



national • birth • defects • prevention • study

# Maternal Use of Acid Reducers Before and During Pregnancy: Trends and Risks for Birth Defects Among Offspring

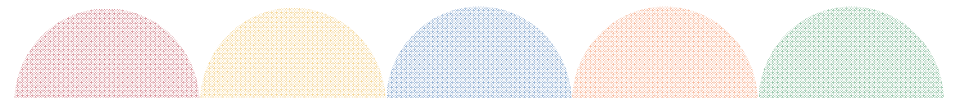
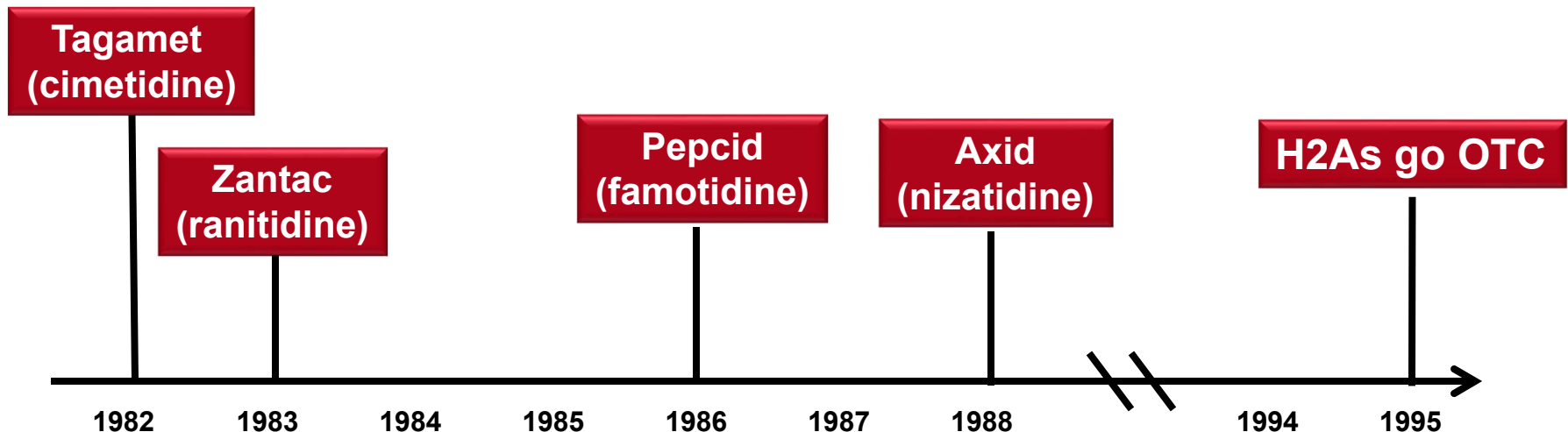
Kelly Getz, MPH  
MA Department of Public Health  
Center for Birth Defects Research & Prevention



# Background

## ● What are acid reducers?

- Medications that suppress gastric acid secretion
- Indications: GERD, erosive esophagitis, ulcers and H. pylori infection (w/ antibiotics)
- (1) Histamine-2 Receptor Antagonists (H2As)
  - Action – block earliest stimuli for acid secretion, histamine
    - Less effective than proton pump inhibitors -- H2As faster acting, but shorter duration

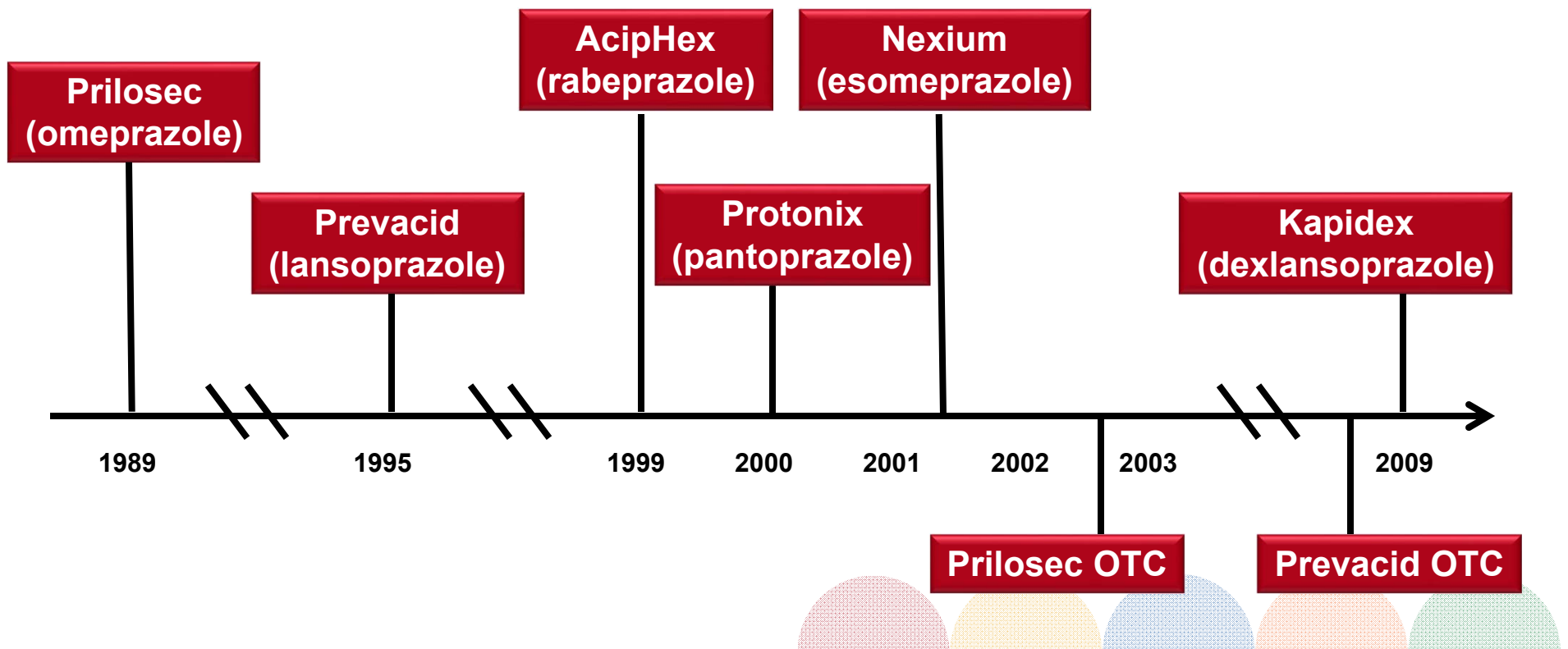


# Background

## ● What are Acid Reducers? (cont'd)

### ● (2) Proton Pump Inhibitors

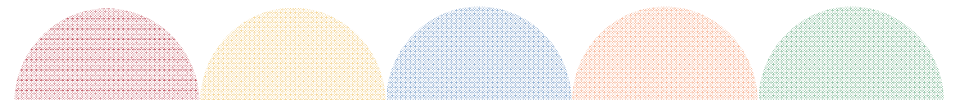
- Action –block the final step in acid secretion pathway in the stomach; shut down the proton pumps leading greater suppression of acid.
- Delayed onset, but longer acting



# Background



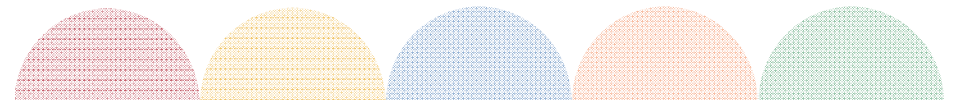
- Many women may be exposed in early pregnancy
  - PPIs and H2As are available OTC as well as via prescription
  - Symptoms of gastroesophageal reflux disorders (GERD) are common during pregnancy and may worsen severity of NVP
- Data on the safety of acid reducers is limited
  - Most studies have shown no significant increase in overall risk of birth defects
  - A recent cohort found a modest increase in overall risk following preconceptional exposure to PPIs (Pasternak 2011)
    - Risk of heart defects and urinary tract defects, but were dismissed as chance findings
    - Few studies have evaluated defect-specific effects



# Objectives



- To describe trends in acid reducer use among NBDPS participants
- To evaluate whether maternal use of PPIs during the periconceptual period is associated with an increased risk of specific birth defects
- To evaluate whether maternal use of H2As during the periconceptual period is associated with an increased risk of specific birth defects

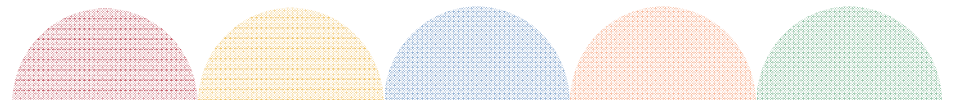


## ● Exposure

- Primary Comparisons
  - Any PPI use B1-P3 (versus no use B3-P9)
  - Any H2A use B1-P3 (versus no use B3-P9)
- Timing
- Specific medications

## ● Outcomes – NBDPS Defects

- $\geq 200$  cases
- $\geq 4$  cases exposed during the periconceptual period, B1-P3



## ● Maternal demographic factors

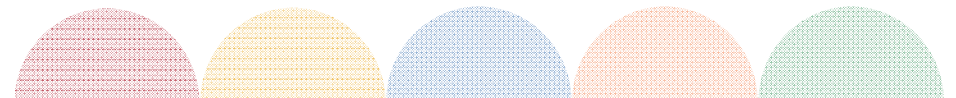
- Age
- Race/ethnicity
- Education
- Center

## ● Behavior and lifestyle factors

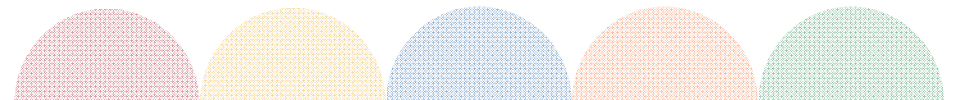
- Maternal smoking
- Maternal alcohol use
- MV/FA supplementation

## ● Reproductive/medical factors

- Gravidity
- Pre-pregnancy BMI
- History of diabetes
- History of hypertension
- Periconceptional Infection

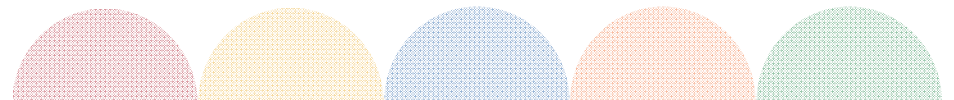


- **Logistic regression used to estimate crude and adjusted odds ratios with 95% CIs**
  - Models adjusted for covariates judged to be both:
    - (1) associated with occurrence of birth defects in at least one organ system
    - (2) associated with exposure among controls

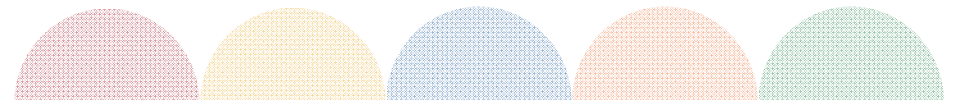




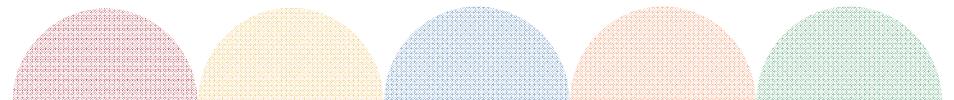
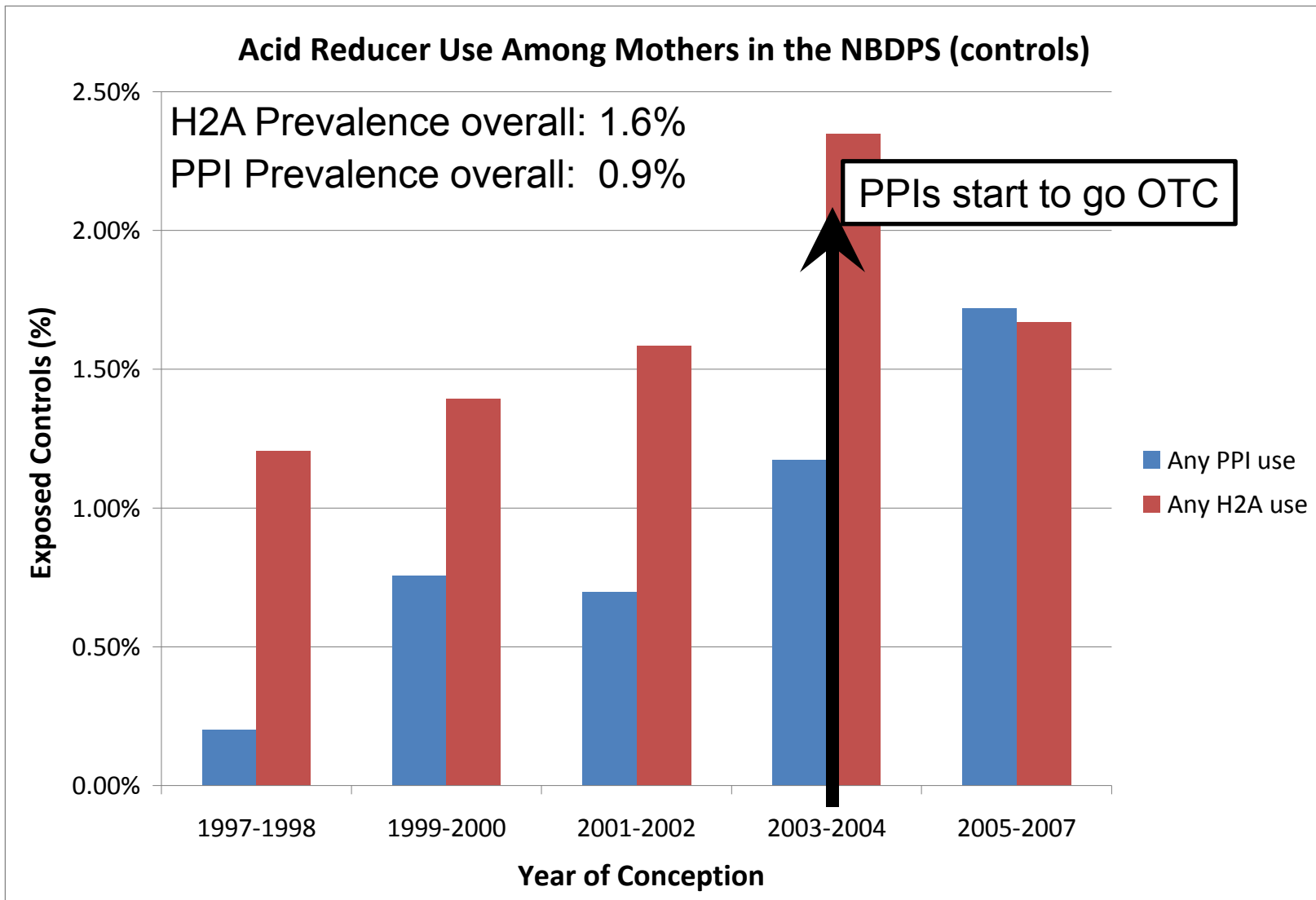
- **Factors associated with periconceptional PPI use**
  - White race, age  $\geq 25$ , BMI  $\geq 30$ , higher education, smoking, study center
- **Factors associated with periconceptional H2A use**
  - White race, age  $\geq 25$ , BMI  $\geq 25$ , higher education, FA/MV use, hypertension, study center
- **Cases and Controls differed on:**
  - Race, age, BMI, education, study center, alcohol use, FA/MV, hypertension, diabetes



## Trends in Maternal Acid Reducer Use



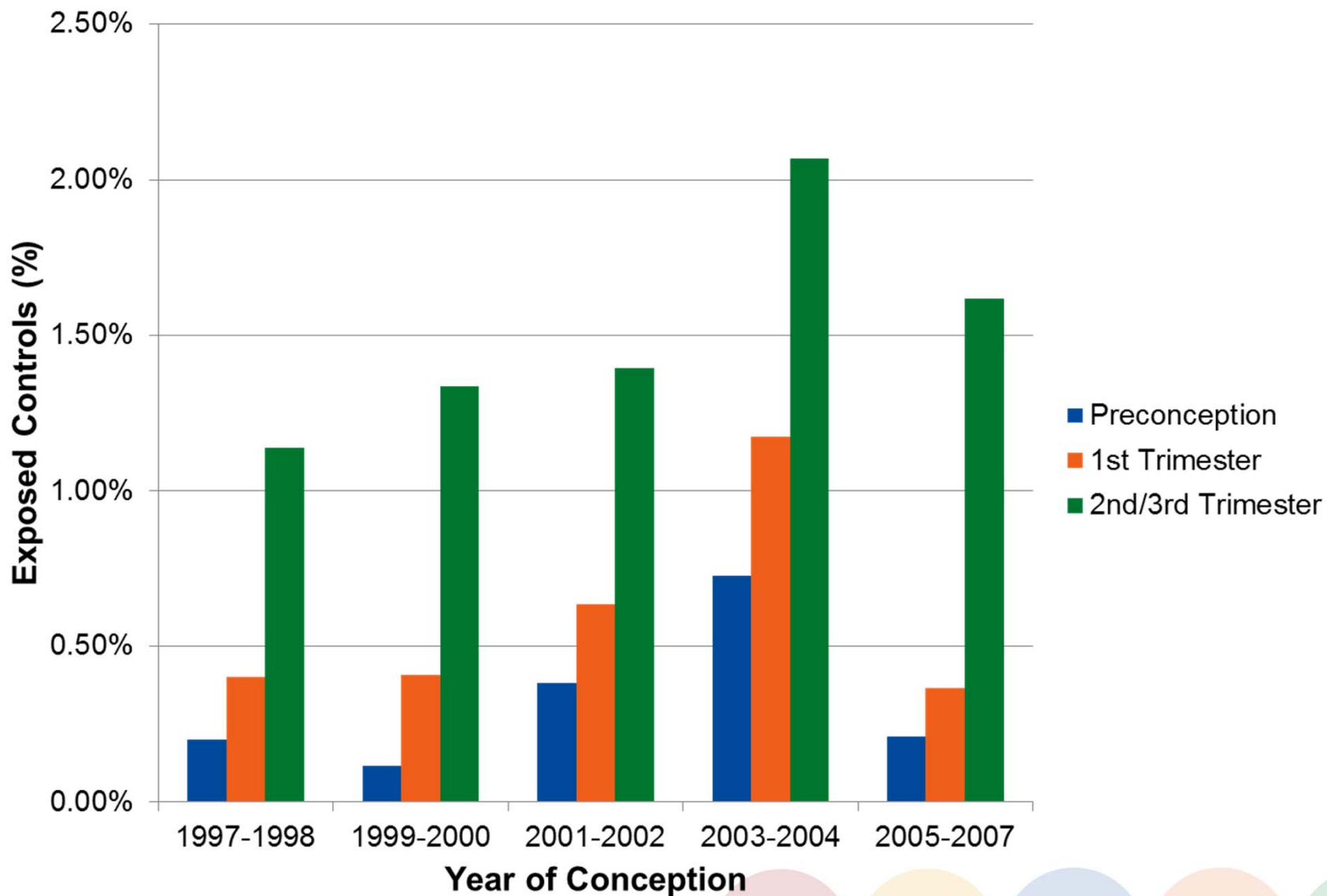
# Results: Trends in Acid Reducer Use



# Trends in Acid Reducer Use

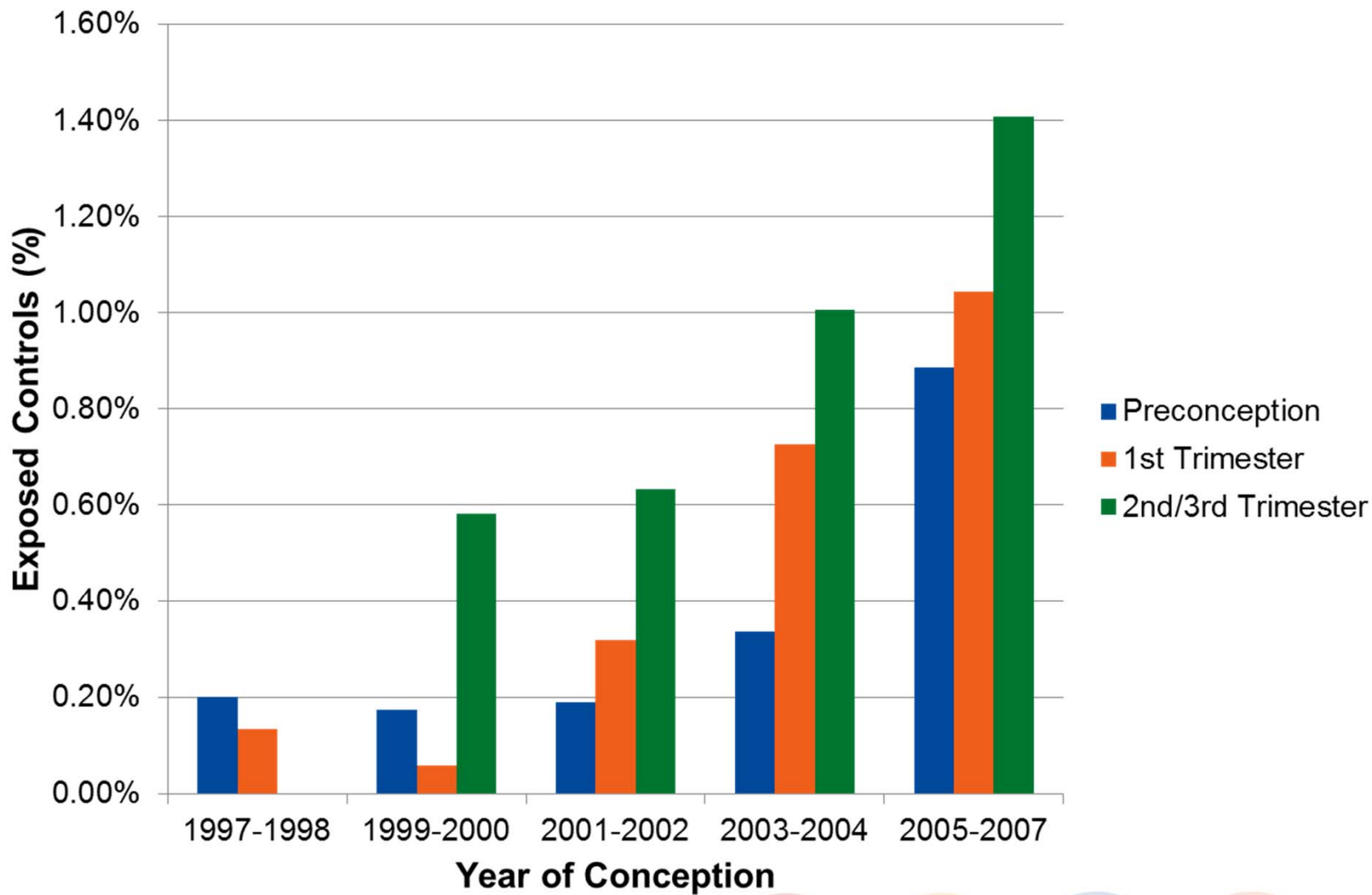


## Maternal H2A Use Before and During Pregnancy

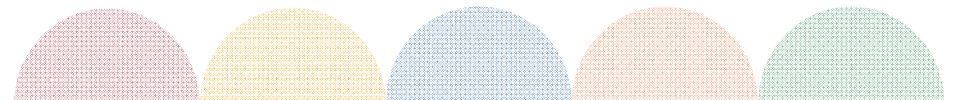
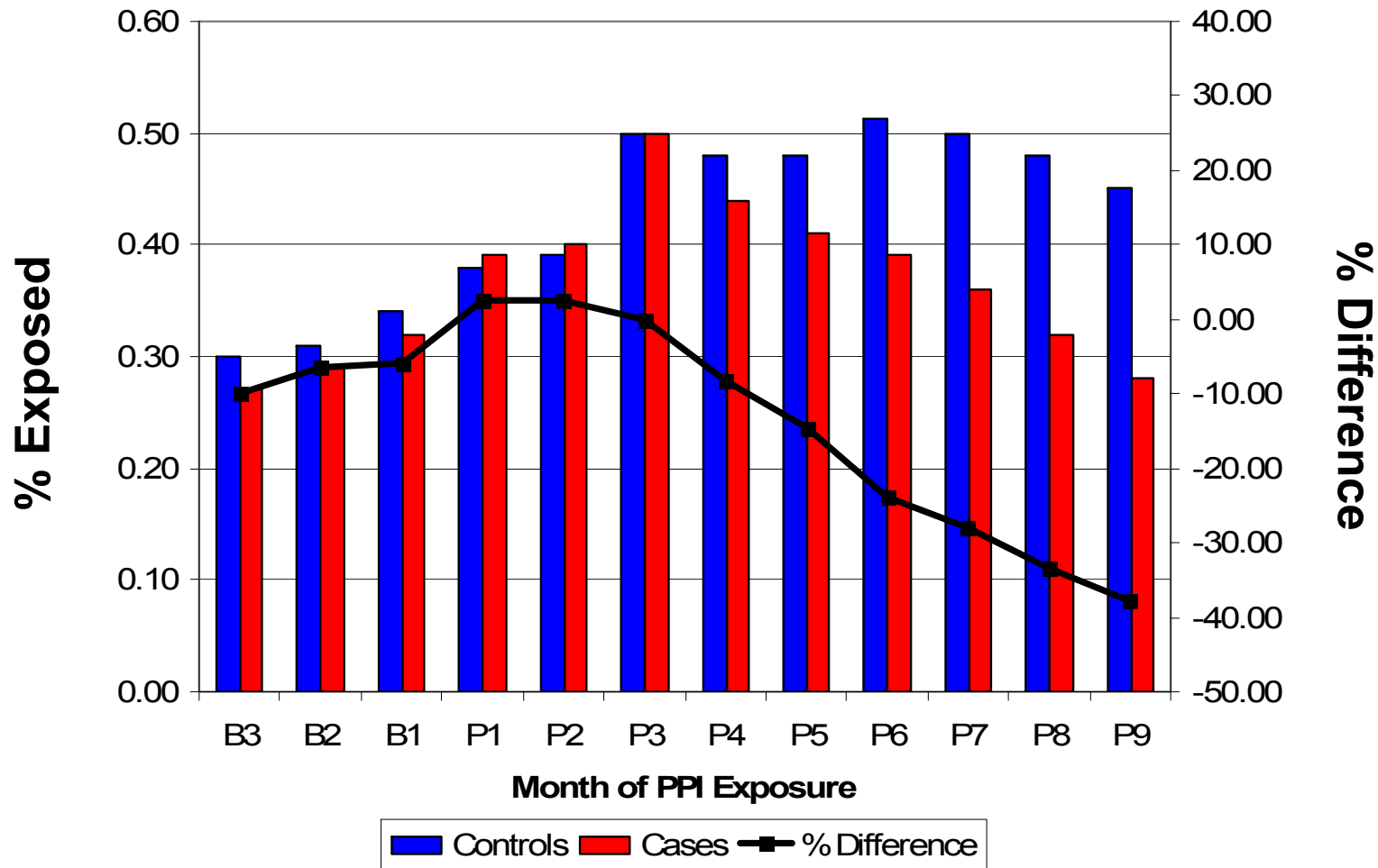


# Trends in Acid Reducer Use

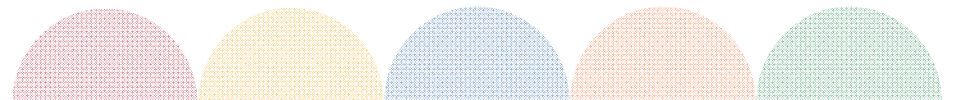
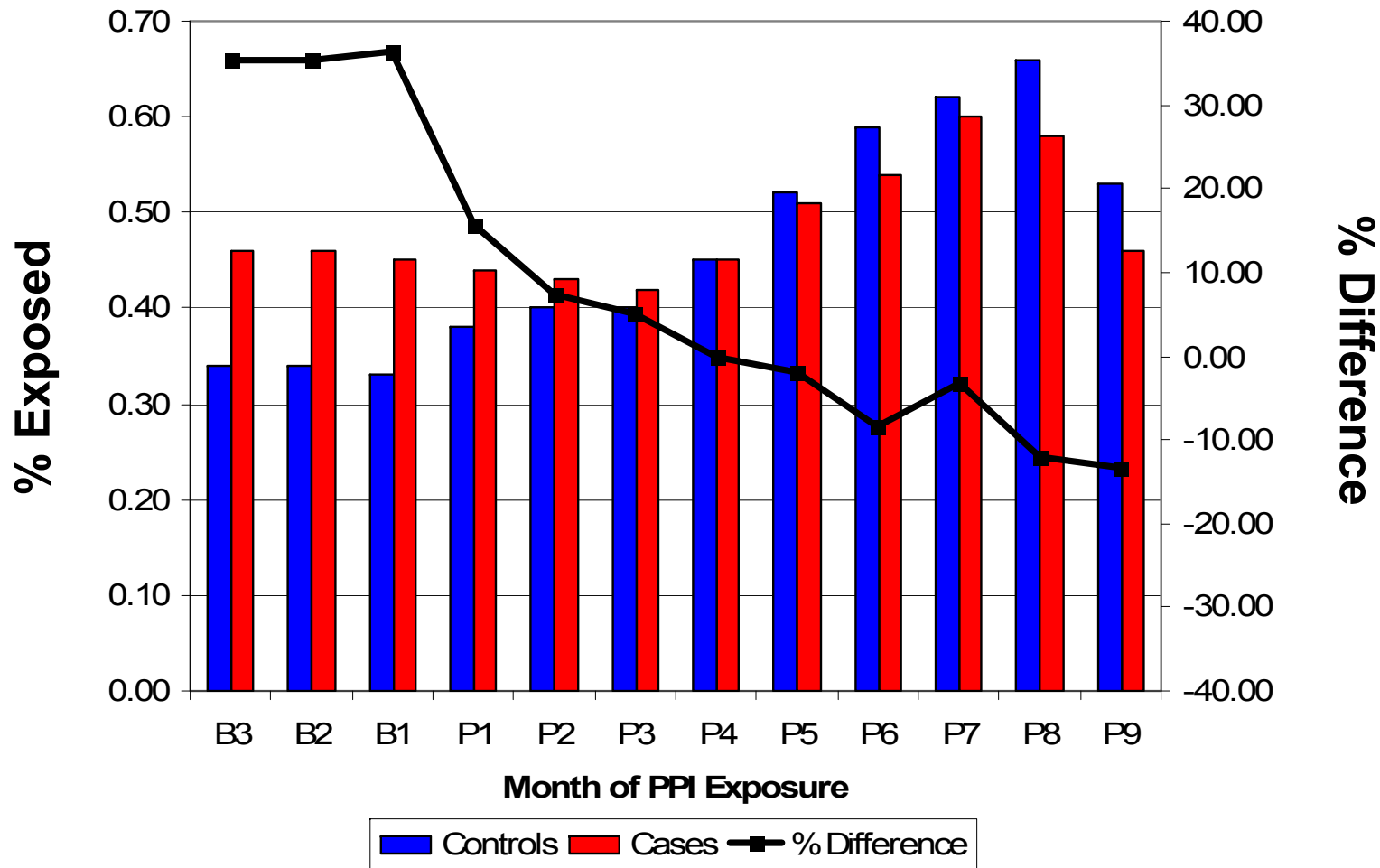
## Maternal PPI Use Before and During Pregnancy



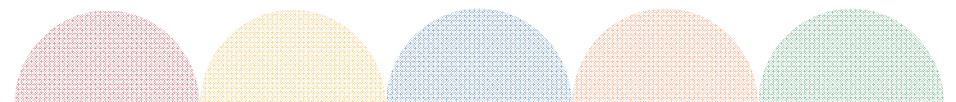
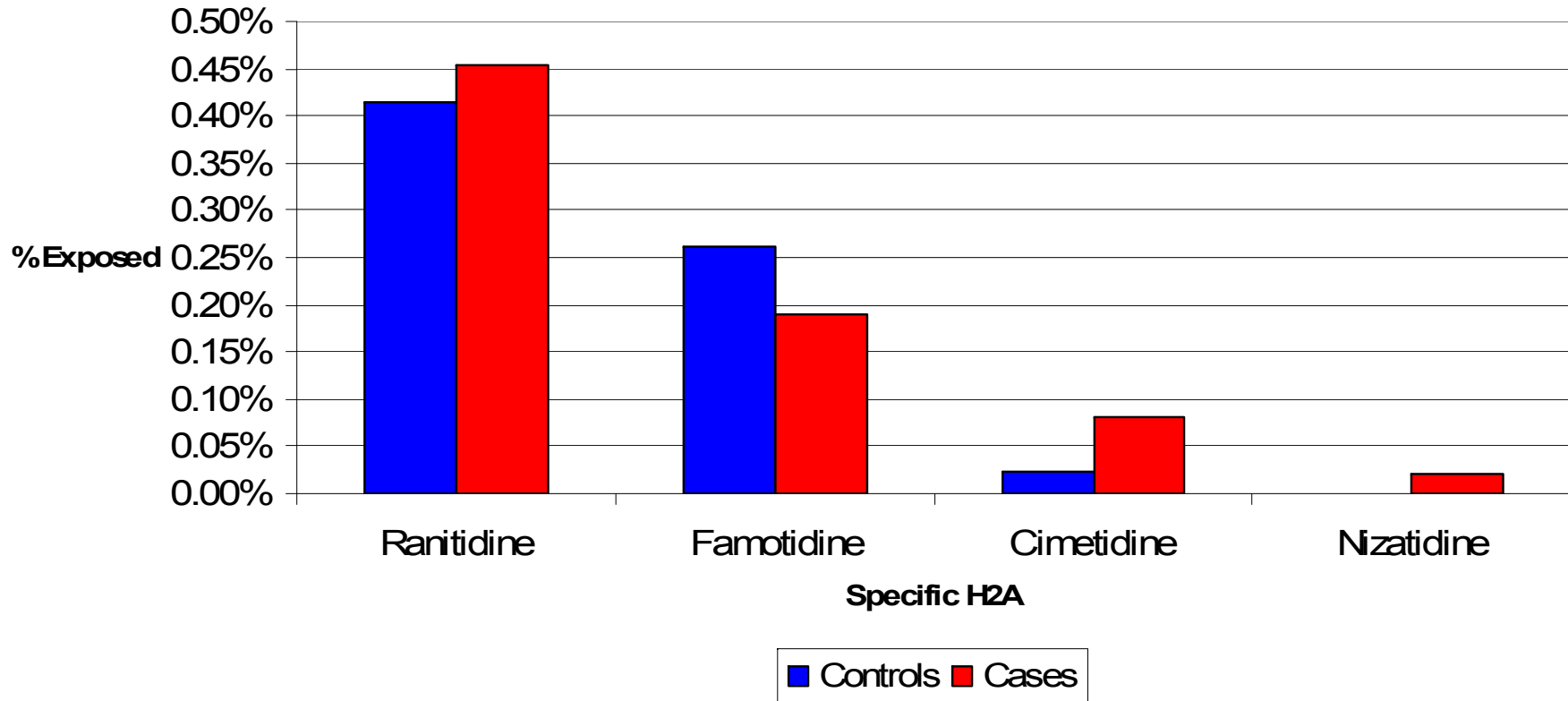
# Results: Trends in H2A Use



# Results: Trends in PPI Use

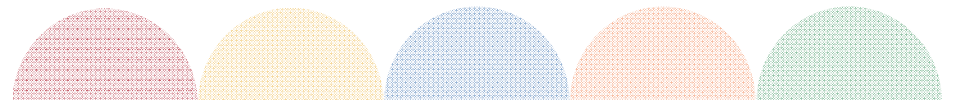
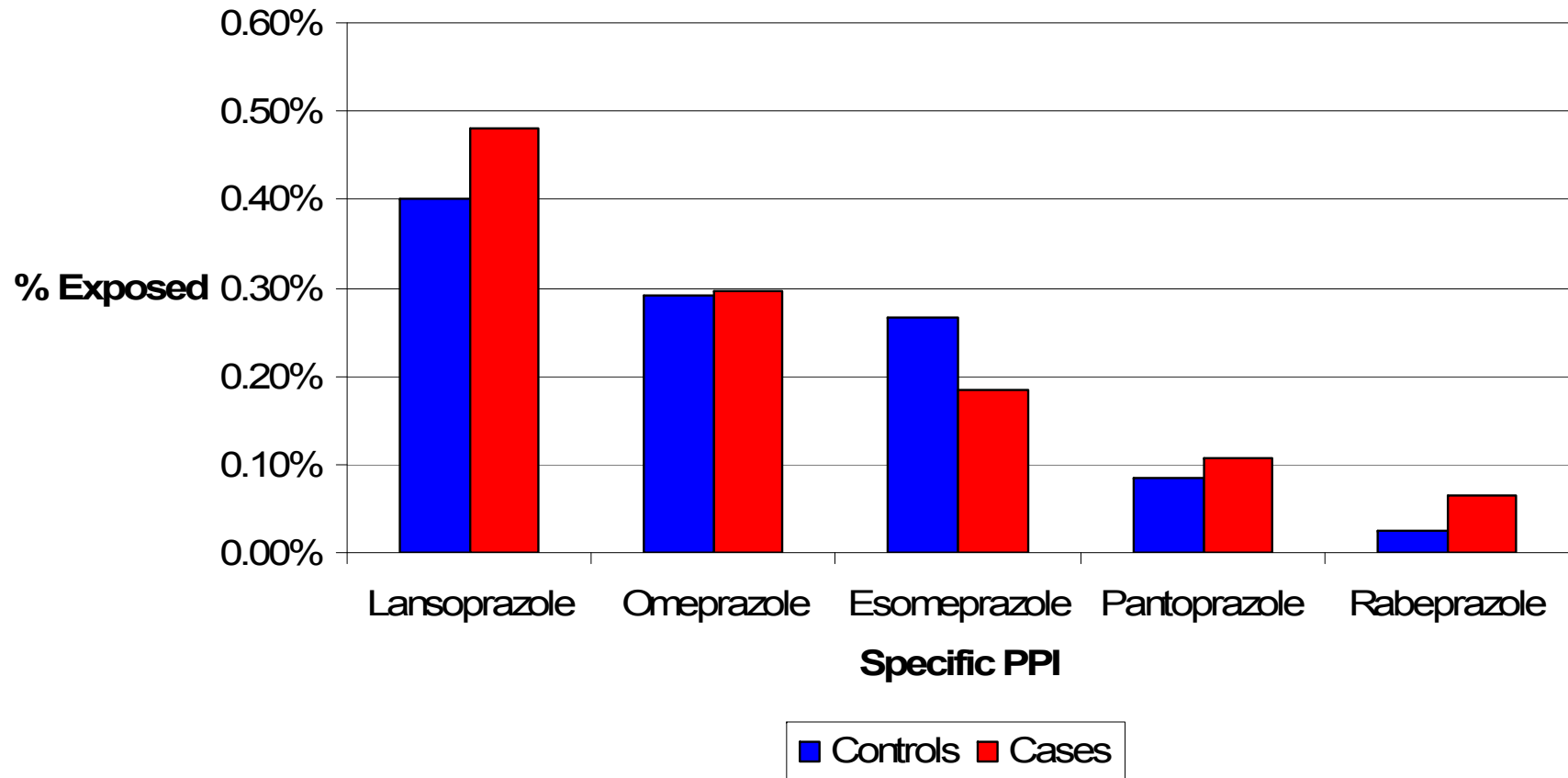


# Results: Periconceptional Use of Specific H2As

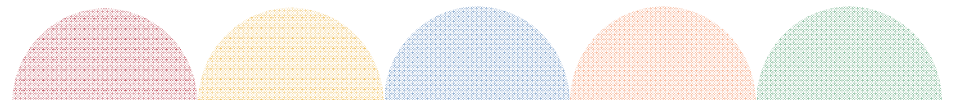




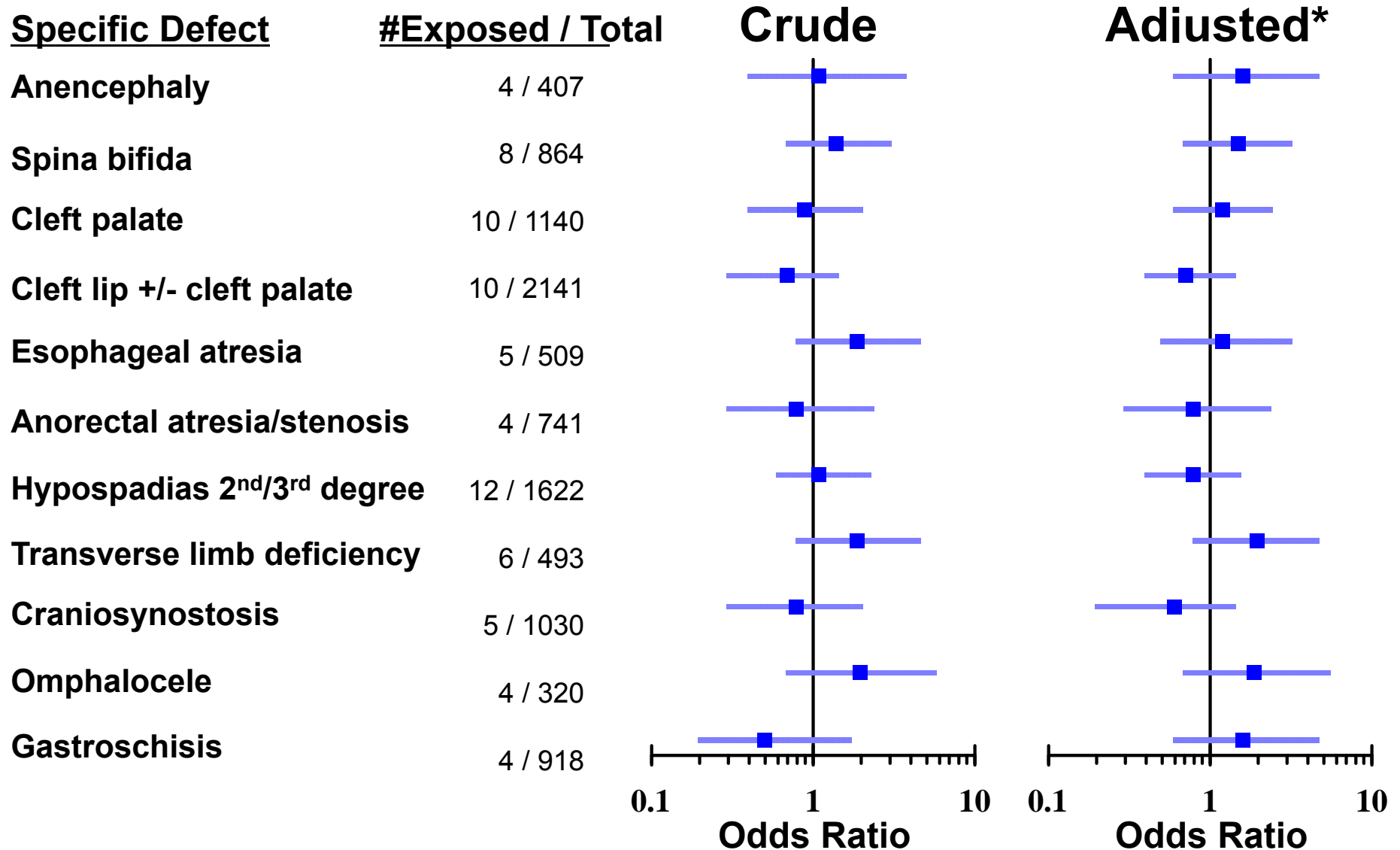
# Results: Periconceptional Use of Specific PPIs



# Maternal H2A Use and Risk for Specific Birth Defects



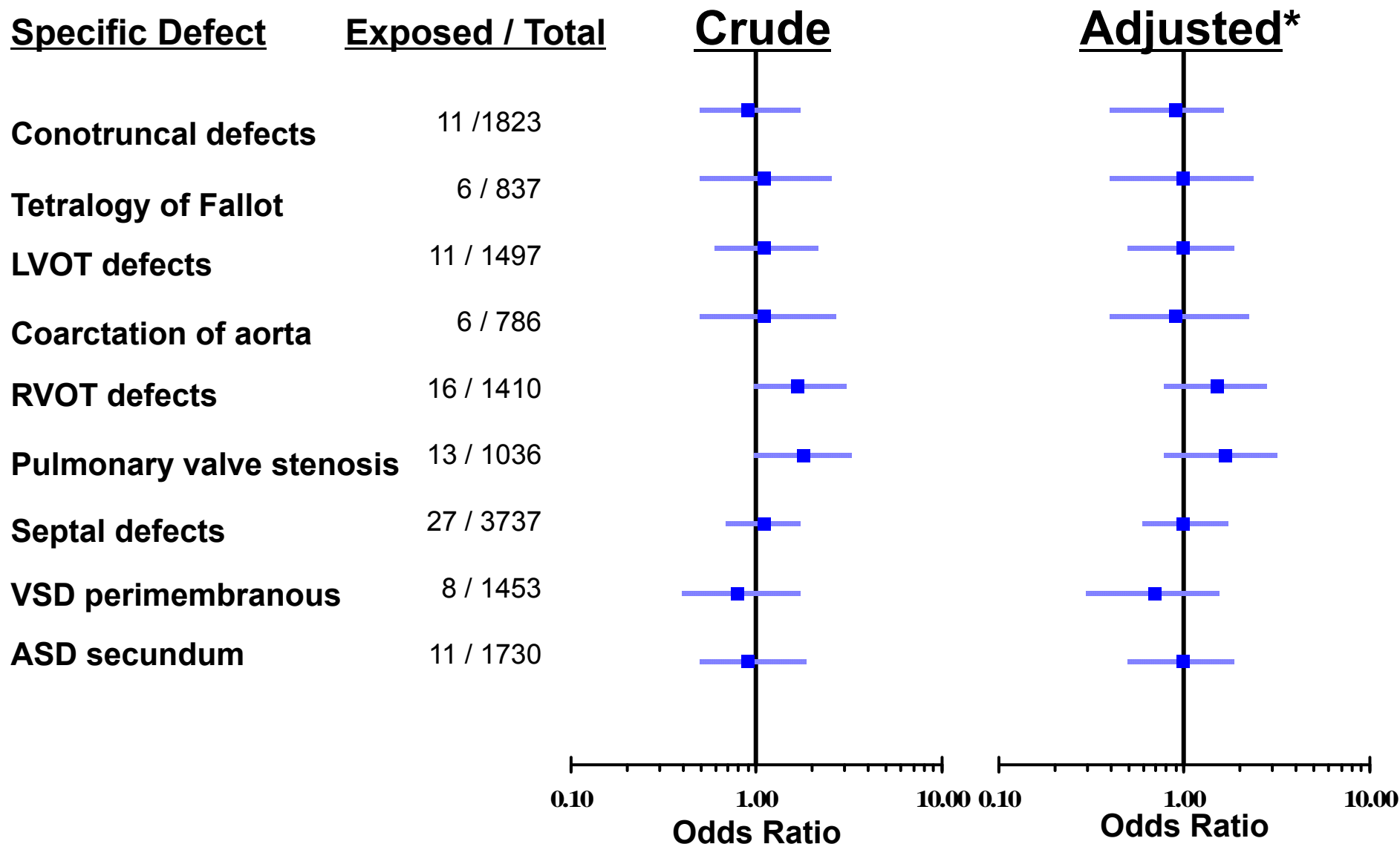
# H2A Crude and Adjusted\* ORs (95% CIs) – Non-heart Defects



Index: Any H2A Exposure B1-P3, Reference: No Acid Reducer Exposure B3-P9

\*Adjusted for race, age, BMI, education, hypertension, smoking, any FAMV use B1-P3 and study center

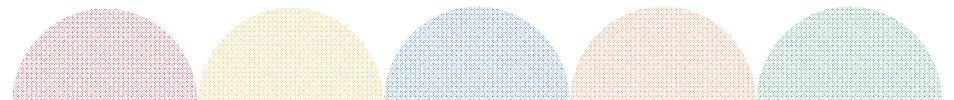
# H2A Crude and Adjusted\* ORs (95% CIs) – Heart Defects



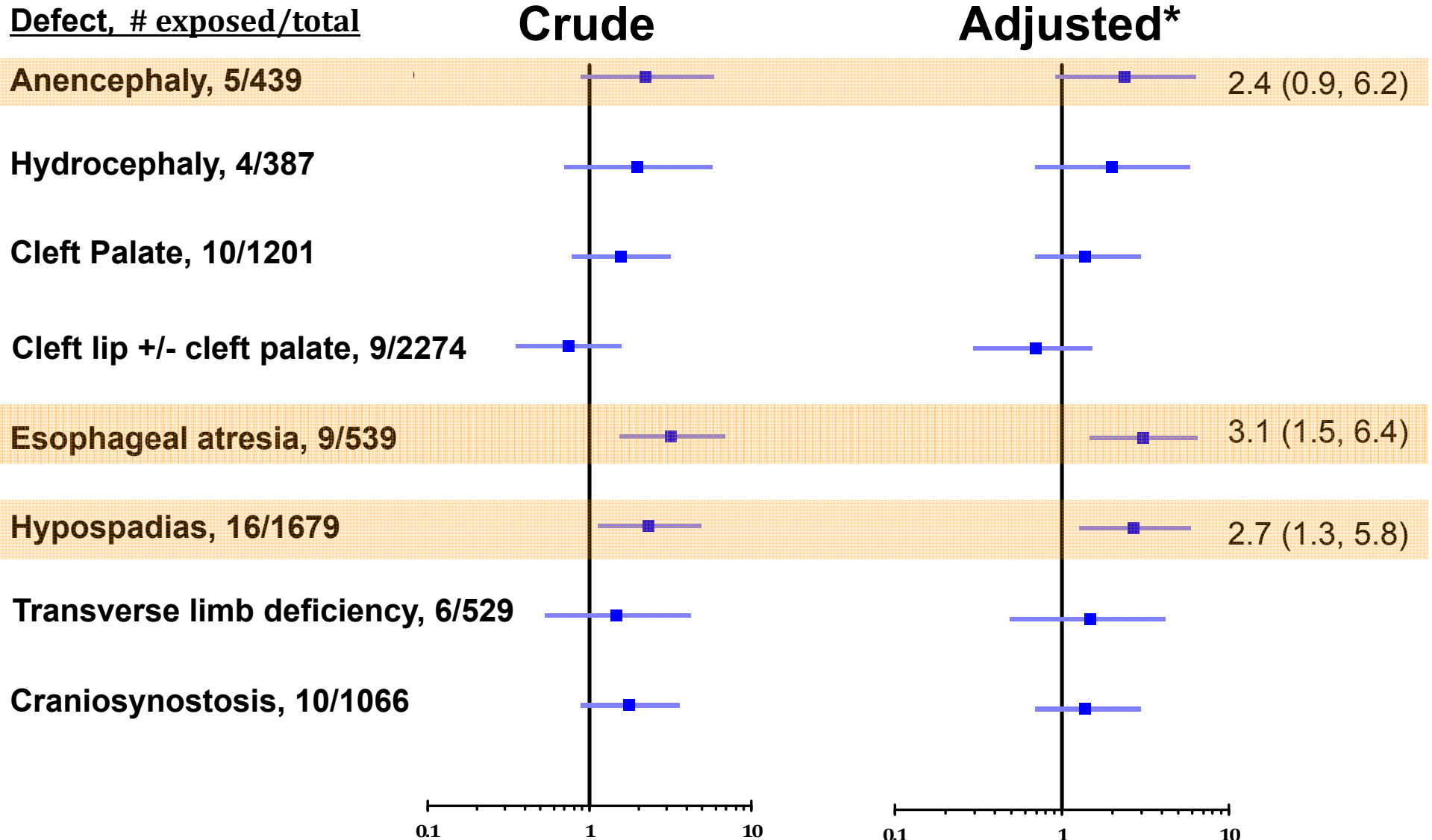
Index: Any H2A Exposure B1-P3, Reference: No Acid Reducer Exposure B3-P9

\*Adjusted for race, age, BMI, education, hypertension, smoking, any FAMV use B1-P3 and study center

# Maternal PPI Use and Risk for Specific Birth Defects



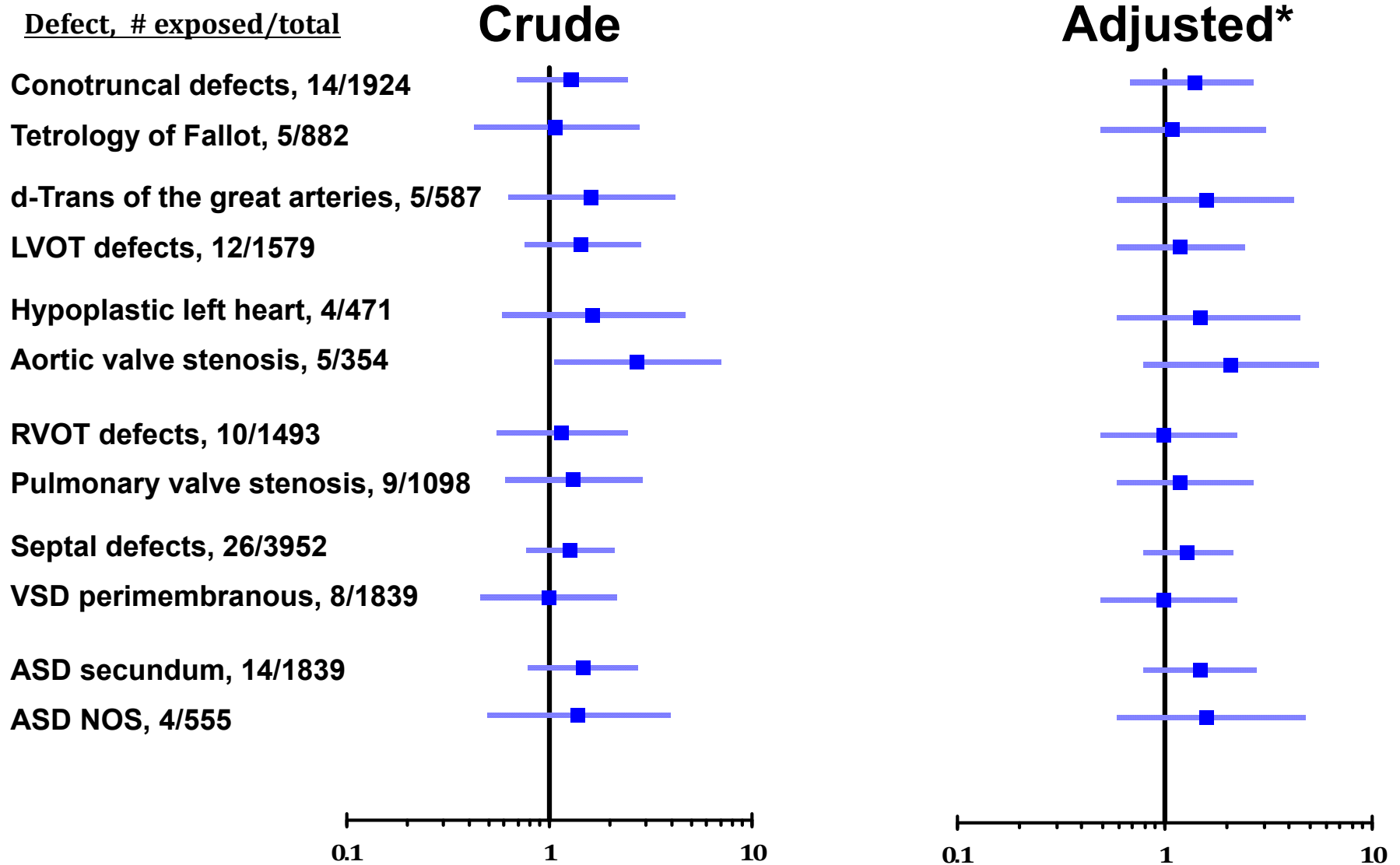
# Crude and Adjusted\* ORs (95% CIs) – Non-heart Defects



\*Adjusted for maternal race, age, BMI, education, hypertension, smoking, FAMV, study center

Index: Any PPI Exposure B1-P3 , Reference: No Acid Reducer Exposure B3-P9

# Crude and Adjusted\* ORs (95% CIs) – Heart Defects



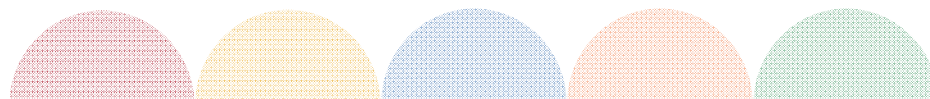
\*Adjusted for maternal race, age, BMI, education, history of hypertension, smoking, FAMV, study center  
**Index: Any PPI Exposure B1-P3 , Reference: No Acid Reducer Exposure B3-P9**

## Results: Timing of Exposure to PPIs



Defect	Any Preconception		1st trimester, no preconception		Preconception & 1st trimester	
	Cases, Controls	cOR	Cases, Controls	cOR	Cases, Controls	cOR
<b>Anencephaly</b>	3, 27	2.3 (0.7, 7.9)	2, 17	2.4 (0.6, 10.4)	2, 23	1.7 (0.4, 7.2)
<b>Esophageal Atresia</b>	4, 27	2.1 (0.7, 6.1)	5, 17	4.7 (1.7, 13.3)	4, 23	2.8 (0.9, 8.1)
<b>Hypospadias</b>	3, 4	1.9 (0.4, 8.7)	5, 8	1.6 (0.5, 4.9)	9, 6	3.0 (1.0, 8.9)

Reference: No Acid Reducer Exposure B3-P9



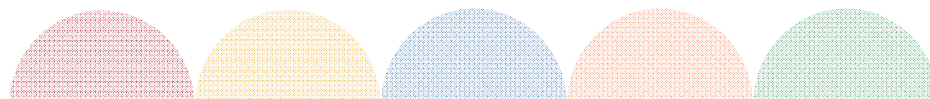


# Results: Specific PPIs

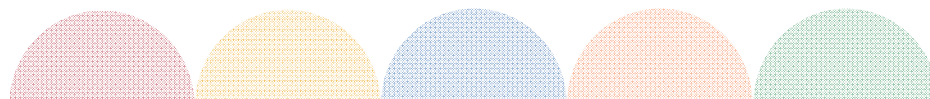


Defect	Lansoprazole		Omeprazole		Esomeprazole	
	Cases Exposed	cOR	Cases Exposed	cOR	Cases Exposed	cOR
Anencephaly		--	3/5	3.2 (0.7, 14.4)		--
Esophageal Atresia	3/9	3.0 (0.9, 10.4)		--	5/9	6.4 (2.2, 18.6)
Hypospadias	6/16	3.0 (0.9, 9.9)	6/16	3.6 (0.9, 14.3)	3/16	2.1 (0.4, 11.9)

Reference: No Acid Reducer Exposure B3-P9



- Provide further reassurance that acid reducers are not likely major risk factors for birth defects
- Some evidence for modest increases in risk for a few specific defects
  - Anencephaly, esophageal atresia, hypospadias



# Acknowledgements



- Marlene Anderka, PI

- Study Collaborators

- Chris Borger
- Sonia Hernandez-Diaz
- Carol Louik
- Allen Mitchell
- Martha Werler

- DPH Colleagues

- Interviewers,  
abstractors, clinical  
geneticists

- Participants

