Author's response to reviews

Title: Effect of ambient temperature on emergency department visits in Shanghai, China: a time series study

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Version: 4
Date: 13 October 2014

Author's response to reviews: see over
Oct 13, 2014

Dear Editors,

We thank the *Environmental Health* for considering another review of our paper entitled “Effect of ambient temperature on emergency department visits in Shanghai, China: a time series study.” We have done our best to revise the manuscript based on reviewers’ suggestions. Below is a point-by-point explanation of our revisions with respect to each comment.

**Editorial’s comment:**

**Format modification:**

Response: Thanks. As for the formatting, we have modified this paper accordingly.

**Reviewer Jeremy Hess’s comments:**

**Major Compulsory Revisions:**

1. The convention in epidemiological analyses such as this is to present the demographic characteristics of the sample in Table 1. I suggested this to the authors in my initial review but they did not make this change. The current Table 1 should become Table 2, and the current Table 2 should become Table 3.

Response: As suggested, we have clarified the demographic characteristics of the sample in Table 1.

2. While the authors did provide more information about their sample, they did not provide information regarding how the sample compares with the other residents of Shanghai. While their sample is large, it is only roughly a quarter of the total population. How do the other residents, registered and otherwise, compare to this sample? Comparisons between their sample and the demographics of the entire population of Shanghai, if available, could be added as one or more columns to the new Table 1.

Response: Thanks for the suggestion. The sample sites of this study included nine urban districts in Shanghai, covering an area of 279 square kilometers with approximately seven million permanent residents. The study population was from nine urban districts (Figure 1) in Shanghai. We collected the daily counts of ED visits for registered residents on the basis of the Shanghai Health Insurance Bureau that provides compulsory universal health insurance and the proportion of registered residents who participated in urban workers’ basic medical insurance was 70.4%. Since the study population was a representative sample of urban residents, it was relatively older than the entire population of the city. Table 1 shows the proportion of females and the elders (≥65 year old) respectively accounted for 55.40% and 32.3%, compared to 48.50% and 10.12% for the entire
population of Shanghai (Shanghai Bureau of Statistics, 2011).
As discussed above, we agree that the selection of sample may be subject to
limitations in the generalization. We have extended the limitation discussion.

3. The authors provided more information about the source of exposure data but it
would be helpful for them to elaborate further. What kind of area is the weather
station located in? How representative of conditions in the rest of Shanghai are
the exposure data? They might consider including a map of Shanghai indicating
the weather station location and highlighting the population centers from which
the sample were taken. Further, they should include information about the
exposure data (e.g., that there were no missing data) in either the Methods or
Results. All of this information is important to help the reader determine how
generalizable the results are.

Response: We thank the reviewer for bringing this point to our attention. As suggested,
we have added a map of Shanghai indicating the locations of weather station and air
pollution monitoring sites (please see Figure S1). The weather data were measured at a
fix-site station located in Xuhui District of Shanghai, a central district of Shanghai
City. Since one monitoring station’s temperature is enough to capture the city-wide
temperature (Guo et al. Spatiotemporal model or time series model for assessing
city-wide temperature effects on mortality? Environmental Research. 2013.120,
55-62.), the monitoring data can represent the entire urban meteorological conditions
approximately. For the calculation of daily concentrations of air pollution, at least 75%
of values must be available on that particular day. If a station had more than 25% of
the values missing for the whole period of analysis, the entire station was excluded. In
addition, we used the daily counts of ED visits on the basis of the Health Insurance
System to measure health outcomes of the residents, there were no missing data. We
have inserted these information on the Methods Section.

4. The authors now include mention of ozone in their paper but incorrectly state that
including ozone is "not likely to attenuate risk estimates." Ozone is a potential
confounded in the relationship between temperature, particularly warm
temperature, and all-cause ED visits, and not controlling for ozone in the analysis
is likely to have resulted in overestimates of the observed association at high
temperatures. This needs to be stated in the Discussion section.

Response: Agree. As suggested, the potential effects of ozone on the all-cause ED
visits have now been discussed as limitations (page 16, paragraph 1).

5. The authors need to include the definition of a case in their Methods section. This
should include the inclusion and exclusion criteria. Moreover, they need to
distinguish between ED visits and hospital admissions (in several places they
seem to use them interchangeably, but these are different outcomes). They need to
state something along the lines of: "We defined a case as any ED visit by an
individual with social insurance on a given day, i.e., from one midnight to the next. Patients were not assigned unique identifiers, so any ED visit during the study period was considered a separate case. Any ED visit, regardless of whether the patient was treated and released, admitted to the hospital, or died in the ED, was included in the analysis.”

Response: We thank the reviewer for bringing this point to our attention. In Methods Section, we defined the study population as registered residents living in the nine urban districts between January 1, 2006 and December 31, 2011 from the Shanghai Health Insurance Bureau. All residents in the study areas who participated in workers’ basic medical insurance, including employees of urban businesses, organizations, institutions, and social organizations (please see page 6, paragraph 1). As suggested, we have added the definition of a case in Methods Section (Page 6, paragraph 2).

6. While the authors do now include more information about other estimates of associations between temperature and ED visits, they need to elaborate further on the estimates in the literature and how these prior estimates compare with their own. Specifically, they need to state the nature of observed associations (i.e., linear relationships, threshold relationships, etc.), the magnitude of effect (in terms of both thresholds and slope of the line/curve), and to compare these prior findings with their own. Are the relationships along the lines of those others have observed? Are they weaker or stronger? If so, what may account for the differences observed? This synthesis should occur in the Discussion section and is lacking from the paper currently.

Response: Now we have extended the discussion accordingly. For example, we compared our estimates with that from the U.S and Australia, in page 13, paragraph 2. In addition, we have inserted a statement to specify the magnitude of effect in terms of both thresholds and slope of the line/curve, and to compare these prior findings with those we found (Page 13, paragraph 1).

7. In the Abstract, the Conclusion continues to overreach the analysis. The Conclusion of the study should relate directly to the data analysis and results. In this case, all the authors can state is that there are observed relationships between temperature and ED visits in Shanghai, whether these relationships are consistent with others in the literature, and that this knowledge has the potential to advance prevention efforts targeting weather-sensitive conditions. The Abstract and Conclusion sections should be congruent and both should be edited to reflect conclusions consistent with the study results.

Response: Agree. As suggested, we have revised the conclusion in the abstract to make it more relevant to the results.
Minor Essential Revisions:

1. The authors should include a statement of whether the study underwent institutional ethics review. If it was exempt from review then they should state this. Either way, the paper needs to include a statement regarding institutional ethics review.

Response: Thanks. We have added the institutional ethics statement in the Methods. In our study, patient records/information was de-identified prior to analysis; then daily aggregated counts for ED visits were calculated and used to conduct the final analysis. We did not access to patient individual information prior to anonymization and data aggregation, and there was no any interaction with the patients for this study (please see page 7, paragraph 2). An exempt from IRB review have been stated in the Methods Section.

2. In regards to the choice of exposure metrics, the authors provide a nice explanation in their response to the reviewer comments but this text is not included in the paper. They should include their reasoning about choosing mean temperature in the paper text and cite the studies they relied on for making this analytic choice.

Response: Thank you. Sensitivity analyses from previous studies using multiple temperature metrics have found that the effect estimates of all temperature metrics were similar (references: Son et al. The impact of heat waves on mortality in seven major cities in Korea. Environ Health Perspect120:566–571. Anderson BG et al. Weather-related mortality: how heat, cold, and heat waves affect mortality in the United States. Epidemiology 20:205–213.). Thus, considering daily mean temperature may be able to provide more easily interpreted results in a policy context and more familiar to the public, we use the ambient temperature for subsequent analyses. As suggested, we have inserted an explanation of exposure metrics in the Data Analysis Section (please see page 8, paragraph 1).

3. The authors provide a justification for choosing all-cause ED visits in their response to reviewers but this should be included in the paper text as well.

Response: Thanks. As suggested, we have clarified this in the Discussion Section (Page 16, paragraph 1).

4. There are several points in the revised version of the paper that need copy editing. In the Background section on p. 4, for instance, the sentence "Even determining the predictors of vulnerability to heat effects would help improve health education and interventions target those who are most susceptible" needs to be revised. There are multiple other locations (pp. 6, 7, and elsewhere) where the language needs to be copy edited.
Response: Thanks. The sentence has been revised as suggested. In addition, we have read through the texts carefully and polished the texts.

Reviewer’s comments:

Abstract:
1. It is unclear why and how a moving average lag model was used to evaluate the lag effects of temperature on EDVs. The reference group needs to be provided when the authors stated “The cold effect seemed to be more acute among individuals aged <45 years”. What is the meaning to say “there were consistent effects on individuals aged ≥65 years”?

Response: Thanks. At present, the models to assess the lag effects mainly included the sing-day lag model and the multi-day lag model (moving average lag model). For example, we used the moving average lag model to evaluate the lag effects, given that single-day lag models may underestimate the cumulative effect of temperature on mortality or hospital admissions (references: Bell et al. Time-series studies of particulate matter. Annual Review of Public Health.2004,25,247-280.). Accordingly, we have revised the statement in the Abstract section.

Methods:
1. More details are needed to explain how they selected a temperature breakpoint (commonly called the “threshold”). Why did they use a linear-threshold model to quantify the effect of ambient temperature as the temperature-EDV relation is likely to be non-linear? How was the lag structure determined?

Response: Thanks. First, we plotted the exposure-response curve between ED visits and ambient temperature based on the GAM. While the relationship between mean temperature and ED visits followed a U-shape curve, we couldn’t get the relative risk (RR) of ED visits per 1°C change in temperature. As a result, we cut the curve into two parts based on the threshold and the each part was similar to linear. Then we used the linear-threshold model to quantify the effect of ambient temperature on ED visits. Lot s of studies have demonstrated the distribution of temperature on mortality or morbidity is nonlinear and usually has a U-, V- or J-shape, the key issue for the study of temperature-related mortality is to define the turning point, which determines the magnitude of the estimated risk below or above the threshold. The threshold temperature is generally the optimum temperature corresponding to the lowest risk of mortality of morbidity. The threshold temperature is often different for different locations and populations because of local climate and population acclimatisation. The lag structure up to 3 days (lag3) was finally selected to assess the effect of ambient temperature on ED visits because the DMT effects appeared to be stable after 3 lag days.

2. They utilized a time series model to assess the relationship between EDVs and ambient temperature, while controlling for air pollutants (PM_{10-2.5}, SO2 and NO2).
relative humidity, rainfall and wind speed. Why did rainfall and wind speed matter? Additionally, how was the multi-linearity issue between humidity and rainfall dealt with in the model?

Response: Thanks. In our model, in order to observe the independent effects of ambient temperature on ED visits, we controlled for potential confounders such as long-term trend, day of week, relative humidity, wind speed and air pollutant. Considering the multi-linearity issue between humidity and rainfall, we didn’t include the rainfall in our model.

3. They stated: “the optimum temperature (OT), corresponding to the lowest point in the E-R curve, was about 12°C”. Was OT only visually observed or tested in the model? The authors claimed that “the risk of ED visits decreased at temperatures below the OT …” Should “decreased” be changed to “increased”?

Response: Thanks. As the exposure-response curve shows, the OT was 12°C as observed. Therefore we have revised the sentence “the risk of ED visits increased at temperatures below the OT and then reversed the trend”.

Results:
1. Why was mean temperature used as an indicator of ambient temperature? The reasons for using mean temperature should be provided in the Methods section. Why and how was lag 0-3 selected? The OT varied with age but how about gender?

Response: Thanks. In some studies, daily maximum or minimum temperature, synthetic measure such as humidex or apparent temperature were used to examined the effects on EDVs. Daily measurements may have different impacts with average ambient temperature on EDVs. Sensitivity analyses from previous studies using multiple temperature metrics have found that the effect estimates of all temperature metrics were similar. Moreover, considering daily mean temperature may be able to provide more easily interpreted results in a policy context and more familiar to the public, we use it for subsequent analyses. We have added the reasons in the Methods section (please see page 8, paragraph 1).

2. Why and how was lag 0-3 selected? The OT varied with age but how about gender?

Response: Thanks. We examined the cumulative effect of ambient temperature on ED visits from lag 0 to lag 3, given that previous epidemiologic studies in China found little evidence of significant associations with a lag over 3 days (references: YZ Mo et al. Relationship between daily mean temperature and emergency department visits for respiratory diseases: a time-series analysis. Journal of Peking University, 44(3):416-419). In addition, the lag structure up to 3 days (lag3) was finally selected.
to assess the effect of ambient temperature on ED visits because the DMT effects appeared to be stable after 3 lag days. Thus, we only calculated the cumulative effect of lag 3 days. In our study, we repeated the same procedure to examine the associations stratified by gender and age (<45, 45-65, 65-75 and ≥75 years). By observing ED visit-ambient temperature curves in males and females, we found that the OT was 12°C. However, the OT varied with age.

**Discussion:**

1. *Most vulnerable groups (e.g., floating population, poor people and unemployed residents) may not involve in this study. Selection bias should be thoroughly discussed.*

Response: The study population was relatively older than the entire population in Shanghai (Page 10, paragraph 3). But we agree with you that floating population and other unemployed residents may have different impacts structures. We have extended the limitations thoroughly in the Discussion section.

On behalf of my co-authors, I thank the reviewers and editors for their insightful comments and suggestions. We feel the incorporation of this feedback has greatly improved this revised manuscript.

Sincerely,

Weibing Wang