Author's response to reviews

Title: Influence of social and material individual and area deprivation on suicide mortality among 2.7 million Canadians: A prospective study

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Author's response to reviews: see over
Dear Editor.

RE: MS: 1882397776508576 - Influence of social and material individual and area deprivation on suicide mortality among 2.7 million Canadians: A prospective study.

Thank you for asking us to revise this manuscript. Amendments made in accordance with the comments received from the reviewers are specified in the attached list. During the revisions, we identified a few errors in the tables that have since been corrected and the text adjusted accordingly.

The revised manuscript has been seen and approved by all authors. We confirm that the manuscript is original, has not already been published and is not currently under consideration by another journal. We hope that, in its revised form, you will be prepared to re-consider the paper for publication.

Sincerely yours,

Stephanie Burrows
Outline of modifications

Specific comments by the reviewers (shown in italics) are addressed below. Changes in the manuscript are marked with tracked changes.

Reviewer 1

Major Compulsory Revisions

1. *Add a theoretical discussion and a further perspective to the discussion/conclusion section. Make clear what your findings were. Do not hide your main findings in long sentences.*

We clarified the main findings in the first paragraph of the discussion, as well as in the conclusion. We have substantially rewritten the discussion to make findings clearer, and included headings to provide greater structure. We have attempted to shorten sentences. It is not clear, however, what the reviewer means by adding a “theoretical discussion and further perspective”. In the discussion we presently address the following theoretical issues: the protective role of marriage; links between lone parenthood, socioeconomic disadvantages and poor health outcomes; as well as possible mechanisms for the protective effects of education and employment. The discussion is, to our knowledge, based on the current literature, and we were not able to identify other discussion elements. If the reviewer can however provide specific examples of added theory that should be incorporated, we would be pleased to do so.

2. *Change the conclusions in the abstract that individual disadvantage was associated with suicide mortality, especially in areas with high level deprivation This is a misleading and not correct conclusion.*

We changed the conclusion of the abstract as follows: “Individual disadvantage was associated with suicide mortality, particularly for males. With some exceptions, there was little evidence that area deprivation modified the influence of individual disadvantage on suicide risk. Prevention strategies should primarily focus on individuals who are unemployed or out of the labour force, and have low education or income. Individuals with low income or who are living alone in deprived areas should also be targeted.” (page 3, lines 1-6).

3. *Expand more on what this study will add to the knowledge of suicide risk, why other studies were inconclusive and what makes this study different.*
To clarify why other studies were inconclusive, we added the following to the introduction: “To our knowledge, only two studies assessed if the effects of individual socioeconomic characteristics vary in socioeconomically different areas [13, 19]. In both studies, there was little evidence that area deprivation modified the influence of individual disadvantage on suicide, and the results that did support interaction were inconsistent, with individual disadvantage a stronger determinant of suicide in deprived areas for some measures and a weaker determinant for others. For instance, in Finland the difference in alcohol-related suicide rates between manual and white-collar workers was larger in deprived areas than in advantaged ones, whereas the difference in non-alcohol-related suicides was smaller in deprived than in advantaged areas [19]. Depending on age and sex, unmarried and unemployed individuals in Denmark had a higher risk of suicide in deprived areas, but low income individuals had higher risk in advantaged areas [13].”

To explain what this study will add to the knowledge of suicide and highlight what makes this study different we added the following:

“There is a need to understand whether individual- and area-level deprivation interact to influence suicide, in order to inform policies and interventions to reduce suicide ... To our knowledge, no Canadian study has used individual and area information simultaneously to investigate suicide. Given that the available evidence on effect modification is limited to two European studies with few measures of social and/or material deprivation, and that the results are inconclusive, we sought to evaluate if more definitive results could be reached in a different setting with a full spectrum of social and material deprivation indicators. The aim of this study was to examine the relationship between individual measures of material and social disadvantage and suicide in Canada and to determine whether relationships were modified by area deprivation.”

Discretionary Revisions

1. **Change the three modifying effects in two.**
   We changed the three modifying effects in two and mentioned that alternatively, there may be no modifying effects (page 5, lines 1-22).

2. **Adjust the method section so that it does not receive so much attention.**
   We have tried to reduce the method section by reorganising or removing some content. However, substantial reductions were not possible as we believe that its present contents...
are required for a researcher wishing to reproduce the analyses. If the reviewer can identify further sections that could be deleted without compromising transparency, we would be pleased to make the changes.

3. **I found the adding of undetermined deaths not necessary. Since no effects were found you can leave this out.**

The reporting of suicide appears to differ across provinces, with, for example, very few undetermined deaths in Québec, but many more in other provinces. Excluding undetermined deaths may potentially underestimate suicide rates (and potentially bias associations). Furthermore, it is common practice in suicide research to include undetermined cases, which helps increase sample size, power and precision (O’Carroll P: A consideration of the validity and reliability of suicide mortality data. Suicide and Life-Threatening Behavior 1989, 19:1-16; Phillips D, Ruth T: Adequacy of official suicide statistics for scientific research and public policy. Suicide and Life-Threatening Behavior 1993, 23:307-319). We therefore did not feel justified to exclude undetermined cases from analyses. If the reviewer can, however, provide evidence that exclusion of undetermined cases would provide a more accurate presentation of results, we could make these adjustments.

**Reviewer 2**

Major Compulsory Revisions

1. **In the abstract, the last sentence of the results and the conclusions would be more useful if made to be a bit more specific. While word count is always an issue statements like “some but not all characteristics” could be more useful if mentioning the most important predictors identified. Likewise, the last sentence of the abstract is pretty general, a conclusion that follows more directly from the findings and is more specific is recommended. This comment also applies to the last sentence of the paper, which is also vague. The results are much more specific and interesting that the conclusion implies. Since the paper does not generally attempt to make causal arguments, perhaps conclusions regarding the populations where prevention should be focused would be one example of a possible type of conclusion**

We have increased the specificity of the abstract as follows:

“After accounting for individual and area characteristics, individual social and material disadvantage were associated with higher suicide, especially for individuals not employed,
not married, with low education and low income. Associations between social and material area deprivation and suicide mortality largely disappeared upon adjustment for individual-level disadvantage. In stratified analyses, suicide risk was greater for low income females in socially deprived areas and males living alone in materially deprived areas, and there was no evidence of other modifying effects of area deprivation” and “Individual disadvantage was associated with suicide mortality, particularly for males. With some exceptions, there was little evidence that area deprivation modified the influence of individual disadvantage on suicide risk. Prevention strategies should primarily focus on individuals who are unemployed or out of the labour force, and have low education or income. Individuals with low income or who are living alone in deprived areas should also be targeted” (pages 2-3, lines 15-24, 1-6).

The last sentence of the manuscript was revised as follows: “Prevention strategies should primarily focus on individuals who are unemployed or out of the labour force, have low education or income. Females with low income and males who live alone in deprived areas should also be targeted” (page 19-20, lines 24, 1-3).

2. It is unclear what the authors used for the time scale in the hazard models. Since not mentioned I would guess that time to event was used. At the end of the results section the authors mention that when using age as the underlying time results did not differ, but the authors should defend why they believe it is more appropriate to not use age as the underlying time when this is likely to better control for age as a confounder. I would suggest that the authors use age rather than time on study as recommended by prior work for the presentation of their primary analyses, since usually age has a stronger effect on the outcome than time on study. Two references for this choice are: Thiebaut AC, Benichou J: Choice of time-scale in Cox's model analysis of epidemiologic cohort data: a simulation study. Statistics in Medicine 2004, 23:3803-3820. Korn EL, Graubard BI, Midthune D: Time-to-event analysis of longitudinal follow-up of a survey: choice of the time-scale. American Journal of Epidemiology 1997, 145(1):72-80.

As requested by Statistics Canada at the time of protocol approval, models were run using the 1991 census date as the start time (i.e. time-on-study). We re-ran final models using age as the underlying time and found similar results, which is in line with literature indicating that there is little difference in estimated regression coefficients between models that use age or time-on-study as the underlying time, as long as adjustment for age
at entry is made, which we did (Pencina MJ, Larson MG, D'Agostino RB. Choice of time scale and its effect on significance of predictors in longitudinal studies. Stat Med 2007;26:1343-59). We modified the methods to clarify that analyses are reported using time-on-study: “Time-on-study was used as the time scale.” (page 9, line 9). In the methods section, we note that “In sensitivity analyses, final models were run … using age as the underlying time” (page 10, lines 4-7) and in the results section we state that “Models … using age as the underlying time showed similar results” (page 14, lines 7-8).

3. The rationale for what covariates were included in the Partially and Fully adjusted models is not provided. There are a number of aspects of this that could be problematic. Standard rules for estimating effects suggest that variables on the causal pathway between exposure and outcome should not be adjusted for, but prior common causes of exposures and outcome should be adjusted for. To give one example where this is problematic, education is a prior of income, but income is not a prior of education. This suggests that if wanting to estimate the effects of income one should control for education, but if one wants to examine the overall effects of education, one should not control for income. I don't consider this particular change compulsory, but the authors should at a minimum have a substantial paragraph in the methods describing how and why particular covariates were included in each of their models and in the discussion regarding the implications of covariate selection for the effect estimate interpretation. As currently written, readers may interpret effect estimates as the overall effect of a particular covariate, when this is not the case given the large number of pathway variables included for some covariate-outcome relationships.

As mentioned by the reviewer in Comment 1, we do not attempt to make causal arguments. Nonetheless, the reviewer may be interested in recent work by Vanderweele, specialist in causal modelling, who explains that adjusted estimates essentially reflect the direct (unmediated) effect of an exposure on an outcome in the absence of interaction between the exposure and mediator (Vanderweele TJ, Vansteelandt S. Odds ratios for mediation analysis for a dichotomous outcome. Amer J Epidemiol 2010;172:1339-1348). The total effect (direct plus indirect) is obtained from unadjusted models. The difference between unadjusted and adjusted models reflects indirect effects (or mediated effects). As partially adjusted models fall in between and are not necessarily needed, we removed them from the tables. We now only show the direct effect (fully adjusted model) and total effect (unadjusted model). We have modified the methods to include a justification for the
covariates and to explain to the reader how the unadjusted and adjusted HRs should be interpreted, as follows: “Covariates were chosen on the basis of their importance in relation to socioeconomic disadvantage and suicide in the literature.” (page 9, lines 2-3); and “In general, fully adjusted estimates reflect the direct (unmediated) effect of an exposure on an outcome), while the unadjusted estimates reflect the total effect (direct plus indirect) [32].” (page 9, lines 17-19). We feel, however, that it is beyond the scope of this analysis to go into greater detail on causal processes, especially considering reviewer 1 who asked for less detail in the methodology, and that our objective was not to elucidate underlying causal processes. In the discussion, we have added to the limitations that “We could not adjust for some covariates that could mediate or confound results, such as substance use or psychiatric illness [10, 11, 14], nor did we test for interaction between exposures and potential mediators [32], hence results from fully adjusted models should not be considered unbiased estimates of direct (unmediated) effects on suicide [42].” (page 19, lines 5-8).

As a side issue, it is clear that education is a prior of income, but we were not able to find literature supporting the notion that income cannot a prior of education (perhaps because low income may lead to reduced opportunities for education – this might happen if a person was forced to drop out of school if income was inadequate, for example). Although such pathways are interesting, we nonetheless focused the discussion on the associations that were measured in the study, since causal pathways were not part of the objective.

4. While subtle, I believe that there is a difference in saying that risk factors are significant in one subgroup and not in the other as compared to saying that effect estimates differ between subgroups. It seems that the latter is more in line with the authors study question, but their analyses focus on the former. I would suggest that the authors are much more specific in quantifying when the effect estimates differ from each other. One such approach is to calculate confidence intervals that when compared for overlap are equivalent to a p=0.05 test of effect estimate difference. Two references for this are: Goldstein, H., & Healy, M. J. R. (1995). The graphical presentation of a collection of means. Journal of the Royal Statistical Society. Series A (Statistics in Society), 158 (1), 175e177. Julious, S. A. (2004). Using confidence intervals around individual means to assess statistical significance between means. Pharmaceutical Statistics,3(3),217e222.
There are other potentially appropriate approaches as well including the evaluation of interaction terms.

The suggested articles are useful for means, but could not be used for our analyses which are based on proportions (not means). We instead used the method proposed by: Altman DG, Bland JM. Interaction revisited: the difference between two estimates. BMJ 2003;326:219 which proposes calculation of a ratio of HRs, with 95% confidence interval, to test for effect modification. The ratio of HRs indicates that effect modification is present when its confidence intervals exclude the null. We added a sentence to the methods which reads: “Differences between HRs from high vs low deprivation strata were assessed by computing the ratio of HRs (95% CI) using the method proposed by Altman and Bland [32]. When the confidence intervals for the ratio of HRs for deprived vs advantaged areas exclude the null, a modifying effect of deprivation is present.” (page 9-10, lines 23-24, 1-2). Tables 3 and 4 have been split into sex-specific tables to accommodate these new results.

5. The primary results presented should account for the clustered nature of the sample.

We accounted for clustering in final models with the sandwich estimator, and results were almost identical with or without it. The length of time it took to run models with the robust option, however, precluded its use for all models, especially since models were run in the offices of Statistics Canada and access was limited to specific times. To be consistent in the presentation of results, we present results that did not account for the clustered nature of the sample.

6. Given the importance for the country context of studies on this subject, I think it is important to include more discussion of how results in Canada differ from other industrialized countries, and why this may be.

We modified the discussion to emphasize differences between our findings and those elsewhere, and tried to propose reasons wherever possible. For example, we discuss differences regarding the results for civil status: “Our results showed that married men and women had lower risks of suicide compared to individuals in common-law unions, or who are separated/divorced/widowed or never married. Other studies also find marriage protective, possibly because marriage confers emotional stability and reduces isolation through opportunities for social and community integration [1, 8, 13, 14, 17, 31, 36]. In our study, effect estimates were of similar magnitude for males and females. This is in
line with studies from Denmark, Sweden and England and Wales [13, 36, 37], but not US research that found non-married status increased the suicide risk only for men. US data suggest that marriage confers greater health benefits to men than women, possibly because women invest time and energy in caring for household members, and males without such social support may be prone to suicide [1]. This may be less the case in Denmark, Sweden, England and Wales, and Canada where there may be greater equality in household roles between the sexes than in the US.” (page 15, lines 2-16). However, reasons for differences in results between countries are not always clear. For the results related to education we stated “Why education plays a role in suicide risk in Canada, and not elsewhere, remains to be explored” (page 17, lines 2-3). If the reviewer is able to identify additional mechanisms, we would be pleased to incorporate these into the discussion.

Discretionary Revisions.

1. *Could the common law union findings be due to confounding by religion? If the authors agree or there is evidence for this, this could be mentioned as a potential explanation for these findings.*

We hesitate to make this assumption as common law union in Canada (especially Quebec, the province with the highest rates) is more likely to be a marker of ethnicity or immigration, than of religion. We adjusted for ethnicity/immigration, which makes it unlikely that these factors confound the relation between individual disadvantage and suicide risk.