Reviewer's report

Title: Effect of prenatal anxiety on lower respiratory tract infections modified by ROS-related genes

Version: 2 Date: 27 June 2014

Reviewer: Thomas Keil

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Major Compulsory Revisions!

The main objective of the current analysis was to examine the association between prenatal anxiety of the mother and respiratory tract infections in the child during the first year (infancy). Secondary objectives included evaluation of interactions with genetic factors.

1. I have one major concern with this manuscript related to the interpretation of the results. The authors write that they found an association between maternal prenatal anxiety and lower respiratory infections in general. This is misleading because the authors examined specific infections and found that the presumed general effect was almost only related to bronchiolitis, however no other specific lower resp. tract infection was associated with maternal anxiety during pregnancy. (Table 3 shows that out of n=14 lower resp tract infections in the whole cohort most (n=9) were bronchiolitis. Throughout abstract and manuscript this needs to be made clearer. It should be pointed out that no other lower or any upper infection was associated with prenatal anxiety! Currently, the reader gets the impression that maternal prenatal anxiety is related to any lower resp. tract infection in the infant, which is the authors’ main conclusion but certainly a rather misleading interpretation.

Specific comments:

2. Abstract, Results: 2 decimals are sufficient for reporting ORs and 95%-CIs (please revise also the tables of the main manuscript in this respect). The first sentence should be revised to reflect more precisely the result, e.g. like this: “Higher levels of maternal prenatal anxiety were associated with a higher occurrence of bronchiolitis with borderline statistical significance (…aOR 1.35; 95%CI 1.00-1.81) but not with other respiratory tract infections. “

3. Abstract, Conclusions, lines 118-120: Both sentences are not interpreting the results correctly (see above); they need to be revised.

4. Keywords: please add “Bronchiolitis”

5. Background, line 128: Is Ref 2 really referring to infectious diseases? It seems to be referring to non-communicable diseases.

6. Methods, line 165: Almost 200 out of 631 participants did not complete the anxiety questionnaire. Why? Did those who filled it out and those who did not
differ? This should be reported in results and discussed as a potential limitation (selection bias).

7. Lines 167-168: Please list which potential confounders were assessed in the questionnaire.

8. Methods, main exposure assessment: anxiety has been assessed in a valid way.

9. Methods, outcome assessment at 1y: please explain in the text if doctor-diagnosed means “parent-reported doctor diagnosis” or “doctor diagnosis from medical records”.

10. Line 191: How often was sinusitis recorded in infants? I learned that infants do not have sinuses, but this may have been questioned recently, however, even if they have very small sinuses that cannot be seen on regular x-rays how valid is the diagnosis of sinusitis in an infant?

11. Statistical analysis, line 109: did the adjustment for parental allergy change the univariate results? Please also describe here which other confounders were considered and how they were defined.

12. Results, lines 230ff: Authors should first report results of main outcome (“any resp tract infection”) before they report results of more specific outcomes.

13. After line 235: authors need to mention that prenatal anxiety was not associated with most of the 7 or 8 specific infections.

14. Discussion: please add at least 3 subheadings to make the long discussion more accessible to the readers. E.g. subheadings such as “Main findings”, “Comparison with other studies” and “Potential limitations” (the latter above paragraph starting at line 318).

15. Under “Potential limitations” it should be mention that the statistical power was much too small to analyze other lower resp. tract infections such as pneumonia and tracheobronchitis in this study. Therefore, this study does not allow us to make valid conclusions on the association with prenatal anxiety with such an underpowered study.

16. Line 332: this is not true for ANY respiratory tract infection, only for “bronchiolitis”. This sentence in the conclusion needs to be revised.

17. Table 1: Should include information on the non-participants and better called “Characteristics of study population and subjects not included in the current analysis”

18. Table 2: The other 7 outcomes need to be listed here as well; otherwise one would get the impression that the presentation of results is a bit selective.

19. Table 3: The title should be more self-explanatory, instead of STAI score better write “Interactions between maternal prenatal stress (STAI score)…” Footnote exposure to tobacco smoking: it should be clearer whether this is during pregnancy or postnatal?

20. Figure 1: this is a good self-explanatory legend, however, the figure should be revised showing results for Bronchiolitis and the y-axis should be labelled
Probability of Bronchiolitis at 1y of life.

**Level of interest:** An article of limited interest

**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.