Reviewer's report

Title: The Association between Maternal Urinary Phthalate Concentrations and Blood Pressure in Pregnancy: The HOME Study

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Reviewer: Kelly Ferguson

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The association between maternal urinary phthalate concentrations and blood pressure in pregnancy: the home study

The present manuscript utilizes a strong cohort study to examine a novel research question, which is whether a relationship exists between maternal phthalate exposure in gestation and changes in blood pressure or risk of hypertensive disorders of pregnancy. The analysis is complete and sound, and the results are supportive of an association between MBzP concentrations at 16 weeks gestation and increased maternal blood pressure before and after 20 weeks gestation, and with increased risk of hypertensive disorders of pregnancy. I have two major comments on the paper which I believe will be easily addressed, but should be necessary before acceptance:

Major compulsory revisions:

1. I very much appreciate the analysis of the blood pressure measurements alongside the clinical outcomes, as this may be more sensitive for detecting effects. However it is somewhat unclear how measurements were abstracted. Please clarify the following in the methods: 1) How many total measurements were available in medical records, before 20 weeks or after? 2) Why was maximum blood pressure post 20 weeks used? Why not maximum in early pregnancy? Was max based on systolic or diastolic, or were they considered independently? I'm mostly concerned about the maximum because it seems to me that this measure could be more erroneous than a measure in the middle (or an average of all measures after 20 weeks). For example, a stressful morning or walking to the clinic could spike blood pressure which would not be related to phthalate exposure, and thus would bias results toward the null.

2. Since this is an online journal presentation of some additional results in the paper and in a supplement would be helpful. The methods shows that associations between phthalates at 16 weeks and 20+ weeks gestation BP measures were analyzed, but these are not shown except in the tercile figure with MBzP and are not described in the results. Also, the associations between other metabolites or sums and the hypertensive disorders of pregnancy should be shown. I think this should go in the primary paper in Table 4. My absolute preference would be for models with continuous phthalates (16 weeks, 26 weeks, average) and the outcome, for each metabolite. (The terciles take up more space and don’t really add much since the associations appear to be linear.) But
continuous or tertiles, all metabolites should be presented in the main paper so that the number of comparisons and directions of other associations can be observed.

Minor essential revisions:
1. Background, second paragraph: Remove “(Table 1)” and cite.
2. Results, second paragraph: “MBzP...significantly associated with increased mean diastolic blood pressure.” The word “mean” suggests that the models were between phthalate levels at 16 weeks and an average of blood pressure measures, but I believe these were linear mixed models? Please clarify.
3. Results, third paragraph: P values for trend do not match those in table 4.
4. Table 2 is not mentioned in the text, and I think it would be nice to show the differences in blood pressure measurements and distributions of hypertensive disorders of pregnancy in association with these covariates. Would also be great to have tests for differences in levels across categories (recommend LMM so that repeated phthalate measures are adequately accounted for in tests), and the description of the summary measures should be moved to the methods. Last, were these in all samples measured or just 16 weeks? Please specify.
5. Discussion, fourth paragraph: If you’re going to mention it please describe how B-hydroxysteroid dehydrogenase is relevant.
6. Discussion, fifth paragraph: Please comment on timing of exposure in relation to your outcomes of interest. Beyond variability, what window do you expect will be most strongly tied to blood pressure changes and do your measurements reflect this?

Discretionary revisions:
1. Discussion, third paragraph: I think the last sentence is worded a little strongly.
2. Table 3: I think this would look better with one column for systolic and one column for diastolic.

Level of interest: An article of outstanding merit and interest 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 that I have no competing interests.