Author's response to reviews

Title: An exploratory spatial analysis to assess the relationship between deprivation, noise and infant mortality

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Author's response to reviews: see over
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**Title:** “An exploratory spatial analysis to assess the relationship between deprivation, noise and infant mortality”

**Editors in Chief, Environmental Health**

Dear Pr Philippe Grandjean and Pr David Ozonoff,

It is a pleasure for us to submit this revised version of our paper entitled “An exploratory spatial analysis to assess the relationship between deprivation, noise and infant mortality”.

We thank the careful and detailed attention that the 2 reviewers have taken in reviewing our manuscript. We substantially revised our paper in response. Also, language revision was done by a native-English speaker. We hope it is now much better and for this we are grateful to our reviewers. We address each point in detail below.

To make your reading easier, we indicated our modifications using highlight in green in the revised text.

With our best regards

Wahida KIHAL
**Reviewer: Alfred Mbah**

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<th>Points</th>
<th>Reviewers Comment</th>
<th>Our Responses</th>
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<td>Results</td>
<td>In the section &quot;Spatial result&quot; (which should read, &quot;Spatial results&quot; to be more grammatically correct), under the sub-section &quot;Stage 1...&quot;, the RR of 3.8 is incorrectly labelled an &quot;infant mortality rate&quot;.</td>
<td>We agree. We revised it in the text.</td>
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<td>Methods</td>
<td>In Table 1, the authors should include a univariate description of the socio-economic characteristics of the study neighbourhoods (e.g., mean and standard deviation). It would also be helpful to know the distribution of the main predictor, noise; perhaps this could be integrated into Table 1. These data would be reported in the Results section, but could be integrated into Table 1.</td>
<td>We agree and added univariate description of socio-economic characteristic of deprivation categories (Mean and 95% CI) in table 1. The distribution of the noise levels across deprivation categories is exposed in the Results section (Now page 9). For more detailed information about the socio-economic characteristics, we refer to our study on the deprivation index. [1] Lalloué et al. A statistical procedure to create a neighborhood socioeconomic index for health inequalities analysis. International Journal for Equity in Health 2013, 12:21.</td>
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<td>Discussion</td>
<td>In the 15th paragraph of the Discussion, when the authors start talking about limitations, the sentence &quot;because baby girls have a lower risk of infant and neonatal mortality, spatial confounding by gender was partially masking the significance of location of the most likely cluster in analysis&quot; is not obvious. Can the authors more clearly explain why they believe this to be the case? Also, unless the lower risk of mortality is thought to be related to how parents treat a female versus male baby, there is likely a biological mechanism that underlies lower risk of mortality in female babies, so the authors should refer to sex rather than gender here.</td>
<td>We agree and now refer to gender instead of sex in the Discussion section. To answer further your question: Because the risk of adverse pregnancy outcome is higher among boys than girls, the spatial distribution of infant mortality can be influenced by gender, should the birth sex ratio vary across census blocks since our rates are not adjusted for gender. We modified the sentence which now becomes “Because baby girls have a lower risk of infant and neonatal mortality [134, 135], and because the birth sex ratio is uneven across the area census blocks spatial confounding by gender may have partially masked the significance of location of the most likely cluster in analysis”</td>
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In the 17th paragraph of the Discussion, I think the authors should also discuss as a limitation the fact that a noise level was assigned to all residents of a building based on the loudest face; whereas individuals within a building may have a lower level of exposure depending on where in the building they live.

Are the authors worried about any misclassification from this method? I.e., might some residents from "high noise" buildings end up with less noise exposure than predicted?

We agree on the fact that some exposure misclassification occurs; we see it as systematic and non-differential. The reason is that the exposure computation procedure assigns to all residents of a building the value of the loudest face. This tends to over-estimate average exposure levels, but we see no reason why this bias should be differential across census blocks. This point has been added in the discussion.

In the 18th paragraph of the Discussion, the author suggest that since noise levels only changed by 0-2 dB (2.97% on average), temporal factors are not likely to change contrasts between spatial units and the lack of data on noise changes is not likely to modify results.

Yet, in the Results, the authors note that the mean noise level across medium and low deprivation neighbourhoods was ~1.6 dB (~2%). Does this not suggest that the temporal change in noise is likely on the same magnitude as the contrast between spatial units of different deprivation levels? If so, is this concerning?

According to the ‘acoustic observatory’, noise levels only changed by 0-2dB. This is a result of experimental tests that were carried out in a few stations; this conclusion is not based a neighborhood measures. This mention was meant to give the reader an idea of noise changes from 2008 to 2011.

We acknowledge that we cannot evaluate the impact of temporal noise changes because we have no data from 2000 to 2009.

Considering the scenario of 0-2 dB change in noise levels, it is true that this change in noise is likely of the same magnitude as the contrast between spatial units of different deprivation levels. However, the noise has not systematically changed according to the deprivation level (e.g. an increase in noise level only among the most deprived blocks).

We suppose that there is no systematic increase in noise levels according deprivation level that would modify the contrast between spatial units of different
<table>
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<th>Conclusion</th>
<th>The authors appear to have no conclusion about direction of relationship between noise and infant mortality based on their analysis, which seems contrary to the Discussion that precedes it.</th>
<th>Thank you for this comment. We revised the conclusion to clarify the relationship between noise and the spatial distribution of infant mortality.</th>
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<td><strong>Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)</strong></td>
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<tr>
<td><strong>Results</strong></td>
<td>In the section &quot;Descriptive results&quot;, under the sub-section of &quot;Neighbourhood noise level&quot;, the sentence &quot;Typically the blocks where noise levels are highest are those in the medium deprivation category&quot; seems inaccurate. The authors base this on the fact that there is a slightly higher mean dB for neighbourhoods in the medium deprivation category compared to the others; but mean values are sensitive to extreme values. Therefore, it seems more direct (and accurate) to suggest that &quot;Medium deprivation neighbourhoods had a slightly higher mean noise level...&quot;</td>
<td>We agree and revised the text accordingly.</td>
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<td>The use of two levels of sub-headings in the Results and Discussion continues to be distracting to the flow of the article, greatly reducing its readability. For example, in the section &quot;Descriptive results&quot;, the sub headings (e.g., Neighbourhood socioeconomic deprivation, Neighbourhood noise level) are unnecessary and could be removed.</td>
<td>We agree and revised sub-headings in the Results section accordingly.</td>
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<td><strong>Background, paragraph 2:</strong></td>
<td>It's unnecessary to report ORs and CIs from other studies in the Background. For example, rather than reporting an OR of 3.12 with a confidence interval, the authors can simply say &quot;a three-fold increase in risk&quot;.</td>
<td>We revised the Background paragraph accordingly.</td>
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<td><strong>Background, paragraph 3</strong></td>
<td>When the authors say &quot;Now, there is also an uneven distribution of noise exposure across socioeconomic groups&quot;, they should specify the direction of this relationship (i.e., that lower SES groups have higher exposure).</td>
<td>We added information about the direction of the association between noise exposure and socio-economic group and provide references.</td>
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<td><strong>Background, paragraph 4, 5</strong></td>
<td>The section beginning with &quot;The paper is structured as follows&quot; in paragraph 4 should come at the end of the Background. Moreover, the description of the theoretical model should come before this statement; and, as a result, the sentences «Firstly, after a literature review...&quot; should be removed from what is currently paragraph 4.</td>
<td>We changed the text “background paragraph 4, 5” accordingly.</td>
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<td><strong>Methods</strong></td>
<td>In the section &quot;Health data&quot;, the authors should be specific rather than saying that there were &quot;several census blocks with 0 deaths&quot;; precisely how many were there?</td>
<td>We added this information in the main text “health data” section</td>
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<td>Results</td>
<td>We think our original text is more accurate given our results and prefer not to change it.</td>
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<td>In the section &quot;Spatial result&quot;, under the subsection &quot;Noise exposure..., it would be more directly concordant with the criteria for evaluation outlined in the Methods to say &quot;We can conclude that noise only partly explains the excess...&quot; rather than that &quot;noise alone does not explain...&quot;.</td>
<td>We now use the term distribution in all sub-section titles.</td>
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<td>In the section &quot;Spatial result&quot;, the sub-section titles change from referring to &quot;spatial distribution of infant mortality&quot; to &quot;spatial display of infant mortality&quot;. This is confusing as I suspect that all titles are referring to the same thing. The authors should make this consistent and I strongly recommend using the term distribution rather than display, which is unclear.</td>
<td>Thank you for your comment and suggestion. We revised the &quot;spatial result&quot; section accordingly.</td>
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<td>In the section &quot;Spatial result&quot;, under the subsection &quot;Unemployment, immigrant status...&quot; the authors should highlight that the decrease in the LR was larger for these factors than for noise by saying that &quot;the most likely cluster kept the same size with a relatively larger decrease in the likelihood ratio&quot;, and also contrast the results of adjustment for noise by saying that &quot;unemployment and immigrant status could explain a relatively large amount of the excess...compared to noise&quot;. This would greatly help the reader understand the narrative of the finding, I feel.</td>
<td>We agree this sub-section was unclear and revised this paragraph to clarify our results.</td>
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<td>The sub-section &quot;Occupation, housing conditions...&quot; in the section &quot;Spatial result&quot; is really hard to follow as written. The several references to Figures in parentheses that do not makes sense. It's hard to know what to make of some of the information provided. For example, why do they start reporting the number of inhabitants in the smaller cluster in Figure 5A when it’s not reported for the larger cluster in Figure 4A? What's the relevance of this data here? Another example is that the authors go from suggesting that controlling for these dimensions of SES resulted in the cluster being &quot;smaller in size by located in the same zone&quot; in the first paragraph, to the cluster being &quot;shifted&quot; in the second paragraph. This is very confusing given the terminology in their criteria outlined in the Methods. My own visual comparison of the clusters in Figures 5A and 4A suggests that the cluster did not shift in</td>
<td>We hope it is now easier to understand</td>
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that the smaller cluster is located within the larger one.

Although the centroid of the cluster does appear to shift - is this what the authors mean?

If so, they should more clearly define what they mean by a shift in the cluster in the criteria for evaluation in the Methodology.

In general, the authors should focus on revising this section with the goal of parsimoniously reporting the results that matter for their narrative.

In the section "Spatial result", under the subsection "Noise, neighbourhood SES characteristics...", the same confusing language is used where the authors simultaneously suggest that adjusting for noise and SES together "shifted" the cluster while it also remained "in the same general location".

How does this result square with the criteria laid out in the methodology for assessing the impacts of covariate adjustment? Also, the description of the results in this section do not prepare the reader for the Discussion.

If I understand the results of this study correctly, the significant finding is that while SES had some impact on the LLR of the most likely cluster alone (as shown in Table 3), further adjustment for noise (in Table 4) reduce the LLr to a larger degree than with SES alone; and also larger than the effect of controlling for noise alone.

So noise contributes to the explanation beyond SES characteristics, and ONLY after first controlling for SES.

If this is accurate, then the authors should include some of this comparative analysis in the Results when discussing of high risk disappears or shifts according to different scenarios".

Is there any more clear take home message about the the pattern of findings than this? The authors do talk more about this, but not until later, under the sub-heading "Noise, socioeconomic characteristics and infant mortality".

Since this theme is the main objective of the
| **Discussion** | In the 19th paragraph of the Discussion, the authors indicate that noise and pollution are collinear and that they examined the impact of controlling for air pollution in another analysis; it would be really helpful if the authors told the reader whether or not air pollution helped to explain infant mortality in that other paper. | We added a sentence in the Discussion section to account for this issue, based on another study of our team (see p 18). |
| **Abstract** | For brevity, in the Conclusion section, the authors should combine the sentences "Because of the scarcity of studies, it is difficult to compare our findings with others" and "These findings require further research for confirmation and interpretation.” | We revised the Conclusion section in the abstract accordingly. |
| **Background, paragraph 2** | The authors devote an entire paragraph to the discussion of evidence of a relationship between air pollution and infant mortality; yet this is not the focus of this manuscript, nor do they have any data on air pollution to include in the analysis. I’d strongly recommend making this a much shorter section to concisely convey the idea that other environmental hazards have been associated with infant mortality; are unequally distributed across SES and may even have an unequal effect across SES. | We shortened this paragraph |
| **Background, paragraph 4** | The sentence "Considering the little amount of research..." is made redundant by paragraph 5. I recommend removing from paragraph 4 (or integrating any unique ideas into paragraph 5) for brevity. | We revised the Background paragraph 4 in the text accordingly. |
| **Background, paragraph 5** | A direct reference to "Figure 1" should be included here. I also recommend swapping the first and second sentence, which would make much more sense to me. | We added a reference to «figure 1” in the Background paragraph 5, now paragraph 4. |
| **Methods** | In the section "Socio-economic data", the last sentence "The measure of neighbourhood deprivation..." is made redundant when this is also stated in the first sentence of the fourth paragraph. | We agree and revised the Methods section accordingly. |
of the section "Analytical strategy and results interpretation". To me, it makes more sense to mention this in the latter section, so it should be removed in the former.

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<th>Section</th>
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<td>Analytical strategy and results interpretation</td>
<td>In the second paragraph of the section &quot;Analytical strategy and results interpretation&quot;, the authors appear to rely on criteria espoused by Kulldorff et al, 1997). If this is the case, then they should state this explicitly in the text. The Analytical strategy and results interpretation section now explains that we rely on criteria from by Kulldorff et al, 1997).</td>
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<tr>
<td>Discussion</td>
<td>In the 20th paragraph, the authors state that the spatial analysis they use has only be described in &quot;only few papers&quot; (which is grammatically incorrect, by the way). Readers might be interested in citations for other studies using this approach. We added the reference of two other study using this approach as Sabel et al. 2007 and Bambhroliya et al., 2012</td>
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"Minor issues not for publication"

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<td>There continue to be a large number of grammatical errors, including many awkwardly written phrases. I have not detailed any of these instances due to the large number of them (actually, a small number are mentioned in passing in the review; but there are no specific comments focused solely on these errors). I recommend that the authors review their manuscript carefully before re-submitting. In the event that none of the authors use English as their first language, perhaps they can ask a native English-language speaker to review the article. Language revisions were performed by a native-English speaker</td>
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<td>Points</td>
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| 6. | Spatial methodology: The authors mention that the differences were “significant”. Here and in several other places in the manuscript it’s unclear if this is based on a statistical test or biological significance. | To answer further the question about “significant”: The significant cluster is evaluated by p-value obtained using Monte Carlo replications \(^{(1)}\).  
<p>| 7. | Stage 1: Does 1.44 refer to a RR as indicated in the abstract? If so, please revise the term higher, to as high or something similar (1.44 times higher indicates an RR of 2.44). Also, I believe that the 3.80 listed in this paragraph is a RR? If so please change the units, if not please add units. This also comes up in the occupation, housing conditions, education, neighborhood… paragraph. | We agree and revised the Results section accordingly. |
| 8. | Noise exposure and spatial distribution of infant mortality: rather than highlight the likelihood ratio it might be more useful to highlight the p-value and RR as in the previous paragraph (and in subsequent paragraphs). | We added some information about RRs and P values, and refer to table 4 which summarizes all this information |
| 9. | Noise, socioeconomic characteristics and infant mortality: this section begins with the authors stating that they found a relationship between noise and the spatial distribution of mortality after adjustment. I am not clear which results this is referring to. My understanding was that adjusting for spatial confounding by noise had no impact on results. It might be helpful to refer back to a specific analysis here. | We agree and revised the first sentence of the Noise, socioeconomic characteristics and infant mortality section. To answer further to your comment: Our result indicate that while SES had some impact on the LLr of the most likely cluster alone, further adjustment for noise reduced the LLr to a larger degree than with SES alone; and also larger than the effect of controlling for noise alone. This means that noise contributes to the explanation of excess of infant mortality beyond SES characteristics, and this only |</p>
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<td><strong>10.</strong></td>
<td>Physiological disruptions...: Paragraph 3: Do the authors suspect that a baby’s gender is related to their census block? If not gender wouldn’t meet the definition of a confounder. Did the authors adjust for gender? I don’t think so, but the final sentence about baby girls seems to imply they did.</td>
<td>We suspect that gender is a possible confounder, but we did not adjust our analysis for it because we do not have any data to do so. It is one limitation of our study we acknowledge.</td>
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<td><strong>11.</strong></td>
<td>Figure 1: This figure is very complicated and is not discussed in detail in the text. It might be useful to simplify or explain.</td>
<td>To answer further to your comment: A figure 1 details some mechanisms whereby chronic exposure to noise might end up in various adverse pregnancy outcomes. Three hypothetical pathways are described and detailed in the Discussion. In the Background section, a last paragraph (now 4) explains this figure 1 which represents the conceptual model.</td>
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<td><strong>12.</strong></td>
<td>Tables: The number of significant digits should be consistent across tables (at least for the same variables, e.g. expected cases).</td>
<td>We revised table 3 and 4.</td>
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<td><strong>13.</strong></td>
<td>Table 3 and 4: Please list adjustment factors with the table.</td>
<td>We revised table 3 and 4.</td>
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<td><strong>14.</strong></td>
<td>Figure 4 and 5: In my original review I enquired about why some block groups in the most likely cluster where not shaded. The figure legends should contain this detail and the figures should have a legend that includes this information. Originally, I thought that these blocks were not included in the most likely cluster because they were missing data but based on the response that doesn’t seem to be the case. Clearly the centroid for some of these blocks falls within the cluster (see the red arrows below), are these blocks in the cluster? Why are they white?</td>
<td>When the centroid for some blocks falls within the cluster and blocks are colored in white, these blocks were not included in the most likely cluster because they were missing socio-economic or noise data. We added this information in the figure legends.</td>
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