Author’s response to reviews

Title: Morbidity burden of respiratory diseases attributable to ambient temperature: a case study in a subtropical city in China

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Author’s response to reviews:

Dear editors:

Thanks for the reviewers’ and your comments on our manuscript entitled "Moderate hot rather than extreme hot is mainly responsible for temperature-related excess outpatient visits for respiratory diseases: a case study in a subtropical city of China" (ENHE-D-18-00434R1). Those comments are all valuable and very helpful for revising and improving our manuscript. We have carefully revised our manuscript according to the comments raised by the reviewers, which are highlighted in red in the revised manuscript. We hope that the revision is acceptable and look forward to hearing from you soon. The point to point responses to the reviewers’ comments are listed as following:

Comments from the reviewer #1:
1. I think the results that both low and high temperature were associated with an increased risk of morbidity of respiratory diseases and that respiratory morbidity risk for young population mainly caused by hot weather, but a reverse J-shaped was observed for the elderly are good enough. The conclusion and the title of the paper are misleading. Moderate hot contributed most of excess respiratory outpatient visits caused by ambient temperature exposure just because most of days in the study time series are at moderate hot temperatures. There is also a lack of biological explanation for this conclusion. I do not see necessity of paying attention to moderate hot days.

RESPONSE: Thanks for the important comments. The results of the relative risks revealed that both low and high temperature were associated with an increased risk of morbidity of respiratory diseases, and younger people and the elderly have different susceptibility temperatures. But, from the results of the attributable risks, we found moderate hot was responsible for the major part of excess respiratory visits (7.5%) comparing with other temperature components (0.9%). There are many studies which have revealed that exposure to extreme temperature may increase the relative risks of a range of respiratory diseases. Our results suggest that public-health policies and adaptation measures should be extended and focused to take account of the whole range of effects associated with temperature. Therefore, we should be wary of adverse health effects caused by moderate hot.

We have revised the sentence and added the biological explanation in the Discussion section: “The most morbidity burden of respiratory diseases was caused by moderate hot (7.5%) comparing with other temperature components (0.9%). The result can be understood as that most of days (about 82.2%) are at moderate hot temperatures, whereas extreme temperatures are about 10.2% in our study time series. In other words, most of the attributable risk occurring in moderately hot days. One possible explanation is that cold air, could heat up in the nasal cavity and may not irritate the respiratory system. In contrast, hot air is not easily cooled by the body, so hot temperatures may be more important to respiratory health[27]. Besides, the patients with respiratory diseases, have poor heat dissipation and circulatory function in hot temperature weather, the resulting heat stress and peripheral blood deposits may significantly increase pulmonary vascular resistance, leading to aggravation of the disease[28]. Because of moderate hot days is the major part of time series, these physiological responses could persist for longer than other temperature components.”.

2. The disease investigated should be clearly described. The authors investigated total respiratory diseases, and some individual respiratory diseases including bronchiectasis, chronic obstructive pulmonary disease (COPD) and asthma, but this is not clearly described in Abstract (Page 2, Line 26, 'morbidity for respiratory diseases' should be 'morbidity for total respiratory diseases').

RESPONSE: Thanks very much for your comments. In the Methods section of Abstract, we revised “A standard time series quasi-Poisson regression with distributed lag non-linear model (DLNM) was applied to estimate the associations between daily mean temperature and morbidity for total respiratory diseases, bronchiectasis, chronic obstructive pulmonary disease (COPD) and asthma.”.
3. Earlier comment about the geographic area from which the municipal hospital drew cases which is important for readers to understand the results is not addressed.

RESPONSE: Thanks for your valuable comments. Due to medical insurance policy and convenience, most of the patients in this study came from local area. We were unable to obtain home address of the patients because of the privacy, so the geographic area from the municipal hospital drew cases was not addressed.

In the Hospital outpatient visits data section, we added “Because medical insurance policy and convenience, most of the patients in this study came from local areas.”.

4. From the location of the hospital and air monitoring stations, why used the average air pollutants from five stations rather than data from the nearest station.

RESPONSE: Thanks. The department of respiratory medicine of the Dongguan Fifth People's Hospital is a key specialty in Dongguan city. The municipal hospital cases for total respiratory diseases might came from all districts of Dongguan city, so we used the average air pollutants from five stations of the city.

5. Calculation of AR should be briefly described rather than citing a reference.

RESPONSE: Thanks very much for your comments. We have added the formula of AR in the Estimation of AR section, and depicted the calculation of AR based on a backward standpoint.

Comments from the reviewer #2:

1. Line 56, p5: “The hospital is one of the first-class hospitals in Dongguan.” How many hospitals are in the city? What is the proportion of patients in this hospital to all patients in the city? Are the patients a representative sample of all patients in the city? Did all the patients live in the city before visiting the hospital so that they had the exposure to the hot?

RESPONSE: Thanks. There are eight high level hospitals in Dongguan, and the Dongguan Fifth People's Hospital is one of them. The department of respiratory diseases in the Dongguan Fifth People's Hospital is a key specialty in Dongguan City. Therefore, many patients with respiratory diseases went to this hospital for medical treatment in Dongguan. We are unable to obtain all respiratory cases of Dongguan hospital, so there is no way to assess representation of patients in our study. This is a limitation in this study, we had mentioned that in Discussion section. Due to medical insurance policy and convenience, most of the patients in this study came from local area.

2. It's not clear what the difference is between "extreme" and "moderate" temperatures. In the methods, the author defined the extreme hot and cold as “…temperatures at 5th percentile or less
of temperature, and at 95th percentile or above of temperature, respectively" (line 12-14, p8) and the moderate temperatures as "the ranges between the optimum temperature with 5th percentile and 95th percentile of temperatures, separately" (line 47-49, p8).

RESPONSE: Thanks for your comments. We defined the extreme hot and cold temperatures for calculating the relative risk caused by extreme weather. Moreover, we defined the extreme hot, extreme cold, moderate hot and moderate cold for calculating attributable risk caused by different temperature range. We have added the Figure S2 to depict them clearly.

The Figure S2 looks like:

Figure S2. The definition of temperature range.

3.Line 28-31, p 11: "Results revealed that a significant fraction (10.4%) of respiratory outpatient visits attributed to ambient temperature within the study period." Should the number be 8.4%?

RESPONSE: Thanks. We are sorry for this mistake. We have corrected this mistake by revising that sentence into: “Results revealed that a significant fraction (8.4%) of respiratory outpatient visit attributed to ambient temperature within the study period.”.

4.Line 39, p 11: "The result can be understood by that most of days (about 89.1%) in our study time series are at moderate hot temperatures." The proportion of extreme and moderate temperatures in the exposures should be reported in order to better understand the results.

RESPONSE: Thanks very much. We have revised that sentence into: “The result can be understood as that most of days (about 82.2%) are at moderate hot temperatures, whereas extreme temperatures are about 10.2% in our study time series.”.

5.Line 42-48, p 11: "This finding has important public health implications: although extreme hot is riskier than moderate hot, moderate hot weather accounts for large proportion of days through a year in tropical regions." Is the study city a "subtropical" one as stated in the title?

RESPONSE: Thank you for your comments. We have corrected this mistake by revising that sentence into: “This finding has important public health implications: although extreme hot is riskier than moderate hot, moderate hot weather accounts for large proportion of days through a year in subtropical regions.”.

6.Line 47-59, p 11: "Therefore, moderate hot is much more important than extreme hot in tropical regions when considering the total adverse health effects exposure to ambient temperature, which indicates that we should pay more attention to moderate hot in planning adaptation strategies and measures to reduce the health risk of ambient temperature." Again, the
study city is not tropical. In addition, the highlighted message is a bit misleading if missing the higher risks from extreme hot. The sentence should be revised.

RESPONSE: Your comments are helpful for us to improve our manuscript. We have revised the sentence as follows: “Therefore, in subtropical regions like Dongguan city, we should be wary of moderate hot when considering the total adverse health effects exposure to ambient temperature. Therefore, we not only focus on extreme hot but also pay more attention to moderate hot in planning adaptation strategies and measures to reduce the health risk of ambient temperature in the context of global warming.”.

7.Line 56, p 12-13: "We postulated that hot temperature generally occurs during daytime, and the younger people stayed outdoor longer and may be less aware of their body temperature changes, so they have more chance to experience hot ambient temperature than the elderly." The interpretation of more burden from cold for older people is not convincing. Was it because that for certain conditions, e.g. COPD, most of the patients were older? Indeed, the findings regarding the impacts of cold on health of older people in the city have not been sufficiently addressed in Discussion.

RESPONSE: Thanks for the valuable comment. We have added these sentences in the Discussion section: “On the other hand, a study found that prevalence of COPD was higher in people aged 60 years or older than in people aged 20–59 years[46]. The airway neutrophils, macrophages and the level of respiratory inflammation have increased in cold environments, and it is easy to aggravate bronchospasm in asthma patients and airway obstruction in COPD patients[47]. Moreover, for the elderly, exposure to extreme cold temperature may increase the risk of developing pulmonary vascular resistance and thrombosis [48, 49].”.