**S2 Text. Statistical analysis plan.**

**Statistical analysis**

**Body Mass Index (exposure) and covariates**
- All statistical analyses to be conducted using BMI, parental age, maternal parity, and offspring’s age at blood collection as continuous variables.
- Potential confounders to adjust models for: parental age, smoking, education, head of household social class, maternal parity, offspring’s age at blood collection and sex.

**Metabolite data (outcome)**
- Exclude ratio metabolic traits with exception of fatty acid ratios.
- Define the list of outcomes (metabolic traits): check the overlap between the different cohorts (not all cohorts have the same metabolites measured).
- Quality control of metabolic traits data: plot concentration or % versus observation number (or box plots) and check for outliers. Do not remove any outliers in the first instance unless there is a clear indication that it is an actual artifact in the data (i.e. observations lying orders or magnitude away from the cloud of data). Perform sensitivity analysis for the other outliers.
- Establish a p-value threshold considering multiple testing and the correlation structure of the metabolic data: perform Principal Component Analysis (PCA) on z-scored metabolic trait data and extract the number of principal components (A) that explain at least 95% of the variance, the corrected p-value threshold is given by \( \alpha/A \) where \( \alpha = 0.05 \).

**Relationship of parental BMI and metabolic traits**
- Analysis to be performed on trios of mother-father-offspring who have no missing data on at least one trio of exposures/outcome/covariables.
- Models will be computed for standardized (z-scored) and un-standardized metabolic traits.
- **Conduct a one-stage and a two-stage individual participant data (IPD) meta-analysis.**
- **Two-stage IPD meta-analysis:** perform all analyses individually on each cohort and for mothers and fathers separately.
o Standardize metabolic traits separately for each cohort and for mothers and fathers.

o Use linear regression with robust standard errors to estimate associations between parental BMI and offspring standardized (z-scored) and unstandardized metabolic traits. Adjust models for parental age, smoking, education, head of household social class, maternal parity, offspring’s age at blood collection and sex.

o Combine the results of each linear regression in each cohort and parent, test for heterogeneity ($I^2$) and meta-analyze the results using random effects for mothers and fathers separately.

- **One-stage IPD meta-analysis**: Vertically concatenate individual cohort data after variable harmonization.
  
o Standardize metabolic traits across cohorts. Standardize paternal BMI across cohorts, separately for mothers and fathers.
  
o Compute adjusted models using linear regression with robust standard errors for mothers and fathers separately, include a dummy variable indicating cohort membership.
  
o Use bootstrap (1000 replications) to compute the difference between the associations of mother and father’s BMI with outcomes.

**Data visualization and results presentation**

- Produce a flow diagram of participant inclusion in the study and a descriptive table with information regarding each cohort.

- Produce forest plots of the results, from the association between parental BMI with standardized metabolic traits, for individual cohort analysis, one and two-stage IPD meta-analysis.

- Produce a scatter plot with regression line of the results of two-stage IPD versus one-stage IPD separately for mother and father, and one-stage IPD father versus mother.

- Produce tables with results, of the association between parental BMI with unstandardized metabolic traits, for individual cohort analysis, one and two-stage IPD meta-analysis.