Reviewer’s report

Title: Personal carbon monoxide exposure, respiratory symptoms, and the potentially modifying roles of sex and HIV infection in rural Uganda: a cohort study

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Reviewer: M. Suter

Reviewer's report:

This is a thorough, well-written, and interesting manuscript that explores correlates of personal CO exposure, as well as the relationship between personal CO exposure and respiratory symptoms in rural Uganda. The authors found high levels of person CO exposure in their cohort. Additionally, CO exposure was correlated with biomass fuel use, and was associated with respiratory symptoms in women and HIV-infected individuals. While this paper is well-written, I think the authors need to be more cautious about the interpretation of their findings, and to frame their analysis as exploratory; I was unclear on the author’s hypotheses going into the study. Also, I think there are some details missing from the introduction to motivate the effect modification analyses, and some portions of the statistical analysis are a bit unclear.

Comments:

1. This is a very small detail, but in your abstract, you begin the results paragraph with a number. This should be written out or the sentence should be rearranged.

2. Your title references the "modifying role of sex and HIV infection," but examining effect modification is not listed in your introduction as one of your hypotheses. The effect modification analysis seems like an exploratory analyses, so I think it should be mentioned in the introduction and identified as such. I would also recommend changing your title to be more in line with the main aim of the study.

3. The introduction is well-written, but I think it is missing some information about the motivations of the study. I would recommend including some information about previously-identified correlates of CO exposure. Also, the background mentions nothing about potential effect modifiers in the CO-respiratory symptoms association. A mention of why you chose to look at certain factors would be helpful. In the conclusion, you include some of this and I think some of it should be moved to the introduction.
4. Are most of the HIV-infected individuals in your cohort virally-suppressed? What percentage are on ART?

5. In lines 115-116, can you mention the specific tests used? In your table 1, you presented descriptive by sex and this should be mentioned.

6. In general, I found your description of the primary outcome of interest a little bit hard to follow (starting in L113). It would be easier to understand if mentioned the two outcomes at the beginning, and then went into more detail about how they were calculated. It would also be helpful if you could mention why you chose 2 different time frames for the outcome.

7. In line 130-131, you should mention the characteristics of interest. I'm also a little bit confused about the purpose of the analysis mentioned here. How is this different from the analysis described in line 133? I think addressing my above comment will help clarify this difference.

8. Do you have any information about compliance with wearing the personal monitors? I might suggest including some of this. It is probably not necessary to include this, but why do some participants have multiple sampling periods, while some only have one?

9. In the paragraph that starts in line 146, I don't see which models were used. You also mention that you explored interaction, but you do not say how this was done. Interaction terms? Stratified analysis? Both?

10. In lines 156-157, you should include some references. As mentioned before, I would also include a mention in the introduction of why individuals with HIV or women would be at a higher risk of harm.

11. In the paragraph that start in line 195, what were models adjusted for? The same things as other models? Also, did you only use stratified models, or do you have some formal test of interaction? If the former, I think this adds to my comment about the slightly misleading title. I would recommend running some formal interaction analyses. I am not convinced your results are due to the statistical precision gained by having higher levels of the exposure and outcome in HIV infected individuals and women, compared to other individuals.

12. Again, I think some of your conclusions about effect modification by sex and HIV infection status are overstated, especially since it was not one of your hypotheses.
identified at the beginning of the study (at least as-written) and no normal interaction analyses were performed.

13. In the conclusion, I would mention something about your biomass-CO finding.

Tables:

1. I am curious why your table one stratified by sex. It might be interesting to see an HIV-status stratified table, especially since the populations were recruited from two difference sources. Differences in demographic characteristics could definitely explain the higher CO levels in the HIV-infected subgroup.

2. A small detail, but I would take the Female sex row out of your Table 1, since your table is sex-stratified.

3. In the footnotes in Table 2, I would include the statistical tests used to obtain p-values. It might also be helpful to include n's in Table 2.

4. In Table 3, why are some of the coefficients missing? I'm guessing this because they were removed from the final model?

5. I'm not sure I follow why some of the correlates of respiratory symptoms are missing from Tables 5-6. Why is this? I think this might become clear when you include more detail about your stratified models in the results section.

6. It seems like Table 7 might be unnecessary, and a mention in the text is probably sufficient.

7. Another small detail, but in Figure 2, change "gender" to "sex."

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