Reviewer's report

Title: The Impact of Long-Term PM2.5 Exposure on Specific Causes of Death: Exposure-Response Curves and Effect Modification among 53 million U.S. Medicare Beneficiaries

Version: 1 Date: 11 Dec 2019

Reviewer: Jonathan Levy

Reviewer's report:

General comments

This is a re-review of a resubmission investigating the association between long-term exposure to fine particulate matter and mortality among the Medicare population. Major comments in my original review related to the need to clearly define the value added of the paper relative to multiple other publications using the same database, to better justify or change the approach for "non-combustion PM", and to better explain why the authors think their findings on things like the shape of the exposure-response function differ from some of the rest of the literature. The authors were generally responsive to these points as well as similar ones raised by other reviewers, though could be a bit more direct about the similarities and more expansive for the reasons for differences (especially in comparison with Di et al., given that they used a very similar dataset).

Specific comments

- Line 23: Note phrase "non-combustion" instead of "non-traffic" here

- Line 51-53: Somewhat misleading sentence, since Di et al. (reference 5) looks at the exact same population as this study, as do other large-scale administrative databases and other cohorts. Text should ideally parse out the studies that focused on white/urban/higher SES populations, and then those that included more diverse populations with their separable limitations.

- Line 59-61: Similarly, I don't think the authors are making the strongest case here. Many studies have done these things, individually or together (again, Di et al. looked at SES surrogates, race, lower PM, and urban vs. rural populations). The case needs to be made that what the authors are doing here involves novel methods to better elucidate these effects, versus just saying that studies haven't done this.
- Line 122-130: This is a greatly improved presentation of the approach. I still think there is some overinterpretation, as the authors could be capturing primary vs. secondary PM rather than traffic vs. non-traffic, but I think this can be handled in the discussion section (though some caveats could be included here as well). It is also worth being explicit, here or elsewhere, that this approach provides the ability to compare non-traffic (or secondary) PM with total PM but does not provide the ability to compare non-traffic with traffic PM. That would help explain why the tables are presented as they are. Alternatively, NO2 could be used as the proxy for traffic PM in the comparison, though that comes with its own interpretation challenges.

- Line 141: Number needed before "billion"

- Line 195-198: The fact that the associations are greatly attenuated for rural populations for lung cancer and respiratory disease (and are even significant but protective) raises questions about the potential role of smoking as a confounder. Smoking rates are clearly higher in rural settings, where air pollution is generally lower. This could contribute to the non-monotonic patterns for lung cancer and these associations. The authors should at least discuss this point. Di et al. did rule out smoking as a potential confounder in their MCBS analysis, but didn't look specifically at this question of urban vs. rural associations.

- Line 210-211: Per above, it could be argued that the residuals are a surrogate of secondarily-generated PM through the correlation with sulfate, not coal specifically (obviously sulfate is an indicator of coal, but in this context could be more of a secondary formation indicator).

- Line 249-250: This conclusion feels like an overreach, given linear or supra-linear associations in studies like CanCHEC or other studies in the Medicare population that included rural populations.

- Line 276-277: This would be a place to potentially talk about the lack of smoking data and the implications, per the discussion above.

- Line 293-296: This would be a place to acknowledge that you may have developed surrogates for primary vs. secondary PM, rather than traffic vs. coal.

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