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**ANALYSIS PLAN: Arsenic exposure during pregnancy and size at birth: data harmonization across three US cohorts**

## **Hypothesis**

Arsenic exposure during pregnancy is inversely associated with gestational age, and birth anthropometry.

## **Participants**

The study population includes participants of three birth US cohorts (i.e., PROTECT cohort, New Hampshire Birth Cohort Study, and METALS) led by three SRP Centers (i.e., Northeastern University, Dartmouth College, and University of New Mexico).

## **Exposure**

*In utero* arsenic exposure using maternal urinary arsenic concentrations (i.e., total arsenic and arsenic speciation including inorganic arsenic (AsIII + AsV), MMA, DMA, and arsenobetaine when available). Also, maternal inorganic arsenic methylation capacity (i.e., methylation indexes and arsenic species percentages).

## **Outcome**

Infants’ gestational age at birth (weeks, continuous), weight (g, continuous), head circumference (cm, continuous), length (cm, continuous), small for gestational age, ponderal index at birth (kg/m3, continuous), and z-scores of birth outcomes (continuous).

## **Statistical analysis**

Regression analysis including outcomes of interest as dependent variable and maternal urinary arsenic concentrations log-transformed as independent variable adjusting for potential confounding factors.

## **Covariates**

*Maternal*: age (years, continuous), socioeconomic status (categorical), education (categorical), race/ethnicity (categorical), parity (continuous), pre-pregnancy BMI (kg/m2, continuous), smoke during pregnancy (dichotomous), weight gain during pregnancy (continuous), delivery type (categorical), pregnancy complications (categorical), urine specific gravity (continuous), folic acid supplement (categorical) and fish/seafood consumption (continuous).

*Infant*: gestational age (weeks, continuous) and sex (dichotomous).

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