Reviewer's report

Title: Mixed individualized- and group-level-metrics for lifetime exposure to air pollution for use in epidemiologic studies

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Reviewer: Steven L Simon

Reviewer's report:

Here I provide comments on the manuscript "Mixed individualized- and group-level metrics for lifetime exposure to air pollution..."

This is nicely prepared manuscript and it is well written. I am not an expert in air pollution assessment though I am qualified to make comments on the assessment strategy. My interest is basically in the methods described here and how they might be applied more generally. However, it was unclear to me after reviewing it, whether it is a methods development paper or an assessment paper. I think the authors tried to do both in one paper. I'm not sure that is possible. I think its potential value is as a paper focused on methods with an example application. If so, it needs to be restructured with less detail on the assessment itself.

Below, I provide two main points, and a number of small issues. I will try and distinguish each.

My first main point: The concept of "multiple imputation" is obviously not a creation of these authors. For that reason, I first wondered if this paper was necessary or was intended simply just an example of usage of multiple imputation. It became clear that the primary development of these authors is their "incompleteness index" and secondly, a demonstration. Depending on the emphasis the authors want to make in their paper, they might consider rebalancing the detail of the paper. In particular, from the point-of-view of an epidemiologic methodologic paper, I found it to be much too heavy on details about the assessment strategy, i.e., the details about the Z-dose. I would have preferred a shorter and more succinct paper on a possible use of multiple imputation and the "incompleteness index", using the air pollution assessment as an example (rather than the centerpiece). Personally, I was interested in the methodology in a general sense, but not in the air exposure modeling. The emphasis is both a matter of concern for the author and the journal. Who do you want the paper to appeal to?

p. 2. Results section of Abstract. While the paper is overall well written, I found this short "Results" section to be a failure. The paper deserves better than this. It told nothing that I could understand on the first read through, and that's when you read the Abstract. The Conclusions of the Abstract were useful, but not the Results.
p. 4, last line. I wonder why the authors call this a "proposed method." Are you thinking there may be some formal adoption of the method? I don't think there will be. Just say it is a "strategy we developed that may have broader use...".

p. 5, 2nd paragraph. I found the sentence "A key component of the methodology...in the way gaps are filled[9]" to be important and might ought to be highlighted more. However, when I went to look at the title of reference 9, I was disappointed that it not reference of a methodologic paper, but another paper on air pollution which I won't bother to look up. I wonder if the authors could find more general references that readers might find interesting and that would better substantiate their methods.

p. 6, 2nd sentence refers to an "imputation model." I find this provocative and I was interested to see the model. However, I found little discussion that I could say "that is the model" except the Appendix. I was unhappy to see the "imputation model" given so little space and way too much space given to the Z-dose, etc.

My second main point was motivated by the authors statement on p. 6 (2nd paragraph): "Calculation of multiple sets of dose values within a multiple-imputation framework makes possible assessments..." Here I want to ask the authors if they have considered how they (or other investigators) should pick or weight the best set? They seem to imply that just having multiple sets of dose values is enough. Wouldn't it be better if parameters were not just alternatives, but picked from probability density distributions such that the multiple sets could form a PDF of results, rather than just be equally weighted alternatives? I'm wondering if I missed something? If not, the authors should consider multiple imputation based on PDFs as done elsewhere in risk assessments.

p. 7, after eq. 1. The authors state Z(i,y) is a vector of "effective doses." What are effective doses? In other assessment areas, e.g., radiation assessments, "effective dose" has been explicitly defined. I realize it is a different definition here, but I don't know what it means.

I found pp. 8-14 not to be of particular interest to me. I think 2 pages would have sufficed.

p. 15, The "incompleteness index", which is the only new concept introduced in this paper, was finally presented. I think it is much too late. My interest had already waned because of the detail on the assessment model. I would move the assessment model to the appendix and the "imputation model" to the main body.

p. 16. I think the statement "If the results are robust...we can have confidence the imputation is not introducing artificial findings" to be important, but no explained well enough. What if the findings are "not robust"? I think a good methods paper would introduce some strategy here.

p. 17-18, The section "Top 1% dose tail" seems important, but the conclusions of
this section escaped me. I recommend trying to be a little more clear and direct about the value of this (and other) sections.

p. 19, last sentence. It seems, based on the last sentence, that from the authors point-of-view, this paper was about the population, rather than the methods. They could have taken a much shorter route to conclude "the subpopulation is worthy of future attention." I think the authors have really missed an opportunity. They should be concluding about the value of their methods to other studies. As you can see, I see this as a methods paper, rather than an assessment paper. I'm unclear which way the authors see it.

Given that the authors are obviously competent in their field and are good writers, they can assuredly improve this manuscript to qualify for publication.

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests.