Author's response to reviews

Title: Air pollution exposure estimation using dispersion modelling and continuous monitoring data in a prospective birth cohort study in the Netherlands

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Author's response to reviews: see over
Dear Dr. Francesco Forastiere,
Associate Editor Environmental Health

Thank you very much for reviewing our manuscript: “Air pollution exposure estimation using dispersion modelling and continuous monitoring data in the Generation R Study” (MS: 1650623880595891).

We are grateful for the extensive and useful comments of the reviewers. We have made changes in our manuscript in response to these comments. Most importantly, we have now focused on the air pollution exposure assessment, and we have shortened the description of the noise exposure assessment and the corresponding results. Furthermore, we have reduced the description of the air pollution exposure assessment and we have included citations to the previous publications that describe this methodology. In addition, we have made several textual modifications to improve clarity. We feel that these suggested changes have improved the quality of the manuscript.

Attached and in response to the reviewers’ reports, you will find our specific responses to all the questions and comments from the Editor and the Reviewers. We hope you will find the revised manuscript acceptable for publication in Environmental Health.

With kind regards,
Yours sincerely,

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RESPONSE TO REVIEWERS

We thank the Editor and the Reviewers for the comments. Our specific responses to these comments have been inserted in blue and underlined. The bold sections are added compared to the first version of the manuscript.

Formatting comments

To ensure that your revised manuscript conforms to the journal style see the Instructions for authors at (http://www.ehjournal.net/info/instructions/).

On the title page, please left justify all the text. The title should include the study design, for example "A versus B in the treatment of C: a randomized controlled trial X is a risk factor for Y: a case control study." For the institutional addresses, remove the colons after each address and insert below the phrase *Corresponding author, removing all other information and placing the * after the corresponding author's superscript number(s). Beneath insert the authors' email addresses listed under the heading Email addresses as author's initials:email address e.g. JS: joe.shmoe@university.edu.

Only the first letter of headings should be capitalized. There should be separate Methods and Results sections under separate headings. To help the flow and make the manuscript easier to read, please reduce the number of subheadings. Please consolidate the number of subheadings as too many headings make reading the manuscript choppy and interferes with the language flow.

Above the Competing interests section insert a List of Abbreviations listing the abbreviation: term and separating the pairs with semi-colons in sentence format. In the References section, the References should be formatted as number, period, space (not tab) and reference. For the tables, all horizontal lines should be visible indicating that each data point is in its own cell. It is important that your files are correctly formatted.

We have made all the formatting adjustments mentioned above to conform to the style of Environmental Health. This means that we have considerably reshaped the manuscript, so that
the new version of the manuscript contains a separate Methods and Results section. We have reduced the number of subheadings, and we only use a few subheadings for the section that describes the air pollution exposure assessment, in order to promote readability and clarity.

Editor

As mentioned by you, the authors, this manuscript includes data that have already been published. As such, since there is the issue that both the methods section and some of the results have already been published as supplemental material in one of the two studies that have used these exposure estimates, we suggest that the paper be reshaped considerably and ask you to review the paper and provide full assurance about double publications.

We thank the Editor for reviewing our paper. We understand the concern about double publications. The present paper had several aims: 1) to describe the air pollution exposure assessment in detail, 2) to provide the distribution of exposure levels for various relevant exposure periods in the prenatal and postnatal phase, 3) to present exposure levels according to maternal and infant characteristics. We have addressed the first aim in our previous papers, but we have now revised this information and give a more detailed description in the present paper. Besides, we have not addressed the second and third aim in previous papers. In response to this comment and the comments of the reviewers, in the new version of the manuscript we have omitted a large part of the description of the air pollution exposure assessment and we have added information that has not been described earlier or that has been revised as compared to the previous publications. In addition, we have included the appropriate citations to our previous publications (van den Hooven et al. 2011a, van den Hooven et al. 2011b).

Reviewer 1

This is an interesting article on air pollution exposure assessment (PM10 and NO2) in the Generation R Study.

We thank the reviewer for the comments. Our specific responses are given below.
Major revisions

1. I found the paper not so easy to read, probably because it contains many issues: the fine spatial and temporal contrasts in air pollution exposure, the noise exposure, comments on mechanisms of the effects on health both for adults and for pregnancy and children. I think it could be improved keeping a more clear focus throughout the paper. If the focus of the paper is the methodology of both air pollution and noise assessments for the cohort of pregnant women and children, I suggest to stick with from the title and the background to the discussion. It is very important to disentangle the effects of air pollution and noise during pregnancy, I would stress the need of both exposure assessments more than general issues on the adverse health effects of traffic exposure from the beginning.

We agree with the reviewer that the paper would benefit from keeping a clearer focus. The main aim of our paper was to describe the air pollution exposure assessment, as the majority of our research is focused on the impact of air pollution exposure on pregnancy outcomes. Noise exposure is mainly assessed because this is an important potential confounder in the associations between maternal air pollution exposure and pregnancy outcomes. Therefore, we now focus more clearly on the air pollution exposure assessment. We merely present maternal noise exposure as one of the maternal characteristics that are described in Table 3. We have considerably shortened the description of the noise exposure assessment and included a citation of the previous publications in which the noise exposure assessment has been discussed.

In the Discussion, we have included:

“There is increasing awareness of the importance to incorporate information on noise exposure in studies on traffic-related air pollution exposure and health [10-13]. Thus far, few studies have included both air pollution and noise when investigating health outcomes [10, 40-42]. In our previous studies on air pollution and pregnancy outcomes, we included information on noise exposure, in order to adjust for its potential confounding effect [18-19].”

Furthermore, we have deleted the results for noise exposure in Tables 1, 3, and 4. Accordingly, we have omitted the discussion of these results in the Results and Discussion section. We feel
that throughout the manuscript, there is now a clear focus on the air pollution exposure assessment, which has increased the readability of the paper.

Methods

2. The approach of air pollution assessment, which uses dispersion modelling and continuous monitoring data, is very interesting. However it has been already used for two publications. The authors could shorten the description, citing the previous publications, and could add what has been done in addition to previous works.

We have substantially revised the description of the air pollution exposure assessment. As suggested, we have shortened the description and included the citations of our previous publications. In response to comment comment 1 and 2 of the second reviewer, we have revised some information to clarify the steps in the exposure assessment procedure. We have revised the following paragraphs (revised sentences are bolded):

“Air pollution exposure assessment

**Individual exposures to PM$_{10}$ and NO$_2$ levels during pregnancy were assessed at the home address,** using advanced spatiotemporal dispersion modelling techniques in combination with hourly air pollution measurements at three continuous monitoring sites. *The exposure assessment procedure has been described previously [18-19].* Below, we give a brief update on the procedure, including some revised information that better describes the individual steps.

**Spatial pattern**

Annual average concentrations of PM$_{10}$ and NO$_2$ for the years 2001-2008 were assessed for all addresses in the study area (Northern part of Rotterdam), using GIS and the three Dutch national standard methods for air quality modelling (considering intra-urban road traffic, traffic on highways, and industrial and other point sources) [20]. Subsequently, in order to obtain spatiotemporal patterns, spatially resolved annual concentrations were calculated for eight different wind conditions, resulting in an averaged spatially resolved concentration pattern for each wind class. **Various input data was taken into account in the calculations as described**
earlier [18-19], including annual data on traffic intensities and annual emissions from traffic, shipping, industry, and households. The traffic intensity data was supplied by the DCMR Environmental Protection Agency Rijnmond (DCMR), and emission sources and emission data were obtained from the National Institute for Public Health and the Environment (RIVM) and the DCMR. Hourly meteorological data was obtained from observations at Rotterdam The Hague Airport, performed by the Royal Netherlands Meteorological Institute (KNMI).

**Temporal pattern**

To account for temporal variation due to different wind conditions, for each hour we derived the corresponding spatial distribution for the prevailing wind direction and wind speed at that specific hour, by means of interpolation between the eight characteristic spatial distributions. Subsequently, the spatial distributions that corresponded to the hourly wind conditions were adjusted for fixed temporal patterns of source activities. In this way, we accounted for temporal fluctuations in the contribution of air pollution sources during the month, week (e.g., working days and weekend days), and day (e.g., morning and evening rush hour). The adjustment for temporal patterns was performed for traffic and for household emissions. Traffic is the source with the strongest fluctuations in emissions within 24 hours. This 24h-pattern is fairly stable for working days and weekend days. Hence, the contribution of traffic was scaled using an average hourly traffic intensity pattern (based on traffic counts), thereby deriving hourly intensities. We also considered the time dependence of household emissions, by applying a 24h-pattern, and we applied a function for outdoor temperature dependence to account for seasonal fluctuations. These functions were derived from energy use statistics. In this way, hourly household emissions were estimated from annual household emissions. Emissions from industrial sources do not contribute significantly to small-scale variations in air pollution concentrations. Emissions from shipping are quite stable over time and also display relatively small temporal fluctuations. Therefore, these emissions were not adjusted for fixed temporal patterns. Nevertheless, even if some small-scale variations would have occurred as a result of these emissions, the difference would have been corrected for in the next step (adjustment for hourly background concentrations).
Adjustment for background concentrations

The modelled hourly concentrations were adjusted for background concentrations (see also \[18-19\]) using continuous hourly monitoring data from three monitoring stations in the study area. This served two main purposes. First, the temporal fluctuations in background concentrations were taken into account and second, the modelled concentrations were adjusted for background concentrations. The measured air pollution concentrations at the monitoring stations are considered as the sum of the background concentration and the contribution from local emission sources. We also modelled the contribution of local emission sources to the PM10 and NO2 concentrations at the three monitoring stations. Subsequently, we subtracted the hourly modelled contributions from the hourly measured concentrations at the stations, thereby deriving an hourly estimate for the background concentrations. The hourly estimates for the background concentrations at the three stations were averaged, which yielded an average hourly background concentration for the study area. In the adjustment procedure, this average hourly background concentration was added to the modelled hourly contributions at the home addresses, in order to take into account the background concentration.

Continuous air pollution monitoring data was provided by DCMR. Missing values for PM10 concentrations at the three monitoring stations were imputed, as described earlier \[18-19\].

Modelling performance

Previous studies have reported a good agreement between annual average PM_{10} and NO_{2} concentrations predicted by a related dispersion modelling approach and concentrations measured at monitoring stations in the larger Rotterdam region \[21-22\]. As mentioned previously \[18-19\], it can be expected that the estimated hourly PM_{10} and NO_{2} concentrations will be even more precise than estimated annual average concentrations.”

Results

3. I suggest to present both the air pollution and noise exposure in the cohort after the exposure assessment, and to add the figures of population in tables 3 and 4.
See also our response to the first comment of this reviewer. To keep a clearer focus throughout the manuscript, we have decided to focus on the air pollution exposure assessment. Therefore, we have shortened the description of the noise exposure assessment, and we have deleted the results for noise exposure in the tables.

Regarding the figures of population, we have now included a separate column with the number of subjects for every subgroup in Tables 3 and 4.

4. I suggest to eliminate the two maps and the flow chart (already published in ref 38).

As suggested by the reviewer, we have omitted Figure 1 (flow chart of air pollution exposure assessment) and Figure 2 (maps illustrating the air pollution concentrations in the study area), and we have included a reference to the previous publications in which these figures have been published.

Discretionary revisions
4. A short discussion of results presented in table 2 could be added.

We agree that we should comment on the correlation coefficients that are presented in Table 2. In the Discussion, we have included the following sentence (see bolded):

“In our air pollution exposure assessment procedure, we are able to consider fine spatial and temporal contrasts in exposure by using a combination of dispersion modelling and continuous monitoring. The high temporal resolution enables investigation of relatively short exposure windows (e.g., total pregnancy, trimesters, or months), that are particularly of interest in pregnant women and children. It also facilitates identification of critical windows of exposure. These short-term exposure windows cannot be examined in studies with only annual average concentrations. In examination of the different exposure windows, the (possibly) moderate to high correlations among some of the exposure averages need to be taken into account when interpreting the results.”
Reviewer 2

This paper assesses air pollution exposure in a mother and child cohort study from Rotterdam, the Netherlands. The combination of dispersion modeling and GIS data allow for considering both spatial and temporal variation in air pollution exposure, which is a key issue to advance in the research area of air pollution and perinatal outcomes, where exposure periods are well defined and there are potential windows of susceptibility.

We thank the reviewer for the comments. Our specific responses are given below.

My main comments are related to the potential limitations and to the calibration of the model. Besides, I am also concerned about the fact that both the methods section and some of the results have already been published as supplemental material in one of the two studies that have used these exposure estimates, as mentioned by the authors.

See also our response to the Editor and to comment 2 of the first reviewer. We have shortened the description of the air pollution exposure, and we have included citations to the previous publications. In the new version of the manuscript, we now describe the air pollution exposure assessment more briefly and we present some information that has been revised as compared to the previous publications.

Major comments
1. According to Jerrett et al. (2004), one of the limitations of dispersion models is that temporal mismatches in the two main sources of data (emissions and meteorology) can cause estimates errors. That is, whereas meteo data are collected at an hourly basis, emission data are usually obtained at larger time-scales. Can authors be more specific of the quality and time-scales of the different input data? If time-scales are different they should discuss the potential implications of this issue.

We understand the concern of the reviewer. However, we were able to overcome this problem by estimating hourly emission data, so that both hourly meteorological data and hourly emission...
data were used in the modelling procedure. In the manuscript, we have now included a more detailed description of the input data, and a description of the step in which hourly emission data was derived for traffic and household emissions.

We have included the following in the paragraph on Spatial pattern:

“Various input data was taken into account in the calculations as described earlier [18-19], including annual data on traffic intensities and annual emissions from traffic, shipping, industry, and households.”

In addition, we have included in the paragraph on Temporal pattern:

“Subsequently, the spatial distributions that corresponded to the hourly wind conditions were adjusted for fixed temporal patterns of source activities. In this way, we accounted for temporal fluctuations in the contribution of air pollution sources during the month, week (e.g., working days and weekend days), and day (e.g., morning and evening rush hour). The adjustment for temporal patterns was performed for traffic and for household emissions. Traffic is the source with the strongest fluctuations in emissions within 24 hours. This 24h-pattern is fairly stable for working days and weekend days. Hence, the contribution of traffic was scaled using an average hourly traffic intensity pattern (based on traffic counts), thereby deriving hourly intensities. We also considered the time dependence of household emissions, by applying a 24h-pattern, and we applied a function for outdoor temperature dependence to account for seasonal fluctuations. These functions were derived from energy use statistics. In this way, hourly household emissions were estimated from annual household emissions. Emissions from industrial sources do not contribute significantly to small-scale variations in air pollution concentrations. Emissions from shipping are quite stable over time and also display relatively small temporal fluctuations. Therefore, these emissions were not adjusted for fixed temporal patterns. Nevertheless, even if some small-scale variations would have occurred as a result of these emissions, the difference would have been corrected for in the next step (adjustment for hourly background concentrations).”

2. The calibration of a dispersion model is a very important step; however, the explanation of model calibration is vague. Why authors did select only three stations for calibration, which were
the selection criteria? Please provide some results on the differences between modeled and measured concentrations. Did authors identify any differences in calibration either by pollutant or type of station?

We understand the confusion. Actually, the term ‘calibration’ may not correctly reflect the procedure. Rather, in this step we determined the average background concentration of the modelled area. We needed to determine this in an additional step, as the background concentration was not estimated in our modelling procedure. To avoid confusion, in the manuscript we have omitted the term ‘calibration’ and we now refer to this step as ‘Adjustment for background concentrations’. We have substantially revised the relevant paragraph (‘Adjustment for background concentrations’), as is shown in our response to comment 2 of the first reviewer.

Furthermore, in selecting the monitoring stations for calibration, the criterion was to select background stations. In other words, the stations needed to be situated far enough from the modelled emission sources, in order to reflect mainly background concentrations, with only a small contribution from local emissions sources. As background concentrations are assumed to be constant within the modelled area, theoretically it would suffice to use only one background station to determine the average background concentration in the area. However, to better take into account the time fluctuations in air pollution concentrations, we used three background stations in our procedure. We have described the detailed procedure in the paragraph on Adjustment for background concentrations.

Minor comments
3. Although the final purpose of the study is to derive air pollution exposure estimates in a cohort of pregnant women, this is a methodological paper so authors should focus the discussion on exposure assessment. Thus, the paragraph about potential biological mechanisms is out of the objective of this paper. Regarding the introduction, it is fine to start with a summary of the current knowledge on health effects but I would focus only on pregnant women and children. In relation to children’s health effects, effects on the immune system (as a potential biological
mechanism by which air pollution can cause other outcomes in early life) as well as effects on
cognitive function have been reported later than many studies on perinatal outcomes.

We agree, and we have now sharpened our focus on the methodology of the exposure assessment.
In the Discussion, we have omitted the paragraph on potential biological mechanisms. In
addition, in the Introduction we now concentrate on the health effects of air pollution in pregnant
women and their unborn children. We have revised the following:

“Air pollution exposure has been associated with several adverse health effects, such as
cardiovascular disease, respiratory disease, and total mortality [1-4]. Certain subgroups of the
population, including pregnant women and their unborn children, have been suggested to
be more susceptible to the adverse effects of air pollution [5-6]. Literature on the specific
effects of air pollution exposure in pregnant women on outcomes such as inflammation markers,
placental function, and blood pressure, is scarce. In contrast, research on the impact of air
pollution exposure on birth outcomes has increased in the last decade, which has led to a number
of reviews summarizing the available evidence [7-8].”

4. Abstract: delete first line, it is a very general statement.

According the suggestion, we have deleted the first sentence of the Abstract.
REFERENCES


http://dx.doi.org/10.1289/ehp.1003316.