Reviewer’s report

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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Reviewer: James Wetmore

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Summary

In this large very retrospective study using a VA database, the authors investigate the issue of differential classification of CKD, using the KDOQI stage classification, by employing what have emerged as the 2 major eGFR equations, namely the MDRD and the CKD-EPI formulas. They are prompted by this vexing data in which prevalence of CKD in blacks appears to be lower at earlier stages of CKD relative to whites, and yet the evidence is conclusive that incidence of new ESRD, as well as prevalence of ESRD, is much higher in blacks than whites. It is certainly possible that some race-based differential misclassification could be occurring, especially at higher levels of eGFR.

Major Compulsory Revisions

Abstract

1. The conclusions of the abstract do not appear to actually reflect the abstract results presented; or if they do, they seem too opaque for an abstract, where clarity is key. We are told that black CKD prevalence = white CKD prevalence by CKD –EPI, but that blacks outstrip whites at stages 3b, 4, and 5. Thus whites, presumably, outstrip blacks at 3a? The authors toggle between overall prevalence (“overall prevalence of CKD is lower when CKD-EPI…”) and racial differences in prevalence; this is confusing. In order to justify the conclusion that “MDRD overestimates the prevalence of CKD among whites” I would expect to see a clear sentence in the abstract results that prevalence of CKD in whites was X% by MDRD and Y% by CKD-EPI, versus A% by MDRD and B% by CKD-EPI in blacks.

Methods

2. The operational rules for determining comorbidities must be described. What algorithms were used? Many times, a single inpatient ICD-9 or two outpatient ICD-9 codes (at least 30 days apart) are used to establish a comorbidity. Does the VA in the VISN database use ICD-9 codes – if not for billing, then for tracking diagnoses? More specificity is needed here.

3. Are the Cr values referable to IDMS? The coefficient changes for the MDRD
formula depending on whether the Cr values are standardized, so it is important
that the right version of the MDRD formula is used, and stated.

Results, Tables and Figures

4. Table 3: I am not sure why results of tests of inference (p-values) are not
shown here. If the goal of listing all these comorbidities is to build a case that
these may influence estimates of eGFR – and I did not detect this theme in the
manuscript – then this table is needed. I am not sure, indeed, that the table is
needed at all. But if it is kept, there should probably be p-values tested just as
they were for all the covariates in Table 2. I realize that Table 2 is for the whole
sample, and Table 3 only for patients with eGF < 60 by CKD-EPI.

5. Tables 4a and 4b should be combined in my view. Simply make 3 columns
with strata of eGFR on left, and AORs for EPI and MDRD in columns 2 and 3.
This improves the presentation very much for the reader for the purposes of
comparison. More importantly, rather than simple bivariate splits, the cohort
should be divided into exclusive strata, unless the authors can make a
compelling case otherwise. If I really want to track how patients are classified into
CKD stages as they progress – as a way of gaining insights into where and how
this CKD/ESRD discordance occurs in blacks and whites – then splitting people
into > or < than 30 seems less helpful than assessing the AORs for blacks versus
whites in 15-30, 30 -45, 45-60, etc. It is much more logical, in my view, to think
about it this way; I would be interested in the author’s responses. Whatever the
presentation, the reader needs to lead carefully through this key table in the
Results. Statements such as, “Table 4 shows that for CKD-EPI, there is no
difference (AOR = 1.057, 95% CI 0.981-1.139) between blacks and whites at a
cutpoint of eGFR = 60, but that for MDRD, there was a significantly lower AOR
(0.67) for blacks to have CKD compared to whites at this cutpoint for eGFR”, etc,
are helpful to guide the reader through the evolution of the results.

6. All figures were very difficult for me to see on my hard copy, I was able to
expand them 600% online but the pink Figure label consistently obscured part of
the figures. For Figure 1, since the number of whites is much greater than the
number of blacks, the combined part looks mostly like the whites. The results for
the whites swamp out the results for blacks, so I would eliminate the combined
group – it does not seem informative for this reason. The authors should highlight
how much lower CKD prevalence is using 2 measurements.

7. Figures 3 and 4 were a little difficult to interpret for me. Is the estimated
parameter the difference in eGFR between the 2 formulas? And in what race is
the 11.5% percentile (eGFR of 48.31). I think there might be valuable information
in these figures but they need to be adequately interpreted for non-statisticians.
Clarity is needed for these potentially-important figures.

8. Is Figure 5 even referred to/explained in the text? I was unable to locate a
reference to this.

Discussion
9. It seems to me that if blacks = whites for CKD (eGFR < 60) prevalence, and if blacks exceed whites in CKD using both formulas at stages 4 and 5, that the main “superiority” of CKD-EPI comes at stage 3b, where blacks exceed whites; there seems to be no difference in 3b between whites and blacks for MDRD at stage 3b. Is this correct? This point would need to be made explicitly since the main point of the manuscript is that CKD-EPI may do a better job of classifying CKD than MDRD, and as a result, would provide insight into the “paradox” that there is a greater prevalence of black ESRD than white ESRD, despite a greater CKD prevalence overall in whites.

10. Overall, I do think the discussion could be focused and shortened. For example, I think the second paragraph the results of previous studies could be synthesized and shortened more effectively, and the following 2 paragraphs beginning “This inconsistency…” and “There are various reasons…” could probably be combined into one paragraph.

11. I am an adherent of the approach of assisting the reader throughout the results section. I realize that some “reductionists” think that the results section be a sterile presentation of just the raw data, but the problem is that all investigators are inevitably more familiar with their results than the reader. So it seems to me that statements such as “In the overall group, 44.4%...(CKD stage 3a by MDRD method” are very quantitative and belong in the Results section rather than the discussion. The implications of this detailed quantitative data should then be placed in the Discussion in most cases.

Minor Essential Revisions

1. There is occasional use of slang terms, such as “till” (page 6), which I am sure means “until”.

2. In the paragraph immediately before the conclusions, there is no need for a comma after “Although”.

3. I am perplexed by Figure 2. On the y-axis, the label is age. Can the authors confirm that several patients had a first Cr measured at between 100 and 110 years of age? And that no individuals < 40 years old had measured values? Could the axes be mislabelled? In any event, the choices of labels should be consistent – discrete values (70, 80, etc) on one axis should not be used when intervals (e.g., 50-59) are used on the other. I suggest consistently using discrete values.

Discretionary Revisions

Introduction

1. I do not have much to dispute about this section since I think the investigative question has been set up, but the massive single introductory paragraph should probably be broken down. I would probably de-justify the right margins throughout and make clear indentations on the left to help the reader. One
potential place to break the intro into 2 or more paragraphs might be just before, “The above studies also employed….”

Results, Tables and Figures

2. Table 1: Classically, study designs are better shown as figures (with boxes around discrete groups, connected by arrows) than tables, for example, as is done in NEJM.

3. Table 2: The heading might best be changed to “Demographics of final sample” with no need for a capital S or the word “size.” Also, the table would look neater, I think, if subheadings are indented. For example, strata of age (4 groups) could be indented under Age, the 4 strata of BMI indented perhaps 3 spaces under the heading “BMI”, etc. Then the p-value could be placed on the row that contains the master heading (e.g., “BMI”).

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

**Quality of written English:** Needs some language corrections before being published

**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.