Reviewer's report

Title: A birth cohort study to investigate the association between prenatal phthalate and bisphenol A exposures and fetal markers of metabolic dysfunction

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Reviewer: Elizabeth Hatch

Reviewer's report:

Overall, this is a well-written and interesting paper on the association between first trimester levels of several phthalate metabolites, BPA and cord blood levels of adiponectin and leptin. The analysis appears to be well conducted although there are a few concerns.

• The 10% and 90% cutpoints for adiponectin and leptin seem quite arbitrary. It would be preferable to explore the data first using both continuous outcome and exposure measures, for example using LOESS or spline regression.

• Given that the leptin levels are so different in males versus females, it would be useful to see the results separately by infant sex. Just testing for statistical significance to determine whether there is an ‘interaction’ isn’t the right approach since it depends upon the statistical model used (e.g. additive vs. multiplicative scale). It would be useful to see both leptin and adiponectin stratified tables or at least present them in the text, especially given previous findings showing differences by gender in BPA results (ref 25).

• Table 2: p-values are unnecessary and don’t tell the reader anything about the direction of the association. Frequencies and %s are enough. Also, the % of current smokers with high leptin levels must be wrong…15.3%?

• in general, there is too much emphasis on statistical significance in the paper. Relying on p-values blends information about effect size with precision (sample size) yet fails to provide clear evidence about either parameter. In addition, the reliance on p-values is discouraged in the ICMJE’s Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals, which encourage authors to “When possible, quantify findings and present them with appropriate indicators of measurement error or uncertainty (such as confidence intervals)...Avoid relying solely on statistical hypothesis testing, such as p-values, which fail to convey important information about effect size and precision of estimates.”

• It is somewhat unclear why GWG was chosen as a confounder since it occurs after the measurement of phthalates and BPA...e.g. could be a downstream variable.

• On page 8, it is stated that the formula for adjustment for specific gravity ‘applied to phthalate concentrations in descriptive but not mv analyses...’ Was BPA supposed to be in this sentence also?

• p. 13, re: non-differential misclassification...this sentence implies that bias
would be to null, but this is true only for extreme categories (highest to lowest quartile). NDM can cause upward bias in intermediate categories, which might explain lack of dose response, e.g for MBzP.

- The statement in the conclusion, ‘While we did not observe any evidence of a monotonic dose-response relationship between prenatal exposure to phthalates or BPA and fetal adipokine levels’ would be more convincing if some of the data were shown graphically. For example, MBzP and MCPP both appear to be associated with lower odds of ‘low leptin’ and higher odds of high leptin, so I’m not convinced there’s no dose-response for those metabolites.

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

i declare i have no competing interests