Reviewer’s report

Title: Very Low-Level Prenatal Mercury Exposure and Behaviors in Children: The HOME Study

Version: 0 Date: 23 Apr 2018

Reviewer: David Bellinger

Reviewer's report:

This is an excellent paper from a group that is highly experienced in addressing the methodological challenges of conducting, analyzing, and interpreting studies such as this one. Although the findings are largely null, except for the suggestive findings with regard to prenatal methylmercury exposure and anxiety, it nevertheless is an important contribution by providing information about a portion of the dosing range about which little is known. The findings suggest that any threshold for adverse effects becomes detectable somewhere between the exposures studied in the HOME study and those in the studies cited that reported significant adverse associations.

Comments for the authors’ consideration.

1. Justification should be provided for the choice of cut-points for maternal age and income. Were these, like the one used for HOME scores, based solely on the distributions of these variables or were these motivated by some other consideration?

2. The mixed models combined children's BASC scores at 2, 3, 4, 5, and 8 years. It is likely that BASC scores are not equally sensitive at all ages, especially for internalizing behaviors. Were analyses conducted that focused solely on scores at 8 years of age (all BASC scores, not just the anxiety scale), as I would expect that scores at this age might provide the best opportunity to evaluate an association with prenatal mercury.

3. Table 1 could be made more informative. Given that 320 women contribute data to both columns, the absence of important differences found it is not surprising. It would be more helpful to compare the 320 women/children for whom data were available to the 69 of the women who delivered singleton children. In the text (first paragraph of Results), who the 320 dyads are needs to be explained.

4. The difference in the directions of the findings for parent reports and child reports of anxiety is interesting. I agree that the findings of less anxiety among children with higher prenatal mercury is probably spurious. I think children under the age of 10 tend not to be very reliable informants of their own strengths and weaknesses. This cannot explain the direction of the association, of course, but it does reduce confidence that the association is real.
5. When the critical exposure biomarker is measured in the mother and the critical endpoint is maternal ratings of child behavior, one always has to consider whether the toxicant might have affected maternal perceptions and interpretations of that behavior. The inclusion of (self-rated) maternal depression as a covariate appears to have been an effort to consider this, but there are other possibilities. Some mention of this in the Discussion could be considered. Also, use of a higher cut-off other than 13 (minimal depression) could be considered, as it is not obvious that that is the best choice.

Level of interest
Please indicate how interesting you found the manuscript:

An article of importance in its field

Quality of written English
Please indicate the quality of language in the manuscript:

Acceptable

Declaration of competing interests
Please complete a declaration of competing interests, considering the following questions:

1. Have you in the past five years received reimbursements, fees, funding, or salary from an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

2. Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

3. Do you hold or are you currently applying for any patents relating to the content of the manuscript?

4. Have you received reimbursements, fees, funding, or salary from an organization that holds or has applied for patents relating to the content of the manuscript?

5. Do you have any other financial competing interests?

6. Do you have any non-financial competing interests in relation to this paper?

If you can answer no to all of the above, write 'I declare that I have no competing interests' below. If your reply is yes to any, please give details below.

I declare that I have no competing interests.

I agree to the open peer review policy of the journal. I understand that my name will be included on my report to the authors and, if the manuscript is accepted for publication, my named report
including any attachments I upload will be posted on the website along with the authors' responses. I agree for my report to be made available under an Open Access Creative Commons CC-BY license (http://creativecommons.org/licenses/by/4.0/). I understand that any comments which I do not wish to be included in my named report can be included as confidential comments to the editors, which will not be published.

I agree to the open peer review policy of the journal