Author's response to reviews

Title: A big temperature decrease between two neighbouring days may increase the risk of childhood pneumonia

Authors:

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Author's response to reviews: see over
Dear reviewers,

Thanks for your valuable comments. We have revised our manuscript accordingly, and all the major revisions have been marked red.

Reviewer: Yasushi Honda

Reviewer's report:

Major Compulsory Revisions:

1. Additional sensitivity analysis

   The relation between TCN and EDV was mainly determined by the latter half of the period, where there is a huge pneumonia EDV spike. Although TCN seasonality is not apparent compared with daily mean temperature, there is still seasonality and winter has higher TCN in Brisbane. This suggests that the huge EDV peak during winter may have confounded the relation between TCN and EDV. To refute this possibility, the authors can conduct the sensitivity analysis without including 2009 data.

Response: We have specifically looked at the TCN impact on childhood pneumonia in summer and winter (Figure 6) (Page 5, Lines 14-17), and commented on the findings (Page 6, Lines 16-18). A sensitivity analysis excluding 2009 data was also conducted (Figure 8) (Page 5, Lines 22-24).

   When we look at the lag pattern on Table 3, except for female, lag 0-7, the relative risks (RRs) are in order of lag 0-10, lag 0-7 and lag 0-1. This implies that the RR is larger when lag is larger. It is understandable that there may be incubation period for the exposure to the onset for pneumonia, but it is unlikely that the incubation period is mainly more than one week. This also suggests that the relation would be confounded by the sharp pneumonia peak in 2009. Another concern is that, since the larger RR for
longer lag, limiting the lag to ten days would also questioned; longer than 10 days of lag would have higher RR.

Response: We have added the “pattern of lagged effect of TCN on childhood pneumonia” (Figure 4) to the revision, and this figure shows that the TCN effect on childhood pneumonia lasted for around three weeks. Thus, we re-ran the model and used lags for up to 21 days in all subsequent analysis (Page 4, Lines 17-18). The mechanism underlying the lag effect was discussed (Page 6, Lines 12-16).

2. Lag structure

Although the authors showed Table 3 for lag analysis, they did not mention at all about this table or lag in the main text. Also, since the authors used DLNM, they can show the lag pattern of the TCN effect for, say TCN = -5, not just the aggregate effect of 0-1, 0-7 and 0-10. At least some discussion on the lag structure is essential.

Response: Table 3 has been removed from the revision. The pattern of lagged effect of TCN on childhood pneumonia is displayed in Figure 4, and the mechanism underlying the lagged effect has also been discussed (Page 6, Lines 12-16).

Minor Essential Revisions:

3. Comparison with other papers

More discussion on the comparison with other papers that address DTR and TCN (and mortality) would be desirable. The authors cited some papers in the introduction, but not mentioned in the discussion. Of course, EDV is different from mortality, but considering that pneumonia EDV should have similar pattern to mortality from respiratory diseases, and that some of the cited papers addressed the relation with respiratory mortality, the authors can compare the results of this paper with those from these papers.
Response: As suggested, we have compared our study with more previous studies in the revision (Page 6, Lines 19-29).

4. Degree of freedom (df) for time

The authors described that the df for time is 8, and they claimed that it controls the long-term trend and seasonality. However, the observation period is 10 years, and it is not possible to control seasonal variation. Or, was the df eight per year?
Response: Yes, it was eight df per year, and it has been clarified in the revision (Page 4, Lines 10-11).

5. Trend of TCN (Figure 1d)

The author did not specify how they did the decomposition analysis, but usually the trend panel should include the average value well within the range, as shown in the panels of other variables (such as Figures 1a, 1b and 1c). However, for TCN, the trend showed that the lowest value is 0.0, which is the period average value of TCN.
Response: As suggested by Reviewer two, we have simplified Figure 1 and only plotted out the original time series, leaving out the seasonality/tend/residual.

Also, although there is rather a sharp peak for TCN, it is only 0.2 degree C. When we are talking about -2 or -5 degrees C drop for the possible effect, this size of the long-term trend would be negligible.
Response: Thanks for pointing it out. We agree that long-term trend may be negligible. To check whether controlling for long-term trend may bias the TCN effect on childhood pneumonia, we did the sensitivity analysis adjusting the df for long-term trend, and found TCN effect did not change much.

Discretionary Revisions

6. Future temperature projection
The authors cited Epstein's paper from NEJM dated 2005. There should be newer and more relevant articles by the climate modellers for describing future temperature pattern. Here, it is desirable that many models have the same tendency that the climate variability is getting larger.

Response: We have cited more recent papers to support our argument (Page 6, Line 8).

7. Figure 4

It is helpful for the readers what "relative" means in this graph. Probably the same as Table 3, but still, it is better to have the note here.

Response: Done. Table 3 has been removed from the revision.

Reviewer: Wan Yang

Reviewer's report:

Major Compulsory Revisions:

(1) A lot of confounding factors, e.g. temperature, RH, PM10, etc., were considered in the DLNM. This is a nice feature of the study. However, the equation is quite confusing to this reader. What does the term ‘DTRt,l/TCNt,l’ mean? Is it a division operation between the two matrices? If so, could authors explain the rationale behind this operation? It doesn’t make sense. From what I read though, it seems the slash between the two matrices (‘/’) was used as a notation for ‘or’. If this is the case, authors should rewrite the equation to make it clearer. Also, the term ‘ns(Tt,l, 3)ns(RHt, 3)’ doesn’t make sense. Should there be a plus sign in between? And should the term ‘ns(Timet, 7)’ be ‘ns(Timet, 8)’ as stated in the text following the equation?

Response: We have revised the equation to make it clearer (Page 4, Lines 1-2). Thanks.

Another perhaps not so relevant question on the model, the lag effect was considered for the variable of interest (in this case, temperature variability), but not for the
‘confounding’ factors. I wonder if the lag effect is considered for all factors—be it ‘confounding’ or not—would the same association be found for the variable being tested?

Response: Yes, we have considered the lag effect for all confounders as well. For relative humidity, PM$_{10}$, NO$_2$, and O$_3$, we used lags up to 10 days. For mean temperature, we used lag up to 21 days. This has been clarified in the revision (Page 4, Lines 17-19).

(2) There is no reference to Table 3 in the text. It seems authors accidentally left the results on the lag. Besides 1, 7, and 10 days lags, did authors perform a sensitivity analysis on the lag, i.e., the lag-sensitive effect?

Response: Table 3 has been removed from the revision. We have looked at the pattern of lagged effect of TCN on childhood pneumonia (Figure 4) in the revision (Page 5, Lines 9-11).

(3) Authors found a more substantial adverse effect of TCN for 2006-2010 than 2001-2005. Looking at Figure 1a, the pneumonia incidence records were not very different across years expect for mid-2009. Given the 2009 peak coinciding the 2009 pandemic and the similar symptoms of influenza and viral pneumonia, it is likely that the 2009 peak was actually due to the 2009 pandemic (e.g., misclassification of ICD 9 code, increased pneumonia complication cases following pandemic influenza infection, or increased consultation due to fears of the pandemic, etc.). Have authors checked on these possible factors? If the 2009 episode is left out of the analysis, what would the impact of TCN look like for 2006-2010, compared to that for 2001-2005?

Response: We did a sensitivity analysis excluding 2009 data and found the magnitude of TCN effect on pneumonia decreased greatly (Figure 8), but the shape of TCN-pneumonia relation remained the same (Page 5, Lines 22-24). The impact of TCN on pneumonia for 2006-2010 was still significant and was greater than it was for 2001-2005. As we have presented both the results excluding 2009 data, and the comparison between TCN effects for...
2001-2005 and for 2006-2010 (with 2009), we did not present the results comparing TCN effects between 2001-2005 and 2006-2010 (without 2009).

(4) Pneumonia has a profound seasonality, with a peak in winter. Have authors considered comparing the TCN impact in different seasons? Would the TCN effect be more significant in winter vs. summer, or the other way around? Could authors plot the distribution of days with a temperature drop >2 °C in each season/month, maybe in lieu of Figure 3, and comment on this?

Response: We have plotted the distribution of days with a temperature drop >2 °C in each month (Figure 3) and commented on this (Page 5, Lines 7-9). We have also specifically examined the TCN effect on childhood pneumonia in summer and winter (Page 5, Lines 14-17).

(5) In the discussion, authors mentioned that previous studies reached different conclusions on the impact of TCN. Could authors comment on what lead to such a disparity? What are the differences between this study and prior works that would make the conclusions of this work stronger?

Response: The possible reasons for the disparity and the strengths of this study have been discussed (Page 6, Lines 21-29).

Minor Essential Revisions:

Page 2, second sentence in the first paragraph of Background, 120 million episodes of pneumonia in 2010 leading to 1.3 million deaths in 2011. I guess these two figures are two separate estimates; but putting them together sounds confusing in terms of timeline.

Response: We have revised this sentence (Page 2, Lines 19-21).

(2) Page 3, ‘10µm’, should put a space between number and unit.

Response: Done (Page 3, Line 21).
(3) Page 5, last sentence in paragraph 3, should it be the other way, i.e., effect of TCN during period two greater than period one?
Response: We have revised it (Page 5, Lines 20-21). Thanks.

(4) Page 6, top paragraph, “Respiratory diseases are mainly caused by immune system’s resistance to respiratory infection …”: This statement is incorrect. Immunity plays an important role in respiratory infection; however, infectious respiratory diseases are caused by infections of pathogens. Climate factors, such as temperature and humidity, could affect the transmissibility of infectious diseases and the human immunity may fluctuate over seasons, e.g., due to change in vitamin D level or melatonin level.
Response: We have revised the statement accordingly (Page 6, Lines 29-31). Thanks.

(5) Page 7, last sentence in paragraph 2: what do the authors mean by ‘ecological design’?
Response: An ecological design means that we collected the aggregated data on temperature and daily EDVs for pneumonia and used a time-series approach to quantify the relationship between TCN and childhood pneumonia. This is a population rather than individual-based study. This has been clarified in the revision (Page 8, Lines 1-2).

(6) Table 1 is not very informative. Perhaps it would be better to show the values for each month instead, or just leave the table out.
Response: We have removed this table as suggested.

(7) Figure 1: can authors compress all sub-plots into one panel, perhaps only plot out the original time series and leave out the seasonality/trend/residual?
Response: Done.

Discretionary Revisions

(1) Could authors explain briefly the mechanism underlying the DLNM? It would put readers without prior knowledge on the model into context better.
Response: It has been explained in the revision (Page 3, Lines 25-27).

(2) Some tables (e.g. Table 1) and figures (e.g., Figure 3) are not necessary.

Response: We have removed previous Table 1 and Figure 3.

Best regards,

Zhiwei Xu (On behalf of all co-authors)