Author’s response to reviews

Title: Mortality Associated with Wildfire Smoke Exposure in Washington State, 2006-2017: a case-crossover study

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Author’s response to reviews:

Reviewer Comments:

Reviewer #1:

Point 1: Summary: This study adds to the relatively scant literature on the effects of wildfire smoke exposure on mortality. This is incredibly important as wildfire smoke is becoming more of a problem in western North America, contributing to more of the air pollution that populations breathe. Additionally, most of the literature examining mortality impacts from wildfire smoke has been done in other countries and not the US, so this is an important study in that way. However, I have some concerns about the exposure assessment (which was not explained clearly enough in the methods to truly understand what was done) and the interpretation of the results, particularly in the discussion section, which implies a misunderstanding of the information one can derive from a confidence interval. I provide specific suggestions and comments below.

Response 1: Thank you for your positive comments and helpful critiques. We address your specific comments below.

Major Points:

Point 2: The results section has good information but it could benefit from reorganization. I would suggest presenting the distributed lag analysis first, then a table of all of the results for lag day 0 and lag day 1 in separate columns for each endpoint studied and each individual group (but
for all causes of death). Then in the next table, put in the analyses (again with separate columns for lag day 0 and lag day 1) for the specific causes of death within respiratory by different age groups and race groups. This would also require reorganizing the writing in the results section.

Response 2: Thank you for your suggestions. We have reorganized the results section according to your suggestions, starting with the distributed lag analysis, then the main analyses, showing both lag day 0 and lag day 1 results, and then the secondary analyses.

Point 3: Some more clarity on the exposure assessment in the methods and also on the statistical analysis is warranted (please see specific comments to this end below). The discussion section does a good job of highlighting the limitations of this exposure assessment, but that revealed much more to me about the exposure assessment that was lacking from the methods section. It is also unclear how the sensitivity analysis is different from the regular analysis as the threshold of 20.4 ug/m3 is referred to for both of these thresholds throughout the paper.

Response 3: Thank you for your comment. We agree that the explanation of the exposure assessment in the methods was insufficient. We have added additional detail for clarity, including supplemental material, and believe that this portion of the methods section is much improved.

Point 4: Also, please see the comments in the discussion section on the interpretation of the confidence intervals.

Response 4: Thank you for your comments. We address the specific comments with regards to the discussion section below.

Point 5: Abstract: The findings of associations for different age groups seems very important to me and should be emphasized in the abstract if possible given word count restraints.

Response 5: Thank you for your comment. We agree, and have added the following sentence to the Results section of the Abstract to highlight this finding:

“When stratified by age group, we observed a 35.0% (95% CI: 9.0 - 67.0%) increase in the odds of same-day respiratory mortality for adults ages 45-64.”

Point 6: Introduction: The referenced Haikerwal paper focused on cardiac arrests, but not just cardiac arrests that resulted in death. This should be noted as the authors are trying to paint a picture of what is known about the association between wildfire smoke and mortality specifically.

Response 6: Thank you for pointing this out. We’ve added the following clause to clarify that the cardiac arrests in the Haikerwal paper did not all result in death:
“Further, Haikerwal et al. observed an increase in risk of cardiac arrests, especially in older adults in Australia, although not all resulted in death.”

Methods:

Point 7: Lines 131-132: Please justify the use of just June - September for the fire season in Washington.

Response 7: Thank you for giving us the opportunity to justify the fire season period. We worked with colleagues from the Washington State Department of Ecology on this study, and they have been documenting smoke in the state for several years. Their historical records indicate that smoke is most common in the months of June-September. Further, months before or after the aforementioned period may have smoke attributed to other sources, such as prescribed burns or residential wood combustion, which we tried to exclude from our analysis. Additionally, in an interagency operating plan, peak fire season is referred to several times, as generally including most of June-September. We’ve added in the following sentence to the methods to clarify this: “Historically, wildfire smoke has been documented in Washington during these months, and is described in an interagency operating plan as “peak fire season” in the Pacific Northwest (29).”

Point 8: Lines 144-147: Please provide in the text the spatial resolution of the grid as this is important to determine if this exposure method is appropriate for assessing exposures across the population.

Response 8: Thank you for your comment. We have added the spatial resolution of the grid in the text:

“The AIRPACT-4 model domain is composed of 4x4 km grid cells. Each AIRPACT-4 model grid cell was matched to one of the three air quality monitoring sites closest to it and to the monitoring site’s nearest National Weather Service meteorological site in order to obtain meteorological variables (see Text S1 for additional detail).”

Point 9: Lines 149-151: Which grid cell were excluded? A map would be helpful. How many people live in those grid cells and/or how many deaths were dropped due to dropping those grid cells? Over the years studied, how affected were those grid cells by wildfire smoke? Again, knowing the size of the grid cells is important to know how much this exclusion may have biased the study.

Response 9: Thank you for your comments. This is a great point, and consequently we have added additional detail on grid cells that were excluded and the subsequent deaths left out. We have added the following sentence in the methods section:

“About 1.5% of person-days across the study time period were not considered to be represented by any monitoring site, and were excluded from the analysis (see Figure S2, Additional file 1, for
a map showing areas excluded). This resulted in the exclusion of 1.2% of total non-traumatic deaths in Washington during the study period (see Figure S1, Additional file 1).

As noted above, we’ve also added a map in Additional file 1 (Figure S2) showing how many years of the study period each grid cell was represented by a monitoring site.

Point 10: Line 191: I thought that 20.4 ug/m3 was the threshold for defining a wildfire smoke affected day in the original analysis. Please clarify which is the main threshold and which is the sensitivity analysis.

Response 10: Thank you for the opportunity to clarify. We’ve included more detail about our main wildfire smoke day definition in the methods section, and added in a clarifying clause about the threshold for the sensitivity analysis. It now reads:

“We also conducted a sensitivity analysis, setting 20.4 μg/m3 for PM2.5 as the wildfire smoke-affected day threshold without additional criteria for days between 9 and 20.4 μg/m3, to assess whether our results were sensitive to the exposure definition (see Table S1, Additional file 1).”

Point 11: In the statistical analysis section, I couldn’t tell if the exposure was wildfire-smoke affected day or PM2.5 that is then interacted with the binary variable of wildfire-smoke affected day. Please clarify this.

Response 11: Thank you for the opportunity to clarify. The exposure is indeed wildfire-smoke affected days, not the interaction between wildfire-smoke affected days and PM2.5. We’ve added in the following clause in the statistical analysis section for clarity:

“This study design compares wildfire smoke exposure, defined as the binary wildfire smoke day classification described above, on the day of death, the day prior to death, and on the four days prior to death, to wildfire smoke exposure on referent (non-event, or control) days for the same decedent.”

Point 12: Also, more needs to be said about how the exposure data was spatially merged with the health data. Please state the software that was used and how the data were spatially analyzed.

Response 12: Thank you for your comment. We have added information on how the exposure data and mortality data were spatially merged. The updated text now reads as follows:

“We then joined this dataset with the above described mortality data using a spatial join in ArcGIS (version 10.5.1; Esri, Redlands, CA), assigning the latitude and longitude of the residence of each decedent to the nearest grid cell and corresponding PM2.5 concentration and humidex value.”
We’ve also added additional text in Additional file 1 (Text S1) explaining the details of our methods. While we felt that this level of detail was indeed important to include, we thought it would be better suited for the supplemental materials rather than the main text.

Results:

Point 13: Table 2 says that the average PM2.5 was 3.39 ug/m³ on referent days, but on line 172, it says that there were on average 3.39 referent days per decedent. I believe the statement on line 172 is correct. Please clarify what the average PM2.5 levels were on the referent days for Table 2 (although I think this is on the line above, so the third line in that section doesn't fit in that section which has a title of PM2.5 mean for that column).

Response 13: Thank you for your comment. Yes, you are correct. The average number of referent days per decedent is 3.39, and the labeling in Table 2 is incorrect. We’ve deleted this row in Table 2 for clarity, referring to it in the text instead.

Point 14: Lines 229-231: Please clarify the wording here. The text reads: "The results indicate some evidence for an effect at two days prior to death, with no evidence for an effect in the preceding days." I think what the authors mean to say is: "The results indicate some evidence for an effect of exposure at two days prior to death, with no evidence for an effect of exposure during in the preceding days on death." Or something to that effect…

Response 14: Thank you for your helpful comment. Your suggested wording increases the clarity of this statement, and we’ve modified the sentence accordingly. The sentence now reads as follows:

“The results indicate some evidence for an effect of exposure at two days prior to death, with inconclusive evidence for an effect of exposure in the preceding days on death.”

Point 15: I suggest putting all of the findings related to Table 3 together, perhaps after the discussion of the lag days?

Response 15: Thank you for your suggestion. After reorganizing the results, we have incorporated more findings into Table 3, and have grouped them together, following the findings of the distributed lag model.

Point 16: Given the evidence from the lag analysis that most of the effect on mortality is for exposure to wildfire smoke the day before death, why were the main analyses done for same day exposure? Additionally, when doing same day exposure, sometimes the death occurred so early in the day that the person was not truly "exposed" to the smoke that day. I would suggest moving the results for lag day 1 to the main results and putting the same day in the extra table. Or better yet, put one column in Table 3 for same day and one column for lag 1. Then Table 4 could be
specifically looking at the stratified analyses by cause of death and by age/race/income etc. I think this would clarify the results better.

Response 16: Thank you for your helpful comment. We agree that reorganization of the results will increase clarity, so we have decided to follow your suggestions. We've re-ordered our results as follows: lag results, then the findings listed in Table 3 (including results for same day and lag day 1 in separate columns), and then we placed the secondary stratified analyses in Table 4.

Point 17: Lines 217-218: the negative sign on the 1 in the confidence interval gets lost as it is on a different line than the rest of the confidence interval and when I first read it, I thought it was 1-4 instead of -1 - 4, which has a different interpretation.

Response 17: Thank you for your comment. We realize this is difficult to read, and we will ensure in the final review that the formatting is easy to read.

Point 18: Line 242-243: The finding for respiratory mortality was already stated prior to Figure 1. I think it fits better here. I would suggest moving the finding about CVD mortality to this section as well.

Response 18: Thank you for the suggestion. We moved the discussion of CVD and respiratory mortality to after Figure 1, where we discuss findings presented in Table 3.

Point 19: Lines 252-254: Please clarify - are these stratified analyses?

Response 19: Thank you for the opportunity to clarify. Yes, these are stratified analyses. We’ve updated the text to increase clarity.

Point 20: Table 4 - presumably these are results from an interaction term and the age group 5-14 is the reference group? Please state that somewhere to clarify. Also, should there also be a hyphen for the reference group for race (I think Other/Pacific Islander)?

Response 20: Thank you for your comment. As stated in Response 19, the results presented in Table 4 are the results of stratified analyses, not the result of an interaction term. We’ve updated the title of Table 4 to increase clarity. Further, the Other Pacific Islander is exactly that – other Pacific Islanders not captured in other race categories. Thank you for checking.

Discussion:

Point 21: Lines 273-274: I would not say that there is a protective effect of wildfire smoke on mortality. The confidence interval includes 0, which just means that we have 95% confidence
that the true value falls within that confidence interval and because that interval includes 0, we can't say with confidence that the true value is positive - it does not mean that wildfire smoke is sometimes protective of mortality and sometimes adverse for mortality, as this statement implies. Lines 275-277 imply the same misunderstanding of confidence intervals that needs to be rectified.

Response 21: Thank you for your helpful comment. We agree that our statements here are misleading, and we have reworded them for accuracy:

“These estimates indicate that we cannot state with confidence that the true odds from same-day exposure are positive…Other studies examining the association between wildfire smoke exposure and non-traumatic mortality report similar results.”

Point 22: Lines 281-285: My reading of the three papers cited here is that all of them demonstrated null associations (read confidence intervals that included the null) between wildfire smoke and respiratory mortality, such that the findings in those other papers is in line with the findings in this paper (that we cannot say with confidence that we can reject the null of no association). Again, this paragraph is showing a misinterpretation of confidence intervals. This paper does observe a borderline significant increase in respiratory mortality associated with wildfire smoke, which I think is stronger than can be said for those other studies. As for the cardiovascular findings, this paragraph is better - some of the previous papers have found borderline positive associations, whereas this paper finds a null association.

Response 22: Thank you for your helpful comments. This is a great point, and we agree that this paragraph needs some re-framing. We’ve changed this paragraph to more accurately reflect the findings in these papers. The paragraph now reads as follows:

“In our additional primary analyses, we observed a 1.0% (95% CI: -6.0 - 4.0%) decrease in the odds of same-day (all-ages) cardiovascular mortality, and a 2.0% (95% CI: -3.0 - 7.0%) increase in the odds of all-ages cardiovascular mortality from previous-day exposure, both indicating null associations. However, other studies find evidence for a borderline significant association for both same-day and previous day exposures (18,21,23). We also observed a 9.0% (95% CI: 0.0 - 18.0%) increase in the odds of same-day (all-ages) respiratory mortality, and a 5.0% (95% CI: -3.0 – 15.0%) increase in the odds of all-ages respiratory mortality from previous day exposure, indicating borderline significant associations, particularly for same-day exposure. Other studies largely report null associations with respect to same-day and previous-day exposure associated with respiratory mortality (18,21,23). Each of these studies employed different methods for assessing exposure, which may account for some of the observed differences in the effect estimates (18,21,23).”

Point 23: Lines 317-319: See (Henderson et al. 2011; Mott et al. 2005; Rappold et al. 2011; Reid et al. 2016) for studies that shows higher effects of wildfire smoke for adults under 65 than for ages 65+ for some specific endpoints. Also check out a recent review that may have more citations (Reid and Maestas 2018).
Response 23: Thank you for including these references. We have incorporated many of them into the discussion in this paragraph, and we think it is much improved. This portion of the paragraph now reads as follows:

“In our secondary analyses, we found a 35.0% increase in the odds of same-day respiratory mortality (95% CI: 9.0 - 67.0%) among individuals ages 45-64. Several papers find higher effects of wildfire smoke exposure among adults under 65 compared to adults over 65, albeit for different health endpoints. Henderson et al. report the largest ORs for respiratory physician visits among adults ages 30-40 year (42), while Mott et al. find asthma and COPD hospital admissions greatest among adults ages 40-64 (43). Rappold et al. find higher increases in respiratory ED visits (including asthma, COPD, pneumonia, and acute bronchitis) among individuals under 65 compared to those over 65 (44), and Reid et al. report higher COPD ED visits associated with PM2.5 in those ages 20-64 compared to over 65 (41).”

Reviewer #2:

Point 1: The authors have investigated the association between exposure to wildfire smoke and non-traumatic mortality over 12 years by combining geo-coded mortality data (N = 171804), gridded PM exposure data and census tract level median household income data. This analysis is important and timely as climate change is increasing the risk of wildfires. The authors used a time-stratified case-crossover design - for each individual case (death), exposure on the day of the event (smoke day yes or no) and on the four days before the event is compared with exposure at control days (smoke day yes or no). The referent days were selected as those days that had the same day of the week, same month and same year as the event day. This design controls for time-invariant confounders (gender, age, individual risk factors) and for time-dependent variability in air pollution. The authors used conditional logistic regression and adjusted for perceived temperature. The authors examined subgroups, ran secondary analyses and conducted sensitivity analysis. The manuscript includes most items recommended by the STROBE Statement — Checklist of items that should be included in reports of case-control studies. The writing is comprehensible and the work represents a useful contribution to the field.

Response 1: Thank you for your positive summary of our work.

Specific comments

Point 2: The statistical methods appear valid, but require some further clarification.

The odds ratio in a case-control or case-crossover design usually informs us how much higher the odds of exposure (smoke day yes) are among cases (case days, deaths) than among controls (referent days, no deaths). On line 177 the authors write that they report results as the change in odds of mortality (outcome) on smoke-affected days versus non-smoke-affected days - if the authors wish to present the results this way, it may be more appropriate to use the term ‘relative
Response 2: Thank you for your comment. Yes, mathematically when an outcome is rare, as it is in this case, the relative risk approximates the odds ratio. However, reporting our results as a relative risk is misleading, and thus, we do not think appropriate. Upon reviewing several other papers that report odds ratios, we have decided that our current wording accurately portrays the findings.

Point 3: The manuscript could be improved by providing more details on the calculation of the PM2.5 gridded exposure data and on the wildfire smoke day classification (STROBE item 7). In the present manuscript, the authors refer to an unpublished study (Doubleday 2019) for further details. The methods should clearly state how PM data was assigned to grid cells; how many grid cells were omitted from the analysis because of missing data; how the threshold of 20.4 µg/m3 was selected to define wildfire smoke days; and what the additional criteria were to capture low PM wildfire smoke events.

Response 3: Thank you for your helpful comments. We have added a significant amount of detail regarding the exposure data in the methods section (under “Exposure data” and “Wildfire smoke day classification”), as well as in Additional file 1 (Text S1), and we believe the methods are much improved.

Point 4: Consider performing additional analyses with the modeled PM values as the independent exposure data.

Response 4: Thank you for your comment. This is a great suggestion, and one that we considered. However, given the scope of our paper, we have decided not to pursue this analysis at this time.

Point 5: The authors should discuss the performance of the smoke day classification protocol.

Response 5: Thank you for your comment. Following your suggestion, we’ve included a longer description in Additional file 1 (Text S1) which includes more detail about our smoke day classification method.

Point 6: Clarify how the sensitivity analysis differs from the formal analysis as both analyses set the wildfire smoke affected day threshold to 20.4 µg/m3 (STROBE item 12).

Response 6: Thank you for the opportunity to clarify. We have added detail to the methods section regarding the smoke affected day classification definition used in our primary analysis, which now makes it clear how it is different from the threshold in the sensitivity analysis.
Point 7: Report numbers of cases at each stage of study and consider using a flow diagram (STROBE item 13).

Response 7: Thank you for your comment. We have included a flow diagram in Additional file 1 (Figure S1) to aid readers in understanding the number of cases at each stage.

Point 8: In Table 2 also present the outcome data (STROBE item 15): number of smoke and non-smoke days on event days; number of smoke and non-smoke days on control days.

Response 8: Thank you for your suggestion. We have added the percent of event days that were classified as smoke days, as well as the percent of referent days classified as non-smoke days to Table 2, as you suggested.

Point 9: Table 2. Note that officially the humidex is dimensionless (not °C).

Response 9: Thank you for your comment. We’ve removed the degrees C from the table and instead added a footnote to explain.

Point 10: In Table 2 also provide the average number of wildfire smoke days per grid cell (is it 102 days? What is the SD? Does this correspond to 8.5 smoke days per year? Is there spatial autocorrelation in the distribution of smoke days?)

Response 10: Thank you for your comment. We have added the average number of wildfire smoke days per grid cell and the SD to Table 2, as you suggested.