Maternal and Paternal Preconception Endocrine Disrupting Chemicals Exposure and Birth Outcomes

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PLAN

01
BACKGROUND (CM)

02
STUDY DESIGN (CM)

03
METHODS (YZ)

04
MXITURES ANALYSIS (YZ)

05
PRETERM BIRTH AND BIRTHWEIGHT (YZ)

06
CONCLUSIONS (CM)

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Works to understand how the Environment impacts reproductive health from the very earliest stages of life – from the formation of gametes and embryos – to the birth of infants and throughout child health and development.

Our mission is to Use cutting-edge evidence to inform clinical practice, translate science into policy action, and implement prevention strategies to improve the health of mothers, fathers, and their children.

SEED
Scientific Early Life Environmental Health & Development Program

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01

BACKGROUND

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Pregnancy and Birth
Couple-based outcome

Birth Outcomes
Prenatal period
Preconception period

Preconception Period
Oogenesis
Spermatogenesis
Uterine receptivity
Overall health

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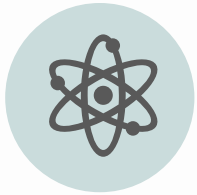
BACKGROUND



EDCs

Exogenous chemicals that interfere with any aspect of endocrine system or hormonal action

PHTHALATES

High Molecular Weight
Medical devices, toys

Low Molecular Weight
Paints, adhesives
Personal care products

BPA

Plastic bottles
Food packaging
Toys

MIXTURES

Beyond a single-chemical problem, real word exposure scenarios are much more complex

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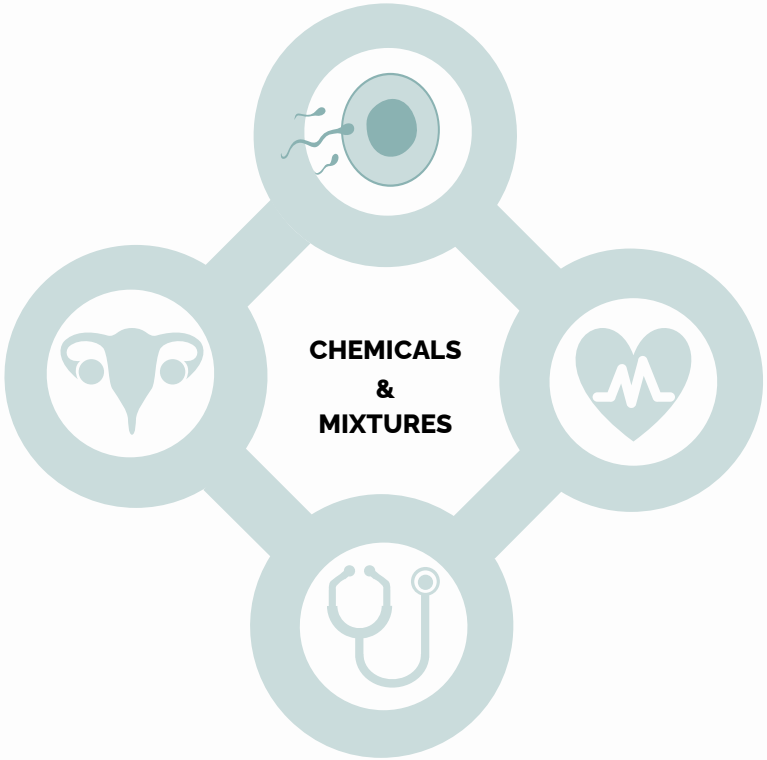
BACKGROUND

ENDOCRINE
Alters any aspect of endocrine function

EPIGENETIC
Alters epigenetic regulation

Genomic imprinting required for embryo-fetal development



IMMUNE
Impacts inflammation and immune function

METABOLIC
Impacts metabolic processes and regulation

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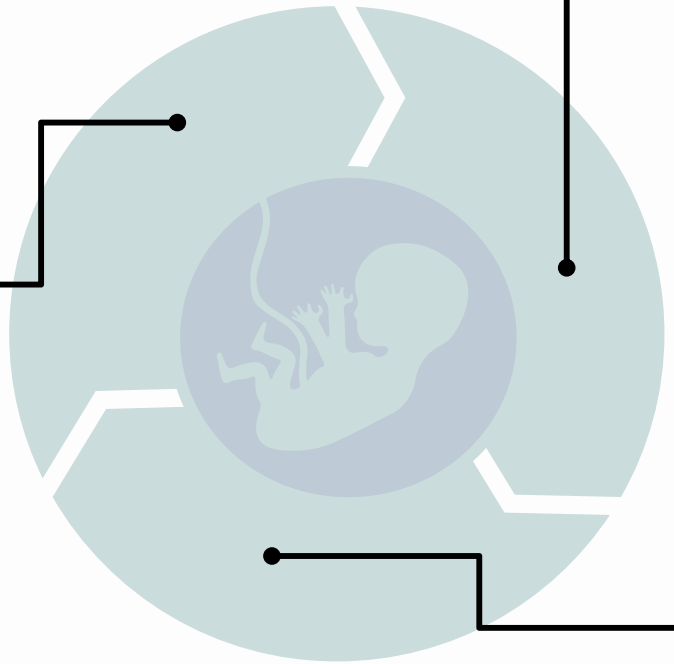
HYPOTHESIS



PRECONCEPTION

Chemical mixtures impact reproduction before conception

DISCRUPTED EPIGENETICS

Oocytes and spermatozoa
Uterine receptivity

DISRUPTED PREGNANCY

Fertilization, implantation, embryogenesis

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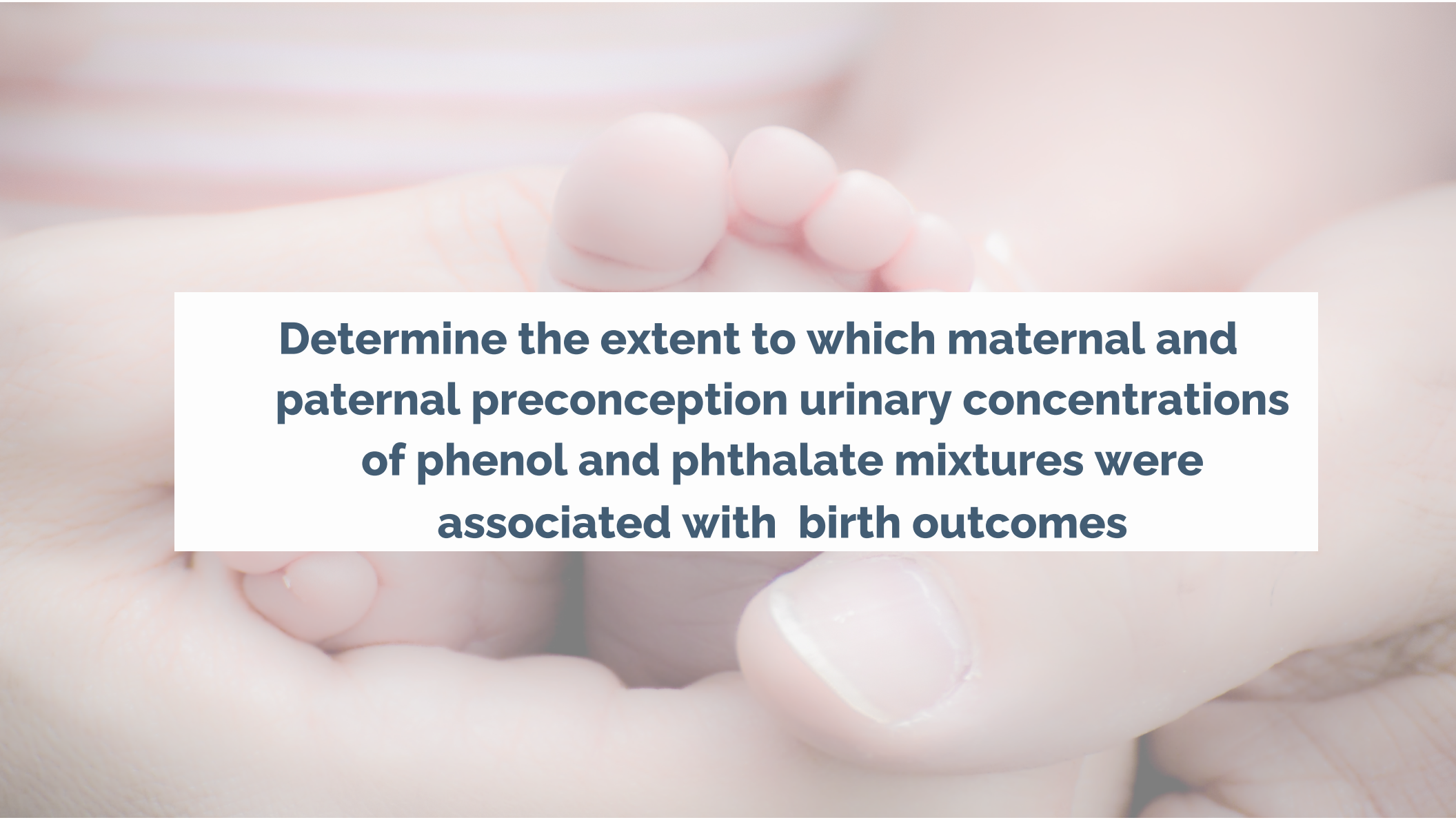

Determine the extent to which maternal and paternal preconception urinary concentrations of phenol and phthalate mixtures were associated with birth outcomes

02

STUDY DESIGN

PROSPECTIVE PRECONCEPTION COHORT
EARTH STUDY

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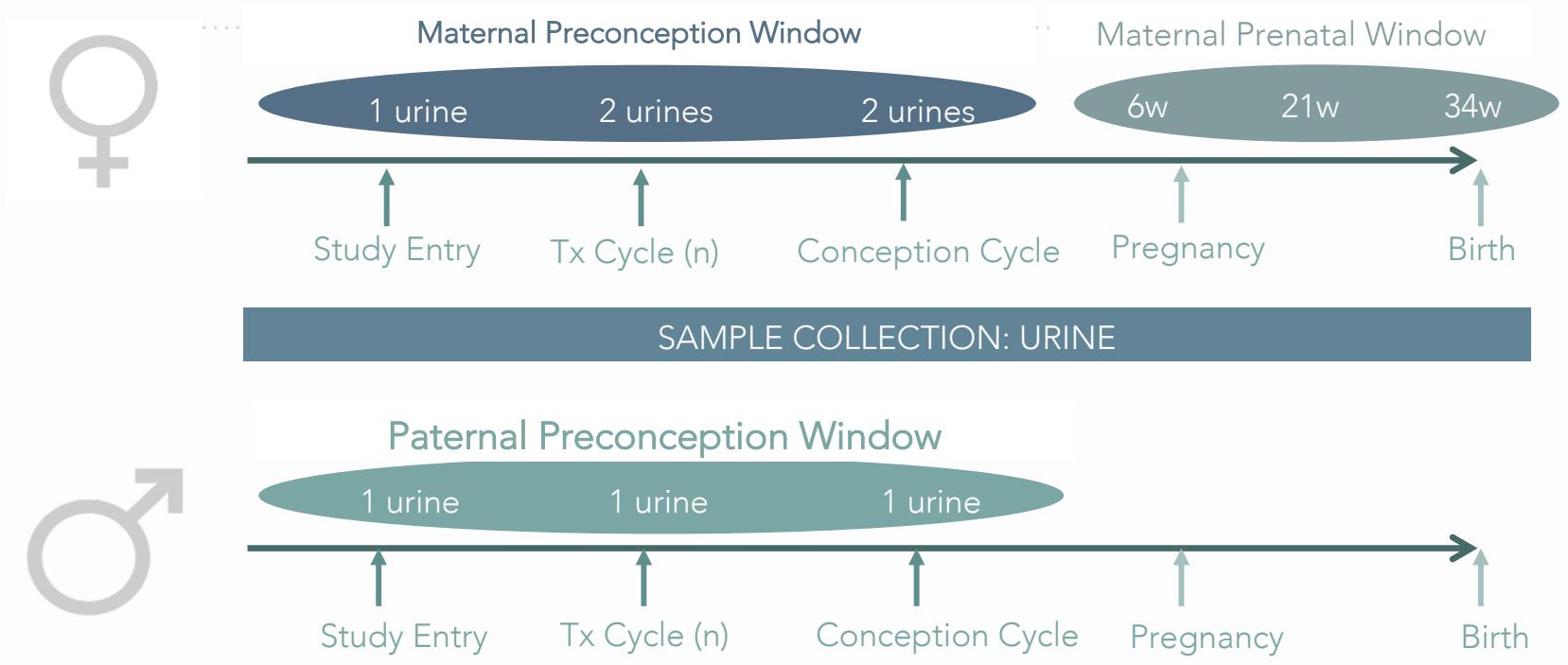
STUDY DESIGN



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03

METHODS

EXPOSURES, OUTCOMES

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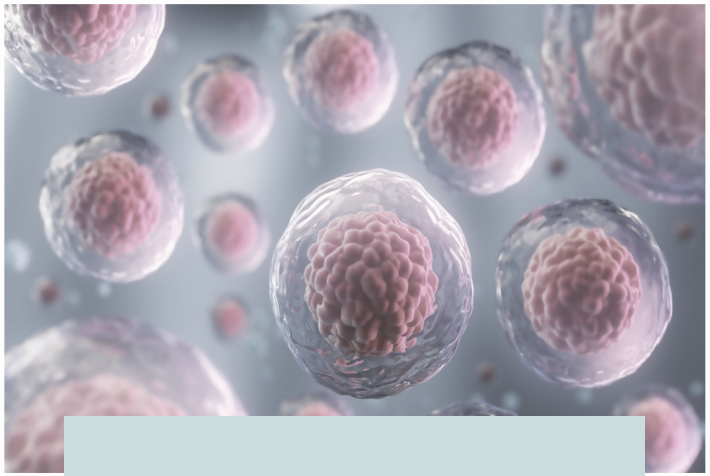
METHODS



EXPOSURES

Urinary Concentrations
11 phthalate metabolites
BPA
Parabens
Mixtures

OUTCOMES

Medical Records
Birthweight (g)
Gestational age accuracy
Preterm Birth (<37 weeks)

04

ANALYSIS

SINGLE CHEMICAL AND MIXTURES

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ANALYSIS

MIXTURE OF CHEMICALS
Individual preconception windows
Couples' joint window

PRINCIPAL COMPONENT ANALYSIS
PCA

BAYESIAN KERNAL MACHINE REGRESSION
BKMR

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MIXTURES METHODS

PCA

- Reduces individual biomarker concentrations into uncorrelated groups (factors) based on the correlation structure
- Useful for the real-life exposure patterns and potential shared sources
- Regression models were fit to examine the association between the PCA-derived groups and birth outcomes

BKMR

- Univariate associations, interactions, and cumulative effect of the mixture
- Hierarchical variable selection in BKMR compares the relative importance of groups (e.g., maternal group vs paternal)
- PCA-derived factors informed groups within in maternal and paternal BKMR models
- Permits examination of relative impact of maternal vs paternal mixture groups on outcomes

ANALYSIS

COVARIATES

Selected a priori w casual diagram
Maternal covariates added to paternal models

MATERNAL AND PATERNAL

Age, BMI, education, smoking, race, fertility treatment

COUPLE MODEL

Adjusted for all maternal and paternal covariates

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RESULTS

PRETERM BIRTH AND BIRTHWEIGHT

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RESULTS

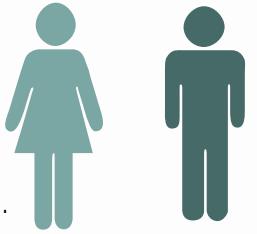
FEMALE

N=384
83% Nulliparous
~ 35 years of age

MALE

N=211
27% Male Factor
~ 36 years of age

COUPLES



N=203
White
Educated
Non-Smokers

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PRETERM BIRTH

RESULTS

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PCA MODELS

Table 1. Risk Ratio of Preterm Birth for every unit increase in PCA Factor Score

PCA-derived factors	Adjusted RR (95%CI) Preterm Birth	
	Maternal	Paternal
DEHP-BPA factor	1.36 (1.00, 1.84)	1.47 (0.90, 2.42)
Paraben factor	0.93 (0.65, 1.32)	1.43 (0.86, 2.38)
High molecular weight phthalate factor	0.88 (0.61, 1.26)	0.67 (0.38, 1.17)
Low molecular weight phthalate factor	0.96 (0.65, 1.41)	0.89 (0.51, 1.52)

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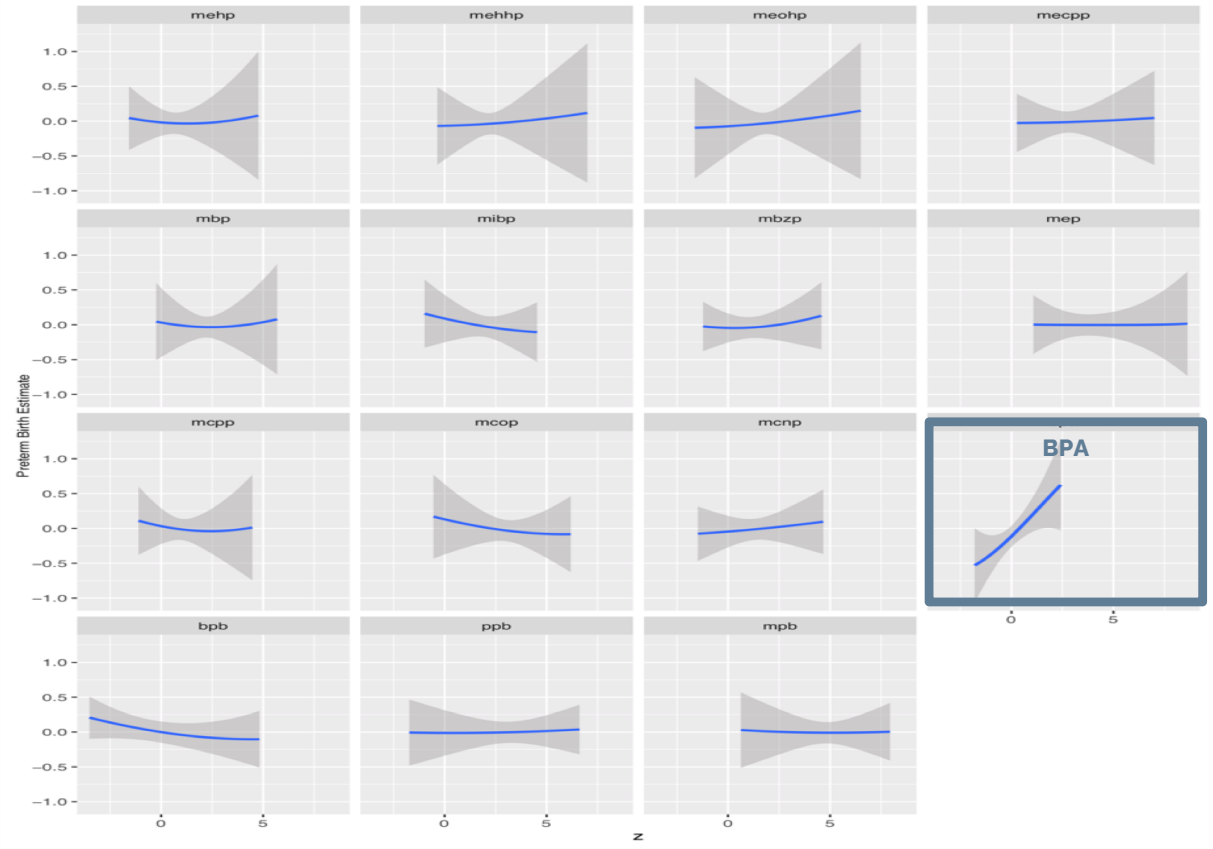
MATERNAL EXPOSURE – PRETERM BIRTH

This BKMR derived figure depicts the association between a given exposure concentration and preterm birth, holding all other individual biomarkers at their median concentration



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PATERNAL EXPOSURE – PRETERM BIRTH

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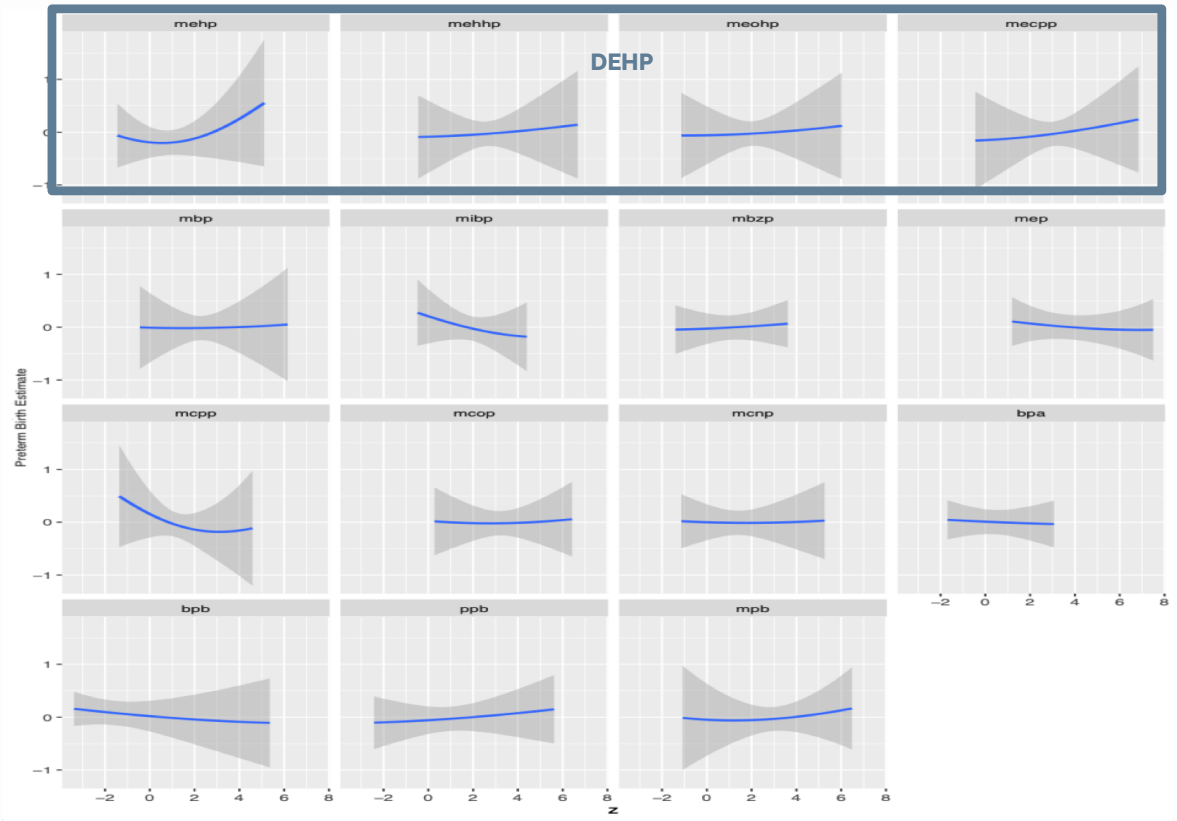

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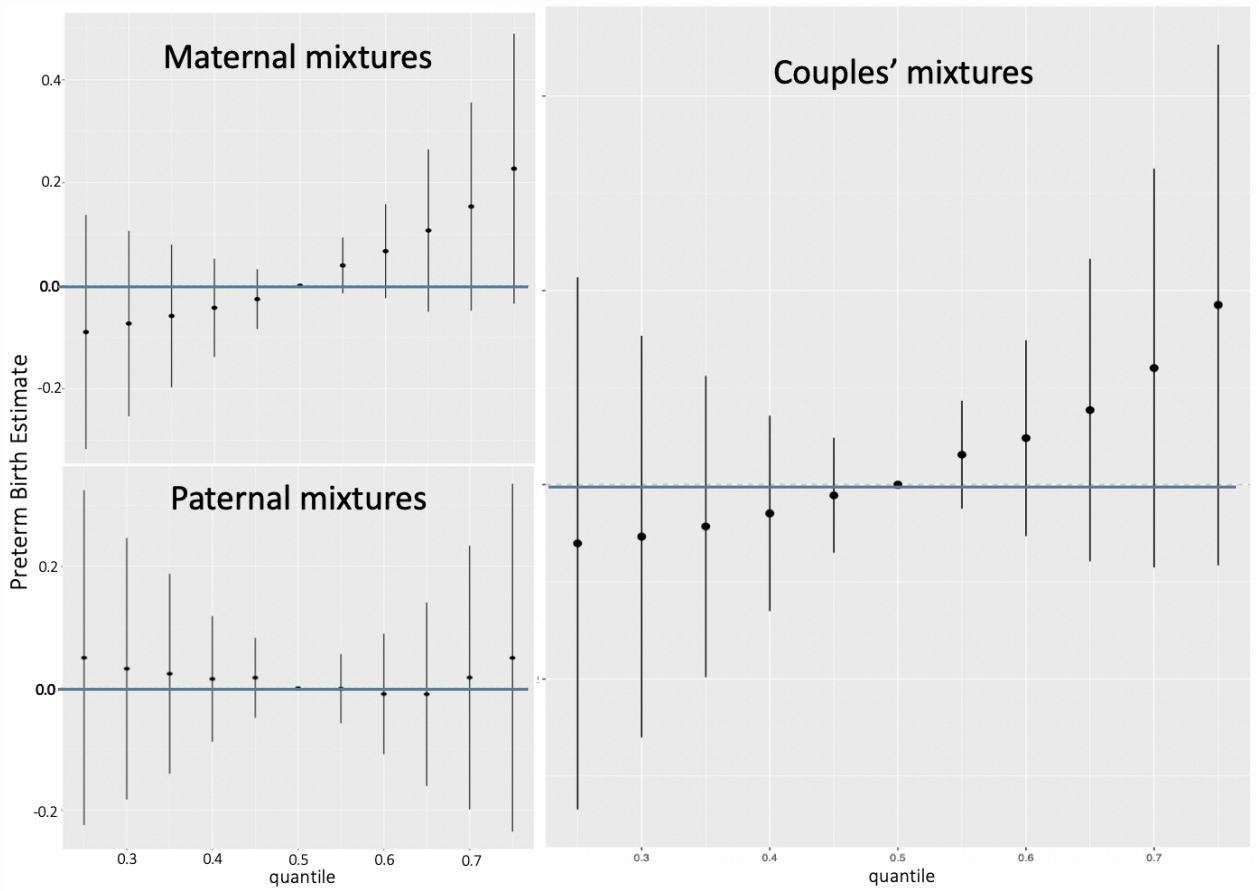
RESULTS – PRETERM BIRTH

CUMULATIVE EFFECT OF TOTAL MIXTURE



Increasing trend of **preterm birth** estimate across quantiles of **maternal** and **couples**' total preconception mixture concentrations

RESULTS

BKMR – Posterior Inclusion Probability (PIP)

Maternal preconception model: DEHP-BPA high PIP

Paternal preconception model: DEHP-BPA high PIP

Couple-based model: similar PIP for maternal and paternal groups

BKMR - SUMMARY

Maternal preconception **BPA** – associated with higher preterm birth risk, holding all other biomarker concentrations at their median

Paternal preconception **DEHP** metabolites – associated with higher preterm birth risk, holding all other biomarker concentrations at their median

Higher preterm birth across quantiles of **maternal** and **couples' total mixture** concentrations

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BIRTHWEIGHT

RESULTS

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PCA MODELS

Table 2. Change in Birthweight (g) for every unit increase in PCA Factor Score

PCA-derived factors	Adjusted Change in Birthweight (gram)	
	Maternal	Paternal
DEHP-BPA factor	-1.99 (-55.51, 51.53)	-63.29 (-133.82, 7.24)
Paraben factor	-18.60 (-72.58, 35.39)	16.21 (-51.57, 83.98)
High molecular weight phthalate factor	16.95 (-37.31, 71.22)	-48.69 (-116.11, 18.73)
Low molecular weight phthalate factor	-51.45 (-105.09, 2.18)	-72.92 (-141.39, -4.45)

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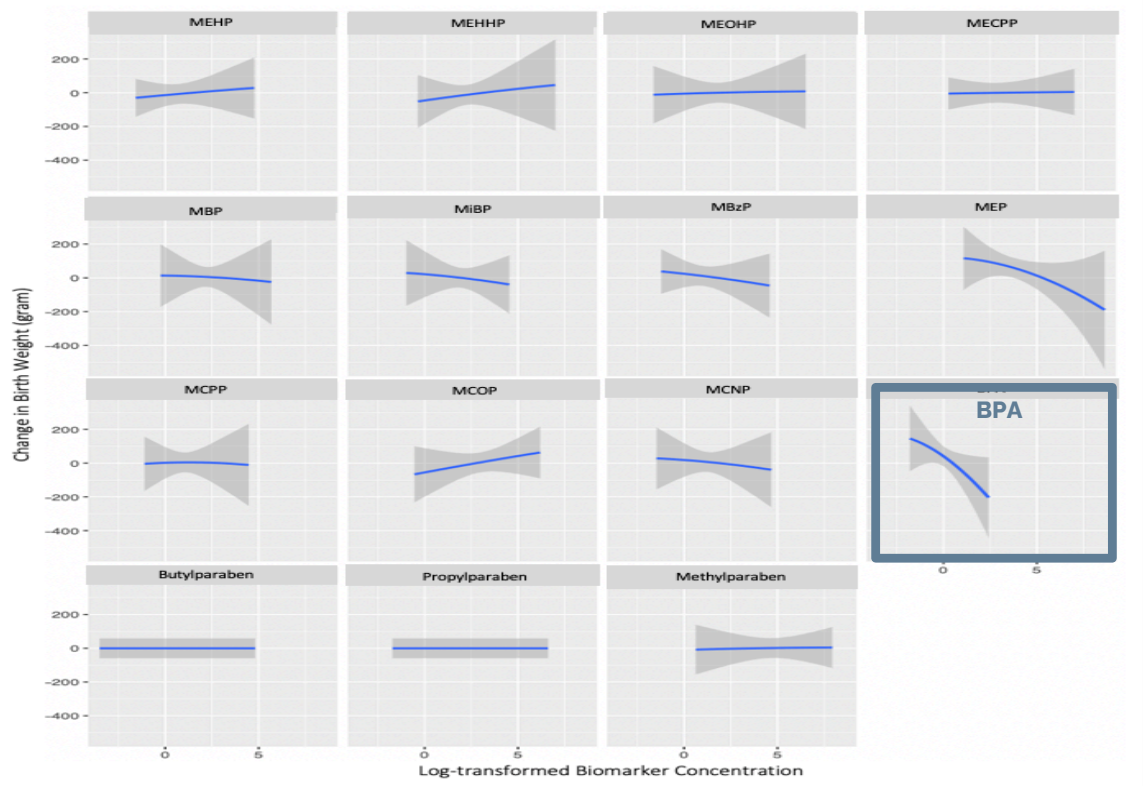
MATERNAL EXPOSURE – BIRTHWEIGHT

This BKMR derived figure depicts the association between a given exposure concentration and birthweight, holding all other individual biomarkers at their median concentration



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PATERNAL EXPOSURE – BIRTHWEIGHT

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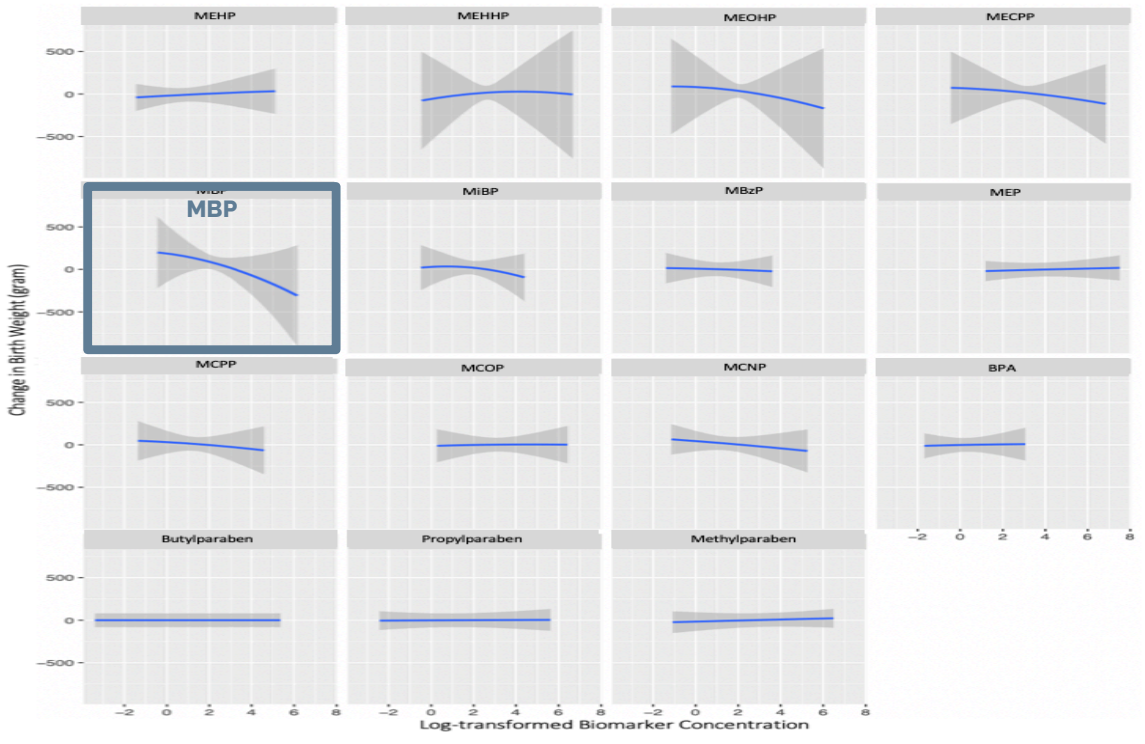

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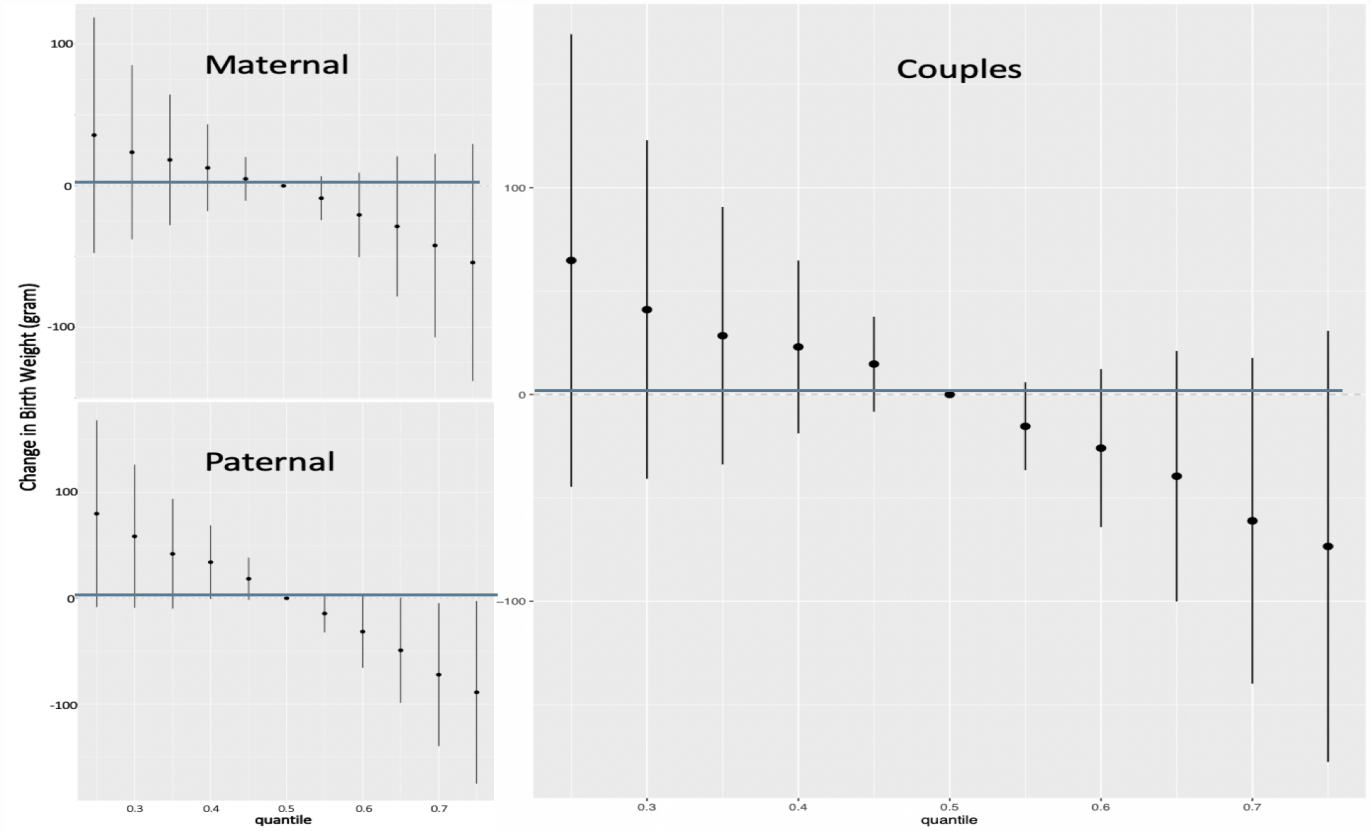
RESULTS - BIRTHWEIGHT

CUMULATIVE EFFECT OF TOTAL MIXTURE



Decreasing trend of **birthweight** across quantiles of **maternal**, **paternal** and **couples**' total preconception mixture concentrations

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SUMMARY

BKMR– Posterior Inclusion Probability (PIP)

Maternal preconception model: DEHP-BPA high PIP

Paternal preconception model: DEHP-BPA and low molecular weight phthalate - high PIP

Couple-based model: higher PIP for **paternal mixture group** than maternal mixture group

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SUMMARY

Maternal preconception **BPA** exposure associated with decreased birthweight, holding all other biomarker concentrations at their median

Paternal preconception **MBP** exposure associated with decreased birthweight, holding all other biomarker concentrations at their median

Lower **birthweight** across quantiles of **maternal**, **paternal** and **couples' total** mixture concentrations

06

CONCLUSIONS

INTERPRETATION AND IMPLICAITONS

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CONCLUSIONS

PRETERM BIRTH

MODELS	WINDOW	BIOMARKER/FACTOR	FINDING
PCA	Maternal	DEHP-BPA	↑ Preterm birth
PCA	Paternal	DEHP-BPA	↑ Preterm birth
PCA	Paternal	Paraben	↑ Preterm birth
BKMR	Maternal	BPA	↑ Preterm birth
BKMR	Maternal	Total Mixture	↑ Preterm birth
BKMR	Paternal	DEHP	↑ Preterm birth
BKMR	Couples	Total Mixture	↑ Preterm birth

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PRETERM BIRTH RISK

CONCLUSIONS

Maternal : DEHP-BPA, BPA, and Total Mixture

Paternal: DEHP-BPA, Paraben, DEHP

Couples: Total Mixture

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FINDINGS

BIRTHWEIGHT

MODELS	WINDOW	BIOMARKER/FACTOR	FINDING
PCR	Paternal	DEHP-BPA	↓ Birthweight
PCR	Paternal	LMWP	↓ Birthweight
BKMR	Maternal	BPA	↓ Birthweight
BKMR	Paternal	MBP	↓ Birthweight
BKMR	Maternal	Total Mixture	↓ Birthweight
BKMR	Paternal	Total Mixture	↓ Birthweight
BKMR	Couples	Total Mixture	↓ Birthweight

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BIRTHWEIGHT

CONCLUSIONS

Paternal : DEHP-BPA, LMWP, MBP, and Total Mixture

Maternal: BPA, and Total Mixture

Couples' Total Mixture

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IMPLICATIONS

CONCLUSIONS

Fathers and Mothers phthalate and phenol mixtures contributed equally to preterm birth risk

Couples' total mixture associated with lower birthweight

Fathers' phthalate and phenol exposure reduces birthweight more than mothers'

Couples' preconception health is a modifiable exposure

Interventions at the couple level before pregnancy attempt may improve perinatal outcomes

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