Author’s response to reviews

Title: Associations of greenness, greyness and air pollution exposure with children’s health: a cross-sectional study in Southern Italy

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Author’s response to reviews:

Manuscript Number: ENHE-D-18-00280.

Manuscript Title: “The effect of greenness, greyness and air pollution exposure on children’s health: a cross-sectional study in Southern Italy”.
Journal: Environmental Health.

We thank you for reviewing the manuscript. We have read and appreciated the important comments from the Editor and the Reviewer: the manuscript has been modified according to the suggestions as closely as possible. We have also corrected minor mistakes or inaccuracies.
Please, find enclosed our point-by-point responses and the revised manuscript (version with changes marked in yellow).

Editor report:

While we see merit in your paper you need to significantly adapt the paper. The reviewer has raised a number of issues you need to address. I share those concerns and would like to highlight the following issues:

Comment: the study is conducted in a small area of a major city. You need to describe the study area qualitatively better for the reader to interpret what the different variables mean in reality. I assume this is about a suburb of Palermo with relatively high rise apartment buildings? Is it close to the sea, extends to the hills? Industry included? Put in some perspective.

Reply: We thank the Editor for the suggestion. In view of this, we have better described the study area (pag 6).

Comment: the term greyness is relatively new. I would appreciate a critical discussion of the usefulness of this concept in practice, as it contains a wide variety of non-green, non-blue objects. What would be the practical advice if we found associations in studies? Add some reflection on this metric (which does not have to agree with my as you can guess negative view). The same applies to the evaluation of the land use categories based upon the rather crude Corine classification.

Reply: Thanks to the Editor for this comment. We have added some clarifying sentences about this topic in the “Discussion” as well as in the “Conclusion” sections (pages 17, 19-20).

Comment: following an issue of the reviewer on Multi exposure models: I interpreted your models as multi exposure models. if so, please clarify and add single exposure models.

Reply: Thanks to the Editor for this suggestion. We have added a table showing the single exposure models in the supplementary material (Table S1).

Comment: the choice to use quartiles but present only two (grouped) comparisons is a bit hard to accept. I see you have a fairly small population, so could you not specify linear models and use the full quartile analyses as a check? If linear is not appropriate, you need to show full quartile analyses (possibly in a supplement)

Reply: Thanks for the suggestion. Following it, we have added two tables showing full quartile analyses on the supplementary material (Table S2- S3).
Comment: it is not obvious that the correlations between stressors are so high you cannot perform simple logistic regression. If so, please add these.

Reply: We thank the Editor for this comment. The ridge estimator restricts the length of the coefficients estimator in order to reduce the effects of multicollinearity. In addition, ridge regression estimation method has better performance than other approaches when the sample size is small, irrespective of different correlation levels. The following table illustrates the multivariable logistic models with very high estimates and wide CI due to the small sample size and the correlation between stressor. For this reason we preferred to use a penalized model as the ridge regression.

<table>
<thead>
<tr>
<th></th>
<th>Ocular symptoms</th>
<th>Nasal symptoms</th>
<th>Pulmonary symptoms</th>
<th>General symptoms</th>
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<tr>
<td><strong>Definition of abbreviations:</strong> NDVI: Normalized Difference Vegetation Index; DUF: Discontinuous Urban Fabric; CUF: Continuous Urban Fabric; RSG: Residential Surrounding Greyness; HTRs: High traffic roads; NO2: Nitrogen dioxide; FSES: Family’s Socio-Economic Status. Significant effects are in bold. Values represent odds ratios, with 95% confidence intervals shown in parentheses. *Accounting for gender, age, FSES, atopy, doctor diagnosed.</td>
<td></td>
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</tbody>
</table>
asthma, parental history of allergy and preterm born. Reference group: Female, NDVI >0.15; Discontinuous Urban Fabric, No RSG, HTR>200 m, NO2 <60 µg, FSES > 49, no sensitization, no asthma, no parental history of allergy and term born.

Comment: give a bit more detail on the LUR model

Reply: Thanks to the Editor for the observation. A detailed description of the LUR model has been included in the “Methods” section (page 10).

Comment: the discussion is long

Reply: Thanks to the Editor for the suggestion. We have reduced the discussion section.

Reviewer #1:

This is an interesting study that examines the associations of several urban-related environmental exposures with symptoms in children. The inclusion of both "green" and "grey" spaces is novel. The analyses have been performed properly, but some aspects need more clarification (see also my comments below). Also, the manuscript should be checked by a native English speaker in order to improve the English language of the manuscript. I have a suggestion for the analyses for this study: The aim of the study is to "simultaneously evaluate the associations between indicators of urban-related environmental exposures with symptoms in schoolchildren". However, as far as I understand, you have only performed single-exposure models (i.e. one exposure per regression analysis). Because the environmental exposure are correlated, it would be interesting to perform multi-exposure analyses. You could, for example, include the NDVI and NO2 concentrations in one model.

You can find the remainder of my comments below:

Comment: Line 7: "A comprehensive approach is advisable to estimate..." Why?

Reply: We thank the Reviewer for this comment. We have changed the sentence in order to clarify the background section of the abstract.

Comment: In the Methods section of the abstract, please mention the country in which the study has been performed.

Reply: Thanks to the Reviewer for the observation. We have added the country in the Methods section of the abstract.
Comment: Line 16/17: "Exposures to greenness and greyness..." Add: at the home addresses.
Reply: Thanks for the suggestion. We have added the sentence in the abstract.

Comment: Results section: You use 'risk of symptoms', but you show OR's. A better term is the 'odds of symptoms'.
Reply: Thanks for the suggestion. We have modified the text accordingly.

Comment: Conclusion: I would not use the words 'account for', but 'are associated with'.
Reply: Thanks to the Reviewer. We have modified the text according to this suggestion.

Introduction:
Comment: Page 4, line 31: I would start the alinea with: "Because of the increasing urbanization, there is growing interest on environmental exposures within urban settings, such as traffic intensity, household density and natural and green space."
Reply: Thanks to the Reviewer for the suggestion. We have modified the text accordingly.

Comment: Page 4, lines 41-46: Remove the sentence about the NDVI. This sentence is more suitable for the Methods section of the manuscript.
Reply: Thanks to the Reviewer for this comment. We have moved the sentence into the Methods section, as suggested.

Comment: Page 4, lines 58-60: Remove the sentence about CORINE, this sentence is more suitable for the Methods section of the manuscript.
Reply: We thank the Reviewer for this comment. We have moved the sentence into the Methods section, as suggested.

Comment: Page 5, line 26: "LUR modeling was applied to explain..." Remove this sentence.
Reply: Thanks for the suggestion. We have deleted the sentence, as indicated.

Comment: Page 5, lines 33-34: "emphasizing that NO2 exposure can cause adverse respiratory outcomes". This implies causality. Remove this part of the sentence.
Reply: Thanks to the Reviewer for the suggestion. Accordingly, we have removed this part of the sentence.

Comment: Page 5, lines 50-51: Change "using the three aforementioned indicators (NDVI, CORINE and LUR)" into "using green, grey and air pollution".

Reply: Thanks for the suggestion. We have changed the text accordingly.

Materials and Methods:

Comment: Page 6, lines 45-53: When did the parents complete the questionnaires (what year, which months)?

Reply: Thanks to the Reviewer for the observation. We have added the requested information in the text.

Comment: Page 8, lines 1-24: I would remove the formula and the technical description of the NDVI (until reference 32).

Reply: Thanks for the suggestion. We have removed this part of the text, as indicated.

Comment: Page 8, line 33/34: "The NDVI assessment was based on individual addresses". I don't understand this sentence. I would assess the average NDVI in a circular buffer (or multiple) around the children's homes. I do not understand what buffer you have chosen, and what the reasons are for this buffer size.

Reply: Thanks for the suggestion. We have clarified this sentence.

Comment: Page 8, lines 43-50: The alinea about CORINE is very vague. Please add some information about the land-cover classes, especially information about the classes mentioned in Table 1. What do the classes DUF and CUF exactly comprise?

Reply: Thanks for the suggestion. We have modified the text for improving the level of information.

Comment: Page 10, alinea "Statistical power": This is very short and unclear. If you want to say anything about statistical power, please give more information.
Reply: Thanks for the suggestion. We have removed the subsection "Statistical power", including the statistical power calculation in the “Statistical analysis” section and clarifying the unclear sentence.

Comment: Page 10, line 55/56: "the highest FSES (>49.5, 1st quartile)". FSES is not an exposure, so don't use it in this sentence.

Reply: Thanks to the Reviewer for the observation. We have removed this sentence, as suggested.

Results:

Comment: Page 11, lines 11-25: I would skip a few descriptive statistics in the text of the Results (for example about passive smoke and maternal smoking during pregnancy) and include the median (IQR) of the NDVI and NO2 levels in the text. The exposures are of interest.

Reply: Thanks to the Reviewer for the observation. We have removed some descriptive statistics and we have added median and IQR of the NDVI and NO2, as suggested.

Comment: Page 11, lines 26-42: The alinea about the self-reported symptoms is very long. The reader can find the numbers in Table 2, so please shorten this part of the Results.

Reply: Thanks to the Reviewer for the advice. We have shortened the text by removing this part of the Results.

Comment: Page 12, line 4/5: "only one house was exluded since.." Do you mean excluded from the analyses?

Reply: Thanks to the Reviewer for the observation. We have specified the reason why the house was excluded from the analysis.

Comment: Page 12, lines 14-16: I would mention in the text whether the correlations are positive or negative. "A significant positive correlation was found between NO2...”.

Reply: Thanks to the Reviewer for the observation. We have added the requested information in the text.

Comment: Page 12, lines 25-41: You use the term 'risk of symptoms', but it should be 'odds of symptoms'.
Reply: Thanks for the suggestion. We have modified the text accordingly.

Discussion:

Comment: Page 13, lines 29-32: Could you say something about the study population from the study by Lovasi et al.?

Reply: Thanks for the suggestion. We have specified the type of study and the population involved.

Comment: Page 13, lines 49-57: Do you have a possible explanation why you found that a very low exposure to greenness was associated with a higher risk of self-reported nasal symptoms?

Reply: Thanks for the question. We have explained our hypothesis in the text (pag 16).

Comment: Page 14, lines 24-29: Could you say something about the study population (e.g. the age of the children) from the study that used pooled data of European birth cohorts?

Reply: As the Reviewer suggested, we have specified characteristics about the study population.

Comment Page 15, lines 41-47: "These results are in agreement with numerous studies demonstrating that elevated concentrations of traffic-related air pollutants in the near-road environment are associated with numerous adverse human health effects". However, in your study, you do not find statistically significant associations of NO2 with the symptom score. Only living in proximity to HTRs (and not the air pollutants) seems to be associated with the symptom score. So, if it is not the higher NO2 concentrations near high-traffic roads, what does explain the association between distance to HTR's and a higher symptom score?

Reply: Thanks to the Reviewer for the observation. We presumably did not find statistically significant associations of NO2 with the symptom score because of the small sample size; indeed, the estimate become significant if we set confidence intervals at 90%. Moreover, irrespective of HTRs which is a measured variable, NO2 concentrations were estimated using a LUR model. Finally, the observed effects in our study are possibly due to co-pollutants other than NO2, whose role remains controversial when considering general population. NO2 may be considered a good marker of traffic air pollution exposure, however it is not the only one. Moreover, the variable HTRs includes several risk factors specifically associated with traffic, such as noise, stress and other pollutants we did not estimate in the current study.

Tables and Figures:

Comment: Table 1: Please do not use the term 'Host'.
Reply: As the Reviewer suggested, we have substituted the term “Host” with “Personal”.

Comment: Table 1: Remove the three rows with the n(%) of children within quartiles of exposures (for example: "NDVI: <0.1504 (1st quartile)"). By definition, each quartile should include approximately 25% of your study population.

Reply: Following the Reviewer advice, we removed the three rows with the n(%) of children within quartiles of exposures.

Comment: Table 1: In the row 'Residential surrounding greyness (300-m buffer), n(%)' I expected a 'median (IQR)'.

Reply: We thank the Reviewer for this comment. The variable “Residential surrounding greyness (300-m buffer)” was dichotomized based on the simultaneous presence of industrial, commercial and transport units, dump and construction sites and urban fabric related features. We included this information in the text.

Comment: Table 3: Please also show the unadjusted results.

Reply: We thank the Reviewer for this comment. We added a table showing the unadjusted models in the supplementary material (Table S1).

Comment: Figure 2: The Figure legend (on the right side of the Figure) only includes numbers and is not clear. I would make a legend only for the three classes of interest (DUF, CUF and coniferous forests) and not use numbers but text in this legend.

Reply: Thanks to the Reviewer for this suggestion. We have modified Figure 2 accordingly.