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

The Impact of Birth Defects and Current Understanding of their Causes

Marcia L. Feldkamp, PhD, PA
Associate Professor
Division of Medical Genetics
Department of Pediatrics
University of Utah

THE UNIVERSITY OF UTAH

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

Acknowledgment and Disclaimer

❑ **Data were provided by the Utah Birth Defect Network (UBDN), a project of the Utah Department of Health (UDOH). This project is supported by the Health Resources and Services Administration (HRSA) of the U.S. Department of Health and Human Services for the amount of $3.046,261.**

❑ **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
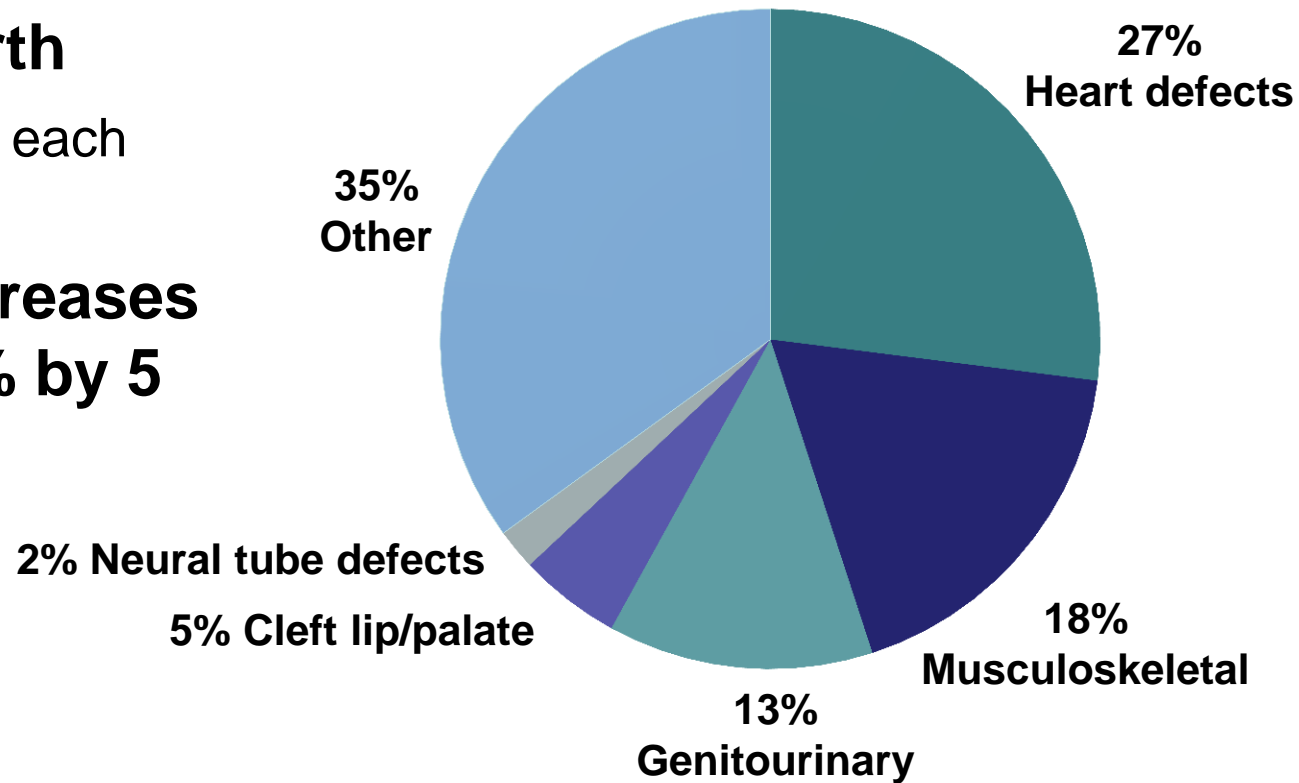

Single palmar crease

Major Birth Defects Are Common

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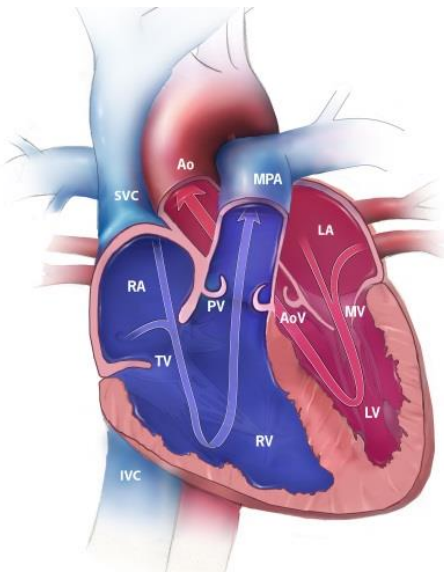 - ➤ 120,000 babies each year in the US
- ❑ **Prevalence increases to 1 in 20 or 5% by 5 years of age**
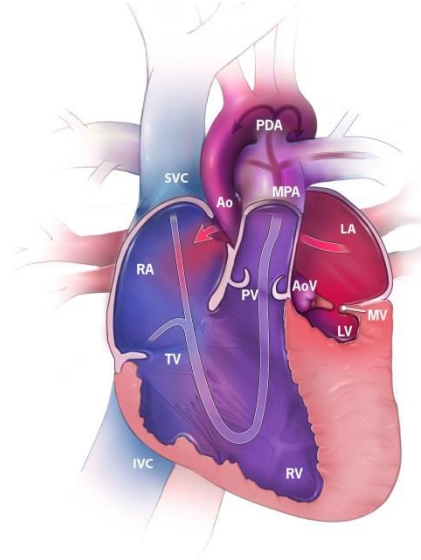
Type of Birth Defect

- 27% Heart defects
- 35% Other
- 18% Musculoskeletal
- 13% Genitourinary
- 5% Cleft lip/palate
- 2% Neural tube defects

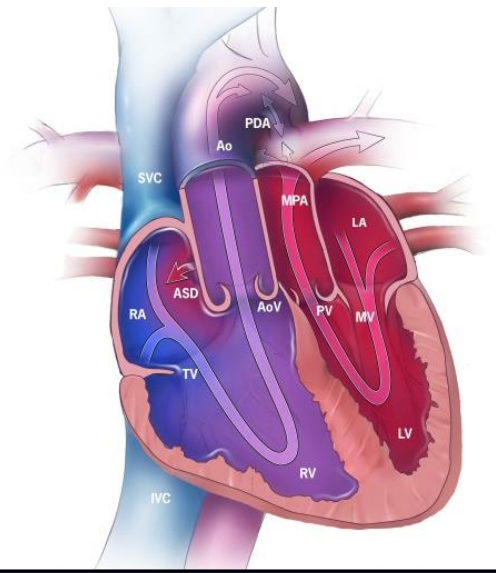Kucik et al. Public Health Reports. 2012.

Heart Defects

Normal Heart
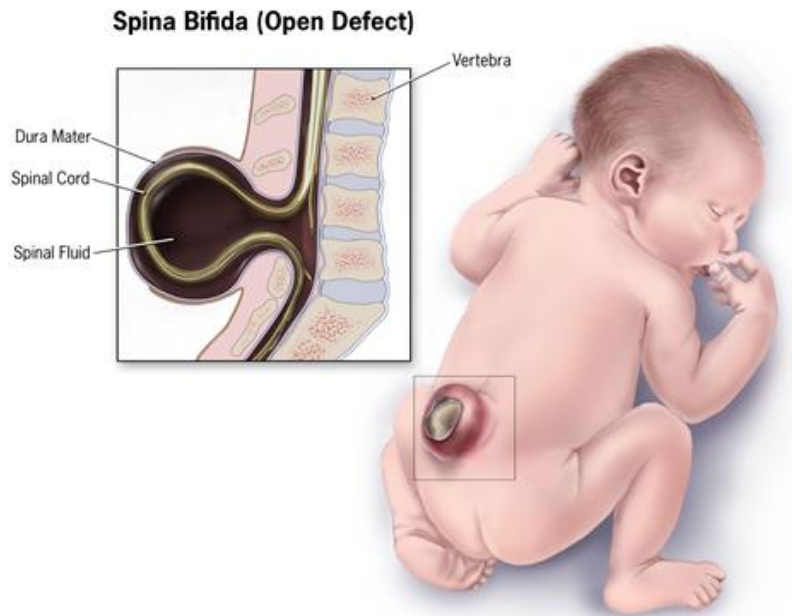
Hypoplastic Left Heart Syndrome

Transposition of the Great Arteries

These types of defects will require surgical repair
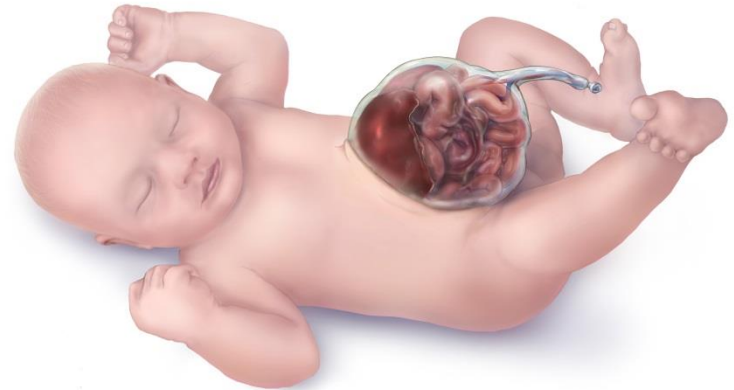
Neural Tube Defects

Spina bifida

Anencephaly

Spina Bifida (Open Defect)

Vertebra

Dura Mater

Spinal Cord

Spinal Fluid

Abdominal Wall Defects

Gastroschisis

Omphalocele

Birth Defects Are Costly

Average daily hospital charges per newborn

Condition	Charge
Uncomplicated birth	$878
Gastroschisis	$3,795
Esophogeal atresia	$4,337
Omphalocele	$4,360
Bladder exstrophy	$4,598
Pulmonary valve atresia	$6,453
Diaphragmatic hernia	$6,508
Coarctation of the aorta	$6,562
Truncus arteriosus	$6,670
Hypoplastic left heart	$6,954
Transposition of the great arteries	$7,523
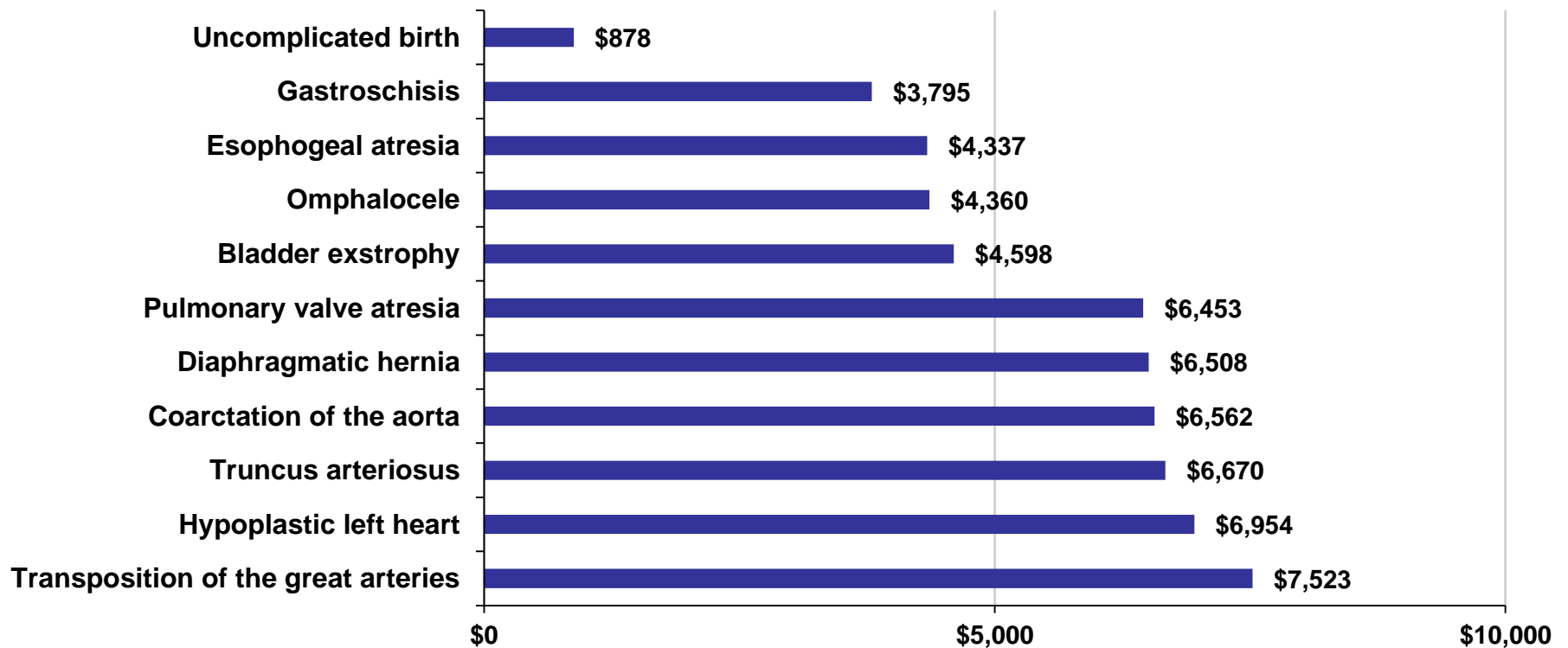
CDC. *MMWR Morb Mortal Wkly Rep.* Jan 19, 2007

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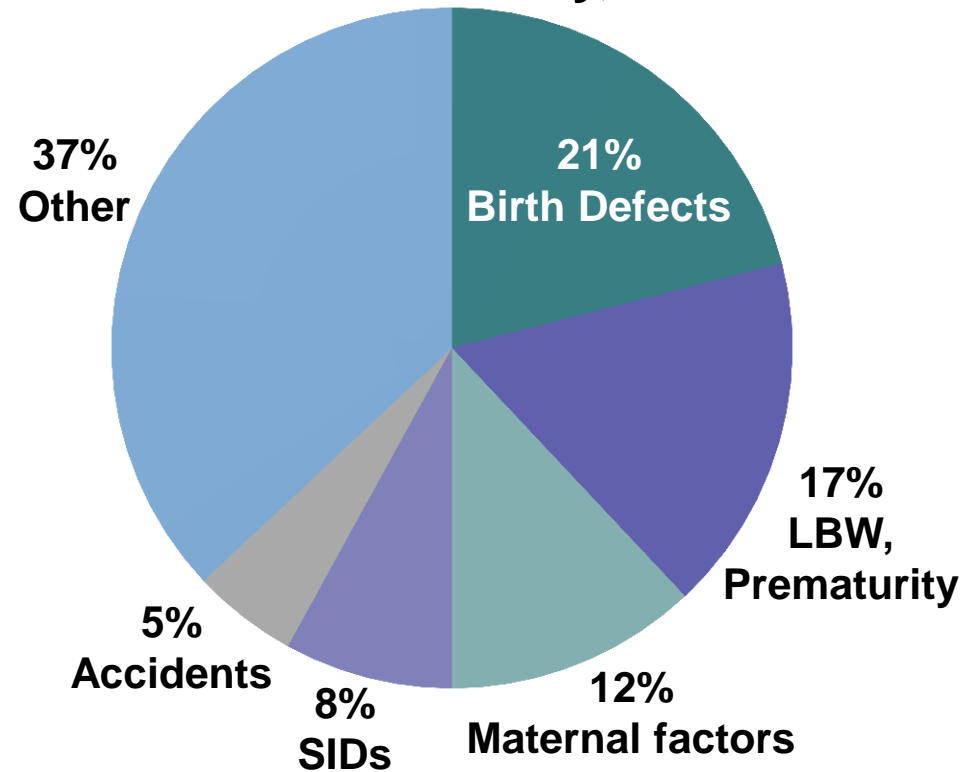
Russo CA, Elixhauser A. HCUP Statistical Briefs : Agency for Health Care Policy and Research (US); 2006-.2007 Jan.

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

Leading Causes of Infant Mortality, 2011

- 37% Other
- 21% Birth Defects
- 17% LBW, Prematurity
- 12% Maternal factors
- 8% SIDs
- 5% Accidents

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

Most Major Birth Defects Occur Early in Pregnancy
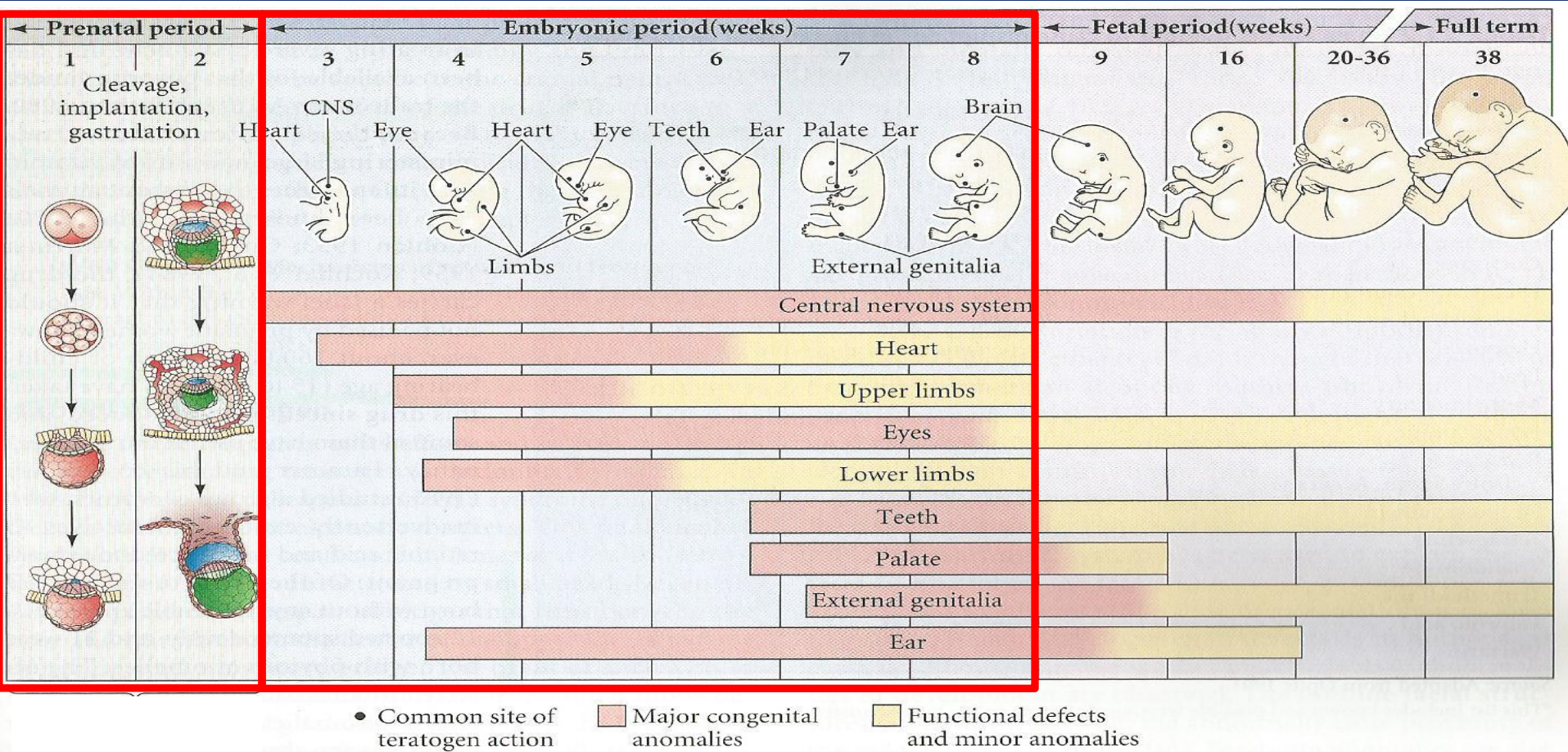
Pregnancy Planning is Primary Prevention of Birth Defects

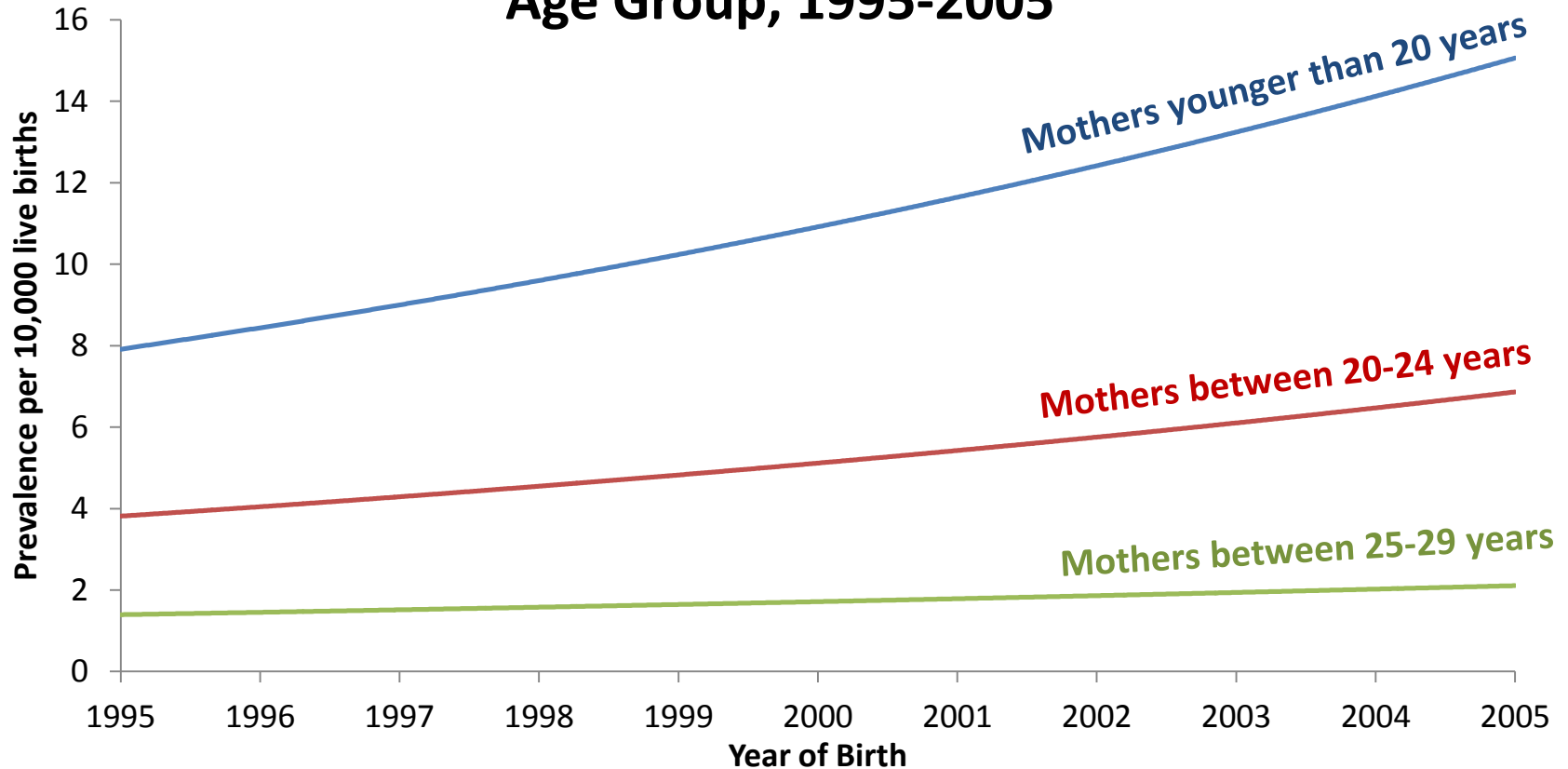- ❑ **The critical time period for all women to reduce their risk is before they become pregnant**

- ❑ **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

Trends in Gastroschisis Prevalence by Maternal Age Group, 1995-2005

Kirby et al. *Obstet Gynecol.* 2013

The Majority of Birth Defects
Do Not Have an Identifiable Cause

Legend: Genetic, Twinning, Teratogen, Unknown

Utah 2005-2009

Genetic: 21.9
Unknown: 76.8
Twinning: 1
Teratogen: 0.83

Pregestational diabetes — 74%
Cytomegalovirus — 19%
Valproate/carbamazepine — 6%

0% 20% 40% 60% 80% 100%
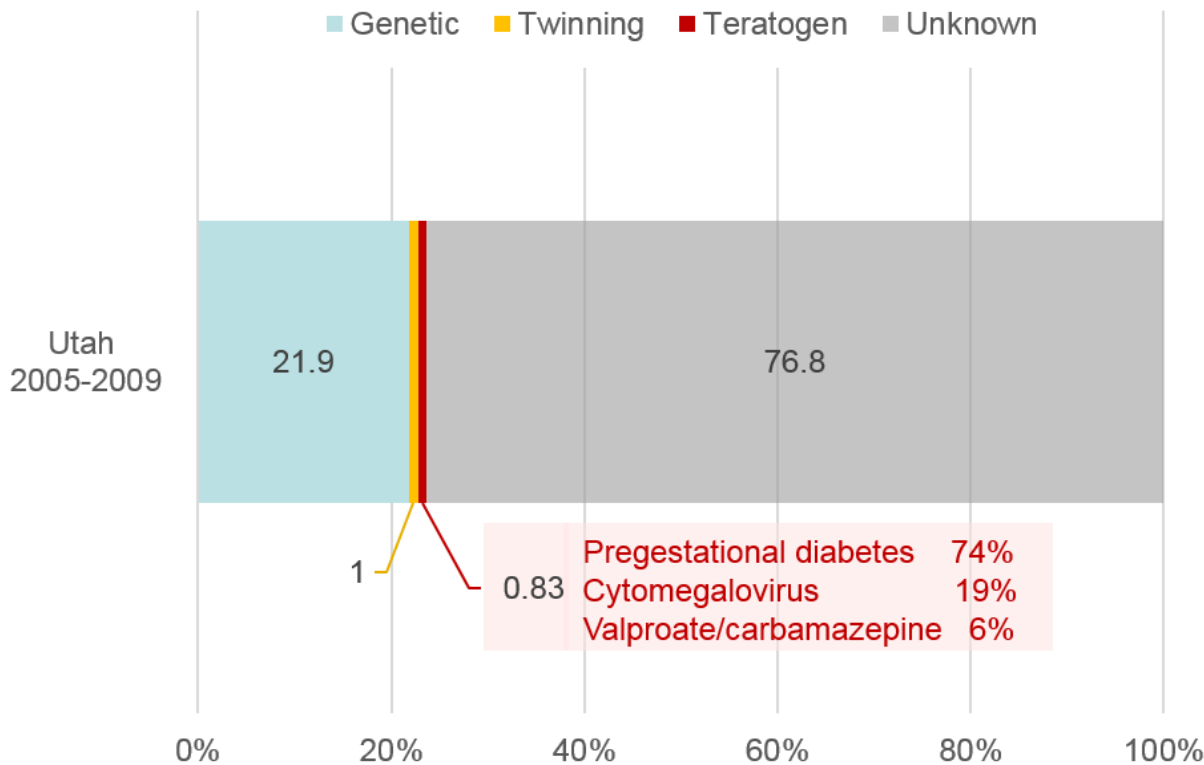
Teratogen: an agent or factor that causes a malformation in an embryo

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
Centers for Disease Control and Prevention

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
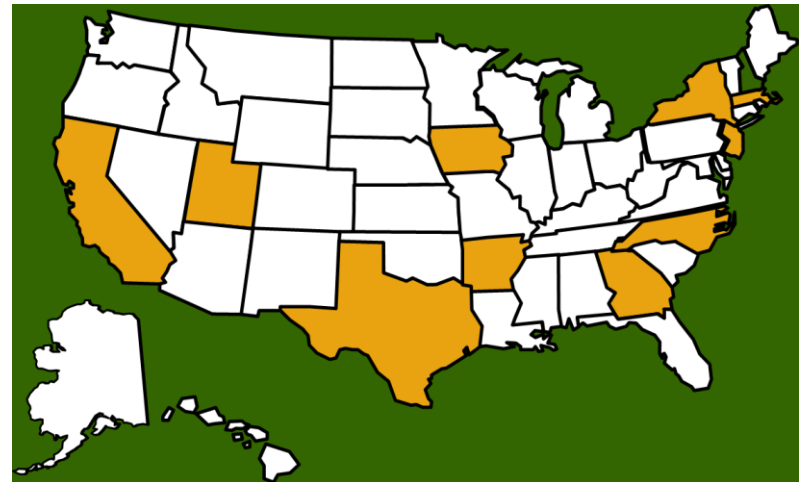
NBDPS Data Collection Methods

❑ **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
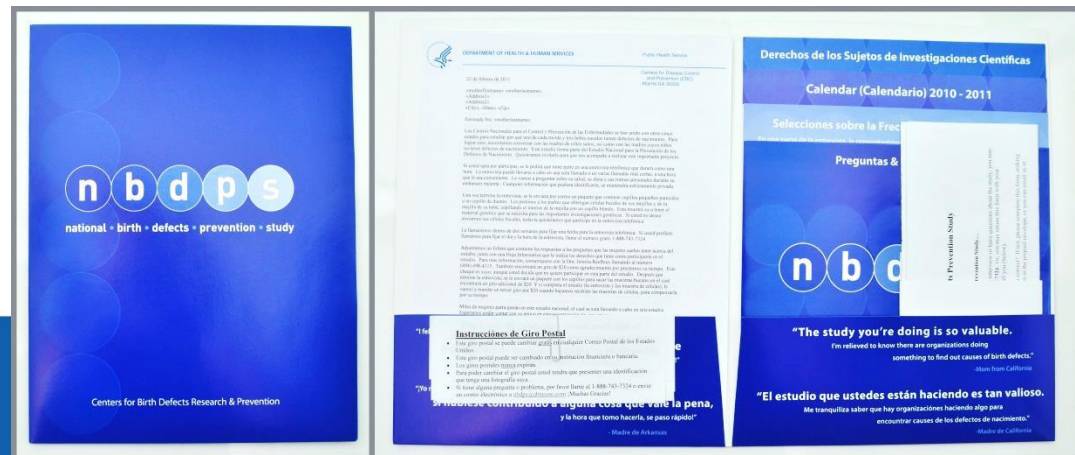
Selected NBDPS Results

❑ **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)

NBDPS Results: Exposure to Opioid Medications

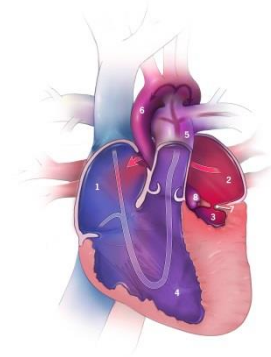❑ **Hypoplastic left heart syndrome**

  ➢ 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

BETTER RESEARCH

RELIABLE GUIDANCE

INFORMED DECISIONS
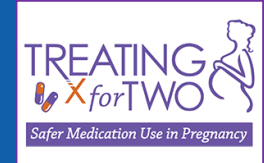
- ❑ **Expand research to fill knowledge gaps**
  - ➢ Accelerate epidemiologic research into medication use and pregnancy outcomes

- ❑ **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**
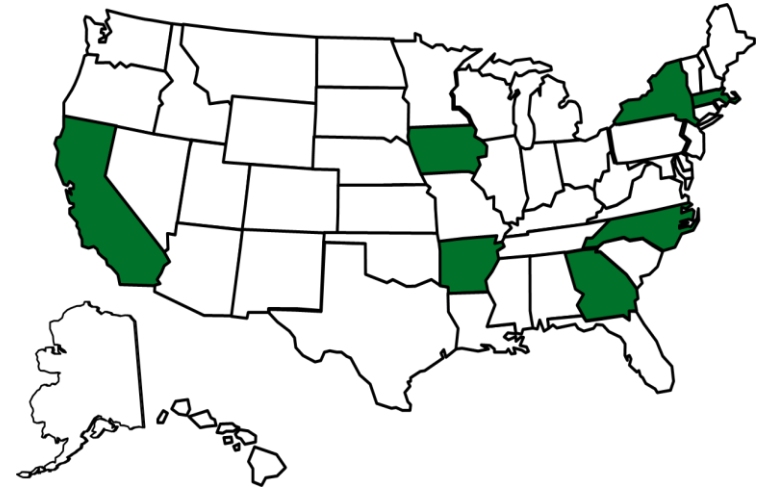
Exploring Modifiable Risk Factors
Maternal Disease and Treatment with Medications

❑ **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

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
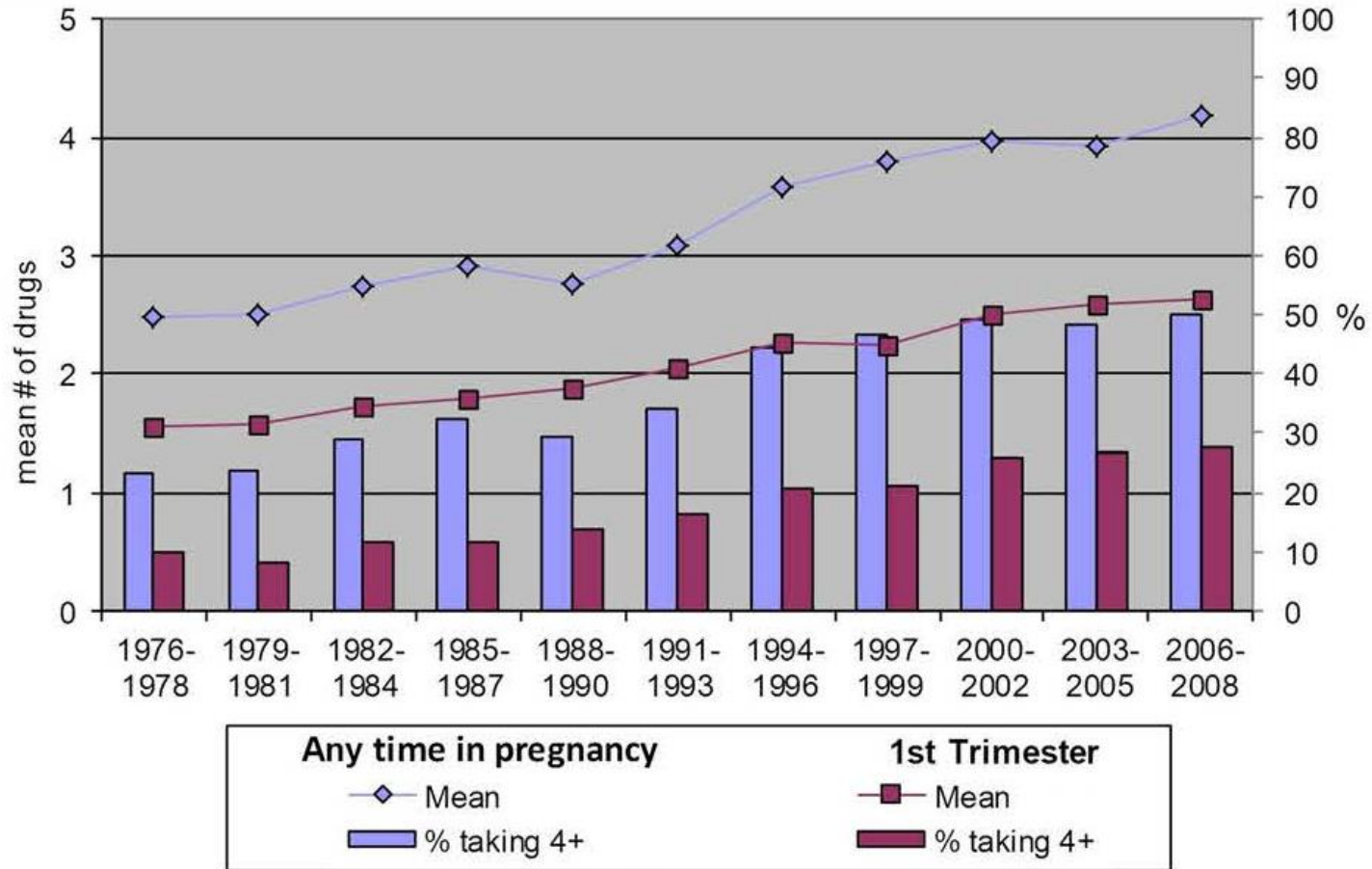
Specific Examples

❑ **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
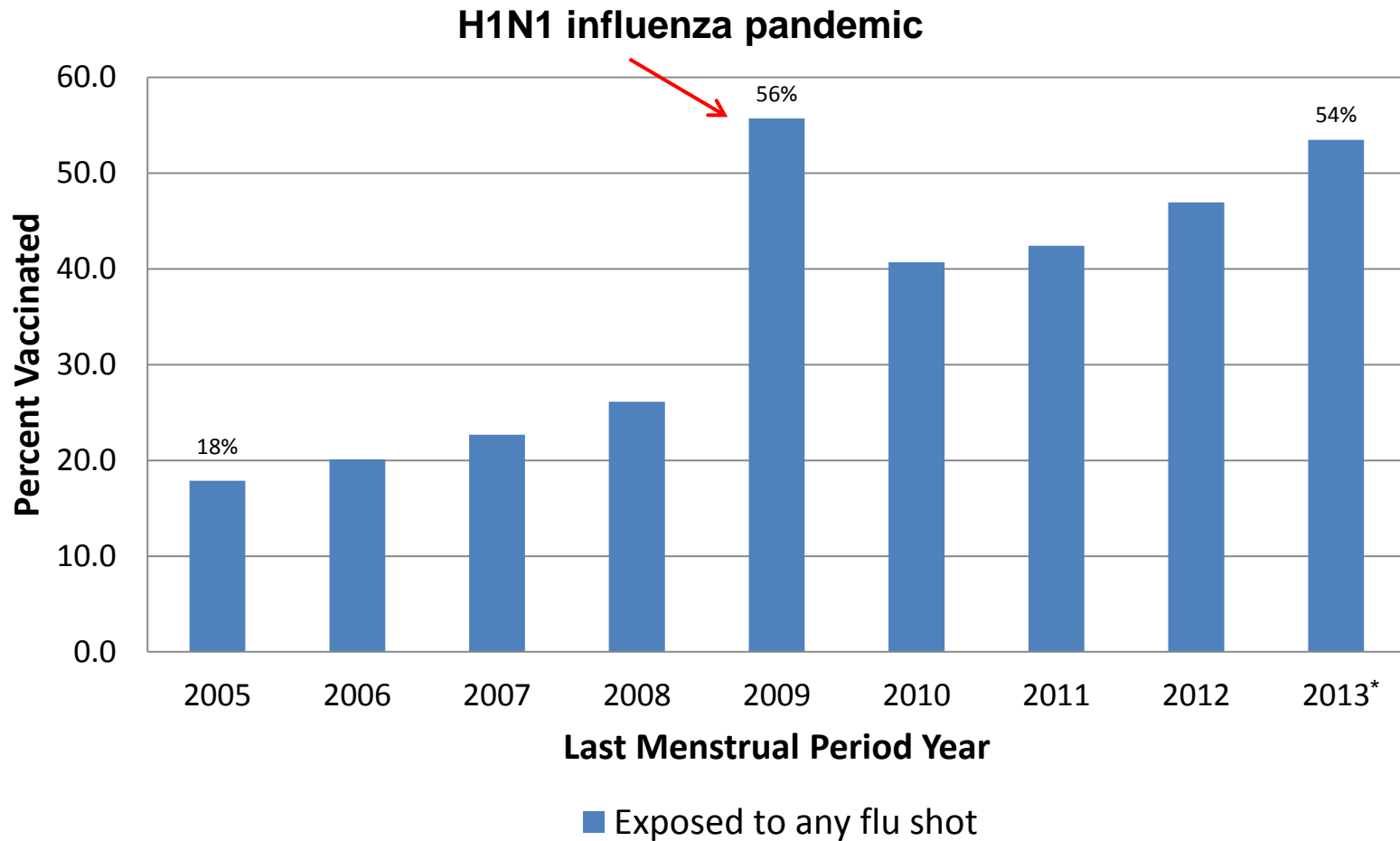
H1N1 influenza pandemic

Legend: ■ Exposed to any flu shot

X-axis: Last Menstrual Period Year (2005–2013*)
Y-axis: Percent Vaccinated (0.0–60.0)

Labeled values: 18% (2005), 56% (2009), 54% (2013*)

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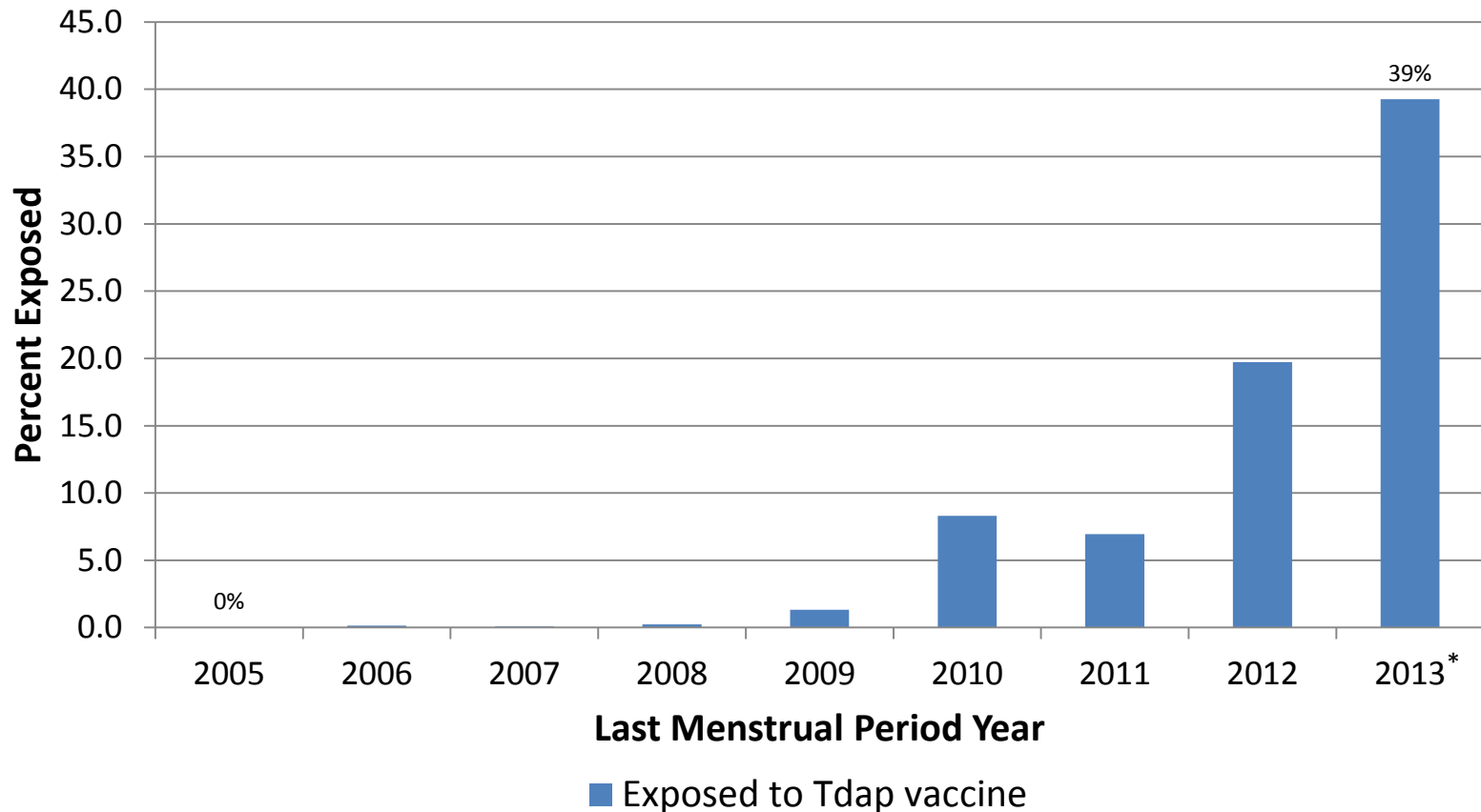
Unpublished data; Birth Defects Study, Slone Epidemiology Center, Boston University
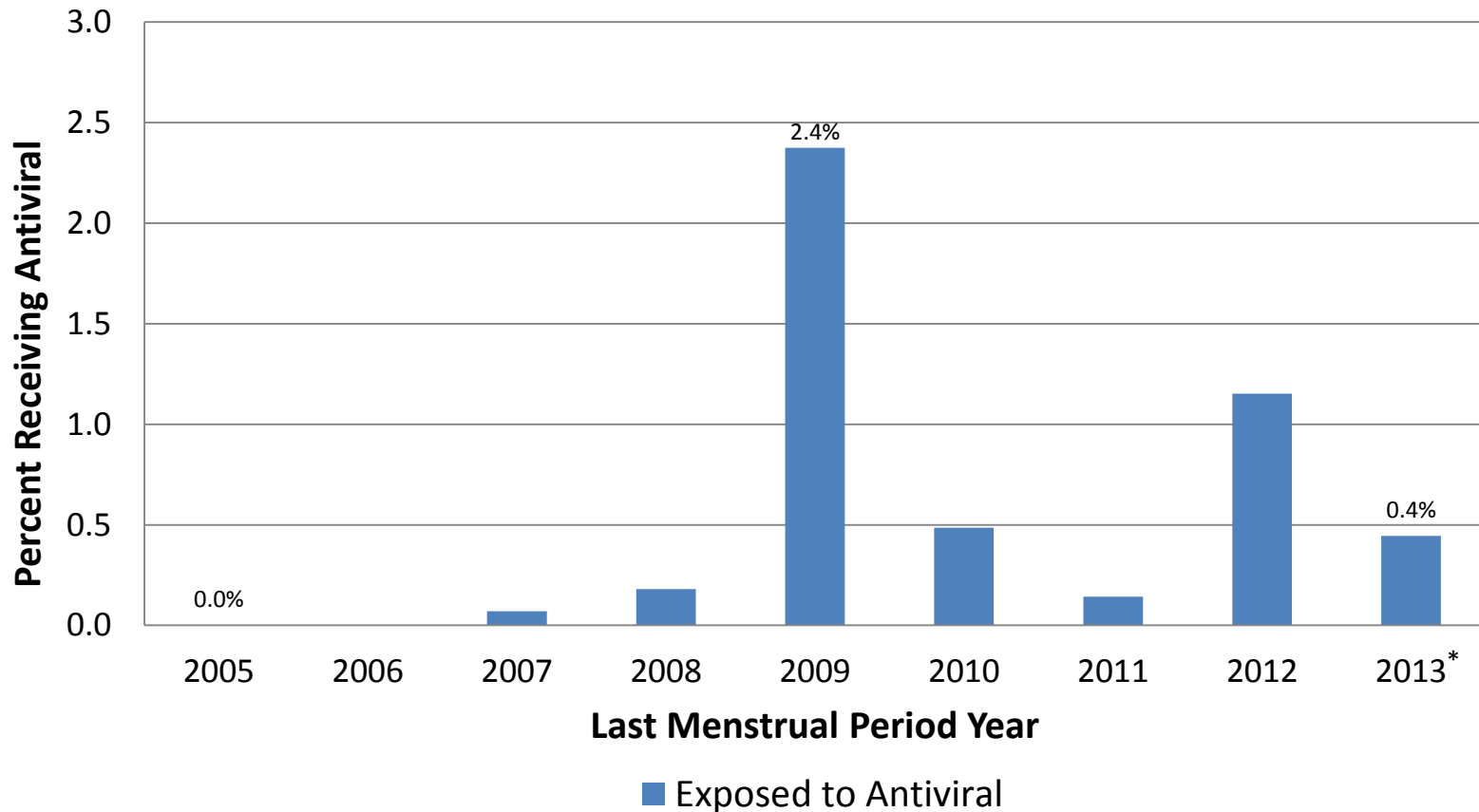Tdap: Tetanus Toxoid, Diphtheria Toxoid, and Acellular Pertussis Vaccine
* Incomplete year

38

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**
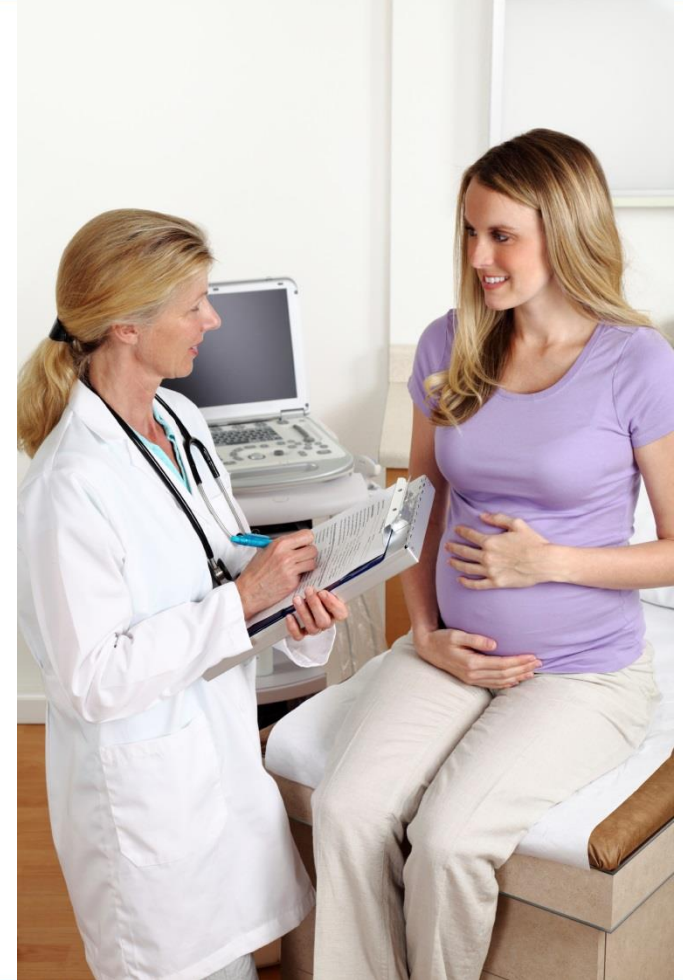
Vaccines and Medications in Pregnancy Surveillance System (VAMPSS)

❑ **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**

VAMPSS: Vaccines and Medications in Pregnancy Surveillance System

Structure of VAMPSS

American Academy of Allergy Asthma and Immunology
Michael Schatz, MD, MS

Prospective Cohort

Organization of Teratology Information Specialists Research Center at the University of California San Diego
Tina Chambers, PhD, MPH
Kenneth Lyons Jones, MD

Case-Control Study

Slone Epidemiology Center at Boston University
Allen A. Mitchell, MD
Carol Louik, ScD

Independent Advisory Committee

Includes:
CDC
NICHD
NIAID
ACOG
AAP
Biostatistician
Consumer Representative

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 <u>wide range of medications and vaccines</u> with respect to the <u>wide range of specific birth defects</u>

➢ 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

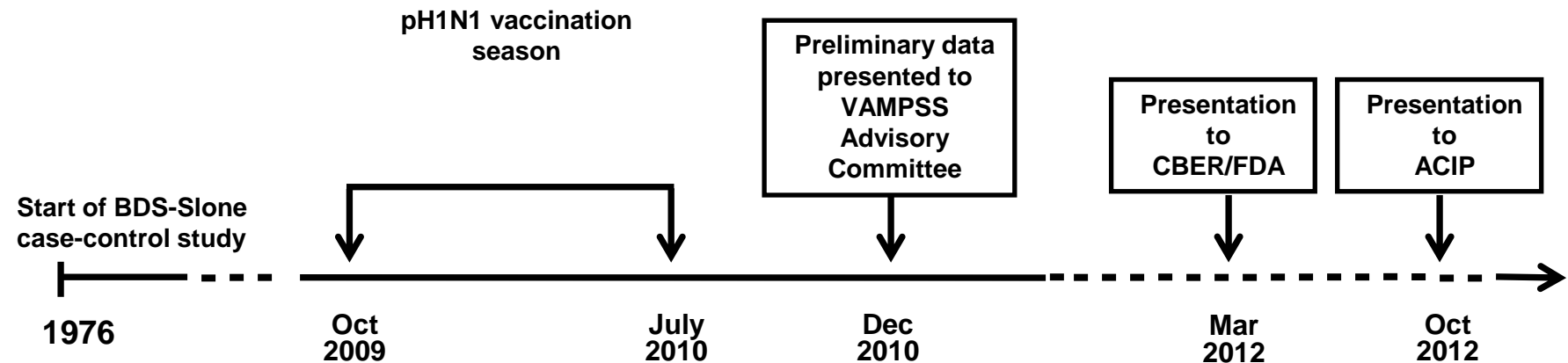❑ **Interview data include**

  ➢ 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

Suzanne Gilboa, PhD, MHS
*Partnerships and Applied 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
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 <u>required</u> to be fortified at 140μg per 100g serving**

- ❑ **Ready-to-eat cereals were <u>allowed</u> to be fortified up to 400μg per serving**

Impact of U.S. Folic Acid Fortification on NTD

Prevented 15,000 cases of NTD since 1999

Pre-fortification

Optional fortification

Post-fortification
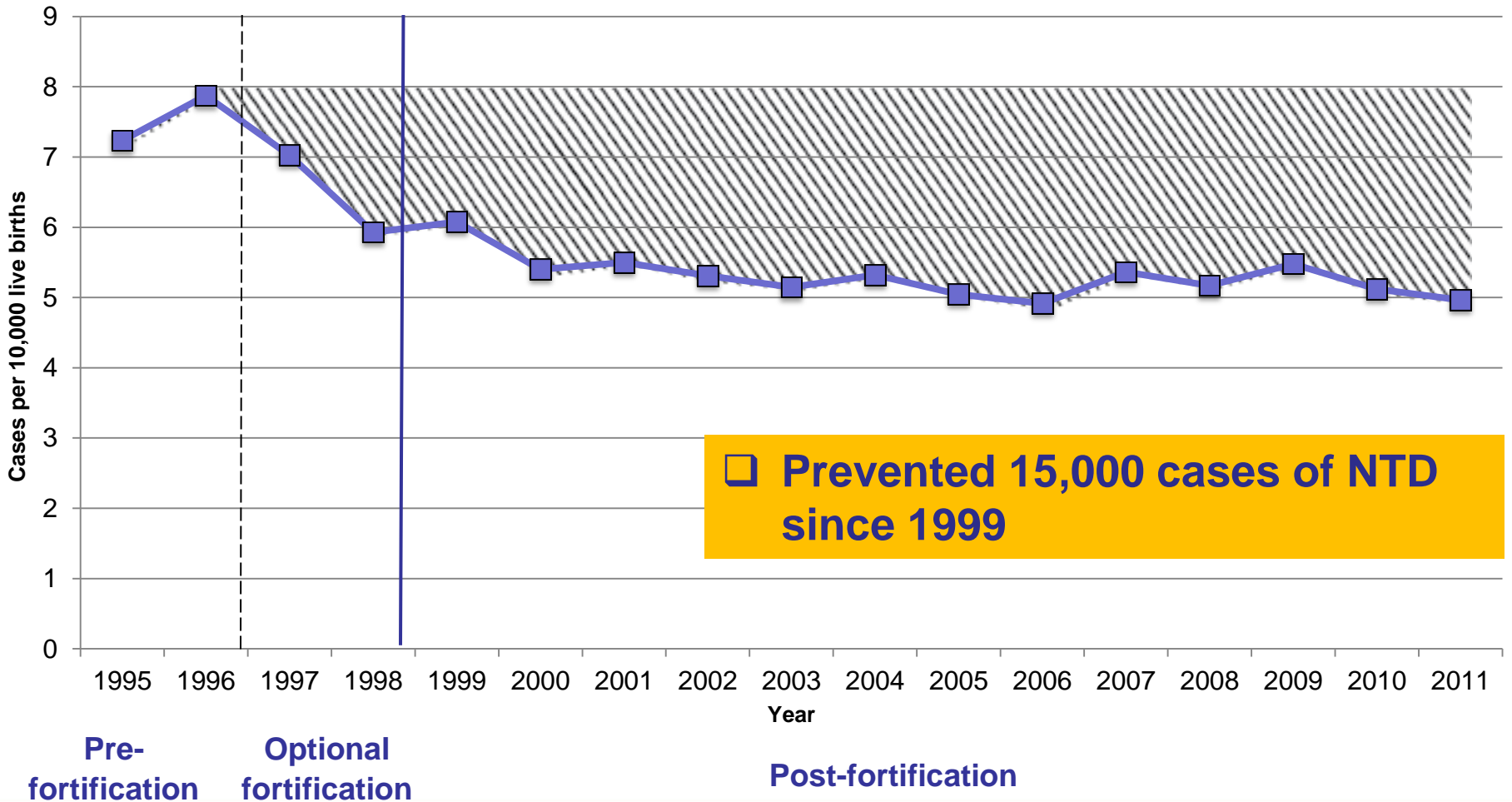
NTD: Neural tube defects
MMWR **January 16, 2015 / 64(01);1-5**

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**
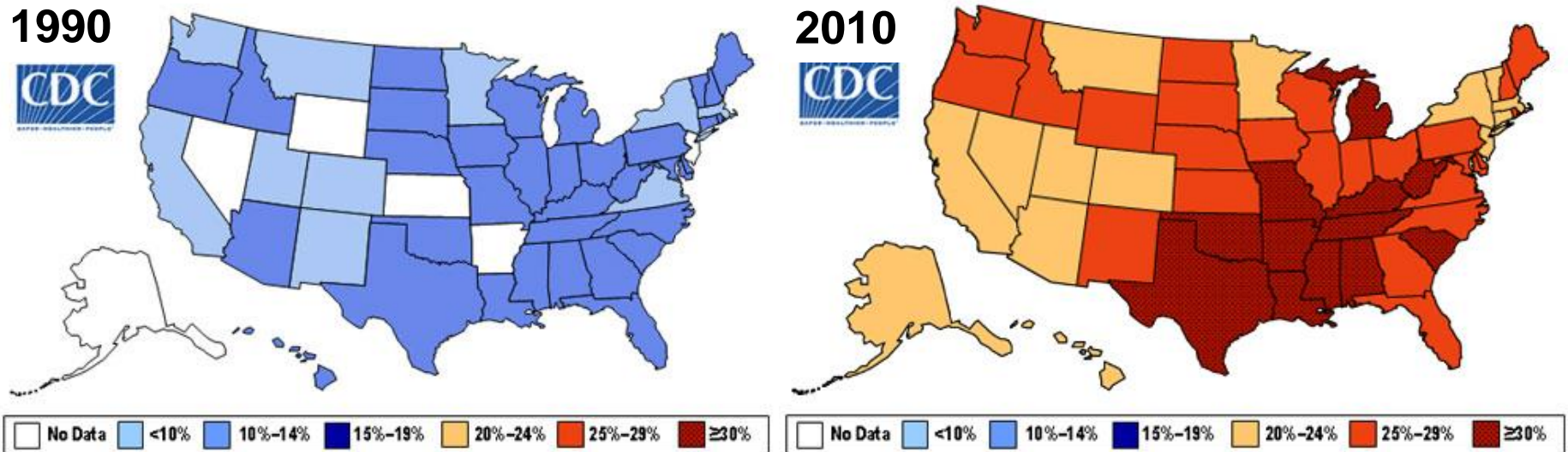
➢ Obesity
➢ Pregestational diabetes
➢ Smoking

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

1990

2010

Legend	
No Data	
<10%	
10%-14%	
15%-19%	
20%-24%	
25%-29%	
≥30%	

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

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

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

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

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**

Birth Defects are **Common, Costly, and Critical**

Birth defects are common

Every 4½ minutes, a baby is born with a birth defect in the United States.

Birth defects affect 1 in every 33 babies born in the United States *each* year.

That translates into about 120,000 babies.

Birth defects are costly

Each year, total hospital *costs* for U.S. children and adults with birth defects *exceed* $2.6 billion, not including outpatient care or many provider charges.

Birth defects are critical

Birth defects cause 1 in every 5 deaths during the *first year* of life.

Birth defects are *critical* conditions that can cause *lifelong* challenges.

Birth defects affect us all. What effect will *you* have on birth defects?

Learn more about birth defects: www.cdc.gov/birthdefects

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