Author's response to reviews

Title: Gaseous air pollution and emergency hospital visits for hypertension in Beijing, China: a time-stratified case-crossover study

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Author's response to reviews: see over
In response to reviewer #1:

1. Since the pollutants’ concentrations were high correlated with each other (Table 2), the authors should be cautious in their conclusion that “Our results suggest that NO2 is more important for health than SO2. Also, PM10 can enhance the health impact of NO2, and share the effect of SO2”.

[Response] We have deleted this statement and mentioned the possible co-linearity between pollutants in the revision. (page 8)

2. Since the emergency-room visits were obtained from only one hospital rather than from the whole city, the authors should discuss the limitation of this (e.g. the baseline population may change)

[Response] We agree that using just one hospital may limit the generalisability of the results. We discussed the limitation in the revision. (page 10)

3. The authors adjusted for temperature as a linear variable which might not be correct. It is widely acknowledged that the relationship between temperature and adverse health outcomes are nonlinear and generally U-shaped. So I suggest the authors use nature spline to treat temperature and humidity in the regression model.
**Response** In factor, we used the polynomial distributed lag model in this study. The polynomial smoothing was used for controlling temperature and humidity. We have added the related information in the revision. (page 6)

In response to reviewer #2:

1. Abstract: Accurately summarizes results.

**Response** We have made this small revision to the abstract (page 2).

2. Background: Adequately covers rationale, and why it matters both to the target audience (US) and to the study population (China).

**Response** We have added some text to the background (page 3).

3. Materials and Methods: From the information given, the methods are fairly clear and appropriate, but need much more detail. It is unclear how the exposure was determined. It is described that there is a pollution monitoring network, but not much about them or how the data from these monitors were applied to determine each participant’s exposure. Spatially: How are the monitors spatially distributed (how many, where located, etc…). Did the authors use the entire city-wide network to determine a city-wide value? If so, how did they use all of the city’s monitors to obtain this single value? A simple city-wide average? If they used a local rather than city-wide pollution value, did they use the hospital location or the patient residences? To determine this local value, did they simply use the closest available monitor available to determine the value, or create a GIS-generated surface? Temporally: what is the temporal distribution of the monitors? Do they take hourly readings? Daily? Weekly? Different for different monitors? How much of the monitoring data for this study was missing? More description of the monitoring network is needed

**Response** There were 8 air pollution monitoring stations. The air pollution concentration used in the study was averaged from these 8 sites. Most studies worldwide have used the average pollution concentration as exposure, because it is very difficult to get individual pollution exposure. We have been trying to spatially model air pollution using GIS in ongoing work. We did not get the original data. The data supplied by Beijing Public Net for Environmental Protection has no missing, because if there were missing data from a
monitoring station on a given day, then the values from the remaining monitors were used to calculate the average concentration. We have cited our previous study in this part (page 5).

4. Case selection could use a bit more elaboration. For example: Is hypertension the primary reason for the EHV used in this analysis, or is any EHV for any primary reason, but with a patient that was hypertensive used as a case?

[Response] We only used the EHV with primary reason for hypertension, which is also the primary diagnosis. The EHV for hypertension were diagnosed by the visits’ symptoms, inquiries, and medical inspections. About 95% of visits for hypertension are diagnosed only with hypertension, while 5% have accompanying heart failure, myocardial infarction or other diseases. We have added this information in the revised version. (page 4)

5. In addition, the selection of the control time periods need further elaboration. The method is a time-stratified case-crossover, and they used the day of the week within a 28 day strata, and 3 control days were chosen. Does this mean that if the EHV occurred on a Monday, Jan 22, that Jan 8, Jan 15, and Jan 29 were used? How is this 28 day strata chosen?

[Response] 28 days is the strata length of the time-stratified case-crossover. Cases are only compared with controls in the same 28 day strata. For example, there were 365 days in 2007, the total number of strata is 365/28≈13. The first strata is Jan 01 to Jan 28, the second strata is Jan 29 to Feb 25. For an EHV on Jan 31, Feb 7 14 and 21 were the control days. We have added these details in the data analysis section. (page 5)

6. What is the typical population of this hospital? Are they a genuine cross-section of this area of Beijing, consisting of all those who live and work in the area? Or do certain sub-populations (higher or lower SES, certain occupations, etc…) tend to visit this particular hospital?

[Response] The EHV of this hospital are residents living around the hospital. Most of them are working or living in the local area. There should be no certain sub-population tending to visit other hospital, as Peking University Third Hospital is one of the largest hospitals in Beijing even in China. Also, there is a special regulation that the emergency patient should go to the nearest hospital, and the designated hospitals for health insurance are the nearest from their homes.
7. Results: Clearly presented. The extensive paragraph regarding Table 2 might be unnecessary. One could simply refer to the general findings one would be interested in when looking at Table 2, rather than restating what has already been displayed in the table.

[Response] We have simplified this paragraph. (page 7)

8. It is mentioned that for multiple pollutant models, the current and 3 day lag values were chosen for SO2 and NO2. From Figure 2, 2 and 3 day lag values for NO2 look similar, so choosing the 3 day lag value may be appropriate. However, for SO2, the 2 day lag value appears larger than the current day value. Why was the current day SO2 value chosen for adjustment, if ORs were used for selection of lag day value?

[Response] We choose the adjustment not only considering the mean ORs, but also the 95% confidence intervals of the ORs. Even though the current day’s OR is similar to the lag 2 day, the 95% confidence interval on current day is narrower than lag 2 day. (page 7)

9. Discussion: Paper presents a clear review of past literature. Discussion of limitations could be expanded. Specifically, how much of a participant’s actual exposure is determined by what is captured by the outdoor air pollution network? Is indoor and outdoor pollution different for many potential hospital patients? Is it common for Beijing residents to stay indoors during extreme weather conditions, when air pollutants might also be more extreme? This would potentially bias the results towards the null, if indoor pollution varies less than outdoor pollution. Are different types of people who have differing exposures (e.g. construction workers vs. office workers) more or less likely to visit the hospital due to cultural or social factors (e.g. differing government support due to urban vs. rural hukou, financial considerations of hospital visits, family support and cultural differences)? What is the population that is actually likely to visit the hospital for hypertension, an issue that by itself might not have obvious or immediately pressing symptoms? Again, is hypertension the primary reason for the EHV’s used in this analysis, or is any EHV with a hypertensive patient used as a case? These issues might also introduce bias and need further clarification in the discussion.

[Response] We have discussed the limitation of using outdoor air pollution to represent the individual exposure. There are few available studies on the impact of indoor air pollution on hypertension morbidity and mortality. Few studies in Beijing have reported the change in behaviour when extreme weather and air pollution occurred. Our ongoing study shows that
there is a strong correlation between outdoor air pollution and indoor air. Therefore when extreme outdoor air pollution occurred, the indoor air pollution is also high. We will further our study on which population is actually likely to visit the hospital for hypertension. We only used the EHV with primary reason for hypertension. We have discussed the limitation of socioeconomic influence in the revision. (page 11).

10. Tables and Figures: Tables and figures are mostly clear and present the most important information. As previously mentioned, one important note is to keep the Y axes for similar graphs consistent so that they can be compared. Specifically, the Y axes showing the OR ranges in Figures 2, 3, and 4 should be the same.

[Response] We have changed the Y-axes so that they have the same range, and added the SO\textsubscript{2} into figure 2 and NO\textsubscript{2} into figure 3.

11. Abstract: the last sentence is a bit misleading and might be changed to something such as “However, no research has directly examined the relationship…” Previous research, including research by the authors, have previously examined these relationships, but not as primary exposures.

[Response] We have revised the abstract. (page 2)

12. Methods: While temperature and humidity have been adjusted for as confounders, it might be interesting to explore whether the relationship differs by season.

[Response] This is an interesting point, but because we only have one year of data, it would not be worthwhile to look at any modification by season.

Yours sincerely,

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