives of safety monitoring for pH1N1 vaccines and influenza antivirals in pregnant women**

VAMPSS: Vaccines and medications in pregnancy surveillance system
pH1N1: pandemic H1N1 influenza virus
CBER/FDA: Center for Biologics Evaluation and Research at the Food and Drug Administration
ACIP: Advisory Committee on Immunization Practices

Findings from VAMPSS pH1N1 Studies: No Increased Risk of Birth Defects

Prospective Cohort (OTIS)

Women exposed to a pH1N1 vaccine did NOT have an increased risk of having a baby born with a birth defect

Relative risk = 0.79
95% CI: 0.26 - 2.42

Case-Control Study (BDS-Slone)

For 41 specific defects, most adjusted odds ratios were close to 1.0, and most of those had relatively narrow confidence intervals

Chambers CD, Johnson D, Xu R, Luo Y, Louik C, Mitchell AA et al. Vaccine. 2013 Oct 17;31(44):5026-32.
Louik C, Ahrens K, Kerr S, Pyo J, Chambers C, Jones KL, et al. Vaccine. 2013 Oct 17;31(44):5033-40.
VAMPSS: Vaccines and medications in pregnancy surveillance system
pH1N1: pandemic H1N1 influenza virus

Importance of VAMPSS for Public Health Emergency Response

- Pregnant women may be at high risk for complications that endanger their pregnancies
- Drugs, vaccines, or other medical products might be used in pregnant women with little or no study
- VAMPSS is proven to work in monitoring safety of emergency countermeasures in pregnant women, on short notice
- VAMPSS represents a key tool to maintain confidence among providers and the public that preventive measures are being actively monitored for safety

VAMPSS: Vaccines and medications in pregnancy surveillance system

Identifying What Else We Can Do To Prevent Birth Defects

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Birth Defects Branch

Division of Birth Defects and Developmental Disabilities

National Center on Birth Defects and Developmental Disabilities

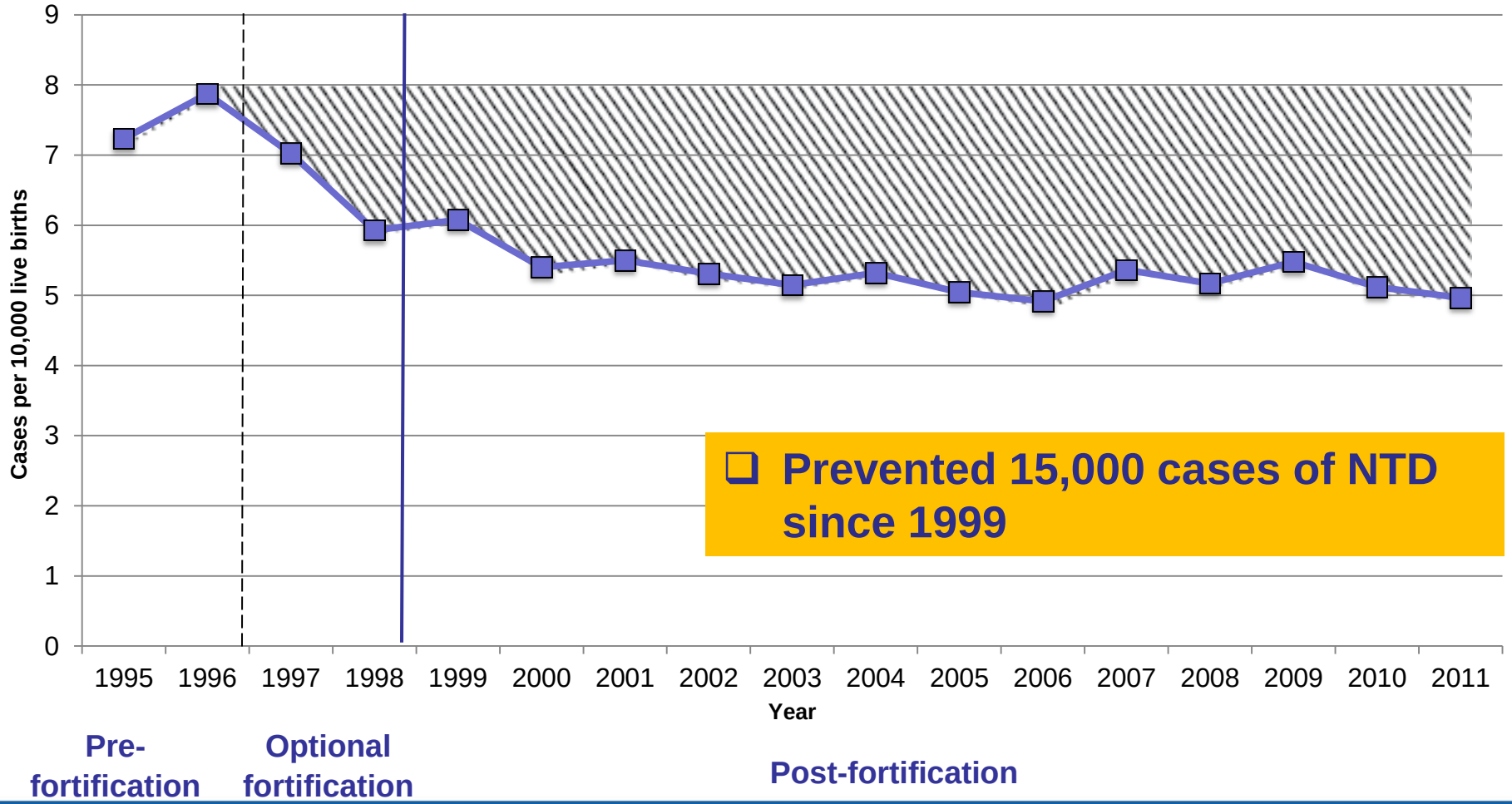
U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

Folic Acid Fortification Prevents Neural Tube Defects

- In 1992, the U.S. Public Health Service recommended all women of childbearing potential consume 400µg folic acid daily
- In 1998, enriched cereal grain products were required to be fortified at 140µg per 100g serving
- Ready-to-eat cereals were allowed to be fortified up to 400µg per serving

CDC. *MMWR* 1992;41(No. RR-14)
µg: Micrograms
g: Grams

Impact of U.S. Folic Acid Fortification on NTD



NTD: Neural tube defects

MMWR **January 16, 2015 / 64(01);1-5**

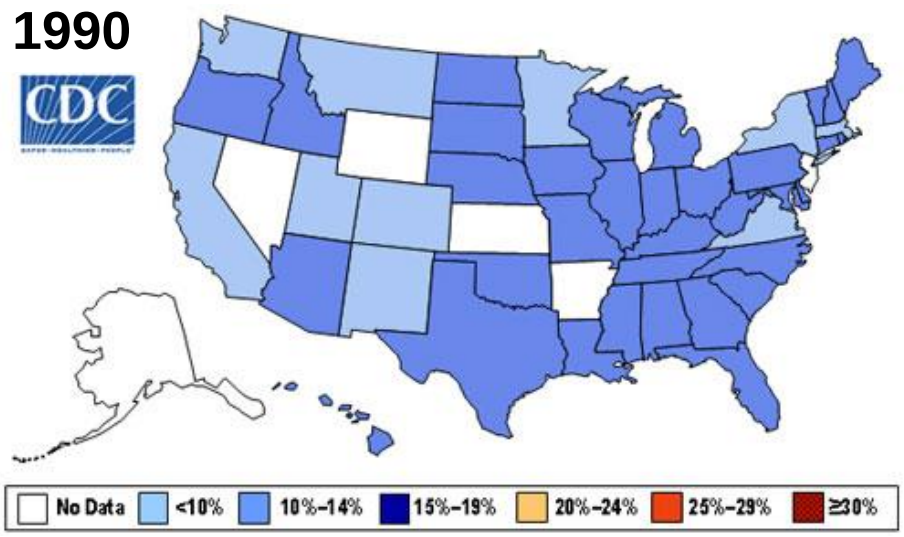
What Else Might Have An Impact on Birth Defects?

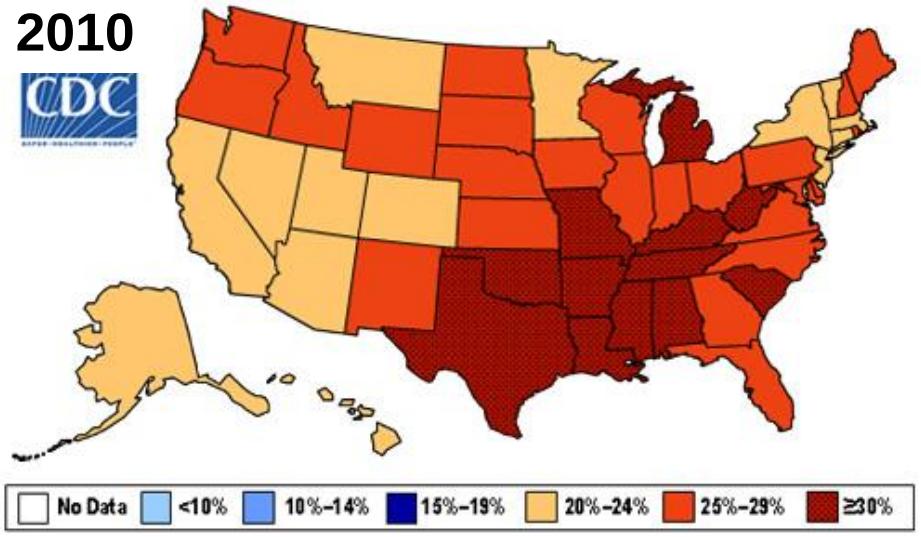
- **Use mathematical modeling of other risk factors to see how we might have a further impact**
  - Obesity
  - Pregestational diabetes
  - Smoking

Basic Modeling Approach

- **Use data inputs from the published literature to estimate**
  - Prevalence of the risk factor
  - Prevalence of the birth defect
  - Magnitude of association between risk factor and birth defects
    - If data not available from published literature, conduct a meta-analysis to obtain a summary measure of association
- **Estimate the population attributable fraction for the risk factor**
- **Estimate the number of preventable birth defects**
  - Modeling incorporates uncertainty (e.g., Monte Carlo simulation)

Overall Obesity Trends in the United States





By 2010, every state had 20% or greater prevalence of obesity

CDC. U.S. Obesity Trends (www.cdc.gov/obesity/data/trends)

Accounting for Uncertainty in the Prevalence of Prepregnancy Obesity

- **For pregnant women, prepregnancy prevalence-18.7%**
  - PRAMS has self-reported height and weight data
- **For U.S. women 20 years or older, obesity prevalence-33%**
  - NHANES has measured height and weight data
- **For U.S. women 20 years or older, obesity prevalence-20%**
  - BRFSS has self-reported height and weight data
- **Model used 18.7% estimate, plus bias factor based on NHANES measured data and BRFSS self-reported data**
  - Bias factor accounts for differences in these estimates

PRAMS: Pregnancy Risk Assessment Monitoring System
NHANES: National Health and Nutrition Examination Survey
BRFSS: Behavioral Risk Factor Surveillance System
Chu et al. *Matern Child Health J* 2009

Input Data to Model the Impact of Prepregnancy Obesity on Birth Defects

Birth Defect	Strength of Association (Odds Ratio)	Estimated Prevalence of Birth Defect in US*	Estimated Annual Number of Children Born with Birth Defect in US
Congenital heart defects	1.30	81.4	33,960
Spina bifida	2.24	3.5	1,460
Cleft lip with or without cleft palate	1.20	10.63	4,437

* per 10,000 births

Honein, et al. *Obesity* 2013.
Stothard, et al. *JAMA* 2009.
Reller, et al. *J Pediatr* 2008.
Parker, et al. *Birth Defects Res A Clin Molec Teratol* 2010.

Estimates of the Impact of Reducing Prepregnancy Obesity on Birth Defects

Birth Defect	Population Attributable Fraction* (95% Uncertainty Interval)	Annual Preventable Number (95% Uncertainty Interval)**	
		If 100% Elimination of Prepregnancy Obesity	If 10% Reduction in Prepregnancy Obesity
Congenital heart defects	**8%** (3%–14%)	**2,850** (1,035–5,065)	**285** (105–510)
Spina bifida	**28%** (21%–34%)	**405** (305–505)	**40** (30–50)
Cleft lip with or without cleft palate	**6%** (1%–11%)	**260** (35–500)	**25** (5–50)

* Population Attributable Fraction: The percent of cases estimated to be caused by prepregnancy obesity
** Rounded to the nearest 5
Honein, et al. *Obesity* 2013

Prevalence of Prepregnancy Diabetes

- Among women of reproductive age, diabetes prevalence estimates vary between 1.9% and 4.0%
- Additional 0.5% to 1% have undiagnosed diabetes
- Model used NHANES race-ethnicity specific prevalence estimates for women aged 20 - 44

Simeone, et al. *Am J Prev Med* 2014.
CDC. National Center for Health Statistics. Health Data Interactive. www.cdc.gov/nchs/hdi.htm.

Input Data to Model the Impact of Diabetes Control on Congenital Heart Defects

Congenital Heart Defect	Odds Ratio (Strength of Association)	Estimated Prevalence of Birth Defect in US*	Estimated Annual Number of Children Born with Birth Defect
All congenital heart defects	3.8	81.4	32,182
Coarctation of the aorta	3.7	4.5	1,767
Hypoplastic left heart syndrome	3.7	2.3	909
Tetralogy of Fallot	6.5	4.0	1,570

* per 10,000 live births

Simeone, et al. *Am J Prev Med* 2014.
Reller, et al. *J Ped* 2008.

Estimates of the Impact of Diabetes Control on Congenital Heart Defects

Congenital Heart Defect	Population Attributable Fraction (95% Uncertainty Interval)	Annual Preventable Number (95% Uncertainty Interval)*	
		If Elimination of Risk Associated with Diabetes (Complete Glycemic Control)	If 50% Reduction in Risk Associated with Diabetes
All congenital heart defects	**8.3%** (5.6%–11.8%)	**2,670** (1,795–3,795)	**1,335** (900–1,900)
Coarctation of the aorta	**7.9%** (2.1%–17.8%)	**140** (35–315)	**70** (20–160)
Hypoplastic left heart syndrome	**8.0%** (1.6% – 20.4%)	**75** (15–185)	**40** (10–95)
Tetralogy of Fallot	**14.8%** (6.6% – 26.3%)	**230** (105–415)	**115** (55–210)

* Rounded to the nearest 5

Simeone, et al. *Am J Prev Med 2014.*

Potential Impact of Preconception Care on Costs Associated with Birth Defects

Input Parameter	Estimate
Prevalence of pregestational diabetes	Diagnosed: 2.9% (2.7%-3.2%) Undiagnosed: 0.5%
Percent of births affected by birth defects among women with untreated pregestational diabetes	7.3%
Preconception care effectiveness, risk reduction	0.25 (0.15 - 0.42)
Lifetime costs of birth defects	$411,723

Peterson, et al. *Am J Obstet Gynecol* 2014.
Hayes, et al. *Prevent Chronic Dis* 2011.
Razzaghi, et al. *Primary Care Diab* 2013.
Wahabi, et al. *BMC Pregnancy Childbirth* 2010.
Waitzman, et al. *Inquiry* 1994.

Potential Impact of Preconception Care on Costs Associated with Birth Defects

Outcome	Estimate
Birth defects averted	**4,731** (4,158–5,215)
Total lifetime costs for birth defects averted	**$1.9 billion** ($1.7–$2.1 billion)

Peterson, et al. *Am J Obstet Gynecol* 2014.

Smoking and Orofacial Clefts

- **50th Anniversary Surgeon General's Report**
  - Released in January 2014
  - Marked first confirmation of causal link between smoking in early pregnancy and orofacial clefts
- **Smoking is one of the few known risk factors for orofacial clefts with potential for prevention**
- **Prevalence of smoking just before pregnancy: 23.2%**

PRAMS: Pregnancy Risk Assessment Monitoring System
The health consequences of smoking: 50 years of progress. A Report of the Surgeon General, 2014.
Tong et al. *MMWR Surveil Summ, 2013*

Input Data to Model the Impact of Smoking Cessation on Orofacial Clefts

Birth Defect	Odds Ratio (Strength of Association)	Estimated Prevalence of Birth Defect in US*	Estimated Annual Number of Children Born with Birth Defect
Orofacial clefts	1.28	17.0	7088

* per 10,000 live births

Honein, et al. *Birth Defects Res Part A* 2014.
Hackshaw, et al. *Human Reprod Update* 2011.

Estimates of the Impact of Early Pregnancy Smoking Cessation on Orofacial Clefts

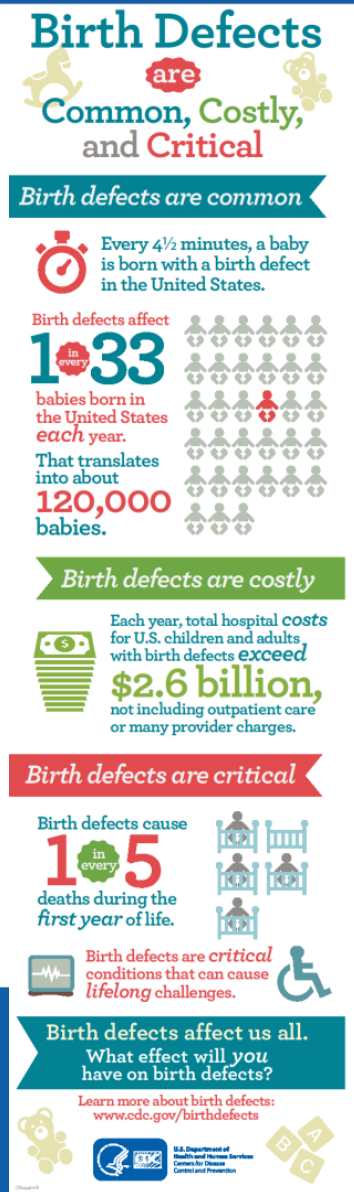
Birth Defect	Population Attributable Fraction (95% Uncertainty Interval)	Annual Preventable Number (95% Uncertainty Interval)* If Elimination of Risk Associated with Early Pregnancy Smoking
Orofacial clefts	**6.1%** (4.4%–7.5%)	**430** (310–550)

* Rounded to the nearest 10

Honein et al. *Birth Defects Res Part A,* 2014.

Advancing Prevention of Birth Defects

- **Birth defects are common, costly, and critical**
- **Majority of birth defects still do not have an identifiable cause**
  - The causes are likely to be multi-factorial with an interaction between genetic factors and modifiable (environmental) risk factors
- **Based on the modifiable risk factors that have been recognized, we <u>know</u> that we can improve prevention**



CDC PUBLIC HEALTH GRAND ROUNDS

Understanding the Causes of Major Birth Defects: Steps to Prevention

January 20, 2015

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention