Author's response to reviews

Title: Chronic Kidney Diseases in Mixed Ancestry South African Populations: Prevalence, Determinants and Concordance between kidney function estimators.

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Author's response to reviews: see over
Dear Dr Deidra Crews


Thank you very much for your letter dated 29<sup>th</sup> December 2012 Re: Paper titled “Chronic Kidney Diseases in Mixed Ancestry South African Populations: Prevalence, Determinants and Concordance between kidney function estimators”. We would like to thank the reviewers for their constructive and valuable comments. We have addressed the concerns raised by the reviewers and these are highlighted in red in the manuscript. Our responses to specific points are below:

**Reviewer's report**

**Title:** Chronic Kidney Diseases in Mixed Ancestry South African Populations: Prevalence, Determinants and Concordance between kidney function estimators.

**Version:** 1  **Date:** 24 December 2012

**Reviewer:** Tariq Shafi

**Reviewer's report:**

This paper by Matsha and Yako provides important information about the prevalence of CKD in South Africa. The paper is clearly written and easy to follow. I think the paper can be greatly improved by some additional information as outlined below.

**Major Compulsory Revisions**

1. CKDEPI and MDRD equations: Please be consistent in the use of “corrected and uncorrected”. I think it may be preferable to use “with race-adjustment” and “without race-adjustment” rather than corrected and uncorrected?

   **Response:** Thank you for raising this point. We feel that scientists in the study setting would be more familiar with ‘ethnicity correction’ than ‘race adjustment’. We have therefore maintained ‘ethnicity correction’ while striving to be consistent as suggested by the reviewer.

2. The biggest strength of the paper is that provides information about CKD prevalence in South Africa from a population-based cohort. I would like to see greater details regarding the prevalence on the cohort itself. Please consider creating a table with prevalence estimates using the attached table.

   **Response:** Thank you for raising this point which we have addressed by providing a new Table 2 showing the crude and age-standardized prevalence of eGFR categories across specified subgroups. Please refer to new Table 2.

3. Table 1 should describe the characteristics of the population overall (first column) and by CKD (>60, <60; by CKDEPI formula) with p values for the univariate associations. The description of the population will be of great interest to the readers. Please remove the word “mean/median” from the description of the variables and put it in footnote to the table.

   **Response:** Thank you for raising this point. We have removed mean/median from the description of variables. We have also added 3 new columns to table 1 and expanded the description of the baseline characteristics of the population to reflect the suggestion of the reviewer. We do feel that
providing comparison of the characteristics by gender is also important and have therefore kept them in the table as originally provided.

4. The methods describe collection of urine and measurement of urine albumin. Why is it not used for CKD classification or reported in Table 1?

Response: Thank you for raising this point. We have now removed the statement on urinary albumin measurement, which was missing for a substantial number of participants and therefore not suitable for use in the current analysis without substantially slashing our sample and inducing selection biases. We do however now acknowledge this as a limitation of the study.

5. In the discussion section, please discuss why there are more women than men in the cohort and how could this selection bias effect your results? For example, is it possible that the men included in the study were perhaps sicker than the general population – this would lead to an overestimation of the CKD prevalence.

Response: Thank you for raising this point. This is not unique to this study but is a general observation in studies conducted across sub Saharan Africa. Females, in contrast to males, are in general more concerned about their health. However we have included this as a limitation to the study.

6. Conclusions: The study provides evidence for support of CKDEPI equation for eGFR reporting and CKD classification (rather than against the current guidelines).

Response: We agree with the reviewer, please refer to the following sentence in our conclusions, “The South African Renal Society CKD guidelines recommends the use of Cockcroft-Gault or MDRD equations, however, our study demonstrated a poor agreement between the two equations in the Mixed Ancestry population groups”.

Minor Essential Revisions
1. Please double check references to all tables. Some of them appear to missing.

Response: Corrected accordingly

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

Reviewer’s report
Title: Chronic Kidney Diseases in Mixed Ancestry South African Populations: Prevalence, Determinants and Concordance between kidney function estimators.
Version: 1 Date: 18 December 2012
Reviewer: Navdeep Tangri
Reviewer’s report:
Matsha et al. present a cross sectional study from a suburb of Cape Town, S Africa, and attempt to describe the prevalence of CKD and associated risk factors in an older community based cohort. The work is of potential interest given the lack of data about the burden of CKD in Africa. However, I have the following major concerns with the manuscript
1)- In the introduction, the authors comment about the lack of information about CKD prevalence in sub-Saharan Africa in contrast to developed nations. However, it would appear that their community based cohort in a suburb of Cape Town is also unlikely to be representative of sub-Saharan Africa.

Response: Thank you for raising this point, this has been addressed in the limitations of the study.

2)- Their comment about the prevalence of CKD being extremely high may not be correct. In fact it is completely dependent on the ethnicity correction in the population. The prevalence is low (< 8 %) with the correction, and only high when the correction is not used. I am not familiar enough with the mixed ancestry population to recommend for/against the use of the ethnicity correction.

Response: Based on the South African Renal Society CKD guidelines that omit the correction factor except for black Africans, the prevalence of CKD stages greater than 3 is the highest reported in Africa thus far.

3)- No GFRs are measured, even in a subset....as such, determining the optimal formula for GFR estimation is not possible.

Response: We do agree on this important point which should be addressed in future studies. We have acknowledged the lack of directly measured GFR as a limitation of our study.

4)- The kappa/agreement analysis is unnecessary. The MDRD and CKDEPI equations use the same variables with slightly different coefficients...As such, it is expected that they would be collinear.

Response: We agree with the reviewer, but believe it to be necessary for completeness in demonstrating the poor agreement between Cockcroft-Gault and MDRD equations that are recommended by the South African Renal Society CKD.

5)- The cohort is predominantly female and obese. As such, the generalizability of the CKD prevalence is unknown.

Response: Please refer to comment number five of reviewer one above.

I would urge the authors to omit table 2, fig 1, fig 2, table 4, and pick an appropriate equation (with or without ethnicity correction)....and focus on reporting the prevalence of CKD and associated factors in this predominantly female South African suburban cohort.

Response: The aim of the present study was to assess the magnitude and determinants of CKD in a community based cohort, and evaluate the agreement between commonly advocated kidney function estimators in a mixed ancestry African population. The South African Renal Society CKD guidelines recommend the MDRD with ethnicity correction factor only in black Africans, it does not account for the African ancestry in the mixed ancestry population of South Africa. The highest agreement was observed when comparing the MDRD and CKD-EPI equations, both with ethnicity correction, followed by their equivalents without correction, thus we believe that these findings should be reported.

Level of interest: An article of limited interest
Quality of written English: Acceptable
Statistical review: Yes, and I have assessed the statistics in my report.
Declaration of competing interests:
I declare that I have no competing interests

Sincerely,

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