Author's response to reviews

Title: Association between socio-economic status and hemoglobin A1c levels in a non-diabetic Canadian primary care adult population

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Version: 2 Date: 16 October 2013

Author's response to reviews: see over
To: The Editor,
BioMed Central

Dear Ms Nolasco

Thank you for the opportunity to respond to the reviewers’ comments. Please find our responses below.

**Reviewer 1 (Joanna Moschandreas):**

Major Compulsory Revisions

1. Previous studies have found evidence that effects of material deprivation on impaired glucose tolerance (and BMI) differ according to gender. Was a possible interaction between gender and deprivation considered in the present context? Were random slopes considered in the model?

We considered several interactions between gender and deprivation with respect to Hgb A1c. In the bivariate models the interaction between gender and any of social deprivation, combined material and social deprivation, or income quintiles and Hgb A1c was largely insignificant (statistically, and clinically).

*Gender and material deprivation, unadjusted models*

There was a marginally significant interaction between gender and material deprivation ($P=0.0587$) and Hgb A1c. That said, the maximum difference in Hgb A1c values between males and females, within a given material deprivation quintile, was 0.06% (i.e. the maximum difference between males and females in Q1, Q2, Q3, Q4 or Q5 was 0.06%). As noted in the discussion, a minimally clinically significant difference is 0.6% or more; thus the difference of 0.06% is not large from a clinical perspective.

*Gender and deprivation, adjusted models*

In the adjusted models, we did not observe a significant interaction effect between gender and any of social deprivation, combined material and social deprivation, or income quintiles – after adjusting for LDL, HDL, TG, BMI, SBP, DBP, Age, Gender, or Family History.

*Gender and material deprivation, adjusted models*

We observed a statistically significant interaction between gender, material deprivation and Hgb A1c after adjusting for other covariates (LDL, HDL, TG, BMI, SBP, DBP, Age,
or Family History). The P-value for the interaction term in this model was P=0.0159. This suggests that the effect of gender on Hgb A1c depends on the level of material deprivation you are in. The maximal difference in Hgb A1c values between gender within a given material deprivation quintile was 0.10%. Again, this difference is clinically very small.

**Multiple interactions**

The interaction effect between gender and income quintile, combined material and social deprivation and social deprivation was non-significant – in any of the bivariate or multivariate analyses. The interaction effect was marginally significant in the unadjusted material deprivation analysis (P=0.06) and was statistically significant in the adjusted material deprivation analysis (P=0.02). That said, in both instances, the magnitude of the interaction effect was small from a clinical perspective. Hence we have chosen to not include it in the material deprivation model or in any of the other models (social deprivation, combined material and social deprivation models, income/SES models).

**Use of random intercept model**

We used a random intercept model to account for the fact that observations (patients) were clustered within a Dissemination Area (DA). That said, the ICC from the random intercept (only) model was approximately 0.005. This is quite small and suggests that there is relatively little DA level variation compared to the total variation in the model.

The model essentially prescribes a different (random) intercept to each individual from a distinct DA.

We did not go any further to estimate random slopes (given the relative paucity of DA level variation).

**Minor Essential Revisions**

1. The title is “Association between socio-economic status and hemoglobin A1c levels in a non-diabetic primary care population”. The sample, however, is not necessarily representative of a primary care population as it consists of non-diabetics aged 45+ with a haemoglobin A1C measurement recorded in the Electronic Medical Records (EMR) system over a recent 3 year period (2009-11). A more appropriate title would be “Association between socio-economic status and hemoglobin A1c levels in a non-diabetic Canadian adult population”

The study’s title was changed to “Association between socio-economic status and hemoglobin A1c levels in a non-diabetic Canadian primary care adult population”
2. Pg 6 paragraph 3. Remove the word “increasing” on the first line.

The word “increasing” was removed.

3. There are mistakes in Table 3. It appears that there are “-“ signs missing at least 6 of the confidence intervals (assuming the confidence intervals presented in the Abstract, pg 3, are correct).

This is not an error. The reference group used in table 3 is lowest income quintile, and highest deprivation quintiles. In the abstract, the highest income quintile and lowest level of deprivation is used for comparison. So we have the same absolute values, but different signs.

We revised the abstract and the result section, and used the same reference groups that are used in table 3.

4. The year of publication is missing in references 1 and 6

Years of publications were added to both references.

5. Page 10 Replace “there were significant associations” by “there were statistically significant associations”. Check the remainder of the text also.

The requested changes were made in the manuscript

6. Methods pg7-8. The description of the SES variables focuses on the ecological aspect. More details should be provided here of the indices themselves e.g. how were they combined (model four in Table 4)? And in the Discussion, a section could be added in which the 4 different SES indices are compared and contrasted to justify why it was necessary to consider all 4 indices in the present study.

We have added a more detailed description of the indices in the Methods section. Changes were made in Methods and Discussion sections to address the reviewer’s concern.

7. Only 37.7% of the sample was male (Table 1). Were males less likely to have the HbA1c screening test? Discuss in the 2nd paragraph of pg 13, in the context of the study limitations (sample representativeness).

This concern was addressed in limitation section.

Reviewer 2 (Sara Willems):
Minor essential revisions:

1) The abstract is not very clear to me. Especially the purpose of the study contains little information. This abstract would not motivate me to read the full paper.

Abstract was revised.

2) Introduction: Based on this introduction it is not clear to me what the point is of this study. The introduction does not convince me this is an important study. This part reads as a number of independent paragraphs where the reader is asked to “jump” from one topic to another. Providing a clear “red thread” for the reader, building the introduction up from a clear problem to the research question is essential.

The introduction was revised.

Major Compulsory Revisions:

1) The methods section misses more detailed information. E.g. which are the covariates taken into the model? Why not including other indicators such as physical activity, smoking, etc.? Or are they included? The method section in the abstract seems to indicate they are (“we adjusted for covariates associated with an increase in the risk of incident diabetes”) but I cannot find them in the tables nor in the text.

Ethnicity, physical activity, and smoking are not included in this analysis due to EMR data limitations. We have mentioned the first two in the limitation part. Smoking history was added to that list.

2) Is this method suited to answer your research question. I am not convinced it is. There might be a major selection bias in the patient group under study. I might be possible that there is a clear independent influence of SES on Hgb A1c, so clear that the lowest SES patients are not in the non-diabetic group but in the diabetic group. The low SES patients left are hardly representative for the low SES patients consulting in the practice and for whom the diabetes risk score is calculated.

We excluded all diabetics from all SES strata, as this study focuses on non diabetic patients. Non diabetic patients were all patients seen in the practices. We have no a-priori reason to believe that there was selection bias by SES or by Hgb A1c testing. The single payer system and universal coverage for medically necessary physician services and laboratory tests in Canada eliminates many financial barriers to attendance in practices or to do laboratory testing. Because the research question was whether there was an association between SES and Hgb A1c levels in non diabetic patients, we did not look for differences in prevalence of diabetes between groups in
different SES strata, only for differences in Hgb A1c levels in non-diabetic persons. We describe the population studied in our article, and this includes all patients consulting in a three year period; we therefore feel that the sample is representative of the patients consulting these physicians during those years.

3) Would it not be more appropriate to use other study designs such as calculating the diabetes risk score with and without SES for all patients fulfilling the requirements for such a test and see what that gives. I need to be convinced your method is suitable.

There are other studies looking at diabetes risk calculation. Our project focused on an independent association between Hgb A1c levels and SES. An independent association would support the inclusion of SES in risk calculators.

4) The ecological phallacy – a major limit of this study- is, to my opinion, underestimated in the conclusion. How could this have influenced your results? I believe the researchers are too strongly convinced that SES should not be included in clinical decision support tools. This cannot be derived so strongly from the results. I also miss a broader reflection on the importance of knowing the patient’s SES for clinical decision making and/or for the treatment of their diabetes.

We agree that ecological fallacy is an important limitation; this is mentioned in the discussion. We do not assert that SES should not be included in decision support tools, only that our data do not support inclusion in diabetes risk calculators in this primary care setting because we did not find a statistically significant association between decreasing SES and increasing Hgb A1c in most models or a clinically significant independent association in any model. We do not imply that SES is not an important determinant of health or that effects of SES should not be considered during clinical care. We were surprised by the results, as they contradict our initial hypothesis. However, in order to avoid publication bias, we believe that negative results as well as results contrary to investigator beliefs should be submitted to the scientific press.

Once again, we appreciate this opportunity to respond to the reviewers’ comments and to resubmit a revised version of the paper.