Author's response to reviews

Title: The MDRD equation underestimates the prevalence of CKD among blacks and overestimates the prevalence of CKD among whites compared to the CKD-EPI equation: A retrospective cohort study.

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Author's response to reviews: see over
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Jigasha Patel, MRCP, Ph.D.
Series Editor, Medicine

Dear Dr. Patel:

We are pleased to submit a revision of our manuscript entitled "The MDRD equation underestimates the prevalence of CKD among blacks and overestimates the prevalence of CKD among whites compared to the CKD-EPI equation: A retrospective cohort study" for publication in BMC nephrology. We have carefully read the reviewers' constructive comments and rewritten the manuscript incorporating their critiques and recommendations. We have attempted to specifically address their comments in the following paragraphs.

From the editorial perspective, we have added the requested statement of ethical approval at the beginning of the methods section. Also, we were unable to upload Table 5 as part of the manuscript, and have uploaded this as a separate document. We have copy-edited the paper to correct grammatical errors.

**Reviewer 1**

**Major revisions**

Methods:
Race was determined by race listed in medical record. In the VA system, this is done by self reporting of the patient. This has been stated in the methods section.

We are not studying the association of comorbidities with prevalence of CKD. In the univariate analysis the prevalence of these comorbidities was found to be higher in CKD patients. The statement "change in race parameter" has been changed.

Results:
Table 3 (now Table 2) has data only on patients with CKD, rather than the entire sample. Thus, we have not combined these tables.

The analysis is of patients > 65 years of age and has been corrected.

Discussion:
We have written the discussion such that there is initially a presentation of clinical factors which may explain the difference in prevalence of ESRD relative to CKD, and then discuss the issue of the differences in prevalence due to the eGFR equations. We have shortened the initial discussion. If the reviewer feels that the manuscript would be improved by starting with the equations, we can certainly alter the order of discussion. We have added further details differentiating the Clase and Coresh studies, including the specific MDRD equation used in the studies (page 12, lines 2-8).

Discussion/Limitations. We have added to the limitations that no actual measured GFR was included and that we have not included proteinuria. The race was determined by patient self report.

**Minor essential revisions**
Overall:
The manuscript has been carefully rewritten to eliminate grammatical errors.
The race terminology has been changed to refer to black and white individuals throughout the text.

Abstract:
VISN and MDRD have been spelled out. Estimated has been added to the GFR terminology.
CKD-EPI equation has been written consistently through manuscript.

Background:
The units of measurement have been made consistent.
The timing of the eGFR measurements has been added early in the methods section.
ICD has been spelled out.
The reviewer is correct that CKD stage 3a and 3b were not in the KDOQI guidelines referenced.
We have added a reference to the NICE guidelines, which included stages 3a and 3b (page 7, line 10).
The clinical variables and the co-morbid conditions have been spelled out. The ascertainment of these conditions has been defined in the methods (page 6, lines 14-18).
The timing of lab values is stated.
Categories of eGFR have been changed to stages of CKD throughout the manuscript.

Results
Table 2 (now Table 1). We agree only one line is needed for gender, but have left both lines in order to show the statistical analysis.
Sentence now reads "logistic regression model for CKD".

Discussion:
The sentence beginning with "several possible factors" has had references added.
The statement "blacks presenting to a primary care physician later" is the correct statement. We are looking at creatinine measurements on entry to the VA system, not at time of referral to the nephrologist.

Discretionary revisions
Background:
The reference by Matsushita has been added to the background.

Results:
The sentence "It has been suggested" has been left in to explain the reason for presentation of the data in Figure 3 (now Figure 4).

Reviewer 2

Major revisions
1. Abstract:
The abstract has a statement added to state the specific prevalences in blacks and whites.

Methods:
2. Comorbidities were obtained from the clinical problem list. This is compiled from inpatient and outpatient visits.
3. The creatinine values were not referable to IDMS over the time period studied. The MDRD formula for non-standardized creatinine values was used.

Results, tables, and figures.
4. Table 3 (now Table 2) has now had p values tested and added.
5. Table 4a and 4b have been combined (now Table 3). We agree with the reviewer that analyzing AORs for blacks versus white by stages may make it easier to understand. We are in the process of analyzing that. We also believe that the way the data is currently presented is a useful way to present the AORs. We have attempted to explain this more clearly in the presentation of the results. If the reviewer strongly feel that it should be presented by stages, we will do so.

6. We have eliminated the combined group in Figure 1 (now Figure 2). We have added a statement in the figure legend to emphasize how much lower the prevalence of CKD is when using 2 serum creatinine measurements. This has also been mentioned in the text (page 9, line 11).

7. We have written a detailed explanation of figures 3 and 4 (intended to be Figures 3a and 3b in the original submission, but now Figure 4 and 5). This has also been added to the results. (page 10, last 2 paragraphs).

8. We had attempted to submit what appears as figure 3 and 4 as figure 3a and 3b. Thus Figure 5 was referred to as Figure 4 in the discussion (page 11, first paragraph). This is now Figure 6.

9. The reviewer is correct that the main superiority of the CKD-EPI is at stage 3b.

10. We have added detail to studies mentioned in paragraph 2 as requested by reviewer 1. Thus, this has not been shortened. We have combined the 2 paragraphs beginning with "this inconsistency" and "There are various."

11. We agree with the reviewer that it is important to assist the reader through the results in this type of study. We have moved some of the discussion to the results section, and have tried to provide clear explanations.

**Minor essential revisions**

1. The manuscript has had all slang terms removed.
2. The comma has been removed.
3. The figure has been revised. The axes were mislabeled. We thank the reviewer for noticing this. The age is displayed in intervals because the figure would be too crowded if discrete age points were used.

**Discretionary revisions**

1. The introductory paragraph has been broken down. The margins have been dejustified.
2. Table 1 has now been made into Figure 1.
3. Table 2 (now Table 1) - heading has been changed. The table has had suggested indentations made.

Thank you for your consideration of this revised manuscript.

Best regards,

Pradeep Arora, MD

James Lohr, MD