PHTHALATE EXPOSURE AND PRETERM BIRTH: RECENT FINDINGS AND FUTURE DIRECTIONS

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OVERVIEW

My overarching research objective is to improve the understanding of how the environment impacts pregnancy and childhood health.

ENVIRONMENT ⟶ **MECHANISMS** ⟶ **PREGNANCY** ⟶ **CHILD HEALTH**

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PHTHALATES ⟶ **MECHANISMS** ⟶ **PRETERM BIRTH** ⟶ **CHILD HEALTH**

PHTHALATE EXPOSURE

Environmental exposure sources

Personal care products
Vinyl plastics
Food and beverage

Absorption and metabolism

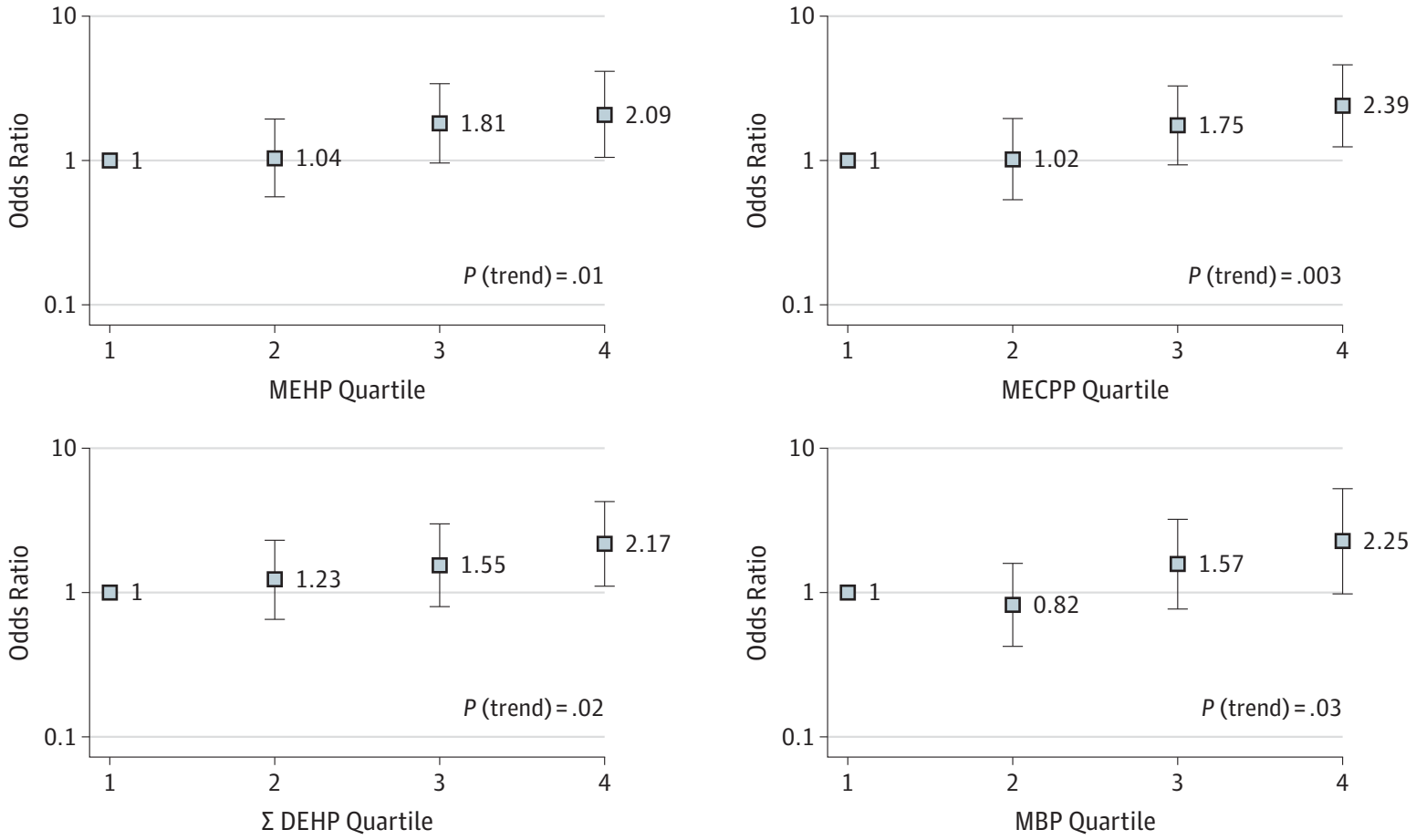
Ingestion
Dermal absorption
Inhalation

Associated health outcomes

Hormone disruption
Infant development
Birth outcomes

PHTHALATE EXPOSURE AND PRETERM BIRTH

Figure 1. Odds of Preterm Birth and 95% CI Levels by Quartile of Average Phthalate Metabolite Level Measured During Pregnancy

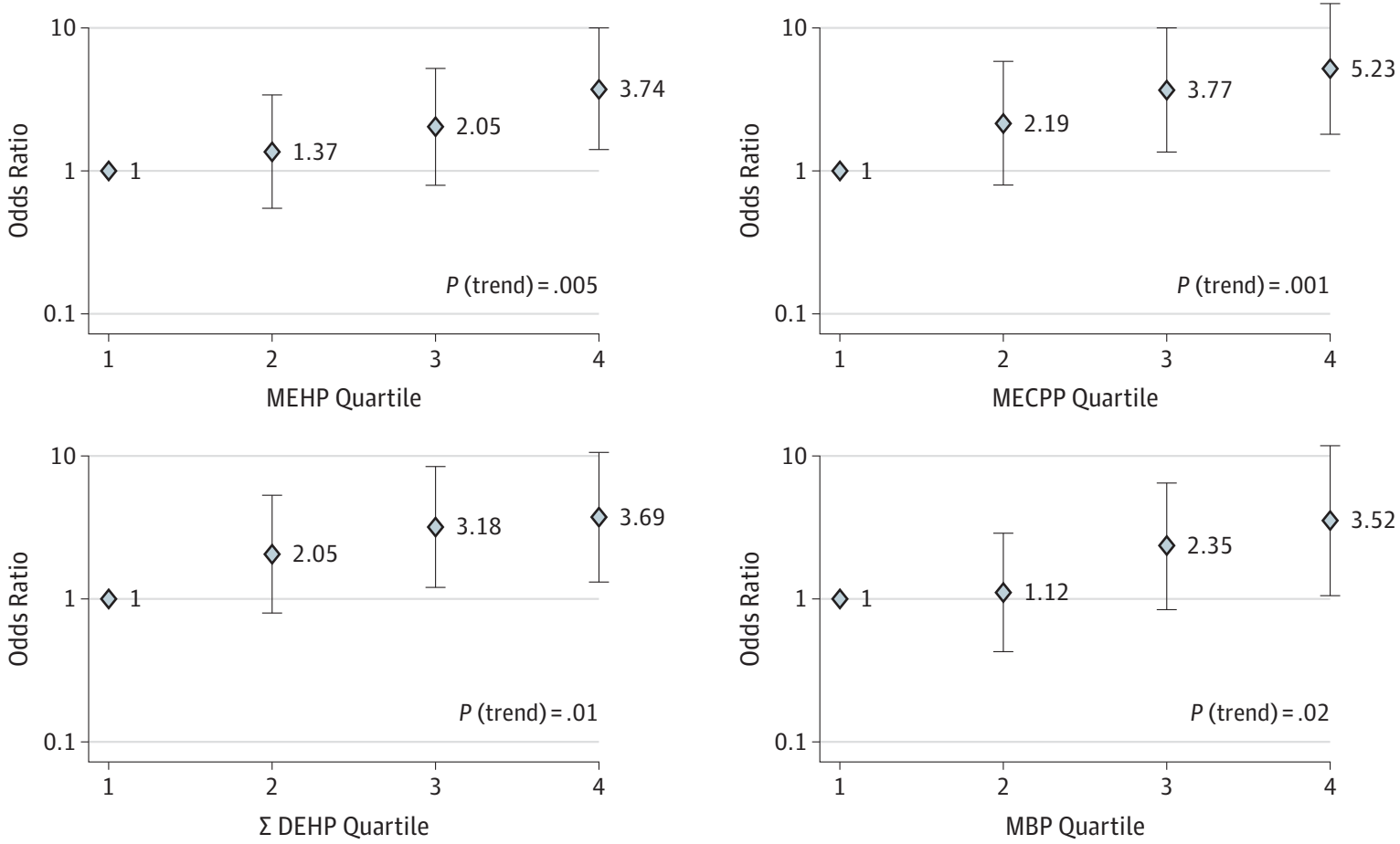


- LIFECODES birth cohort
- N=**130** cases of preterm birth, N=352 controls
- Urinary phthalate metabolites measured at **4 study visits**
- DEHP and DBP metabolites associated with preterm

Ferguson et al. 2014, *JAMA Pediatrics*

PHTHALATE EXPOSURE AND PRETERM BIRTH

Figure 2. Odds of Spontaneous Preterm Birth and 95% CI Levels by Quartile of Average Phthalate Metabolite Level Measured During Pregnancy



- Greater effect estimates observed for **spontaneous preterm birth** alone

Ferguson et al. 2014, *JAMA Pediatrics*

REMAINING QUESTIONS

Do these associations hold in other study populations?

What risk factors make pregnant women more vulnerable to phthalate exposure?

Are there threshold effects or cumulative effects of exposure to phthalates?

PHTHALATES AND PRETERM BIRTH IN OTHER STUDIES

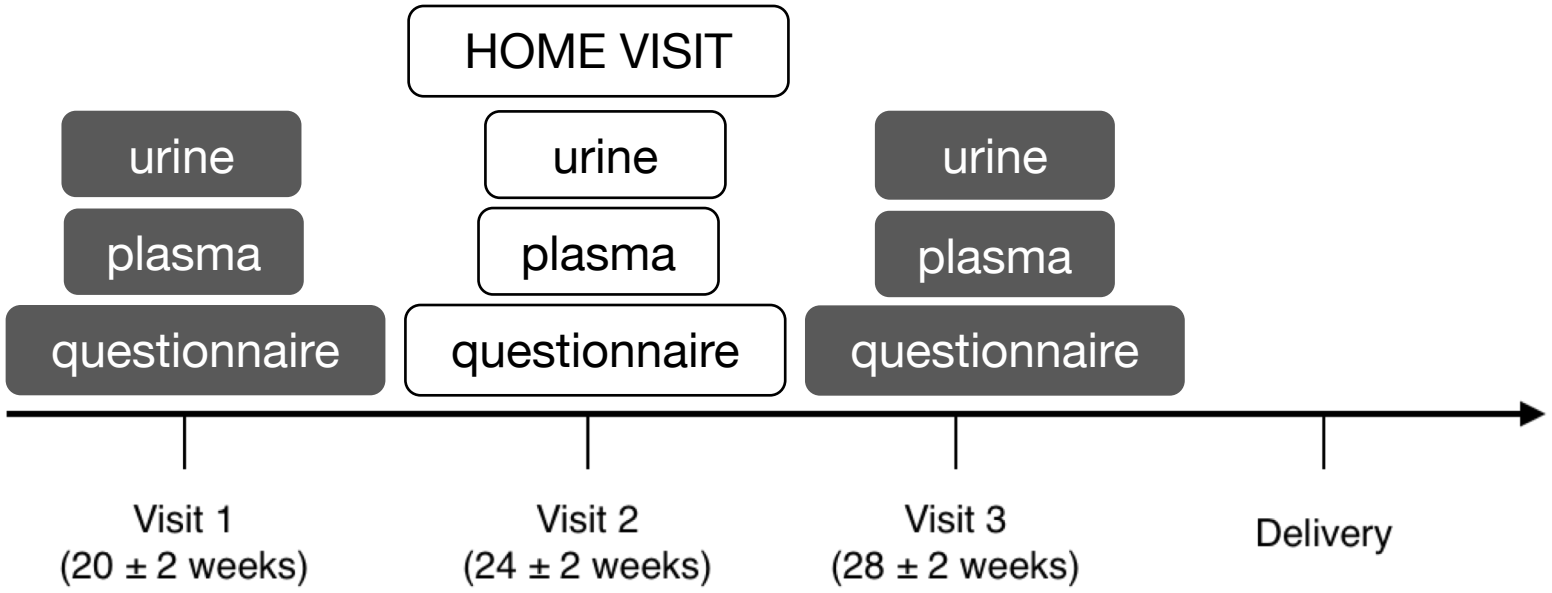
Reference	N (preterm)	Urine time points (weeks)	+ Gestational age	- Gestational age
Bloom 2019	319 (28)	18-22		
Huang 2018	106	delivery	MBzP, DEHP metabolites	
Casas 2016	391	12, 32		
Polanska 2016	165	30-34		MEP
Shoaff 2016	368	16, 26	MBP, MCPP	
Watkins 2016	68 (2)	8-14, delivery		∑DBP (females only)
Weinberger 2014	72 (7)	Not provided		DEHP metabolites
Suzuki 2010	149 (2)	9-40		
Adibi 2009	283	28	DEHP metabolites	
Meeker 2009	60 (30)	3rd trimester		DEHP metabolites, MBP, MCPP
Whyatt 2009	331	3rd trimester		DEHP metabolites
Wolff 2008	382	25-40	∑Low-MWP, DEHP metabolites	

N < 400 preterm ≤ 30

2 urine samples max

Mostly null findings

PROTECT BIRTH COHORT



- Puerto Rico Testsite for Exploring Contamination Threats (PI: Alshawabkeh)
- Recruitment at 2 hospitals and 5 clinics in the Northern Karst region of Puerto Rico since 2011
- Restricted to women without medical complications
- Urinary phthalate metabolites from three study visits
- N=100 cases of preterm birth, N=971 term

AVERAGE ASSOCIATIONS WITH PRETERM BIRTH

- Models adjusted for maternal age and education level

	Odds Ratio (95% CI) of preterm birth
n (preterm, term)	100, 971
MEP	0.98 (0.73, 1.32)
MBP	1.42 (1.07, 1.88)
MBzP	1.09 (0.84, 1.42)
MiBP	1.32 (1.02, 1.71)
∑DEHP	0.92 (0.69, 1.22)
MCPP	1.18 (0.92, 1.51)
MCOP	1.08 (0.83, 1.41)
MCNP	1.14 (0.88, 1.47)
n (preterm, term)	75, 738
MHBP	1.33 (0.98, 1.81)
MHiBP	1.44 (1.04, 2.01)
n (preterm, term)	38, 381
MECPTP	0.65 (0.41, 1.04)
MEHHTP	0.70 (0.44, 1.11)
MONP	0.89 (0.58, 1.36)

Ferguson et al. 2019, *Environment International*

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- No association between DEHP metabolites and preterm birth

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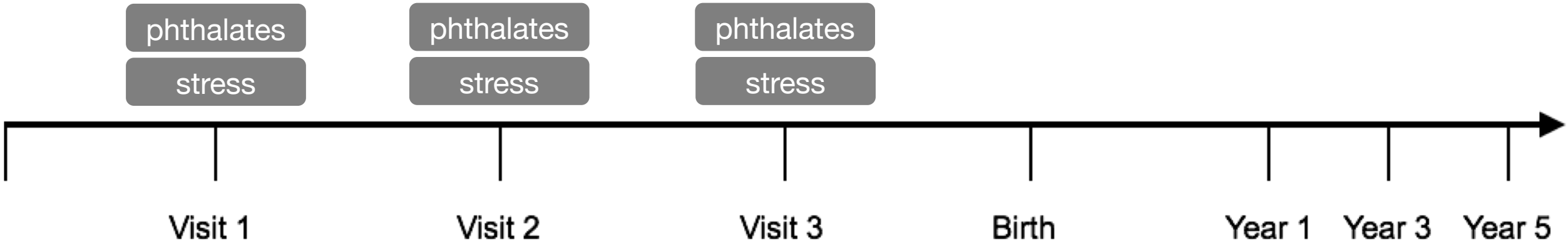
TIDES



The Infant Development and the Environment Study (TIDES)
Collaborators: Shanna Swan, Sheela Sathyanarayana, Emily Barrett, Ruby Nguyen, Nicole Bush

N=57 preterm, N=625 term for present analysis

PHTHALATE ASSOCIATIONS WITH PRETERM BIRTH

	Average
n (term, preterm)	625, 57
MEP	1.12 (0.90, 1.41)
MBP	1.32 (0.93, 1.89)
MBzP	1.06 (0.80, 1.41)
MiBP	1.28 (0.86, 1.91)
ΣDEHP	1.33 (0.87, 2.06)
MCPP	1.07 (0.82, 1.39)
MCOP	1.07 (0.83, 1.40)
MCNP	1.17 (0.85, 1.61)

- Associations were imprecise due to small numbers of preterm births

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- Associations were imprecise due to small numbers of preterm births
- Average MBP, MiBP and ΣDEHP associated with increased OR of preterm

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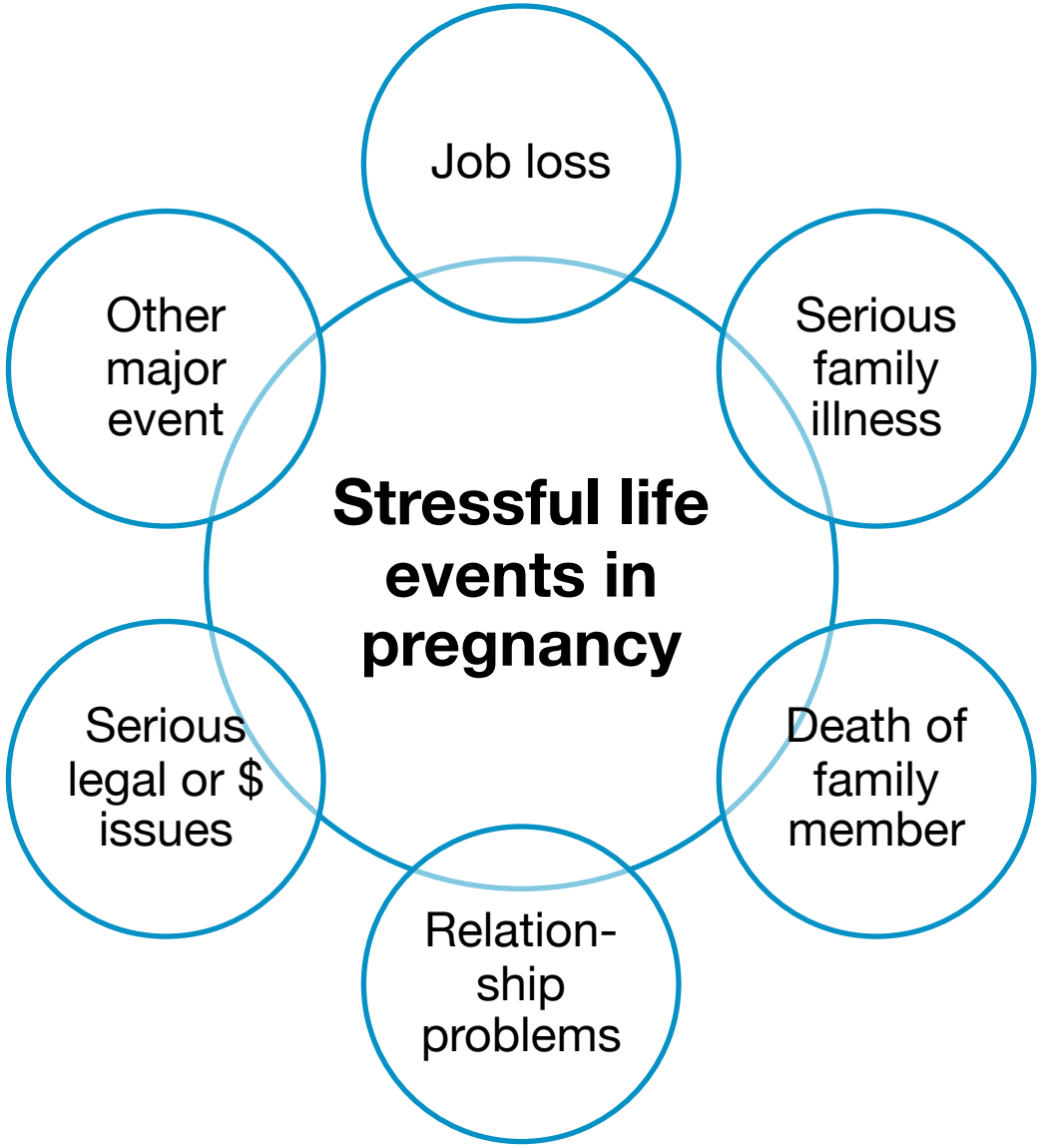
STRESSFUL LIFE EVENTS IN PREGNANCY

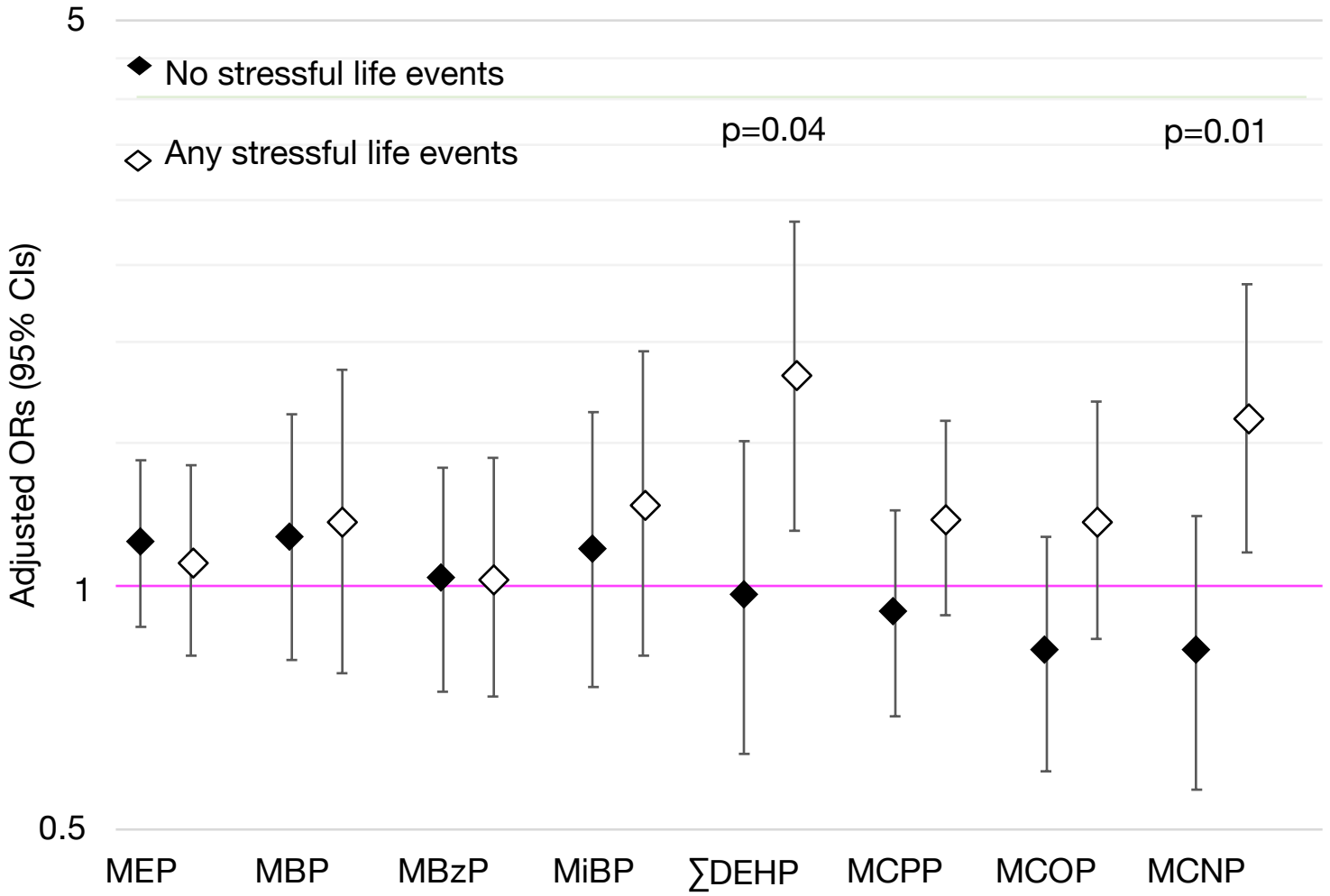


- Assessed via questionnaire at each study visit to determine whether participants experienced SLEs during each trimester
- Summarized as “Any SLE” vs. “No SLE” occurring during pregnancy
- Logistic regression models of phthalates and PTB were stratified by this binary variable

Ferguson et al. 2019, *Environment International*

RESULTS FROM STRATIFIED MODELS

- In general, OR from women experiencing stressful life events in pregnancy were higher than OR from women experiencing no stressful life events



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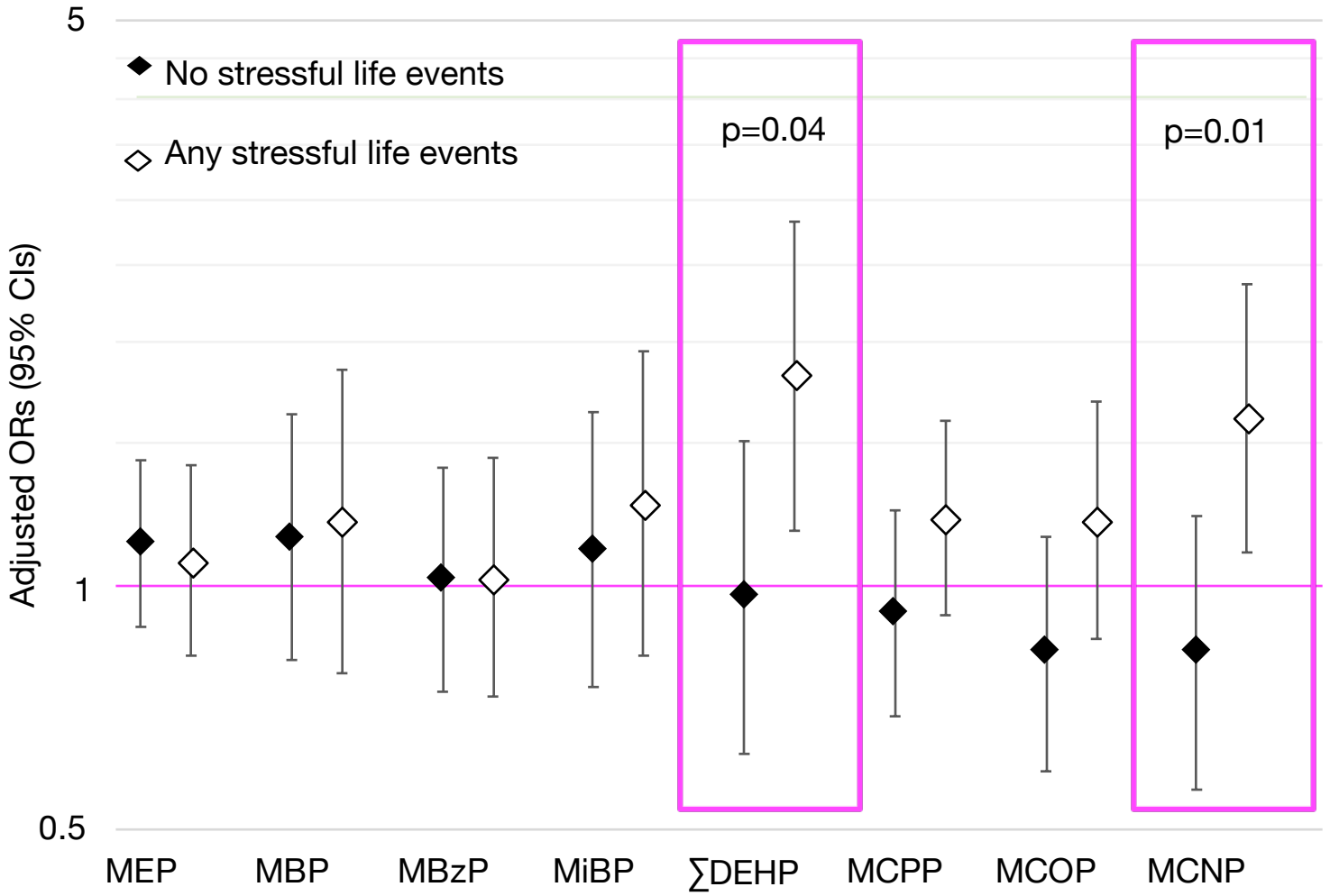
RESULTS FROM STRATIFIED MODELS

- In general, OR from women experiencing stressful life events in pregnancy were higher than OR from women experiencing no stressful life events
- Test for interaction showed that difference between groups was significant for ΣDEHP metabolites and MCNP



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POOLED STUDY OF PHTHALATES AND PRETERM BIRTH

Study cohort	N
PROTECT	1101
TIDES	779
LIFECODES	480
Healthy Start	444
CHAMACOS	429
CCCEH	389
HOME	389
EARTH	385
MSSM	362
MUSC	318
SFF	294
MARBLES	190
HEBC	190
EPS	126
MMP	68
Rutgers	52
Total	**5,996**

- Will utilize US studies with prenatal measurements of one or more urinary phthalate metabolites (16 total)
- Research questions:
  - What are the specific windows of vulnerability?
  - Are there differences by race/ethnicity?
  - Are there threshold effects?
  - Is there a cumulative effect of exposure?
- Current status: Data transfer agreements complete, data transferred to NIEHS, variables harmonized, analysis underway!

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LIFECODES cohort
Thomas McElrath, Brigham and Women's Hospital
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PROTECT cohort
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John Meeker, University of Michigan
Akram Alshawabkeh, Northeastern University
José Cordero, University of Georgia

TIDES cohort
Shanna Swan, Icahn School of Medicine at Mount Sinai
Sheela Sathyanarayana, Seattle Children's Hospital
Emily Barrett, Rutgers University
Ruby Nguyen, University of Minnesota
Nicole Bush, University of California San Francisco

Pooled Study of Phthalates and Preterm Birth
Cohort PIs contributing data!!!
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