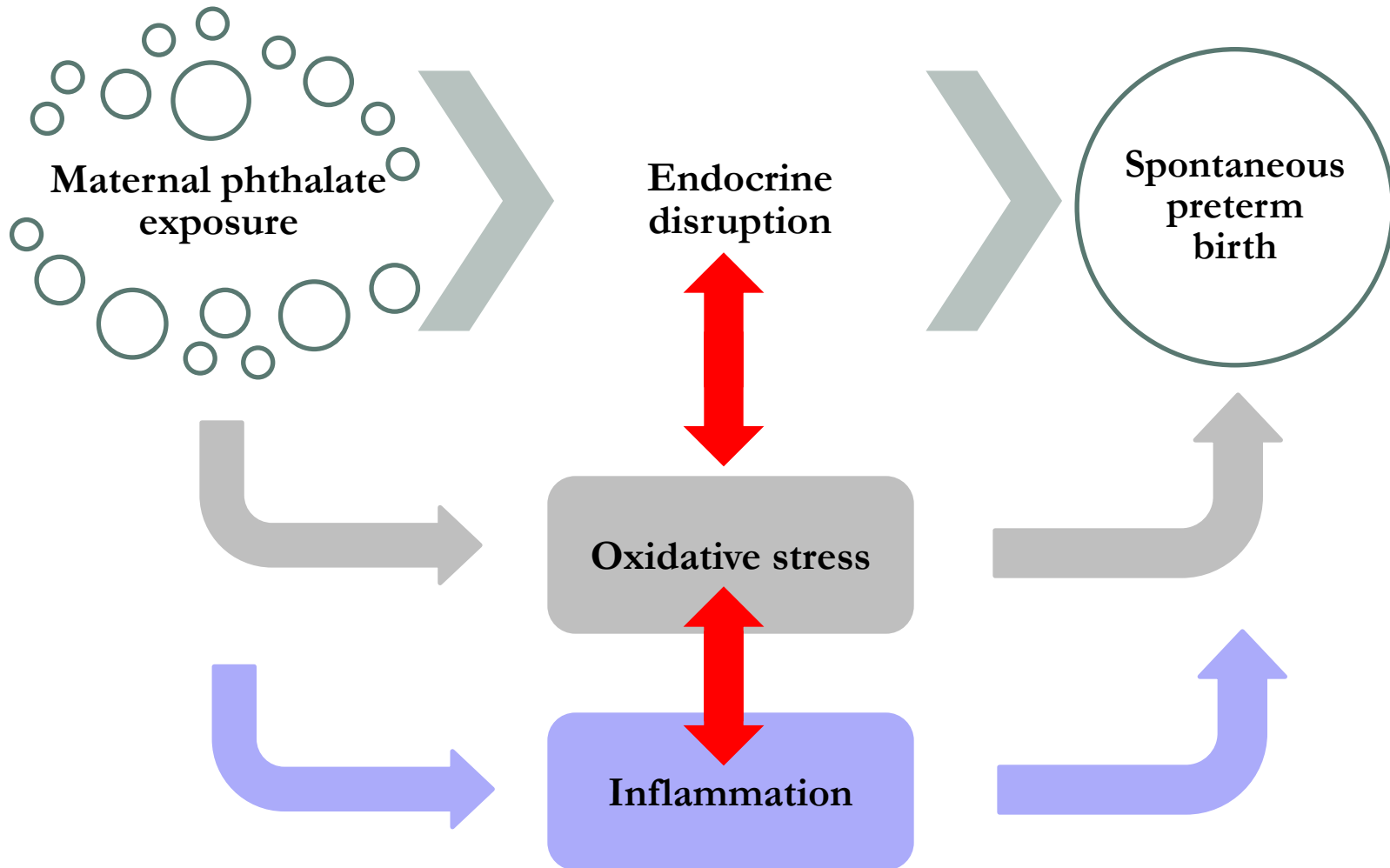


Developmental effects of phthalates: what are the mechanisms?

Kelly Ferguson, PhD
University of Michigan School of
Public Health

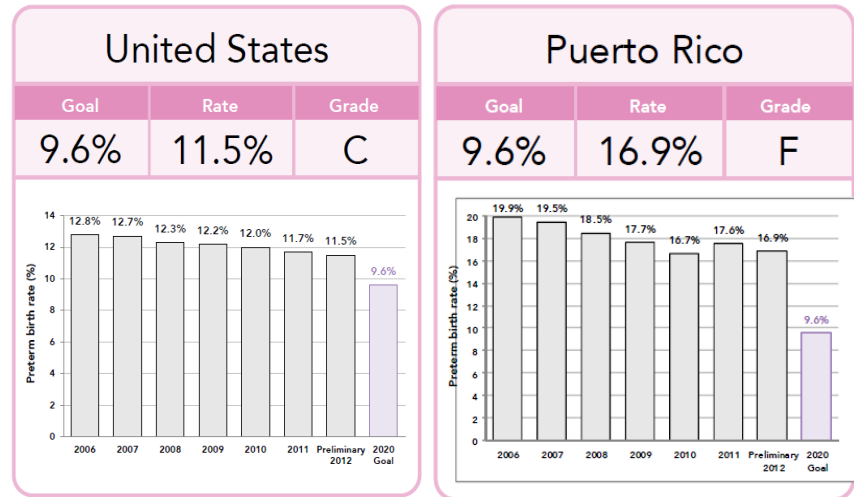


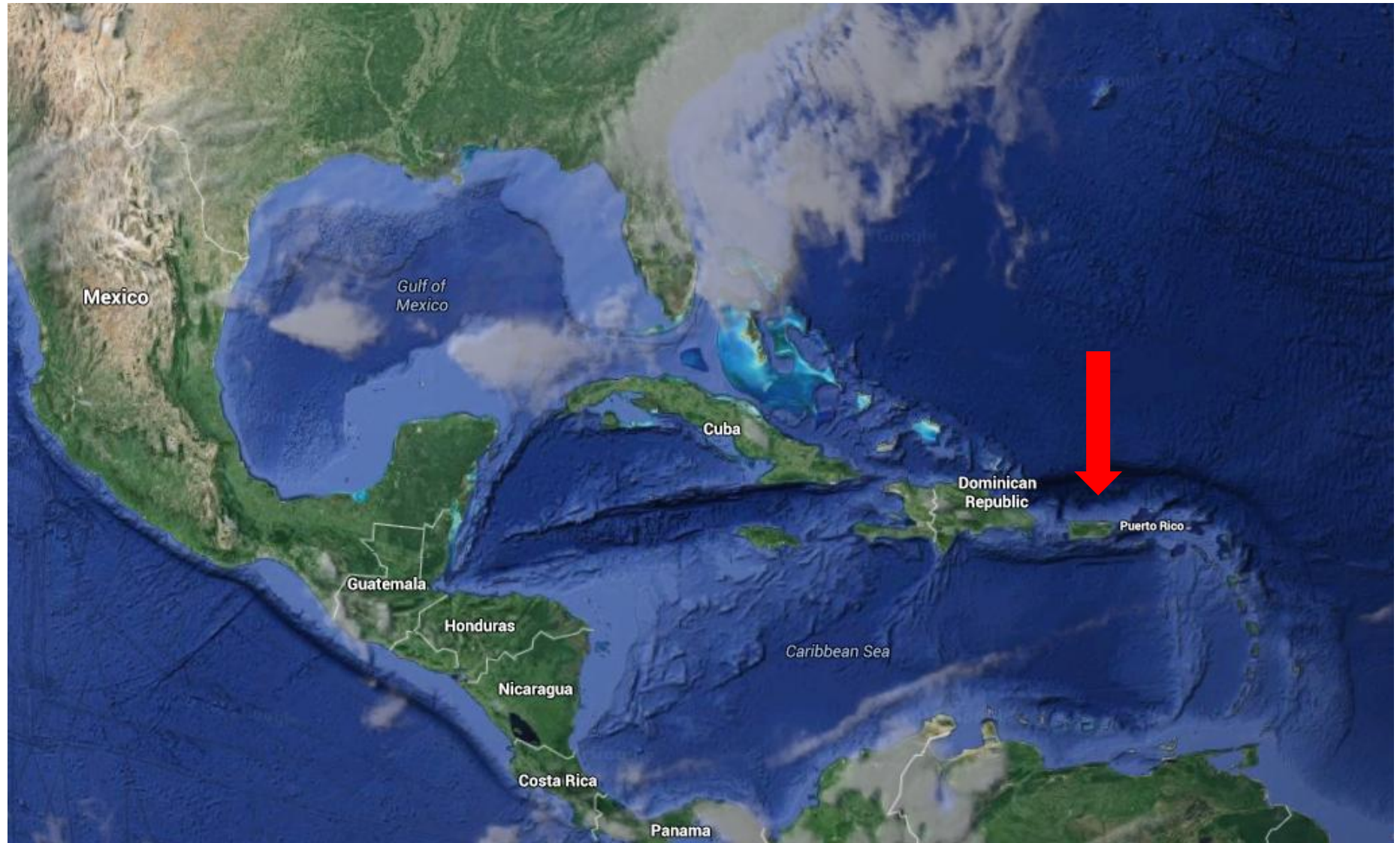
Mixed mechanisms?



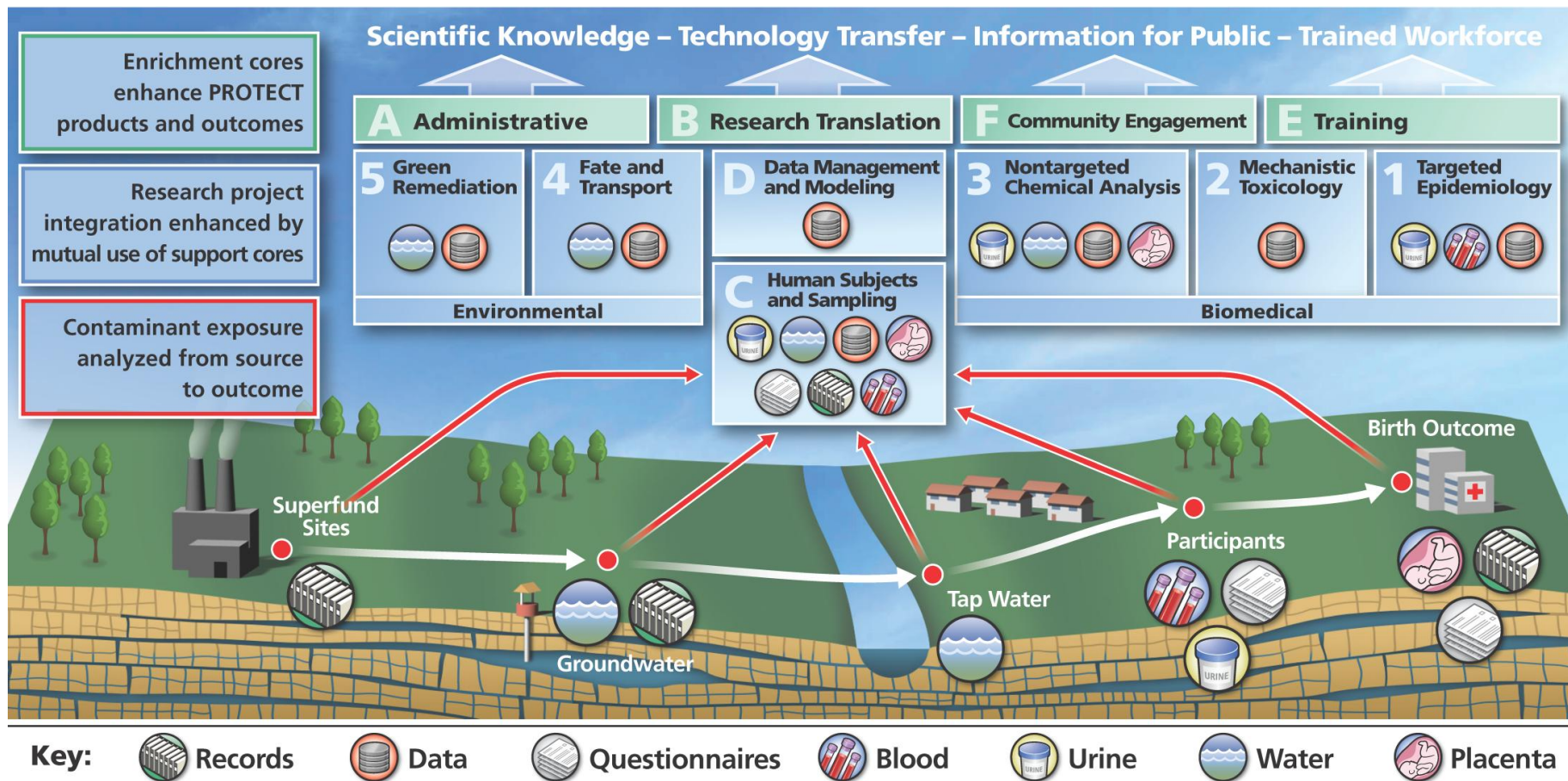
Puerto Rico Testsite for Exploring Contamination Threats

- Second highest rate of preterm birth worldwide
- Densely distributed contaminated waste sites





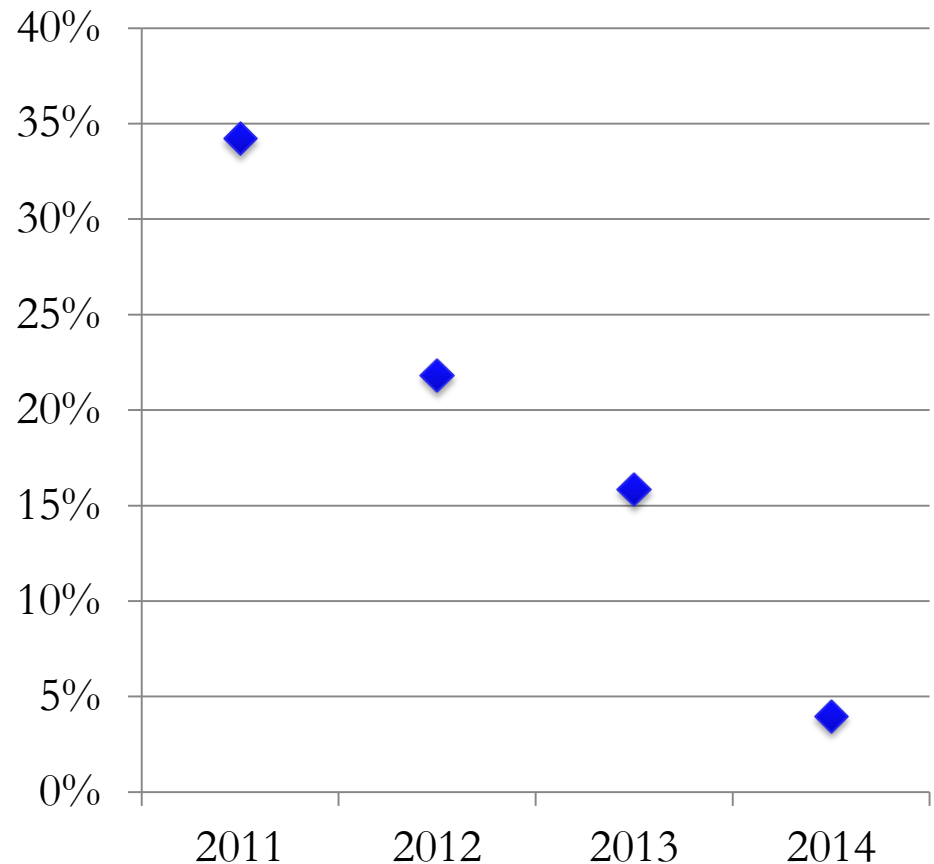
Puerto Rico Testsite for Exploring Contamination Threats



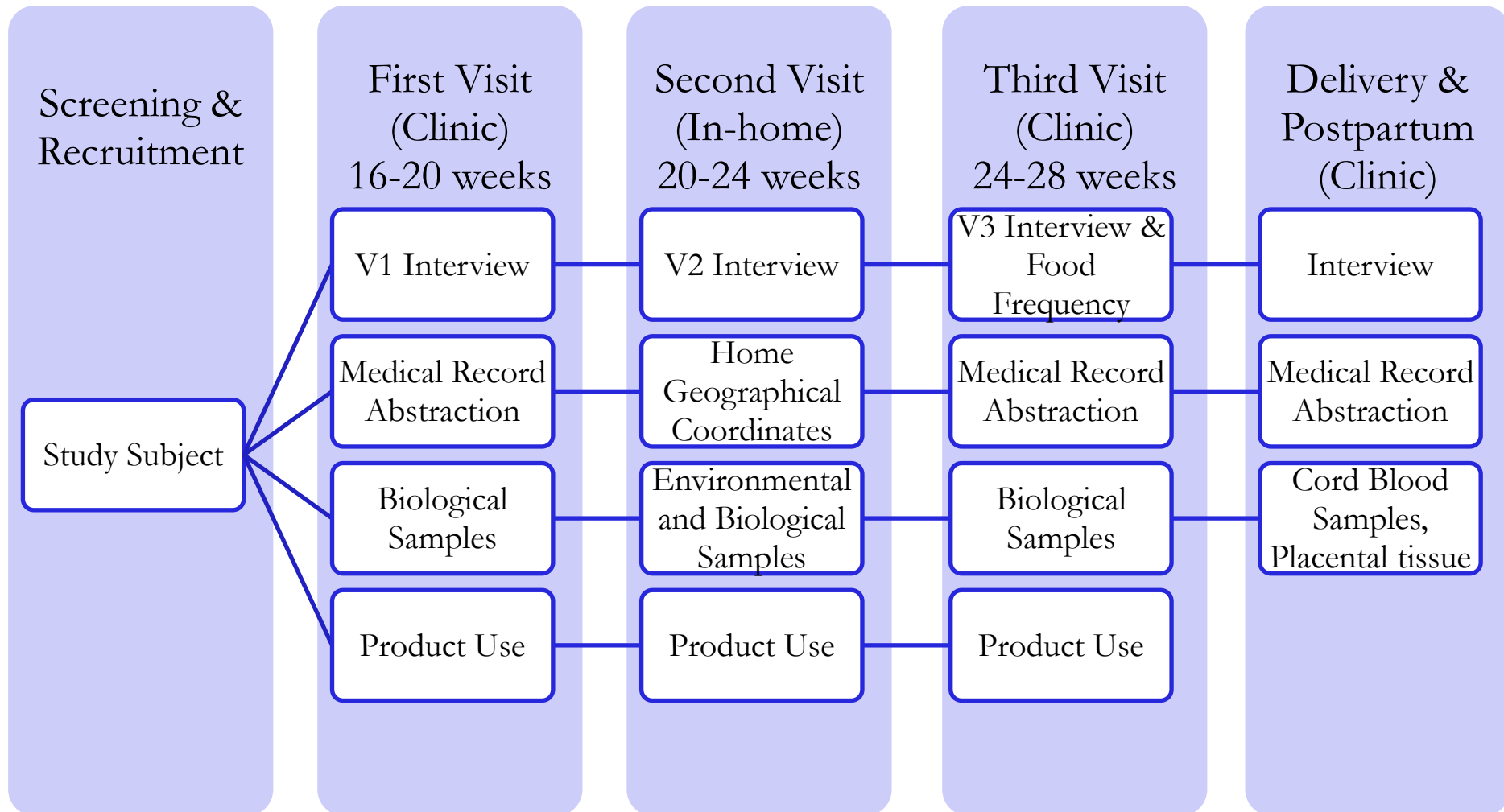
PROTECT Recruitment

STATUS	NUMBER
Recruited (total)	827
Pregnancy completed	569
Live births	539
Early losses and stillbirths	30
Pregnancy in progress	85
Withdrawals	173

Withdrawal Rate



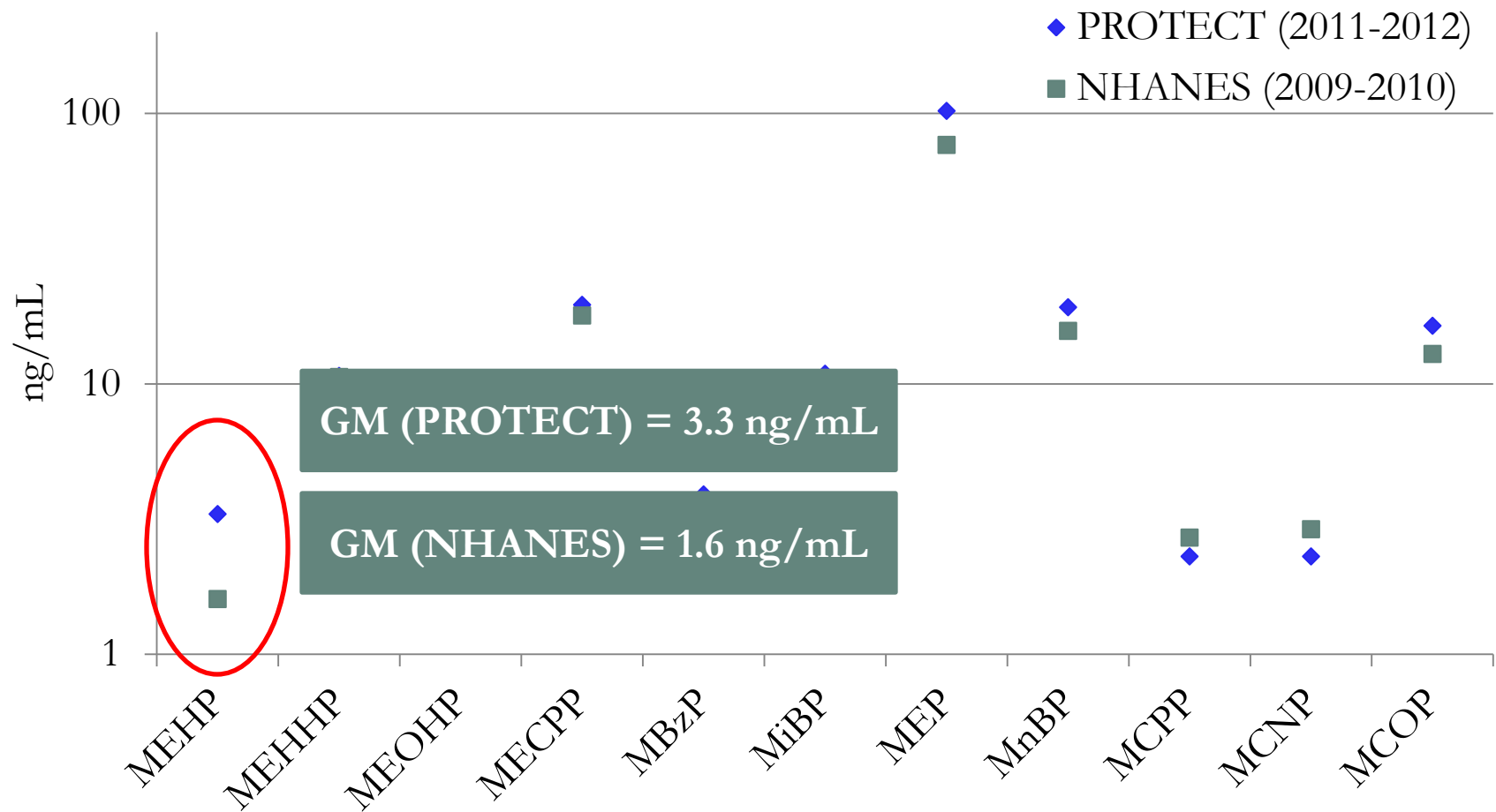
Participant Follow-up



PROTECT Study population 2011-2012

Maternal characteristics	Mean \pm SD or N (%)
Age at enrollment	27.5 \pm 5.2
Education	
< High School	14 (10.7)
High School/equivalent	10 (7.2)
College	115 (92.7)
Household income (\$)	
<\$20,000	57 (40.1)
\$20,000-\$40,000	34 (24.0)
>\$40,000	30 (21.1)

PROTECT urinary phthalate metabolite concentrations 2011-2012



Examining mechanisms of phthalate action in pregnancy utilizing biomarkers

Endocrine disruption

- Thyroid hormones
- Estradiol, SHBG, Progesterone

Serum

Inflammation

- C-Reactive Protein
- Pro- and anti-inflammatory cytokines

Plasma

Oxidative stress

- 8-isoprostane (lipid peroxidation)
- 8-hydroxydeoxyguanosine (8-OHdG, oxidative DNA damage)

Urine

Endocrine disruption results

N=106 women

N=181 observations

+ No clear associations or trends in longitudinal analysis with thyroid hormones, estradiol, SHBG, or progesterone

+ Inverse association between MCPP and Free T3

$\% \Delta = -2.89$, 95%
CI = -5.65, -0.02

+ Inverse association between MEP and progesterone

$\% \Delta = -10.6$, 95%
CI = -17.6, -2.84

Endocrine disruption by study visit: Free T4

Visit 1 (N=100)

Visit 3 (N=81)

	% Δ (95% CI)	% Δ (95% CI)
Σ DEHP	3.09 (-2.17, 8.27)	-9.02 (-15.3, -0.80)
MCPP	1.41 (-2.83, 5.80)	-5.11 (-12.5, 2.22)
MCNP	0.43 (-3.47, 4.37)	-6.34 (-14.0, 0.99)
MCOP	-0.44 (-4.58, 3.76)	-3.02 (-11.5, 5.38)
MBzP	2.44 (-2.77, 7.65)	-2.97 (-12.1, 6.07)
MiBP	4.95 (0.27, 9.28)	-4.70 (-11.8, 2.08)

Inflammation results

N=87 women

N=157 observations

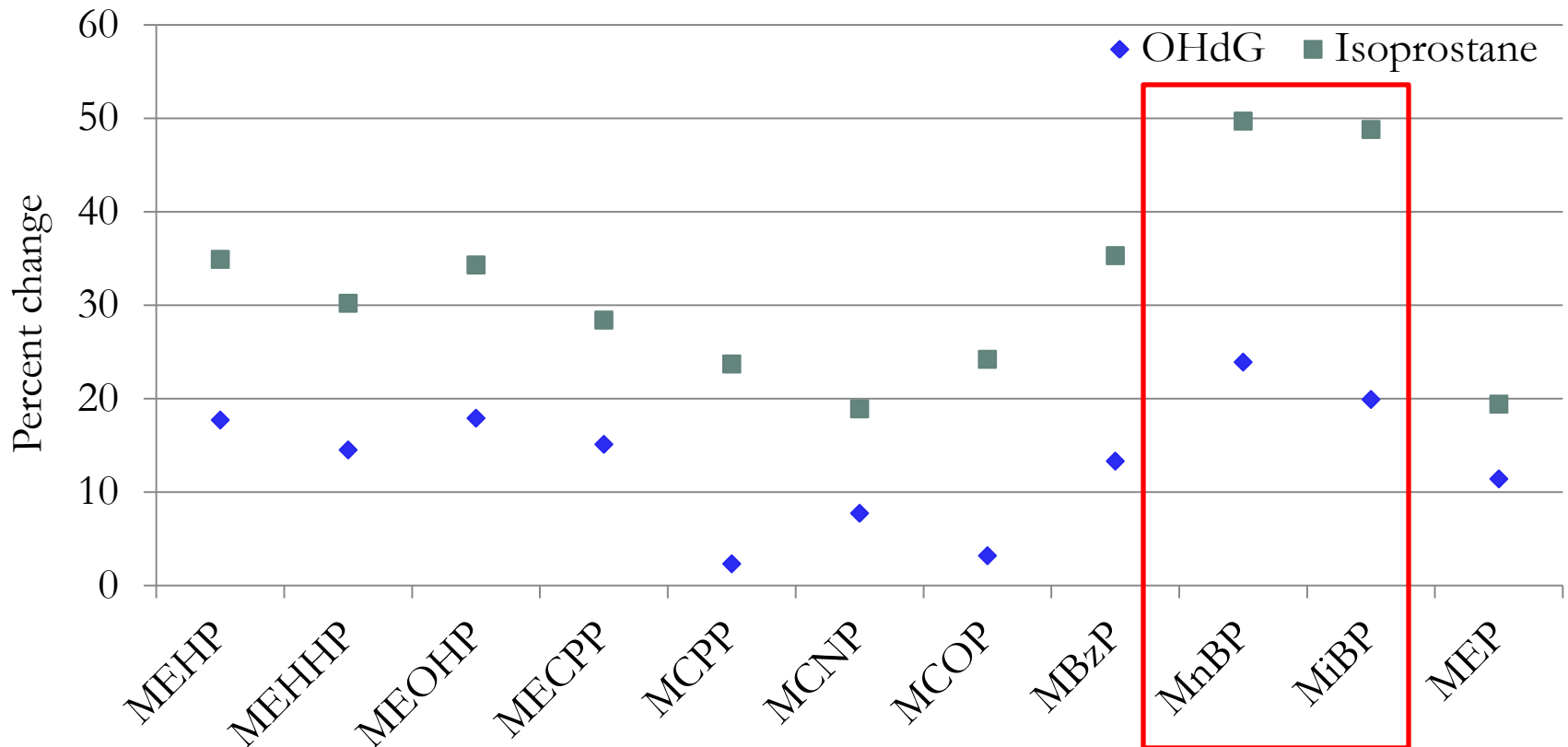
	CRP	IL-1 β	IL-6
	% Δ (95% CI)	% Δ (95% CI)	% Δ (95% CI)
MEHP	8.55 (-7.27, 27.1)	5.41 (-12.0, 26.3)	15.9 (-4.58, 40.8)
MECPP	4.25 (-9.95, 20.7)	8.06 (-8.37, 27.4)	18.8 (-0.59, 42.1)
MCPP	13.0 (-1.23, 29.4)	-4.50 (-18.1, 11.3)	2.87 (-13.0, 21.7)
MCNP	10.1 (-0.86, 22.2)	10.4 (-1.93, 24.3)	16.8 (2.69, 32.9)

+ No associations with IL-10 or TNF- α

Oxidative stress results

N=46 women

N=125 observations



Replication of results in a nested case-control study from Boston

Research

A Section 508-conformant HTML version of this article is available at <http://dx.doi.org/10.1289/ehp.1307996>.

Urinary Phthalate Metabolites and Biomarkers of Oxidative Stress in Pregnant Women: A Repeated Measures Analysis

Kelly K. Ferguson,¹ Thomas F. McElrath,² Yin-Hsiu Chen,³ Bhramar Mukherjee,³ and John D. Meeker¹

¹Department of Environmental Health Sciences, University of Michigan School of Public Health, Ann Arbor, Michigan, USA; ²Division of Maternal-Fetal Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts, USA; ³Department of Biostatistics, University of Michigan School of Public Health, Ann Arbor, Michigan, USA

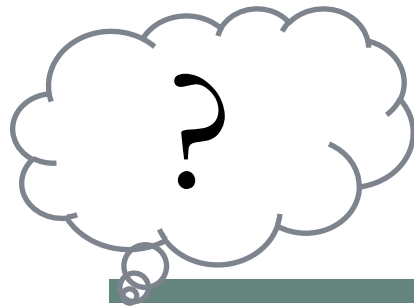
Increased 8-isoprostane and 8-OHdG in association with most phthalate metabolites

+ Inflammation markers and phthalates paper under review

Positive association between MCPP and IL-6, otherwise null

+ Recently completed measurement of thyroid hormones at 4 time points during pregnancy

Analysis underway



Future directions

- Associations with birth outcomes
- Mediation of phthalate-birth outcome relationships by mechanisms examined
- Associations with other and mixed exposures
- Engaging with community and reporting back results
- Follow-up on children

Thank you!

University of Michigan

Dr. John Meeker

Lauren Johns

Dr. David Cantonwine

Dr. Bhramar Mukherjee

University of Puerto Rico

Dr. Jose Cordero

Dr. Liza Anzalota

Northeastern University

Dr. Akram Alshawabkeh

Funding sources

NIEHS P30 Core Center (P30ES017885)

NIEHS P42 Superfund Program (P42 ES017198)

Collaborators

Dr. Antonia Calafat (CDC, Phthalates)

Dr. Dan McConnell (Hormones)

Dr. Joel Whitfield (Inflammation)

Dr. Elizabeth Hurst (Oxidative stress)