Reviewer's report

Title: Age as an effect modifier for renal transplantation in Canada's Aboriginal Peoples

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Reviewer: Lauren Kucirka

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Major Compulsory Revisions

While the analyses presented by the authors clearly show that Aboriginals have less access to transplantation than their non-Aboriginal counterparts, the case for age as an effect modifier of this disparity is less clear. Across age groups, the number who had the outcome of transplantation is small, and especially small in the oldest age group where the effect modification is seen (n=23 Aboriginal patients transplanted). Since the major finding of the paper is the effect modification in the oldest age group, it is critical to know the magnitude of disparity the authors were powered to detect. If they were powered to detect a disparity similar to the younger age groups and they didn't, this would provide strong evidence of effect modification. However, if the analysis is not powered to detect such a difference the message and conclusions of the paper should be attenuated accordingly.

Furthermore, given the small number of outcomes in Aboriginal patients and large number of covariates the authors should indicate what tests/procedures were used to ensure the model was not overfit.

Given that the primary focus of the paper was on disparities in transplant rates for Aboriginals, it is unclear why age and race stratified Poisson regression models giving absolute rates in each subgroup are presented rather than relative rates for which would describe the disparity in transplant rates for Aboriginals compared to Caucasians. Using the current presentation the reader is forced to calculate the relative rate in order to interpret the results. Furthermore, we cannot tell whether rate of transplant for Aboriginals is statistically significantly reduced when compared to the rate for non-Aboriginals. Relative rates should be presented here and the authors should explain what these models add over the Cox proportional hazard and competing risk models (in other words, why didn't they just repeat those analyses stratified by donor type?)

Comparison of the hazard ratios (Cox model) and subhazard ratios (competing risk model) is useful to illustrate how much of the disparity is explained by differential mortality on dialysis between the two groups. For example, if the disparity was much greater when measured in a competing risk model, it would suggest that Aboriginals had higher mortality on dialysis relative to Caucasians. However, there is significant overlap between the 95% confidence intervals of the
two estimates so it is unclear that differential dialysis mortality worsens this disparity; this should be clarified in the results and discussion.

Minor Essential Revisions

The authors perform a very thorough sensitivity analyses to examine the effects of missing data; it would be helpful to know how much data were missing.

Introduction, Sentence 2: needs a citation.

Introduction, Sentence 3: "The Aboriginal ESRD population is in general younger than their Caucasian counterparts and often reside in rural communities." The citation should reference the specific data source within the Canada statistics page that support these statements.

Introduction, Sentence 5: "Despite the fact that Aboriginal population with ESRD is well suited for renal transplantation..

Introduction, Paragraph 3, Last Sentence: "Age has been found to be an important effect modifier with lower rates of renal transplantation demonstrated in elderly women and young African-Americans." Age is an effect modifier of the relationship between gender and transplantation (older women have reduced rates of transplant, younger women do not). However, this is not true for African-Americans who were shown to have similarly reduced rates of transplant at all ages. This sentence as well as sentence 2 of paragraph 6 of the discussion should be modified accordingly.

Discretionary Revisions

Table 1: Since the average age of the Aboriginals is 12 years younger than the average age of Caucasians, the higher rates of comorbidities in Caucasians might be largely explained by differences in age; stratifying Table 1 by age group would help to clarify this.

Since paragraph 1 of the introduction is only 1 sentence, I would combine with paragraph 2.

Introduction, Sentence 4: I think this statement would be stronger if "as such" was replaced with "previous studies have shown" to clarify that this is not just a hypothesis and is actually supported by the study cited.

I would avoid statements such as "the Cox model overestimates the risk" or that "the competing risk model is more accurate" and focus more on the substantive differences between the two. The competing risk model accounts for differential rates of the competing risk (mortality) and thus shows how much of the disparity is explained by differential rates of mortality between the two groups. The estimates from the Cox model are a better approximation of what the hazard ratio would be if mortality were equal between the two groups.

Level of interest: An article whose findings are important to those with closely
related research interests

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests