Reviewer's report

Title: Relative risk of renal disease among people living with HIV: a systematic review and meta-analysis

Version: 1 Date: 16 June 2011

Reviewer: Meredith Shiels

Reviewer's report:

Review for BMC Public Health

“Relative risk of renal disease among people living with HIV: a systematic review and meta-analysis”

This manuscript is a meta-analysis examining the relative risks of renal disease among people with HIV, and by antiretroviral therapy use, tenofovir use and age. Overall, I found the paper somewhat difficult to follow. The authors’ definition of the outcome of interest seemed to be defined differently for each study, and not enough information was included for each individual study in the tables.

Major revisions:

Overall comment: Please add a table with all of the pertinent information for each study included in the study. Please include the name of the cohort or a description of the participants, how the study defined their outcome of interest, age range, HIV risk group, adjustment variable, etc. The version of table 1 given to me is missing the majority of the studies, and does not have complete information.

Methods:

1. Outcome measures: You state that the primary outcome was “the incidence of CKD defined as estimated eGFR<60 mL/min/1.73 m2 for greater than or equal to 3 months irrespective of kidney damage.”
   a. Your outcome should be defined as the disease endpoint, not the incidence of the disease endpoint.
   b. Did every study report eGFR<60 for at least 3 months?
   c. You state that each study included in the analysis used this definition, but then proceed to describe each study’s outcome differently (e.g., kidney disease, chronic kidney disease, HIV-associated nephropathy, all-cause nephropathy, acute renal failure, tubular dysfunction, renal impairment). This is extremely confusing, and it concerns me that you might be combining different outcomes. If each study does use the same eGFR cutpoint, it would be helpful to state up front that the studies name their endpoints differently, but they are all defined the same way and you will be referring to all endpoints as X (i.e., chronic kidney disease).
Results:

1. Meta-regression and subgroup outcomes

a. I would suggest breaking this paragraph up and presenting results with the overall meta-analysis results.

b. Your meta-regression method is very confusing to me. Doesn’t meta-regression estimate the association between study characteristics and the overall RR? You stated that you “identified risk factors on renal function” and that “geographic location and eGFR were significantly associated with the degree of renal disease.” These factors should be estimated in relation to the RR and not with the presence of renal disease alone.

c. Twice you report that you performed “subgroup analysis using these two variables,” and then you provide one estimate. Is this estimate from one of the subgroups? I think you mean that you adjusted for potential confounders and produced an adjusted RR from the meta-regression model. Is that correct? This should be clarified.

Minor revisions:

Abstract

1. Methods: What was the earliest date of publication included in your study?
2. Methods: You state that eligible studies were observational cohort studies here, but later you state that you also included case-control and cohort studies.

Introduction:

1. Please add references to the first paragraph.

Methods:

2. The description of your search strategy does not include CROI abstracts, though this component is included in the abstract and your results. I think that the use of abstracts from a conference should not be encouraged in a meta-analysis. Conference abstracts have not been edited based on peer review, and results often change before manuscript submission. Further, abstracts often do not present the level of detail needed in a meta-analysis.

3. Selection of studies: Did you exclude papers that present results from the same study? For example, if two studies reported results from MACS, did you exclude one of them?

4. Renal outcomes: You mention the differences in how eGFR was estimated. How do these methods compare? Do they produce similar results? Did the prevalence of CKD differ by studies based on their methods use?

5. Quality assessment: Please add the maximum score of the Downs and Black checklist.
Results

2. Effect of antiretroviral treatment:
   a. It is unclear how each study defined ART use. This could be added in the description or to a table.
   b. Did you look at duration of any ART?

Discussion

1. First paragraph: You state that the “relative risk of renal disease for PLHIV was found to be 3.87 times more than that of HIV-uninfected people.” This is not correct terminology, you should either say the risk is 3.87 times more or the relative risk was 3.87.

2. Please add further information to the discussion about the mechanism for CKD in people with HIV infection and the mechanism by which ART reduces risk and tenofovir increases risk.

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

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.