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Invited Commentary | Nephrology

Systemic Kidney Transplant Inequities for Black Individuals: Examining the Contribution of Racialized Kidney Function Estimating Equations

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Kidney transplants, especially from living donors, confer superior outcomes for individuals with kidney failure. Yet Black individuals in the United States, who are 2- to 4-fold more likely to develop kidney failure than White individuals, have been less likely to receive transplants during the last 3 decades.[1] There is an urgent need to eliminate multilevel causes of this profound inequity. To date, most efforts to identify factors associated with racial transplant inequities have implicated a constellation of patient social contexts (eg, lack of insurance, poor knowledge, and financial or logistical barriers) that result from social policies and actions that manifest structural racism. Medical practices have also been found to contribute to racial transplant inequities. For instance, Black individuals are disproportionately harmed by delayed referrals to kidney care and transplant evaluation. Studies suggest delays may be due, in part, to clinicians' implicit or explicit biases, including physician misperceptions about the benefits of transplants for Black individuals or discordant and inaccurate beliefs regarding causes or prevalence of these disparities. However, it has been less clear whether guidelines for clinical decision-making, including racialized kidney function estimates, could systematically bias physicians' transplant referral and evaluation practices, thereby contributing to racial inequities.

The widely used Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation was established in 2009 to calibrate and standardize traditional serum creatinine–based measures of kidney function.[2] Similar to its predecessor, the Modification of Diet in Renal Disease study equation, the CKD-EPI equation incorporates coefficients that adjust individuals' estimated glomerular filtration rate (eGFR) based on Black race or female sex. The race coefficient systematically raises eGFR by 16% for Black individuals compared with all others, conferring an estimate of better kidney function for Black individuals at the same levels of serum creatinine. This race coefficient was incorporated into the CKD-EPI equation in an attempt to account for differences in serum creatinine observed among select research populations enriched with Black individuals. Differences were postulated as potentially related to a number of factors, including increased muscle among Black individuals compared to individuals of other races.[2] However, these hypotheses have not been substantiated by rigorous scientific evidence,[3] fueling concerns about the race coefficient's basis and validity.[4] Equation-based eGFR thresholds trigger key clinical practice guidelines for kidney care, raising further concern about the impact of the race coefficient on the care of Black individuals. For instance, guidelines recommend referrals for nephrology care and the initiation of early patient-physician transplant discussions when eGFR is less than 30 mL/min/1.73 m^2 to allow time to consider and pursue kidney transplantation and living donation.[5] Furthermore, guidelines recommend referrals for kidney transplant evaluation and accrual of time on the kidney transplant waiting list when eGFR is 20 mL/min/1.73 m^2 or less.[5,6] Late or missed referrals have direct implications for transplant receipts. Hence, biased estimates of kidney function could systematically contribute to Black individuals' transplant inequities by promoting delays in these important benchmarks.

This study by Zelnick et al[7] investigated the accuracy of the racialized CKD-EPI equation and its potential contribution to kidney transplant inequities for Black individuals in 3 complementary analyses conducted among 1658 self-identified Black individuals enrolled in the National Institutes of Health-funded prospective Chronic Renal Insufficiency Cohort study.[8] Among 311 of these individuals who had their GFR directly measured using iothalamate (iGFR), Zelnick et al[7] validated the accuracy

of the widely used CKD-EPI equation with and without the Black race coefficient as well as a less-used CKD-EPI$_{CYS}$ equation, which incorporates cystatin-C, a non–creatinine-based biomarker of kidney function, and does not include a Black race coefficient. In their analysis, the CKD-EPI eGFR equation that included the Black race coefficient consistently overestimated iGFR (ie, suggested better kidney function) by 3.1 (95% CI, 2.2 to 3.9) mL/min/1.73 m^2. When the Black race coefficient was removed, the CKD-EPI eGFR consistently underestimated kidney function by −1.7 (95% CI, −2.5 to −0.9) mL/min/1.73 m^2. The less-used CKD-EPI$_{CYS}$ equation also overestimated iGFR among Black individuals by 5.6 (95% CI, 4.6 to 6.6) mL/min/1.73 m^2. These findings highlight potentially significant clinical imprecision conferred by use of the CKD-EPI equations to estimate directly measured kidney function in Black individuals. Separately, among 2 larger subgroups, Zelnick et al[7] also evaluated associations of removal (vs inclusion) of the Black race coefficient from the CKD-EPI eGFR equation with differences in individuals' risks of developing eGFR less than 20 mL/min/1.73 m^2 (ie, the threshold at which clinical practice guidelines recommend patients should be referred for kidney transplant evaluation and begin to accrue waitlist time) and their risks of developing eGFR less than 30 mL/min/1.73 m^2 (ie, when clinical practice guidelines recommend nephrology referrals and early consideration of kidney transplants). In these analyses, removal (vs inclusion) of the Black race coefficient from the CKD-EPI eGFR equation was associated with 35% (95% CI, 29% to 41%) higher instantaneous risk of achieving the transplant referral threshold (eGFR <20 mL/min/1.73 m^2) and 52% (95% CI: 45% to 59%) higher instantaneous risk of achieving the nephrology referral and transplant consideration threshold (eGFR <30 mL/min/1.73 m^2) among Black individuals. Accordingly, when the Black race coefficient was removed (vs included) in the CKD-EPI equation, Black individuals reached the guideline-recommended transplant referral threshold 1.9 years earlier and the nephrology referral threshold 3.6 years earlier. These findings suggest that removing the race coefficient from the CKD-EPI equation could avert potential systematic delays imposed on Black individuals' receipt of transplant care by several years.

The implications of this study by Zelnick et al[7] should raise consternation and prompt thoughtful consideration regarding how race has been operationalized in the measurement of kidney function and in the context of kidney care. It is widely recognized that race is a construct developed to hierarchically categorize individuals for sociopolitical means, and it does not precisely capture individual biological differences.[9] Use of racialized eGFR equations may not only produce biased kidney function estimates, but it may also reinforce the effects of structural racism on Black individuals by systematically and differentially influencing physicians' clinical decisions and practice patterns. Numerous well-documented failures along the multistep pathway to kidney transplantation contribute to kidney transplant inequities for Black individuals, including delayed referrals for timely nephrology care, suboptimal discussions about transplants between Black patients and their physicians, late or missed referrals of Black patients to transplant centers, racism- and discrimination-mediated concerns about trustworthiness, strict sociocontextual criteria for assessing transplant suitability, and historically inequitable organ allocation policies. These systemic deficiencies in clinical practice and policy have been compounded by overarching structural inequities, including Black individuals' limited access to health care, suboptimal health literacy, inadequate treatment decision-support, financial barriers and logistical challenges to completing transplant evaluations, and difficulties identifying potential living kidney donors.

To disrupt profound, complex, and systemic transplant inequities for Black individuals, all potential contributors must be illuminated and dismantled. Some policy efforts to eliminate historic racial inequities in transplant care have already been implemented. Most notably, 2014 changes to the deceased donor kidney allocation system[6] improved racial equity in transplant eligibility by accounting for individuals' time with advanced kidney disease. However, even the progress associated with these policy changes may be diminished through delays imposed by continued reliance on the racialized eGFR equation. Precise and individualized measures of kidney function are needed to guide kidney care. While we await these measures, the study by Zelnick et al[7] provides evidence to support universal removal of the Black race coefficient from the eGFR equation as an

important action toward rectifying longstanding transplant inequities for Black individuals and to ensure we do not unintentionally perpetuate them.

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