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Title	Assessment of the impact of cold and hot temperatures on mortality in Ontario, Canada: population-based study
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Reviewer 1	Monica Campbell
Institution	Toronto Public Health, Healthy Public Policy
General comments	This team of investigators is well qualified to undertake the study and have chosen appropriate methods such as the case-crossover design. That said, the narratives of the paper needs to be improved to ensure clarity for the audience, which is likely the medical and public health sector rather than scientists such as epidemiologists. The paper would benefit from a careful review for clarity and grammar. Specific Comments: 1 - Downplay the comparison between hot and cold-related mortality as both are a serious problem and need to be addressed. Pitting one serious issue (heat) against another serious issue (cold) may undermine support for continued interventions to protect people from heat. Climate change projections clearly show increases in warming for the future. It is fine to suggest that the health sector and others need to pay more attention to cold-related mortality given the relatively high relative risk. However, it is also important to acknowledge that hot weather and cold weather response programs and policies vary across the census divisions in the study. 2 - Address the issue of heterogeneity among the 27 census divisions. If temperature is the key variable in weather-related mortality as the authors suggest, then one would expect a good correlation between the mean temperature for each of the 27 census divisions and their respective excess mortality from heat and cold exposure. Based on Figure 2 and others like it in the appendix, it is not apparent how well these variables correlate. It would be useful to include a figure in the paper that displays temperature (x-axis) and mortality (y-axis) for the 27 census divisions for hot and cold. This graphic along with the R-square value would provide important validation to the authors' hypothesis, as well as provide a clear readily understandable image. 3 - Page 11 Lines 21-26 is unclear "Overall there was no strong evidence of heterogeneity...." What does this mean? 4 - Strengthen the interpretation section by providing some narrative on acclimatization and how it might affect the study findings. Are those communities with a greater range in temperature extremes more at risk early in the cold or warm season due greater need for acclimatization? 5 - Include in the text some reference to morbidity impacts from extreme weather, and note that this paper focuses only on mortality rather than hot or cold-related impact. For example, cold-related health impacts include frostbite, frost nip, trench foot (common in the homeless population). 6 - Page 13 Lines 23-35 the findings related to mortality risk in hospitals do not seem plausible. Unless you have stronger and clear evidence, I suggest downplaying or perhaps eliminating this for this paper. You have not provided any evidence to support the suggestion that ..."it is possible that some hospitals were better able to provide a protective warm environment in winter than a protective cool environment in summer."
Reviewer 2	**Antonio Gasparrini**
Institution	London School of Hygiene and Tropical Medicine
General comments	The manuscript presents results on an assessment of the impact of cold and hot temperatures on mortality in the Ontario region of Canada. The analysis is based on a case-crossover design, assesses the impact on different mortality outcomes, and investigates the effect modification of individual characteristics. The authors provide an original contribution to the research on temperature-mortality

	associations. The manuscript is well written and generally clearly structured. The statistical methods are generally adequate to address the research questions, and the interpretation of the results is appropriate and correctly illustrated. My main doubts relates to the specific effect summaries, in particular in relation to the comparison between the association with cold and hot temperatures,. In addition, I have some reservations on the choice (and motivations) of the lag period, and on the validity of the estimates of attributable deaths. Specific comments are added below. 1. While the analytical approach chosen by the authors is appropriate for comparing the impact across regions, periods, mortality outcomes and individual characteristics, I have some reservations that the hot and cold contributions can be actually compared in this analysis. In particular, their estimates strongly depend on the chosen effect summaries and modelling assumptions, as discussed below. I suggest the authors to shift the focus of the paper to the other comparisons mentioned above, which are of great interest and worth being published. In particular, I suggest excluding the work 'comparative' from the title, as it might sound misleading. 2. The authors choose a very simple definition of the effect summaries, meaning the linear increase in OR for 5°C in the moving average over a short lag period (different for cold and hot). Given the purpose of the study and the specific research questions, I found the choice of these simple and easily interpretable summaries perfectly reasonable. In addition, the results of the sensitivity analysis seems to exclude the presence of substantial biases. However, the author should make clear to the reader that this choice is motivated by the specific objectives of the study, and that their approach does not entirely describe the complex associations between temperature and mortality. More complex effect summary definitions and modelling approaches may be needed in other context. In particular, I suggest the authors to make clear that their model can be too simple to address some research questions, such as the comparison of the impact of cold and hot temperatures (see above) or the computation of attributable mortality (see below). 3. The authors tested the presence of non-linearity in the temperature-mortality associations in the two seasons (cold and hot) by running separate models in the 27 census divisions. This is misleading, as it is likely that most of the non-significant tests can be attributed to the low statistical power. It is not a surprise that the only significant results occurred in Toronto, likely one of census divisions with the largest populations. While the association with cold is generally very close to linear, there is overwhelming evidence that the association between hot temperature and mortality is supra-linear. Although, as commented above, I find the choice of this simple summaries (including the assumption of linearity) reasonable in this analysis, I would make clear the purpose of this simplification. Conversely, I found reassuring that more complex models, such as splines and distributed lag models, provides very similar results. 4. Conventional wisdom among environmental epidemiologists is that in case-crossover analyses the lag period cannot be extended such to include control days. In the time-stratified control selection adopted here, based on the same weekday, this means that the maximum lag should be limited to 6 days. This belief, actually, lacks any theoretical foundation, and it is in fact completely wrong: the lag period can be extended as long as required, the limit being the computational power and the increasing collinearity between terms for temperature and season, as it occurs in time series models. Overlapping control periods are perfectly legitimate. The authors can check this out by extending the lag period to 7 days, and realizing that the model converges and provides reasonable estimates. The authors should revise the sentence in the section Strengths and weaknesses (page 15) on this issue. 5. Previous studies have identified cold effects at lags up to 3-4 weeks. The choice of 6 days as maximum lag may produce an underestimate in the association with cold. As discussed in Comment 2, I agree that this choice is likely to be not too critical in some comparisons. However, the authors may want to extend the sensitivity analysis to longer lag period, as currently it suggests that the association with cold is not limited to 0-6 lags. 6. The computation of attributable deaths in the online appendix is very superficial, and possibly wrong. Estimates of the OR are reported for a 5°C increase, and no specific reference temperature is provided. This reference is required for the definition of the counterfactual scenario, and such temperature is difficult to identify given the linearity assumption and the restriction of the analysis to summer and winter months. This issue is one of the reason of the difficulties in comparing impacts of cold and hot temperatures. I

	strongly suggest the authors to exclude the results on attributable deaths entirely. 7. While the manuscript is well and clearly written, some more structure is needed when reporting their findings. In particular, I suggest to report first the results for primary analysis (non-accidental mortality, all the subjects), and then stratified analyses on different causes and effect modifiers. This structure can help the reader to interpret the long series of results. In particular, it is no clear why the authors failed to include non-accidental mortality as an outcome in Figure 4. 8. The same structure can then be used when discussing the findings in the last section. I suggest to comment, in order, on the primary analysis and then on stratified analyses. 9. The authors report the associations as 'excess mortality'. However, they should bear in mind that they are estimating ORs, not RRs, and I am not sure excess mortality can be easily derived from the former. Maybe 'excess odds of mortality'? 10. More info are needed about the distance (average and maximum, for example) of each subject's residence from the meteorological stations, possibly stratified by census division. 11. The authors should provide a rationale about the selection of the mortality outcomes. 12. I suggest the author to report somewhere the actual figures of the analysis by calendar periods, so that they are available to the reader. 13. In Table 2, I suggest replacing the results of the sensitivity analysis to the lag period of air pollution with the sensitivity to the lag period for temperature, which is more relevant and only reported in the online appendix in the current version.
Reviewer 3	**Yuming Guo**
Institution	The University of Queensland
General comments	This paper is well written and is easy to follow. Also it uses a standard method to address an important topic for temperature and health. Some suggestions are provided as following: 1. In the abstract, the authors should state whether cumulative effects are used for the effect estimates of cold-related and hot-related effects. 2. Line 18, page 8, the authors created a categorical variable for three time periods (1996-2000, 2001-2005, and 2006-2010). But they did not illustrate how they do the analyses for each time period, using interactive terms for the time period and temperature or using simple stratification? 3. The reviewer doesn't think it is suitable to use 5 dg increase as unit, as different cities have different range of temperature. At least, the authors should use a sensitivity analysis to judge which unit increase produced low heterogeneity by a meta-analysis, for example, using 5 dg increase as unit or using SD increase as unit or using IQR increase as unit? 4. Lines 54-56, page 8. the authors stated "Further details on model development and linearity assumption are provided in the online appendix." this part should be provided in the main context. 5. Lines 33-36, page 13. More discussions are needed for the differences.