Reviewer's report

Title: Environmental risk factors of pregnancy outcomes; a summary of recent meta-analyses of epidemiological studies

Version: 1 Date: 20 September 2012

Reviewer: Gayle Windham

Reviewer's report:

This paper takes on the large task of reviewing meta-analyses on a number of chemical risk factors in relation to several adverse pregnancy outcomes. While this is an important topic, the paper suffers from a lack of focus and presentation of new insight or recommendations.

Major Compulsory Revisions:

It is not clear whether the authors wish to present a review of exogenous risk factors for adverse pregnancy outcomes that might be useful as a synthesis of current data for potential policy (or etiological) purposes, or a methodological evaluation of the conduct of meta-analyses in this topic area. Perhaps both, but unfortunately it does not succeed, so further focus would be most helpful.

1. As it is organized by chemical group it would appear to be a review article, but it only summarizes what has already been presented in published meta-analyses (M-A) There is no further synthesis of data into conclusions about risk, by for example, combining the meta-analyses' results, even qualitatively, or comparing meta-analytic results and how those vary by the methodological aspects of the analysis chosen or studies included, or attempting to fill the gaps of meta-analyses examined to draw conclusions or calculate some final summary risk estimate for each of the various chemical groups. When determining risks, it is important that all appropriate data is included—did these meta-analyses do this or are there other papers available, or pooled data not as formal as a meta-analysis? Are M-A from only the last ten years enough to make conclusions? Be clear, in revising, on how this review adds to the understanding about risks of these chemicals.

2) If it is to serve as a methodological piece evaluating meta-analytic practices, much more information about the methods should be provided and explained. For example, “meta-analysis guidelines” mentioned in 2nd para of methods should be spelled out for the reader, as well as the various tests considered. In this case it would not seem necessary to split out the meta-analyses so finely (e.g. only 2-3/chemical), but rather evaluate them as a whole. I found little actual evaluation of the techniques used, but rather just a listing, with no summary. How did the methods affect results of the M-A? Is that M-A of high enough quality to consider in assessing risk? Or going further, can the M-A be replicated from information provided? An evaluation would usually lead to recommendations—what is still needed in this area, e.g. improvements in M-A in order to make conclusions about risks?
The area that becomes the focus of the paper will determine further revisions needed, so specific suggestions are difficult to make.

3) For example, the abstract and introduction will need to reflect the specific aim.

4) Methods section should be expanded as noted. I have some concern that the term “adverse pregnancy outcomes” (or others similar) were not used in the initial search so summary papers may have been missed. This appears to be the case by the 2 additional papers (of only 16 total) picked up by “other sources.” 5) If this becomes more of a review paper, other studies that contribute to risk, not included in M-A’s, should be added.

Results: 6) Might only need 1 of the tables, depending on focus. Table 2 might also be split if there is any way to group more similar exposures. 7) If this is an evaluation, the second paragraph should provide some quantification of the studies that followed guidelines, etc., and then actual assessment of the impact.

8) There may the most studies on ETS, but not the most meta-analyses, what is the evaluation of this result? 9) See comments above if this is to be a review piece. 10) Heterogeneity tests are mentioned, but not with respect to how many studies are included in the M-A, wouldn’t this affect possibility of heterogeneity?

Minor Essential Revisions (not necessarily for publication if fixed):

There were numerous problems with grammar, punctuation, formatting and errors, so these should be reviewed before publication as here I only note some examples. In addition, I note some areas needing clarification.

1. Abstract: Describe direction of associations with birthweight.

2. Introduction: punctuation to indicate associations greatly needed in 2nd sentence.

Methodology: 3. formatting of references with their test in last paragraph, first sentence is very confusing, but improved by end.

4. Last phrase of last sentence is very awkward; I would say “conducting” analyses by sub-groups “defined by....”

5. Define acronyms like MOOSE and ENRIECO.

Results: 6. Spell out all acronyms when first used (or in methods), and define endpoints once (e.g. LBW).

7. Shouldn’t flow diagram be referred to as “figure”?

8. Formatting of studies to list year and ref # is awkward.

9. I2 became I2 in many places, which was confusing.

10. Leonardi-Bee et al. 2008 and 2011 (or 2010 in ref list!) are not cited consistently or correctly in text and tables.

11. Results of ref 17 must be wrong as upper CI is same as OR (in water DBPs).

12. Ref 24 in text has slightly different OR than in table.

13. Throughout, one study is stated as: “conducted meta-analyses”, why plural for one study? Prefer single as for first sentence under occupation—at least
14. “Pesticides” sub-head should be inserted before Ngo studies. Ngo 2010 paragraph: said no heterogeneity, but then try to describe non-Vietnamese studies as having different RR than Vietnamese, so would delete. Results split out by study design—it appears there is only 1 cross-sectional, so add that N or say “study” not studies. The sentence really isn’t very useful, so would delete—e.g. risks all rather similar.

15. Punctuation really needed in third and sixth paras to aide understanding.

Table 2: 16. Hard to read, might consider splitting. 17. List studies in order presented in text.

18. There are several places where the specific outcome is unclear, e.g. Sapkota 2010, no assoc with what? If all congenital anomalies are lumped, so state.

10. In several places “only” appears but is not at all clear what it refers to—col 4 for ETS, or 5 for PM10, etc.

20. Watch the negative sign for bwt CI’s (Pope et al), may need CL’s with comma vs. hyphen.

21. Different fonts in different columns.

22. Under occupation, “Paternal” should be inserted before solvents for Logman.

Discretionary Revisions:

1. Comment about the 2 M-A’s on DBPs and VSDs producing nearly identical results—is this true or a typo?

2. Metals and other water contaminants were mentioned in methods, but not results, were none found? Or PFCs? (If so, lead to a possible recommendation?).

3. Mention results for DDE under POPs.

4. Discussion: another reason for small number of M-A may be only examining 10 years. More studied chemicals may have prior M-A’s.

5. In paragraph 5, say more how approaches followed guidelines even though not explicitly reported.

6. Several statements are rather vague—end of 4th, 6th and last paragraphs.

7. Paragraph 7 has interesting points that could be developed further, possibly into a recommendation.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Needs some language corrections before being published

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.