

## **Author's response to reviews**

**Title:** Spatial analysis of air pollution and childhood asthma in Hamilton, Canada: comparing exposure methods in sensitive subgroups

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**Author's response to reviews:** see over

Dear Editors:

We are pleased you will consider this resubmission. As you know, the paper was submitted two years ago, but due to family and personal health issues, the first author was unable to address all of the concerns until October of 2008.

We again apologize for the inconvenience this may have caused you and Dr. Hoek. In reviewing the comments of Dr. Hoek, we noted a number of new issues raised in his second review that were not mentioned in the first review. These were in addition our previous revisions intended to address his and the Dr. Carpenter's comments. We have undertaken to address as many of these as possible within the time limits and in keeping with the original revisions, and hope you and he will find our revisions satisfactory.

#### Major comments

The authors report on the association between traffic-related air pollution and asthma in children using the ISAAC questionnaire in the city of Hamilton. Significant associations were found only for girls when assessing asthma without hay fever. The topic is clearly of interest and the study generally well-performed.

My main problem with the paper is the presentation of the data and some features of the epidemiological analysis.

1. In the key parts of the paper, formulations differ as to what associations the authors claim to have found. It needs to be clearly mentioned that only in a subgroup and a sub-outcome associations were found, e.g. as in the first sentences of the Discussion.

We have revised to the discussion to include the sentence that leads in the results part of the Abstract as follows:

“There were no significant associations between any of the exposure estimates and asthma in the whole population, but large effects were detected the subgroup of children without hayfever (predominately in girls).”

2. Many readers may interpret the study as largely negative with significant findings in a sub-analysis only. This is enforced by the presentation of especially the significant findings in the tables. I would favour a more detailed presentation of findings. This is also motivated by the Introduction of the authors which says that they will look at different exposure indicators, different outcome definitions and different susceptibility. Only the last topic is well-documented in the paper. A final motivation for this is the sentences in the text about the sensitivity of the results for substituting hay fever with other indicators of atopy.

We agree that the comparison of exposure models is a secondary and less thoroughly developed aspect of the paper. We have therefore removed reference to comparison of exposure models in the Introduction and the Discussion.

As noted in our previous response to reviewers, we presented findings that were significant in the susceptible subgroups with the only exposure model that produced significant results after control for confounding and co-pollutants. Please see the response to the first reviewer on the first resubmission. We also added a new column of descriptive statistics in Table 1 dealing with the hayfever.

We could include appendix tables with the other results if needed, but felt during our internal review all co-authors recommended focusing on significant effects to avoid too many tables and detracting from the main focus of the article. We emphasize that all of these models were tested, but the reporting of them was long.

We have included such an Online Appendix of the bivariate associations in the paper now, and if the editor feels this strengthens the paper, it is available for inclusion. As noted, only the LUR model has significant effects when the confounders and co-pollutants are included, which is our reason for focusing on this finding, without promising the more extensive comparison of exposure models that would clearly make the paper too long.

A suggestion:

a. Change table 4 in a basic table showing the associations with all outcomes and all exposure variables, possibly stratified by gender. Drop the coefficients for the other variables and possibly focus on traffic-related pollutants as suggested in the Introduction, e.g.: listing the outcomes of asthma and exposure, then by specific allergen sorting the data into all OR, all 95%CI, girls OR, girls 95%, boys OR and boys 95%CI.

We have included this in the Online Appendix mentioned above.

b. Please focus on adjusted associations. The study has limited confounder, so fully adjusted associations should be the focus.

The number of potential neighborhood confounders is fairly extensive, and given this we have chosen to include the adjustment variables in Table 4.

c. Then show the same or a smaller table for wheeze (this supports the asthma associations a lot, as there is always discussion about asthma diagnosis!)

At the end of the Results section we have devoted a paragraph to the wheeze outcome. The results generally support the findings for the asthma

outcome and adequately address the concern about questionnaire-based diagnosis. Adding in a Table for this sensitivity analysis may detract from the main focus of the paper on Asthma and would add to the length, which we have attempted to reduce in response to Dr. Hoek's other comments.

3. I am surprised about the lack of individual confounder data given that this is an ISAAC questionnaire. Please comment on this.

The ISAAC study questionnaire and dataset that we used did not contain this information for all of the subjects. These data were collected as part of a prevalence study, and we adapted the data for use in the epidemiological analyses. We have not included a statement to the effect in the methods.

4. How did the analysis take the clustering within schools into account?

With the sample size there was insufficient data to compute a stable random effects variance within the schools. Instead we used a spatial GLM model to remove any spatial trends in the data to account for potential non-independence by proximity. As reported, the main results were relatively unchanged by inclusion of spline surfaces.

5. The point of temporal stability of the spatial contrast is quite crucial. Please document this more than by stating on p. 10 "quite consistent".

We have elaborated this point, and supporting it with the findings of the LUR model.

6. I cannot reconstruct the effect estimates on pages 17 and 18.

We have corrected this where appropriate or removed from the text if it detracted from the focus of the paper.

7. The difference between boys and girls is interesting and has been found before, though not consistently. A more systematic comparison with previous findings would be useful. The explanation offered on p.22 (time outdoors) would likely favour boys as more susceptible.

We have removed the reference to time outdoors. The remainder of this paragraph cites numerous papers, so we are not sure how this could be made more systematic, but would be happy to address this concern if there is another suggestion for improvement.

8. The paper is too long and presents too much detail e.g. criteria for and explaining of confounding; interaction discussion in results; references in results.

We have removed the entire first paragraph, most of the study site description, and parts of the Discussion. There were only 4 references cited in the results, and these were meant to support assertions about appropriate methods for the sensitivity analyses.

9. Please provide site types for the fixed-site monitors

We are uncertain what is meant by “site types”? Do you mean the land use around the monitors or the type of monitors used? The land use classifications are usually industrial, traffic or background, roughly equally distributed. If this is what is intended, we do not customarily include this kind of information because it is publicly available and because we have already published extensively using the same monitoring locations. If something else is intended, please let us know and we can address this concern.

10. Units for PM10 in Table 2 are not ppb, I assume? Maybe drop the boys/girls part of the table, no reason that this should differ. Instead document variability more for whole group than with range.

We have added a footnote indicating **“Particulate matter in  $\mu\text{m}^3$ ; gaseous pollutants in parts per billion.”**

11. Table 4: present for more meaningful ranges than 1 unit as done in text

We would prefer to leave these tables in 1 unit increments and to document differences in the text. This seemed acceptable on the first revision to both reviewers.

12. Please clarify the sentences on p. 22/23 on measurement error in exposure and robustness for confounding. Not sure this is correct.

We have removed this sentence now in an attempt to reduce the length.