Author’s response to reviews

Title: Desert dust outbreaks and respiratory morbidity in Athens, Greece.

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Author’s response to reviews:

RESPONSE TO THE EDITORS AND THE REVIEWERS

We thank the Editors and the Reviewers for the careful review of our manuscript. We have revised the manuscript following these suggestions. Please find in the following the responses to the specific comments. We have highlighted additions or modifications with yellow.

Response to Reviewer #1:

Reviewer’s comment no 1:

“I appreciate the efforts undertaken by the authors to address all my major concerns. I am fine with the answers. There are only a couple of doubts, which the authors might decide to address or not.”

Response:

We thank the Reviewer for this encouraging comment. Indeed, we feel that the revision of the first version of the manuscript based on the Reviewer’s comment has substantially improved the paper.
Reviewer’s comment no 2:

“First, I am not fully sure that the case-control matching cannot be retained in the analysis. Since matching has been done individually based on predefined characteristics, authors should still be able to account for it. In other words, they might be able to define categorical variables identifying the pairs (or triples) of days with same covariates but different dust indicator, and condition on them by use of conditional Poisson regression. In this way, the contrast of analysis would be entirely within group, and adjustment for those characteristics would be achieved by design. I would suggest the authors to at least consider this possibility, and motivate a negative response if they believe it is wrong.”

Response:

We have followed the suggestion of the Reviewer (and that of Reviewer 2, comment no 4) and applied a Poisson regression including indicator variables for matched sets of "dust" and "non-dust" days. We additionally applied a mixed Poisson model approach with a random intercept for matched pairs, as an equivalent approach. We have included the results from the 3 models in the Supplemental Tables S3 and S4. The general pattern of the findings did not change. We have described this approach in the Methods section (lines 106-109) where we write: "As additional sensitivity analyses, we applied two modelling approaches that preserved the matching of "dust" and "non-dust" days but use more degrees of freedom in the models. In the first approach, we added 132 indicators for the matched sets and in the second approach, we applied a mixed Poisson model with a random intercept for matched sets of days." We describe the findings in the Results section (lines 170-171): "The results from the additional sensitivity analysis models applied did not substantially change the main findings (Supplemental Tables S3 and S4)."

Reviewer’s comment no 3:

“Second, it is a pity that the authors could not specify a priori a longer series of data (up to more recent years). In this way, being the study conducted in only one city and over a 10-year old period, its interest is somewhat reduced.”

Response:

We agree with the Reviewer that the points mentioned limit the relevance of the findings. This has been stated in the limitations (line 262 of the revised manuscript: “…renders an extension of the analysis to a longer time period practically impossible restricting the relevance of our findings.”)
Response to Reviewer #2:

Reviewer’s comment no 1:

“The authors are to be commended on their thorough and responsive revision. I have only a few follow-up points”

Response:

We thank the Reviewer for this encouraging comment. Her constructive review has helped us very much improve our manuscript.

Reviewer’s comment no 2:

“In the previous version, I didn't fully appreciate that data were only available for specific dust and non-dust days. This has been clarified well in the revision. As a minor point, I would refrain from labeling this as a 'time-series' analysis (line 94) given the discontinuous data available for this study (only 300 days over 6 years).”

Response:

Following this suggestion, we have deleted the term “time-series“ (line 94).

Reviewer’s comment no 3:

“In my previous review (major comment #4), I questioned the very high magnitude of effects observed for dust days (~50% increased risk on dust vs. non-dust days). In response, the authors have added some text on data limitations that don't allow exploration of potential additional confounders (e.g., pollen levels). I would also suggest, however, that the authors highlight these magnitudes as being exceptionally large in the discussion – they are much larger than observed in previous studies. And, given that they are consistently large across all tested strata (e.g., in Table 3 for male and female, above/below 65 yrs, different outcomes), with no considerable variation, this suggests to me the possibility of a chance finding or uncontrolled confounding”

Response:

Following the Reviewer’s suggestion, we have specifically addressed this point as a limitation of the study writing (lines 263-269): “The observed association of desert dust days and respiratory morbidity was very strong with estimates of approx. 50% increase in risk of emergency room visits or admissions on dust days compared with the non-dust days. These effects although consistent across all tested strata such as male/female or age below/above 65 years as well as across the different outcomes, are much larger than the effects usually reported in the literature.
For this reason, we cannot exclude the possibility of uncontrolled confounding or of a chance finding. However, applying sensitivity analysis, did not modify the magnitude of effects, which remain large.

Reviewer’s comment no 4:

“With the clarification of data availability in the revised text, I also wonder about the analytic design that the authors employed. The current Poisson models, controlling for temporal factors in the model, do not take advantage of the sampling design of case and matched control days. As a sensitivity analysis, can the authors run models in which an indicator variable is included for every matched strata (e.g., 132 indicators), rather than controlling for the matching factors of time, temperature, and humidity in the model? This second model would take advantage of the matched design, and thus would not need to include temperature, humidity, day of week, etc. (though might still include control for calendar month and holidays).”

Response:

We have followed the suggestion of the Reviewer (and that of Reviewer 1, comment no 2) and applied a Poisson regression including indicator variables for matched sets of "dust" and "non-dust" days. We additionally applied a mixed Poisson model approach with a random intercept for matched pairs, as an equivalent approach. We have included the results from the 3 models in the Supplemental Tables S3 and S4. The general pattern of the findings did not change. We have described this approach in the Methods section (lines 106-109) where we write: "As additional sensitivity analyses, we applied two modelling approaches that preserved the matching of "dust" and "non-dust" days but use more degrees of freedom in the models. In the first approach, we added 132 indicators for the matched sets and in the second approach, we applied a mixed Poisson model with a random intercept for matched sets of days." We describe the findings in the Results section (lines 170-171): "The results from the additional sensitivity analysis models applied did not substantially change the main findings (Supplemental Tables S3 and S4)."

Reviewer’s comment no 5:

“Finally, the health data were only collected for adults (line 74) - please clarify the lower age limit in the methods section, and also in tables that specify ‘<65 yrs’, perhaps these labels can be revised to indicate the age range (e.g., 18-64 yrs?)”

Response:

We thank the Reviewer for this suggestion. Accordingly, we have replaced “<65” with “18 – 64” in the text (line 167) and in the tables (Table 3 and Table 4).