Author’s response to reviews

Title: Regional variation of premature mortality in Ontario, Canada: a spatial analysis

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Author’s response to reviews:

Thank you for the opportunity to submit a revision of our manuscript, “Regional variation of premature mortality in Ontario, Canada: a spatial analysis,” for consideration by Population Health Metrics.

We appreciate the thoughtful comments from reviewers. We have responded to all comments and detailed those responses below. The revised manuscript has been uploaded with track changes, as requested. Overall, we believe the manuscript has much improved in clarity and interpretation.

On behalf of my co-authors, I would like to thank you for considering our manuscript.

Sincerely,

Laura C. Rosella, PhD
Associate Professor and Canada Research Chair in Population Health Analytics
Dalla Lana School of Public Health, University of Toronto

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POINT-BY-POINT REVIEWER RESPONSE
Reviewer 1:

Comment 1.1: Define premature mortality in the abstract

   Response 1.1: Good suggestion. We have added the definition to the abstract.

Comment 1.2: Clarify why mortality for those aged under 18 is not considered premature. It is possible that this will bias the results, for example areas with high childhood mortality appear to have low premature mortality as you have defined it?

   Response 1.2: Thank you for identifying this point of confusion. We understand that there are meaningful differences in the risk factors and pathways underlying adult and child premature mortality. Furthermore, the sampling frame Canadian Community Health Survey, which we used to capture behavioural risk factor data, does not include children aged under 12. Thus we chose intentionally to focus on adult premature mortality, defined as death between age 18 and 74. We acknowledge and apologize that this was not clear in the text. Language has been updated throughout to specifically describe our primary outcome as adult premature mortality. The exclusion of childhood mortality has also been discussed in the “Limitations” section of the manuscript.

Comment 1.3: I am not sure what the “excess” computations achieve. Urban centres tend to have higher premature mortality rates for numerous reasons, including deprivation, crime and traffic accidents. When they don't, it's because of health migrant effects (internal and external). Or extreme weather in the case of Canada and poorer infrastructure and difficulties in access to health care? I don't know really, but the point is I don't see how you would argue that this comparison adds anything since you suggest that every other region could be like your comparator, when that is unrealistic. In short, you are comparing pears with apples.

   Response 1.3: Thank you for this astute point. We agree that Ontario is unlikely to achieve equal premature mortality across all regions. However, we believe that from a health policy and planning perspective, including excess death calculations adds value as an absolute measure of the burden of premature mortality across the province. For example, the total 2013 population of Northern LHIN sub-region (which had the highest premature mortality rate for females) was only 13,147, compared to a population of 406,416 in Hamilton LHIN sub-region. As a result, interventions to reduce premature mortality may be more cost-effective if implemented in the Hamilton LHIN sub-region. In this context, we felt it would be appropriate to include the “excess death” data as a supplemental file to accompany our manuscript. This reasoning has been clarified in the Methods section of the text.

Comment 1.4: I would not expect spatial autocorrelation to be an issue, and I am not surprised you get similar results with both approaches. But please report it
Response 1.4: The methods and results sections have been updated to report Moran’s I statistic for residual spatial autocorrelation in all 3 GLMM models. No significant spatial autocorrelation was found in either of the adjusted models.

Reviewer 2:

Comment 2.1: Premature death is an important indicator in this paper. The authors should explain briefly how they evaluate the premature death in the main text, but not referring to a literature.

Response 2.1: Thank you for this suggestion. We have added a sentence to the introduction to more strongly introduce premature mortality. Additionally, we have added a definition of premature mortality to the abstract and expanded the “Primary Outcome” section describing how premature deaths were captured in our study population.

Comment 2.2: Other factors such as material deprivation, current alcohol consumption, excess body weight, inadequate fruit, vegetable consumption, sedentary behavior and ever-smoked status should also be introduced in detail. For example, their definitions and unit.

Response 2.2: Thank you for pointing this out. We have added a section titled “Other Variables” in the Methods section, to more fully define each of the factors included in our models. We have also added a sentence under “Data Sources” describing ON-Marg in greater detail.

Comment 2.3: In the hierarchical Poisson regression model implementation you described in additional file 1, the model estimates $\theta_i$ was defined as "the age-standardized mortality ratio for LHIN sub-region i". However, you "report sex-specific rate, which have not been age-standardized" (statistical Analysis, Line 2). I suggest that you add implementation or relevant references to describe the methods of age-standardization and ensure consistency of related nouns in the article.

Response 2.3: Thank you for this comment. The model estimates are based on age-standardized expected death counts, resulting in age-adjusted coefficient estimates. Conversely, the premature mortality rates, which are intended to describe the crude, overall geographic distribution of premature mortality across Ontario, have not been age-standardized. More explicit reference to the reasons for age-standardizing the expected death counts has been added to the Methods.