

31294-Reply to reviewers

Dear Dr. Fang-Fang Ji;

First, on behalf of all my co-authors and myself I want to express our thanks to the editors and reviewers of this report. We made changes in the text to address the comments of the reviewers. Here we will provide our replies to the comments of the reviewers:

Reviewer 00351120

Thank you very much for the kind comments. In the 1st paragraph of page 18 we had made a comment with a reference (ref. 150) about the computation of low eGFR values by the MDRD formula. However, we want to stress that this may not be applicable to all eGFR formulas unless it is shown to be so in experimental studies measuring GFR by a standard method in healthy individuals. The direction of the error and the degree of deviation of eGFR from GFR values outside those tested during the development of the equations are not easy to predict intuitively. This is true for any regression. We did not add any new comments to the text along these lines. However, we are willing to add additional comments if the editors consider them necessary.

Reviewer 02889203

Thank you very much for the useful suggestions. We made some changes in the text addressing these suggestions. Here we provide answers to the suggestions of the reviewer: (a) The only GFR biomarkers that are in extensive current use for eGFR calculations to diagnose and stage CKD are creatinine and cystatin C, and this is the reason for including only these two biomarkers in the early part of this report. The comments about beta2-microglobulin and beta-trace protein in the late section discussing new GFR biomarkers were expanded, the two references offered by the reviewer were added to the list of references (new references 215 and 216), and their main conclusions were commented upon in the revised text. (b) The second paragraph in the Introduction refers to examples of conditions affiliated with CKD. Cardiovascular disease is the most important of these conditions. We made that clear in the first sentence of this paragraph. (c) The contents of page 9 were shortened. In addition, the three case reports were shortened. The breath of the topic discussed did not allow further shortenings in our opinion.

Reviewer 00503233

Thanks for the favorable reception of this report.

Reviewer 00503312

Thanks for the favorable grading of this report.

We are submitting the revised manuscript with a new –and expanded by one– number of figures. Dr Shapiro discovered and corrected an error in the scaling of the figures. Our figures are now properly scaled and color coded to illustrate where the MDRD and CKD-EPI formulae diverge. We are also submitting the other required documents including the signed copyright assignment form, an audio core tip, the conflict-of-interest statement, and the Google Scholar statement. Please note that this report was not supported by any grants and that a language certificate is not needed because English is the native language of several authors, who made changes in the text.

Please stay assured that we are willing to modify this report by making any other changes that you consider necessary.

Thank you again

Best regards

Antonios H. Tzamaloukas