Black Race Coefficient in GFR Estimation and Diabetes Medications in CKD: National Estimates

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Black adults with type 2 diabetes (Supplemental Table 1). Using race-based eGFR and albuminuria classification, 39.3% (95% CI, 36.2% to 42.4%) were classified as having CKD. This increased to 45.2% (95% CI, 41.9% to 48.5%) using eGFR without the race coefficient. This was an additional 5.9% (95% CI, 4.4% to 7.3%) of the study population classified with CKD—an estimated 235,341 (95% CI, 158,920 to 311,762) individuals. SGLT2i initiation (by the CKD guideline) would be recommended for 35.3% (95% CI, 32.4% to 38.2%) of Black persons with diabetes under race-based GFR estimation, versus 40.3% (95% CI, 37.4% to 43.2%) using eGFR without the race coefficient. GFR without race coefficient would reclassify 0.8% (95% CI, 0.1% to 1.4%) of Black persons with diabetes <30 ml/min per 1.73 m², too low for SGLT2i initiation or metformin continuation, and 0.3% (95% CI, 0.0% to 0.7%) would drop <15 ml/min per 1.73 m², too low for GLP-1ra. Of those newly classified with

GFR from serum creatinine–based equations informs medication management in CKD. These equations include age, sex, and race (Black versus non-Black), and the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation increases eGFR by approximately 16% for Black persons. This has led to concern about systematically different care; however, removal of the race factor has led to concern about medication eligibility and dosing. Glucose-lowering medication recommendations in CKD depend on eGFR. The Kidney Disease Improving Global Outcomes (KDIGO) Guideline for Diabetes Management in CKD recommends medication classes for CKD. Metformin is the first-line medication for type 2 diabetes in general, yet has a lower eGFR threshold (30 ml/min per 1.73 m²). Sodium-glucose cotransporter 2 inhibitors (SGLT2is) and glucagon-like peptide 1 receptor agonists (GLP-1ras) have shown kidney and cardiovascular benefits and are preferred in CKD. However, the KDIGO guideline outlines lower eGFR limits for initiation (30 ml/min per 1.73 m² for SGLT2i and 15 ml/min per 1.73 m² for GLP-1ra). Removal of the race coefficient from eGFR for Black persons means some would newly qualify for CKD-preferred medications (eGFR reduced into CKD range) and some would no longer qualify (eGFR reduced below thresholds). We estimated the proportion of Black adults in the United States with type 2 diabetes for whom medication recommendations could be affected by dropping the eGFR race coefficient.

We used the National Health and Nutrition Examination Survey (NHANES), a study that enables estimates of the United States population. NHANES was approved by the National Center for Health Statistics institutional review board. We combined four 2-year data cycles, 2011–2018, adjusted the weights and applied survey methods to estimate cross-sectional totals and proportions of the population. We included persons aged ≥20 years with self-reported Black race and type 2 diabetes.

GFR estimates used CKD-EPI, and CKD was classified using eGFR and albuminuria. We further classified by metformin, SGLT2i, and GLP-1ra recommendations from the KDIGO diabetes guideline. For those reclassified as having CKD when the race coefficient was omitted, we estimated the proportion with prior indication for SGLT2i or a GLP-1ra based on the American Diabetes Association guideline (for cardiovascular disease or weight loss). Multiple imputation was performed for missing laboratory data (Supplemental References).

We identified 923 observations, representing a cross-sectional estimate of 4,007,966 (95% confidence interval [95% CI], 3,358,243 to 4,657,689)
CKD, 27.8% (95% CI, 15.0% to 40.6%) would qualify for SGLT2i or GLP-1ra for cardiovascular indications, and 93.4% (95% CI, 86.0% to 100%) would qualify for weight loss (body mass index ≥25 kg/m²). Figure 1 presents results in a visual format. We found that omitting the eGFR race coefficient could affect guideline-directed medications for a substantial number of Black adults with type 2 diabetes. An additional one in 20 would be newly classified as having CKD and would potentially qualify for CKD-preferred glucose-lowering therapy. However, most reclassified into CKD had other indications for these agents: one in four for cardiovascular indications and nine in ten for weight loss. Nearly one in 100 would have eGFR reduction substantial enough to no longer qualify for SGLT2i initiation (on the basis of the KDIGO guideline) or metformin continuation. The effect of eGFR without the race coefficient has been noted previously with metformin therapy: 12%–16% of Black persons in a health database with eGFR 30–44 ml/min per 1.73 m² prescribed metformin would no longer be eligible.5 Of note, equitable care in diabetes reduced incident CKD in Black persons to rates lower than White persons in the Action to Control Cardiovascular Risk in Diabetes trial.6 Disease classifications have important effects beyond medication eligibility, influencing anxiety and insurability.

Figure 1. Estimated proportions of Black adults with type 2 diabetes in the US, categorized by CKD status. (A) Tree map representing Black adults with type 2 diabetes in the United States categorized by KDIGO CKD group with eGFR estimated without race coefficient. The areas of the colored rectangles are proportional to the estimated number in each group. The bracket labeled “CKD” identifies the groups that would be considered to have CKD on the basis of eGFR and albuminuria (all groups except the green rectangle). The bright rectangles (with asterisks) represent proportions that undergo CKD classification into a more severe CKD group that could influence diabetes treatment when eGFR is calculated without race coefficient (versus eGFR with race coefficient). (B) Groups undergoing reclassification into a relevant higher CKD stage (eGFR calculated without versus with race coefficient) are highlighted here (same groups and scale as in (A)). Classifications use the KDIGO CKD classification on the basis of eGFR (G1/G2: ≥60 ml/min per 1.73 m²; G3a: 45–59 ml/min per 1.73 m²; G3b: 30–44 ml/min per 1.73 m²; G4: 15–29 ml/min per 1.73 m²; G5: <15 ml/min per 1.73 m²) and urine albumin-creatinine ratio (A1: <30 mg/g; A2: 30–300 mg/g; A3: >300 mg/g).4 eGFR was estimated using the CKD-EPI creatinine equation without race coefficient. The colors (green, yellow, orange, and red) correspond to the KDIGO CKD classification table, where movement from green to red represents worse prognosis. The total area of the colored rectangles in (A) represents an estimated 4,007,966 (95% CI, 3,358,243 to 4,657,689) persons.
subpopulation of interest, and our subpopulation was small, resulting in wide 95% CIs. We were limited to single laboratory measurements. Black persons who also identified as Hispanic or multiracial persons were not identified. Our study does not address how race coefficient removal affects eGFR accuracy. Removal of the race coefficient has been associated with systematic underestimation of measured GFR among Black persons.7

The most important consideration is not guideline drug eligibility, nor accuracy of equations, but how to achieve optimal, equitable outcomes for Black persons. Enrollment of more Black participants in clinical trials is essential for this goal. Further investigations into mediation effectiveness and safety in these individuals are needed.

DISCLOSURES

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SUPPLEMENTAL MATERIAL

This article contains the following supplemental material online at http://jasn.asnjournals.org/lookup/suppl?doi:10.1681/ASN.2020121724/-/DCSupplemental.

REFERENCES
