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Influence of race in the estimation of glomerular filtration rate in patients with a high cardiovascular and renal risk

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The estimation of glomerular filtration rate (eGFR) is usually indirectly calculated from serum creatinine in routine clinical practice. This indirect eGFR determination is then used to perform therapeutic decisions. However, serum creatinine may be influenced by GFR, but also by muscle mass and diet; therefore, age, sex, race (Black/African American vs. other), height, and weight have been used to adjust the eGFR.¹ While age, sex or height are biological variables, race/ethnicity certainly has biological/genetic background but also carries a strong social and psychological burden, and is usually a very sensitive topic. As consequence, many medical centres have removed the race adjustment from eGFR despite the lack of studies assessing the potential clinical impact of this decision.^{2,3}

The Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation to estimate GFR from serum creatinine was developed and validated across 10 studies including people with and without chronic kidney disease (CKD). Race was classified as African American (AA) or other as assigned by the study participants or the investigators.¹ A reassessment of the original CKD-EPI equation excluding the adjustment for race has led to a systematic error in the evaluation of AA participants, leading to an underestimation of the measured GFR and a worse performance of the CKD-EPI equation.⁴⁻⁶ New eGFR equations that omit race but incorporate both creatinine and cystatin C together in the equation were found more accurate.⁷

Given the potential implications of removing race from the CKD-EPI eGFR equation, we aim to replicate previous findings in a broad population of patients with a high cardiovascular and renal risk, including: 1) type 2 diabetes in the ACCORD (NCT00000620) trial, 2) hypertensive without diabetes in the SPRINT (NCT01206062) trial, and 3) heart failure with preserved ejection fraction in the TOPCAT (NCT00094302) trial.

We computed eGFR from serum creatinine using the CKD-EPI equation with and without the race indicator for AA/Black patients. We then compared the distributional eGFR shift, CKD reclassification, and prognostic implications of calculating eGFR with and without race.

ACCORD enrolled 10,251 patients of whom 1,947 (19%) were Black/AA. The inclusion of race adjustment in the CKD-EPI equation gave a mean eGFR of 87 ± 19 ml/min/1.73m², when race was excluded from the equation the mean eGFR was 75 ± 17 ml/min/1.73m² i.e., a difference of minus 12 ± 3 ml/min/1.73m² by excluding race from the equation. *Figure 1A*. Excluding race from the CKD-EPI equation more than doubled the number of patients classified as having CKD stage 3: 378 excluding race vs. 166 including race. A similar pattern was seen in SPRINT and TOPCAT. In SPRINT 9,361 patients were included of whom 2,928 (31%) were Black/AA. Excluding race from the equation led to a difference of minus 10 ± 3 ml/min/1.73m², with many more patients classified as having CKD stage 3 (680 vs. 1048). *Figure 1B*. In TOPCAT-Americas 1767 patients were included of whom 293 (17%) were Black/AA. Excluding race from the equation led to a difference of minus 8 ± 3 ml/min/1.73m², and more patients classified as having CKD stage 3 (187 vs. 145). *Figure 1C*.

In this study excluding race from the CKD-EPI equation systematically led to an underestimation of GFR and classified more patients as having worse CKD stages. These findings have important clinical implications and potential unintended consequences, as Black/AA patients could have received lower drug doses or have a label contra-indication for taking certain drug and some could have been excluded from these trials based on low eGFR.

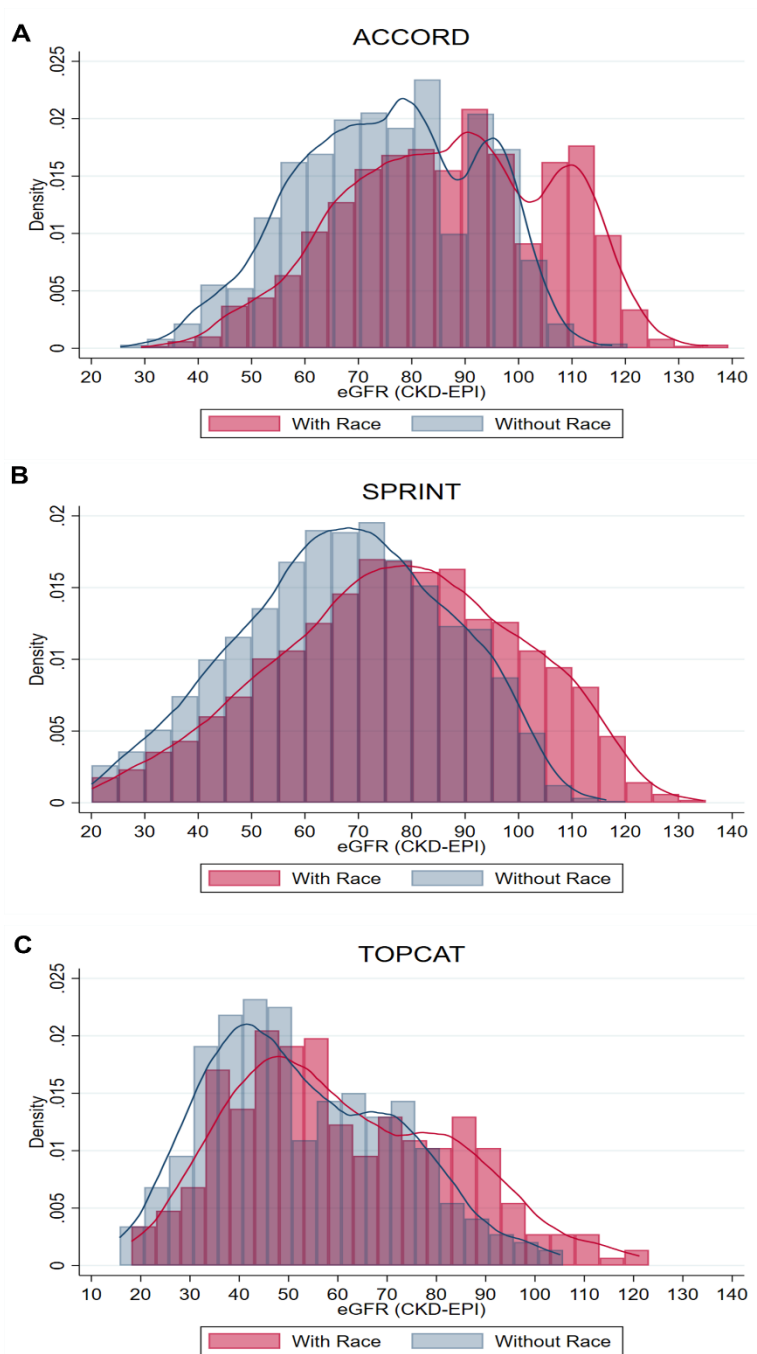
Our findings expands to high CV risk patients previous reports from others,⁴⁻⁸ which led an NKF-ASN task force to recommend immediate implementation of the new CKD-EPI creatinine equation refit without the race variable.^{7,9}

Further research on GFR estimation aimed at eliminating race and ethnic disparities is warranted.

Disclosures

The authors have no potential conflicts of interests regarding the content of this manuscript.

Figure 1. Influence of race in the estimation of glomerular filtration rate



Legend: eGFR, estimated glomerular filtration rate calculated by the CKD-EPI formula and expressed in ml/min/1.73m².
A, ACCORD (Action to Control Cardiovascular Risk in Diabetes); B, SPRINT (Systolic Blood Pressure Intervention Trial); C, TOPCAT (Aldosterone Antagonist Therapy for Adults With Heart Failure and Preserved Systolic Function).
Caption: Calculating eGFR without the inclusion of the race variable (“African American”) leads to a leftward shift in eGFR i.e., African American patients have their eGFR underestimated, which may have major implications for treatment, follow-up, and prognostic assessment.

Note: We used the CKD-EPI formular to compute eGFR, hence these results may differ from those presented in the respective trials, using the MDRD formula.

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