Dear Dr. Smith

Manuscript ID BMJ.2017.039236.R1 entitled "Impacts of London's road traffic air and noise pollution on birth weight: a retrospective population-based cohort study"

Thank you for sending us your paper. We have some further comments from the reviewers, who feel the paper has been much improved by the first round.

I feel we are making progress and almost there.

Yours sincerely,

Rubin Minhas
Dr Rubin Minhas
BMJ Associate Editor
rm1000@live.com

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Report from The BMJ’s manuscript committee meeting

These comments are an attempt to summarise the discussions at the manuscript meeting. They are not an exact transcript.

Members of the committee were: xxx (chair), yyy (statistician), [and list other eds who took part]

Decision: Put points

Detailed comments from the meeting:

First, please revise your paper to respond to all of the comments by the reviewers. Their reports are available at the end of this letter, below.

Please also respond to these additional comments by the committee:

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In your response please provide, point by point, your replies to the comments made by the reviewers and the editors, explaining how you have dealt with them in the paper.

** Comments from the external peer reviewers**

Reviewer: 1

Recommendation:

Comments:

The revision of this manuscript includes many substantial changes that elevate its quality. I have some remaining comments and suggestions.

Comments
Abstract, conclusions: Conclusions are too long. They should be 1 or 2 sentences, not more. Sentence about attributable risk should be moved to the results section. In the light of the associations with non-exhaust air pollution, the reference to diesel should be removed from the abstract.

Study population. I agree with the removal of outcomes in all birth and the restriction of the paper to term births as this makes the paper easier to follow. However, the paper in its current form is not consistent with regard to the inclusion/exclusion preterm birth, for example the study population and Table 1 should still include preterm births. Moreover, line 220 mentions stratified analyses by term/preterm. That does not make sense if all analyses were performed in term births. This needs to be fixed.

Methods, line 127-128. The use of the air pollution model for other epidemiological analyses with other health endpoints does not say anything about the model's validity. Therefore, this sentence including the 5 references should be removed from the paper.

Line 156f. Randomly distributed across what? Could you please clarify that.

Use of noise as a categorical variable. The plots of the GAMs included in the reply and should be included in the (supplement of) the paper. The plots indicate that outcome-noise relationships do not severely deviate from linearity. I think the reasons for continuing to use noise as a categorical variable do not outweigh the limitations of such an analysis, i.e. that the use of air pollution as continuous variables and noise as categorical variables makes it difficult to compare effects and (as mentioned by reviewer 3) and to determine the impact of mutual adjustment. Moreover, the non-normal distribution of the exposure variable is not a requirement in linear (logistic) regression – of course, when using non-transformed noise in linear/logistic regression needs careful checking of associations being driven by extremely high exposures. In the light of the above, I suggest to replace associations with categorical noise variables by associations with continuous noise variables expressed per IQR increase in exposure, or at least to add associations with continuous noise variables to the paper. Moreover, GAMs assessing the functional relationship between outcomes and exposure should be introduced before linear (logistic) regression results.

Discussion, line 401. Add "vehicles" after 10,000.

Lines 430ff. You state that you did not have data on ambient temperature. I assume that routine data is available for the area and period of interest. Do you mean that the temperature data have never been linked to the birth weight data and cannot be linked at this stage? Please clarify.

Line 447, multiple testing. This is very short. I suggest to add why you decided not to adjust for multiple testing despite the limitations of doing so.

Associations with trimester-specific exposures. The relevance of exposure during different trimesters is an important research topic within this field. These associations have been assessed and are presented in supplementary Table 9, but are no longer mentioned in the discussion. I think there needs to be at least some discussion of the relevance of the different trimester together with a summary of the evidence regarding timing from other studies. I agree with reviewer 3 that the paper by Rich et al. is one of the most persuasive papers on this topic and should be added to the discussion - irrespective of the 3rd trimester being most influential in the present study or not.

Additional Questions:
Please enter your name: Ulrike Gehring

Job Title: Associate Professor for Enviromental Epidemiology

Institution: Institute for Risk Assessment Sciences, Utrecht University, The Netherlands

Reimbursement for attending a symposium?: No

A fee for speaking?: No

A fee for organising education?: No

Funds for research?: No

Funds for a member of staff?: No

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Reviewer: 2

Recommendation:

Comments:
The revised manuscript is much improved and presents a more balanced presentation of the study findings. This should be a valuable contribution to the literature. I agree with the authors approach to present results per IQR as this is most useful to compare impacts across the different exposures, including between air pollution and noise. I appreciated very much the inclusion of joint GAM models as these results are, in my view, among the most convincing. I'd suggest that their presentation in the manuscript could be more prominent.

Parity: The authors have now mentioned lack of information on parity as a limitation, but while the authors suggest this is most likely to be related to ethnicity or deprivation (which are accounted for), parity very easily could be spatially variable based on other factors such as maternal age and individual (not neighborhood) income. This could be added to the Discussion.

Air pollution model evaluation: The response to earlier comments and the revision regarding model evaluation should be further improved and authors may have misinterpreted the key point of the prior comment: it is not whether the model is or is not "valid" which is itself a question that cannot be answered directly (all are models and in fact they cannot be "validated" as that implies that truth is known, they can only be "evaluated" against some other measure) but rather whether the model performed better for some pollutants compared to others and if so how this might affect the comparisons between pollutant in the epidemiologic findings. If the model estimates of NO2 are less accurate than those for PM2.5 then that needs to be considered in the interpretation of epidemiologic findings. Within this context correlations are not the metric of interest but rather model RMSE, NMB or some related measure.

From the cited paper describing the air pollution model: "taking the root mean square error as an approximation of this uncertainty gives a value of 17.3 p.p.b. (28%) for NOX, 9.2 p.p.b. (36%) for NO2 and 1.6 μg/m3 (6%) for PM10" This suggests much better performance for PM10 than for NO/NOx. PM2.5 metrics are not reported in the cited publication but some metrics are in the cited internal report which also suggest higher NMB for NO/NOx compared to PM2.5. As such I reiterate the initial comment regarding the pollutant metrics and comparisons between them and suggest that conclusions regarding the impacts of one pollutant compared to another on the birth outcomes need to be addressed within this context and conclusions modified accordingly.

Spatial resolution of the noise model: To say that the model can be applied at a resolution of 0.1 m tells one nothing about the resolution of the model estimates themselves, unless the authors are actually arguing that the model can reliably detect differences in noise over a distance of 0.1m. Is the model actually developed at 0.1 m resolution (meaning that there are actually locations where estimates differ on that distance scale) or as I expect at some larger resolution (for example the paper describing the noise model indicates that some of the input data are at a resolution of 50m so is there some downscaling)? Most important would be some clear indication that the noise model estimates are indeed more highly resolved spatially (and this refers to the model itself, not its application) than the air pollution estimates as that would tend to support the findings by reducing the potential for exposure misclassification to favor the air pollution measures over noise in the joint models.

Abstract: Suggest removing from conclusions: "Our findings suggest that air pollution from road traffic in London, which is dominated by diesel exhaust emissions, is adversely affecting fetal growth. These results may be driven by the fine particulate matter (PM2.5 traffic-exhaust) component rather than the gaseous pollutants NO2 and NOX." While I do not disagree that diesel does dominate road traffic air pollution in London, this manuscript does not specifically address this point nor does the modeling as presented here indicate that diesel is more closely linked to PM2.5 (which the next sentence suggests is driving the impacts) than it is to NO2 or NOx. More generally both of these sentences are too speculative (see above comments regarding model evaluation) to be in the Conclusions of the abstract, although certainly it is reasonable to include them in the Discussion.

L238 (and elsewhere)– NO2 is generally not considered a primary pollutant

Table 2 still contains p-values for joint model results (OK to retain p for trend)

L271 – this should only refer to Figure 2

Additional Questions:
Please enter your name: Michael Brauer

Job Title: Professor

Institution: The University of British Columbia

Reimbursement for attending a symposium?: No

A fee for speaking?: No

A fee for organising education?: No

Funds for research?: No

Funds for a member of staff?: No

Fees for consulting?: No

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