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Title: Neighbourhood level material deprivation and response to combination antiretroviral therapy in the Canadian HIV Observational Cohort Collaboration (CANOC): a longitudinal cohort study
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Reviewer 1: Keyna Bracken
Institution: McMaster University, Family Medicine, Hamilton, Ont.

General comments (author response in bold)

People who injected drugs ever were was part of the data set and presented in Table 2 with a significant p value but this is not commented on anywhere that I can see. Did this vary provincially? I wonder if this may result in some of the difference observed in BC.
We agree that although the multivariable model was adjusted for IDU status, there could be some residual confounding as a result of provincial variation in IDU. However, we did not comment on the significant p-value for IDU as this variable is serving as a confounder not an exposure. In order to avoid the table 2 fallacy, we did not interpret any measures of effect of any factors except our exposure.

Was there any provincial variation in the medication prescribed? How did you deal with changes to the drug regimen that may have impacted immunological response over time?
We appreciate these questions. The proposed analysis did not examine changes in drug regimen over time as we restricted the analysis to treatment response within 6 months after cART initiation. There may have been some individuals who changed drug regimen within the 6 month time window but we did not consider this here. We believe adjusting for enrolling province and era of entry into cohort would account for some spatial-temporal differences in prescribing cART.

Reviewer 2: Zahid Butt
Institution: University of Waterloo, School of Public Health Sciences, Waterloo, Ont.
General comments (author response in bold)

Previous studies using the deprivation index have used social deprivation in addition to material deprivation for SES. Why have the authors chosen to use material deprivation index only as an indicator for SES?
We agree that it would be an interesting study to examine the social deprivation index, as well as the material deprivation index, and its association with immune and virologic response. Due to the complexity of presenting an analysis with a four-level exposure variable (neighbourhood level material deprivation quartiles) and a four-level response (immunologic and virologic response categories), we believe an analysis on the social deprivation index is outside of the scope of the proposed manuscript.

In this study, 22.3 % of the participants were excluded because of various reasons. What impact does this exclusion have on the study results? Could the authors elaborate on this?

We appreciate the seriousness of this comment. We have added additional discussion:

- Page 17: ***A large number of individuals were excluded from the present study (37.0%) which could have introduced bias. Some provinces had very high amounts of missingness (Ontario, 54.0%) whereas others had very little (British Columbia, 9.8%). This can be at least partially explained by the way postal code data was provided to the Centre: some clinics in Ontario only reported the first three digits of the postal code which limited our ability to ascertain their neighbourhood level material deprivation quartile while the population-based cohort in British Columbia had much more complete data. It cannot be excluded that differences in how the data is collected may have contributed to regional differences in study findings. Individuals who were excluded due to insufficient VL and CD4 data may have also introduced bias into this study. Compared to those included, individuals with missing VL and CD4 data were more likely to live in one of the materially deprived neighbourhoods (21.2-22.0% versus 24.9-26.3%), to be female (14.0% versus 29.8%), and to have reported ever injecting drugs (20.5% versus 37.0%). However, we believe there were no variables present in the CANOC dataset which could accurately predict the missingness and as a result, imputation was not utilized. Of note, the additional analysis containing 77.7% of CANOC participants supported the association between neighbourhood level material deprivation and concordant negative response to cART.***

3. For the material deprivation index variable, the authors have categorized it as residence in a materially deprived neighbourhood (index >0) or not (index <0). The index score ranges from - 8 to +8. Can a person who has a score of +2 be compared to a person who has a score of +8? Could the authors elaborate on this?

This is an excellent point. We agree that dichotomizing the deprivation index was likely not the most stringent approach. We have updated the manuscript to include neighbourhood level material deprivation quartiles as the primary exposure. However, we maintained the dichotomized index as an additional analysis which supported the quartiles-based results.

To this end, we have included:

- Page 10: ***Neighbourhoods were then grouped by deprivation quartile from 1 (least deprived) to 4 (most deprived).***

- Page 13: ***Of those included, 2908 (35.1%) individuals lived in the least materially deprived neighbourhoods compared to 1754 (21.2%) who lived in the most deprived neighbourhoods. The remaining participants (43.7%) were evenly distributed among the two intermediate material deprivation quartiles.***

- Page 13-14: ***In the univariable multinomial logistic regression model, participants residing in the second material deprivation quartile had an increased odds of CD4+/VL- discordant response (OR 1.21, 95%CI 1.05- 1.41). Living in the third neighbourhood level material deprivation quartile was associated with increased odds of concordant negative (OR 1.44, 95%CI 1.13-1.83) and CD4+/VL- discordant response (OR 1.19, 95%CI 1.02- 1.38). Individuals living in the most materially deprived neighbourhoods were more likely to exhibit a concordant negative (OR 2.33, 95%CI 1.86-2.91) or discordant response (CD4+/VL- OR 1.32, 95%CI 1.13-1.54; CD4-/VL+ OR 1.45 95%CI 1.19-1.76) to cART (Table 2).***

After adjustment for sex, province of enrolment, whether individuals had ever injected drugs, era of entry into cohort, and age at baseline, living in the most materially deprived neighbourhoods was significantly associated with increased odds of a concordant negative response (aOR 1.45, 95%CI 1.13-1.86) and CD4-/VL+ discordant response (aOR 1.31, 95%CI 1.06-1.62).
- Page 15: ***The additional analysis using a dichotomized material deprivation index included 10 133 (77.6%) individuals from CANOC. Distribution of concordant positive (62.0%), concordant negative (7.1%), and CD4+/VL- (20.5%) and CD4-/VL+ (10.5%) discordant responses were consistent with the primary analysis. There were also no significant differences with respect to baseline characteristics. Consistent with the primary analysis, living in a materially deprived neighbourhood was significantly associated with increased odds of concordant negative response (aOR 1.34, 95%CI 1.13-1.60) in the multivariable model. There were no other statistically significant associations.***

4. Did the cohort have information on co- infections such as HCV or HBV or TB? This may impact the response to ART (measured by CD4 counts and VL) as well as adherence.
We agree that information on HCV, HBV, or TB would be important to include. However, data on comorbid conditions is not available in CANOC. We have added additional explanation in the submitted manuscript to this point:
- ***Treatment adherence and comorbidities that may impact immunologic and virologic response would have been considered as potential confounders in the multivariable model if such data were available*** **(page 12)**

5. The univariable model in table 2 includes only neighbourhood level material deprivation as a variable. The authors need to present the univariable results for the other variables as well.
For example, why was MSM not included in the final model?
We have added the univariable results for the other variables as well (page 27). We did not include additional variables in the final model as we were concerned with being adequately powered among smaller groups (e.g. Saskatchewan).

6. Please add 'logistic' to univariable and multivariable multinomial regression modelling
Agreed, this has been updated throughout the manuscript.