Author’s response to reviews

Title: Associations between short-term exposure to gaseous pollutants and pulmonary heart disease-related mortality among elderly people in Chengdu, China

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Associations between short-term exposure to gaseous pollutants and pulmonary heart disease-related mortality among elderly people in Chengdu, China

Jianyu Chen; Jie Zeng; Chunli Shi; Liu Ruicong; Rong Lu; Suling Mao; Li Zhang

Dear Dr. Hoek,

Thank you very much for your letter and for the reviewers’ comments concerning our manuscript “Associations between short-term exposure to gaseous pollutants and pulmonary heart disease-related mortality among elderly people in Chengdu, China.” We have evaluated the comments carefully and found them all to be valuable and very helpful in improving the manuscript. Accordingly, we have made corrections that are highlighted in red in the revised version. Additionally, point-by-point responses to the reviewers’ comments are provided below.
We wish to re-submit a revised manuscript and hope that it is acceptable for publication in the journal.

Looking forward to hearing from you.

Yours sincerely,

Li Zhang

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Responses to Reviewers:

First of all, we thank the reviewers and editor for their positive, constructive, and insightful comments and suggestions. Accordingly, we have carefully revised the manuscript and made corrections which are highlighted in red in the revised version.

List of Actions (LOAs):

LOA1: Table 3 (formerly Table 4) was revised. The effect estimates of PM2.5 were added in Table 3, and additional descriptions were added to paragraph 3 of the Results section.

LOA2: Descriptions of the results in the Results section were revised. Redundant number descriptions were omitted.

LOA3: Additional descriptions contextualizing the characteristic of pulmonary heart disease were added to the Background section.
LOA4: Additional discussions about the results of effect estimates of air pollutants compared to those from previous relevant researches were added to the Discussion section.

LOA5: Table S1 was added to the revised manuscript, in which the median and IQR of correlations of SO2, NO2, CO, O3, and PM2.5 across the 24 monitoring sites were presented.

LOA6: Table 3 was moved after Table 4 in revised manuscript, and the table numbers changed accordingly.

LOA7: Figure 1 was revised because we found that a monitoring site position was incorrectly marked in Figure 1.

LOA8: Several words or descriptions were revised based on the reviewer’s comments.

LOA9: Monitoring methods for air pollutants were added to the Methods section.

LOA10: We calculated monthly concentrations of SO2, NO2, CO, O3, and PM2.5, and presented seasonal trends of pollutants in the newly added Figure S1. This might be useful to understand the air pollution sources and the influencing factors for seasonal trends of pollutants in Chengdu.

LOA11: Additional descriptions of seasonal trends of SO2, NO2, CO, O3, and PM2.5 were added to the Results section, and additional discussions of pollutant origins were added to the Discussion section.

LOA12: Figures 4 and 5 were combined and the resulting figure renumbered accordingly.
Responses to Reviewer #1 Comments:

The authors performed a time series of pulmonary heart disease, a relatively rarely studied outcome. Five years of mortality and air pollution data in a large city is used and analyzed with state of the art statistical methods. The paper is well written. With a few adaptations I recommend the paper for publication.

Response:

We appreciate the reviewer’s careful and professional review of our manuscript. We are very thankful for the reviewer’s recommendation for publication.

Replies to the Main comments:

1. The focus on only the gaseous pollutants is not appropriate given the interest in PM2.5. I notice you did adjust for PM2.5 so you have the data. You need to add the effect estimates for PM2.5 to the paper (Table 4). That will enrich the strength of the paper.

Response:

We thank the reviewer for this suggestion. As is pointed out, many previous studies have proved the association between exposure to PM2.5 and mortality or morbidity of cardiovascular disease. We therefore concluded that we should present the effect estimates for PM2.5 in the manuscript in spite of PM2.5 being considered as co-variable and that its influence on health effects needed to be controlled. We added the effect estimates for PM2.5 to Table 3 (formerly Table 4), and added the relevant descriptions to paragraph 3 of the Results section, as follows: “Additionally, an association between PHD-related mortality in people aged 60 years and older and PM2.5 was observed in our study. The day corresponding to the greatest effect was one-day lag (Table 3).”
2. In the Results section, you are repeating too many numbers. Numbers that are in a table you refer to should not be in the text. Rewrite with reference to the table and a short statement what the reader should take from the table e.g. significant associations found with …

Response:

Thank you very much for pointing this out. We included too many redundant number descriptions in the Result section. We revised the descriptions of results in paragraphs 2, 3, and 6 in the Results section, which are highlighted in red in the revised manuscript.

The revisions read as follows:

Paragraph 2, “Table 2 shows the Spearman’s correlation coefficients of air pollutants and weather conditions. The correlations existed among air pollutants, and between air pollutants and weather conditions.”

Paragraph 3, “Figure 2 shows the calculated results of association between PHD-related mortality in people aged 60 years and older and ambient gaseous pollutants. After controlling the influence of confounders—including daily temperature, relative humidity, and atmospheric pressure—the associations were between PHD-related mortality in people aged 60 years and older and increases in concentration of IQR in SO2 (13 µg/m3), NO2 (17 µg/m3), and O3 (74 µg/m3).”

Paragraph 6, “For SO2, NO2, and O3, corresponding to their greatest effective days (SO2 at Lag1, NO2 at Lag1, and O3 at Lag2, respectively), we applied a two-pollutant model by adding PM2.5, SO2, NO2, O3, and CO as co-variants, respectively. The health effects of SO2, NO2, and O3 mainly remained in two-pollutant models, although the effects of SO2 became null after adjusting for NO2 (Table 4).”
3. Given the rather new outcome you study, give a bit more background on how common the disease is relative to other cardiovascular diseases.

Response:

We thank the reviewer for this suggestion. We added additional descriptions to contextualize the characteristic of pulmonary heart disease in the Background section, which are highlighted in red in the revised manuscript. The new text reads as follows: “PHD has emerged as a major cause of disability and mortality within cardiovascular diseases [3]. In the United States, PHD is estimated to account for 7% to 10% of all heart diseases, and to be associated with between 10% and 30% of all hospital admissions for heart failure [4]. Autopsy studies in patients who died of chronic lung disease found that 40% were accompanied with PHD anatomically [5].”

4. Note in the discussion that the ORs you present are large compared to other time series studies of CVD mortality, also in China. Discuss a bit more.

Response:

We appreciate the reviewer pointing out these issues. We studied several recent research reports on air pollution and CVD mortality. The reported excess risks ranged between 0.77% and 4.8% for SO2 in 10 μg/m3 increase of concentrations, and between 0.41% and 2.7% for NO2 (see Refs. 1–5 below). Our estimates of effects were relatively higher compared to previous studies. Owing to the insufficiency of our study, we assumed the cause of different study areas, or the effects of gaseous pollutants on PHD-related mortality, might be higher than those on other cardiovascular mortalities. We again thank the reviewer for providing a meaningful and interesting research direction. Indeed, we have expanded our study to multiple cities in Sichuan Basin, and hopefully the effects of air pollution on PHD-related mortality and CVD mortality could be addressed more precisely in further studies.
We added additional content to the Discussion section, which is highlighted in red in the revised manuscript, as follows: “Compared to previous reported effects of air pollution on cardiovascular mortality, our analysis reported relatively higher effect estimates for the same level of increase in gaseous pollutants concentration. The risks of PHD-relative mortality for SO2 were approximately 5.5 times greater than those of cardiovascular mortality derived from the Public Health and Air Pollution in Asia (PAPA) project [26], 2.6 times greater for NO2, and 2 times greater for O3. Cao et al. [27] reported that the excess risks of cardiovascular mortality per 10 µg/m3 increase in SO2 and NOx in China were 4.8% and 2.7%, respectively. The risks of PHD-relative mortality in our study were both 1.3 times greater. Compared to the calculated results of risks of cardiovascular mortality derived from the APHEA (Air Pollution and Health: A European Approach) project [28], those of PHD-relative mortality for NO2 in our study were 9 times greater. Although the results for risks from the aforementioned studies corresponded to the entire population, and those in our studies corresponded to those of only the elderly population, we assumed that the effects of gaseous pollutants on PHD-related mortality might be higher than those on other cardiovascular mortalities. Further studies are warranted to address these differences.”

References:


5. You are calculating one pollution time series for a very large city. This is common in time series study, but it would be useful to add the correlation of the pollutants across stations to judge better how reasonable the use of a single pollution time series is. Add supplement tables presenting e.g. the median and IQR of all correlations between individual stations e.g. NO2 of station 1 v2 2, 1 vs 3 etc. Lots of correlations that you can summarize with e.g. median and IQR.

Response:

We thank the reviewer very much for this suggestion. The convincingness of the use of a single pollution time series in our study would be enriched after the verifying of consistency in correlations of air pollutants across monitoring sites. We calculated correlations of SO2, NO2, CO, O3, and PM2.5 across the 24 monitoring sites, and the results of median and IQR are presented in Table S1.

Accordingly, we added additional descriptions to paragraph 2 of the Results section in the revised manuscript, as follows: “Additionally, correlations of air pollutants existed between each pair of individual sites (Table S1).”

6. Table 3 should be after table 4 that presents all results. In table3 identify the selected lag (the most significant in the current table 4).

Response:

Thank you for pointing this out. Table 3 was inserted after Table 4 in the revised manuscript, and the table numbers changed accordingly. ORs of selected lag days for SO2, NO2, and O3 were identified in Table 4 (formerly Table 3).

Replies to the Minor comments

1. In Intro replace ecological study with time series study

Response:

We thank the reviewer for pointing this out. We have made the required replacements in the revised manuscript.
2. Delete "we are the first researchers" in a very specific sentence, a study is always the first. This is not of interest, the work is why I review this positively

Response:

Thank you for pointing this out. We have made the following revisions in the revised manuscript: “An epidemiological design of time-stratified case-crossover was conducted to assess the association between short-term exposure to ambient gaseous pollutants and PHD-related mortality among elderly people in the central Sichuan Basin of China.”

3. In data collection, replace would be with were

Response:

Thank you for pointing this out. Relevant changes have been made in the revised manuscript.

4. Why did you restrict to 60 yr age?

Response:

We thank the reviewer for pointing this out. In China, 60 years is a common retirement age. Many studies of elderly people in China are also restricted to age 60 years (see references below). Thus, we restricted our study to age 60 years.

References:


5. In data collection, replace monitoring centers with monitoring sites

Response:

Thank you for pointing this out. Relevant changes have been made in the revised manuscript.

6. Add which monitoring methods were used

Response:

We thank the reviewer for pointing this out. We added details of monitoring methods in paragraph 2 of the Methods section, as follows: “Concentrations of air pollutants were continuously monitored 24 hours a day, and the data were recorded in the system automatically in every fixed monitoring site.”

7. Add which temperature and humidity lags you used in the analysis

Response:

We thank the reviewer for pointing this out. The influences of daily temperature, relative humidity, and atmospheric pressure were controlled by using natural cubic splines (ns) with three degrees of freedom in our model equations, in which single- or multi-day lags of weather conditions were no longer applied.

8. Add a bit on important air pollution sources in Chengdu (industry, coal burning, traffic); qualitatively is enough, quantitatively better

Response:

We thank the reviewer for this suggestion. We calculated monthly concentrations of SO2, NO2, CO, O3, and PM2.5, and presented seasonal trends of pollutants in the newly added Figure S1. This might be useful to understand the air pollution sources and the influencing factors for seasonal trends of pollutants in Chengdu. In addition, we consequently added additional descriptions of the seasonal trends of SO2, NO2, CO, O3, and PM2.5 in paragraph 2 of the Results section, as well as additional discussions of pollutant origins in the Discussion section. The new text additions read as follows:

In paragraph 2 of the Results section: “Concentrations of SO2, NO2, CO, and PM2.5 were remarkably higher in winter than those in summer, while concentrations of O3 were contrary (Figure S1).”
In paragraph 3 of the Discussion section: “The major sources of gaseous pollutants comprised of SO2, NO2, CO, and O3 in Chengdu were mainly from industrial emissions and fuel combustion. In addition, NO2 and CO can also derive from traffic emissions [29, 30]. The concentrations of gaseous pollutants showed typically seasonal trends in our study. The concentrations of SO2, NO2, and CO were remarkably higher during winter each year, which may be due to the reduction of air flow diffused dilution efficiency and to the increase of biomass fuel combustion for heating. Higher concentrations of O3 in summer were probably caused by increased sunlight. However, the aforementioned seasonal changes were controlled by using the case-crossover method.”

9. Figure 4 and 5 can combined

Response:

We thank the reviewer for pointing this out. Figures 4 and 5 have been combined and renumbered as the new Figure 4 in the revised manuscript.

10. I find the sensitivity analysis with three fixed controls unnecessary, drop. So drop figure 6

Response:

We thank the reviewer for this suggestion. We omitted descriptions for the sensitivity analysis with three fixed controls in the Methods section and in the Discussion section in the revised manuscript. Figure 6 was dropped accordingly.