Author's response to reviews

Title: Does acute maternal stress in pregnancy affect infant health outcomes? Examination of a large cohort of infants born after the terrorist attacks of September 11, 2001

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Version: 2 Date: 27 May 2009

Author's response to reviews: see over
Dear BioMed Central Editorial Team,

Enclosed please find our revised manuscript “Does acute maternal stress in pregnancy affect infant health outcomes? Examination of a large cohort of infants born after the terrorist attacks of September 11, 2001.” To adequately address the reviewer comments we have incorporated revisions into the manuscript.

The authors appreciate the opportunity to respond to reviewer comments and all authors agree this revision has improved the clarity of the original manuscript. The revised version of the manuscript has been submitted, and a version with tracked changes is available upon request. Our responses (in bold) to each of the reviewers’ comments follow below:

**Reviewer's report**

**Title:** Does acute maternal stress in pregnancy affect infant health outcomes? Examination of a large cohort of infants born after the terrorist attacks of September 11, 2001

**Version:** 1  **Date:** 27 April 2009

**Reviewer:** Andreas Beyerlein

**Reviewer’s report:**

Review on “Does acute maternal stress in pregnancy affect infant health outcomes? Examination of a large cohort of infants born after the terrorist attacks of September 11, 2001”

This is a well-written paper with an interesting hypothesis. The data seem to be of high quality, and the statistical approaches chosen are appropriate. I would like to address only some minor points:

**METHODS**

- P. 7: It was difficult for me to understand your definition of preterm birth. On p. 6 you wrote that your database contained information about children’s EGA, so I assumed that this was recorded in completed weeks.
We agree that this paragraph could be more concise and we have revised it accordingly.

- P. 7: How could it happen that more than one 5-digit code existed for a single infant?

Although not common, infants with more than one provider may receive slightly different ICD-9-CM codes for weeks of gestation and EGA may be clinically revised in the course of obstetric or infant care. Further explanation has been added to the text to better explain this possibility.

- P. 8: Why did you choose only women in the first trimester on 11 Sep for the analyses on male:female ratio and birth defects? Was it because these outcomes are based on events happening mainly in the first trimester? If so, please state this.

Thank you very much for your insightful comments. Your assumption is correct, and we have added a sentence to clarify this point. In addition, there is a description included in the discussion that provides further explanation.

- P. 9-10: Please give an example of what you concluded from chi-square tests. Which variables showed multicollinearity, and what did you conclude from this? Since the final models obviously contained the same variables (tables 1-3), I don’t think you need to give the information on chi-square tests and regression diagnostics.

This is an important point. The presence of multicollinearity was assessed for all variables simultaneously and deemed a potential problem if the associated variance inflation factor was found to be 4 or more. It should be noted that in general a level of 10 for variance inflation is suggested and we used a level of 4 as a conservative approach. We found no variables having potentially problematic influence on the model. Since chi-square statistics (or other non-adjusted statistics) are an important part of the initial steps of any epidemiologic investigation, we would like to request that we leave the statements in so that the readers may see we did perform a thorough analysis.

RESULTS

- P. 10: Please give OR and CI of male:female ratio in your logistic regression analyses.

Thank you; we have added the OR with CI for this outcome as requested.

DISCUSSION

- P. 13: You write that the male:female ratio may be an indicator of pregnancy losses. For the non-clinical reader, it would be helpful if you stated this earlier, e.g. in the Introduction.

We appreciate you pointing this out, and we have now briefly defined the use of the sex ratio as a marker of pregnancy loss in the introduction.
- P. 14: You refer to a study having shown that “military members … experienced healthy psychological responses” after 11 Sep. However, 82% of the mothers in your data were only related to military members (p. 5-6), but did not do military services themselves. Could it be possible that, while male military members reacted (at least partly) in a positive way, their wives’ reactions would be rather negative (e. g. fearing that their husband has to leave for a long time etc.)? This might confirm the validity of your approach.

This is a great point and we have rearranged the text to better emphasize this point.

- P. 14: You might state somewhere that the 11 Sep probably did not put as much stress on women as a natural disaster would (although I find it surprising that assassination of politicians might do). This might explain your insignificant findings.

Thank you for your suggestion. We’ve modified the text on page 14 to address your comment.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:
I declare that I have no competing interests.

Reviewer's report
Title: Does acute maternal stress in pregnancy affect infant health outcomes? Examination of a large cohort of infants born after the terrorist attacks of September 11, 2001
Version: 1 Date: 5 May 2009
Reviewer: Jana Vignerova

Reviewer's report:

Minor essential revisions:

1. The bad arrangement of the text is evident. Parts “outcome definitions” and “defining exposure and referent populations” is too long. It is very difficult to understand the principle of the problems defined there. There are some sentences which repeat the same information in other words. Please consider the necessity of the diagnoses codes publication.

We acknowledge that the ICD-9-CM coding system can be somewhat cumbersome. To make the outcome definitions easier to understand, we have modified this section leaving only the essential codes.
2. Part “defining exposure and referent populations”: The referent group is twice defined as 1 year prior and 1 year after the exposed group. The part is closed by the sentence “Therefore, alternative analysis limited the referent group to only those infants conceived 1 year prior to exposed group.” I think, that such referent group would be better than reference group defined above (for the reason mentioned by authors - ... “that infants conceived in 2002 would still be “exposed” to the stress of September 11, 2001,...”). Please, consider this alternative.

In case your analysis will be based on reference group defined as 1 year before and 1 year after 2001, put the explanation why you prefer the first alternative to the discussion.

Thank you for this suggestion; we have conducted further analyses and attempted to revise based on this comment. Although it appears redundant, our use of four outcomes with two different exposure windows necessitates a detailed description. We feel it is important for the reader to know exactly what dates the referent group are comprised of for the different outcomes. We did, however, modify the section to better reflect why both 2000 and 2002 were used as the referent group for the primary analysis. In addition, we have performed alternative analyses using a referent group composed only of infants conceived in 2000, and the lack of significant findings is now reported in the results section.

3. Why are results divided in two parts ... from 0 to 13 weeks, and ... from 0 to 36 weeks? It is not clearly mentioned in methods. It would be better to arrange the results by investigated health problems (sex ratio, birth defects, preterm birth, growth deficiencies).

4. The first paragraph of the part “Infants in utero, from 0 to 36 weeks...” belongs to Methods.

In response to points 3 and 4, we have added the suggested text indicating 0 to 36 weeks to the methods. As currently written, the results are presented by investigated health problem under the sub-heading of their specific exposure window. The findings are presented in this way to make it clear to the reader which outcomes used which exposure window.

Discretionary Revisions:

5. The legend of the figure: “Male/female sex ratio of infants born to military families after stress.” After stress born children were those exposed in September 2001 only.

Thank you for your comment; our new title addresses your point.

6. Tables: 2nd column – “all infants” involves including infants in column 3 (with health problems)? It would be more clear to put in column 2 number of children without problems only.

We value your opinion on the best way to present a table, and have debated the options for this particular one many times. We feel presenting the information in the current format allows an opportunity for a quick comparison of our exposed population to all referent infants.
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 that I have no competing interest's below

We appreciate the opportunity to respond to the comments and suggestions provided by the reviewers. As corresponding author, please contact me if I can provide any additional information.

Respectfully,

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