VIEWPOINT

Reconsidering the Consequences of Using Race to Estimate Kidney Function

Nwamaka Denise Eneanya, MD, MPH
Renal-Electrolyte and Hypertension Division, Perelman School of Medicine, University of Pennsylvania, Philadelphia; and Palliative and Advanced Illness Research Center, Perelman School of Medicine, University of Pennsylvania, Philadelphia.

Wei Yang, PhD
Department of Biostatistics, Epidemiology, and Informatics, Perelman School of Medicine, University of Pennsylvania, Philadelphia.

Peter Philip Reese, MD, MSCE
Renal-Electrolyte and Hypertension Division, Perelman School of Medicine, University of Pennsylvania, Philadelphia; and Department of Biostatistics, Epidemiology, and Informatics, Perelman School of Medicine, University of Pennsylvania, Philadelphia.

Corresponding Author: Peter Philip Reese, MD, MSCE, Center for Clinical Epidemiology and Biostatistics, University of Pennsylvania, 423 Guardian Dr, 917 Blockley Hall, Philadelphia, PA 19104 (peter.reese@uphs.upenn.edu).

Clinicians estimate kidney function to guide important medical decisions across a wide range of settings, including assessing the safety of radiology studies, choosing chemotherapy, and reviewing the use of common nonprescription medications such as nonsteroidal anti-inflammatory drugs. Because direct measurement of kidney function is infeasible at the bedside, the usual approach involves using estimating equations that rely on serum creatinine. These equations assign a higher estimated glomerular filtration rate (eGFR) to patients who are identified as black. Yet in some medical and social science disciplines, a consensus has emerged that race is a social construct rather than a biological one.[1] In this Viewpoint, we argue that the use of kidney function estimating equations that include race as a variable cause problems for transparency and unduly restrict access to care in some cases, yet offer only modest benefits to precision.

Estimated GFR equations fulfill an important need for clinicians to conveniently assess kidney function and, secondarily, for public health authorities to assess the prevalence of kidney disease. These equations, such as the Chronic Kidney Disease Epidemiology Collaboration equation (CKD-EPI) and its predecessor, the Modification of Diet in Renal Disease Study (MDRD) equation, were generated in large cohorts of individuals who underwent gold-standard measurement of "true" GFR by infusing iothalamate or another chemical into the blood and quantifying its urine clearance. Investigators found that black race was independently associated with a slightly higher GFR at the same serum creatinine level. This association has been justified by the assertion that black individuals release more creatinine into the blood, perhaps because of more muscle mass, although data remain inconclusive.[2-4] The CKD-EPI equation includes a race coefficient that increases the eGFR in black patients by about 16%. Estimated GFR equations also include age and sex because older individuals and women, on average, have less muscle than younger individuals and men, respectively; these generalizations have a stronger empirical basis than that for race.

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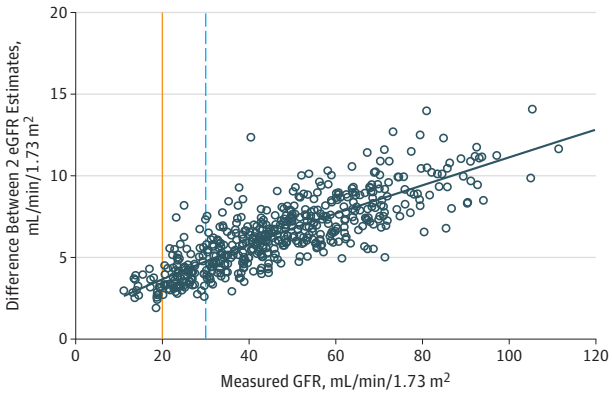
Classifying patients according to ancestry (rather than race or ethnicity) has legitimate purposes to identify individuals at risk of complications from rare gene mutations like sickle cell trait or cystic fibrosis. However, eGFR equations are distinct because they instead assert that existing organ function is different between individuals who are otherwise identical except for race. Population studies reveal only small differences in gene distributions between racial groups while showing greater variation between individuals of the same race. Meanwhile, the history of medicine offers abundant evidence that racial categories were often generated arbitrarily and at times implemented to reinforce social inequality.[5]

Racial categorization is often used in a nonstandardized way. Consider a hypothetical 50-year-old woman with a creatinine level of 2.0 mg/dL and no proteinuria. Her father self-identified as black race and her mother self-identified as white race. If this patient is admitted to the hospital, an administrator or clinician may assess the patient's skin tone or hair and label her as black in the medical record. Alternatively, the patient may be asked to identify her race. Yet she would have no way to know that her answer would affect assessments of her organ function or treatment. Furthermore, 3% of individuals in the United States identified as multiracial in the 2010 Census, whereas in Brazil and some other countries, the multiracial category exceeds one-third of the population. Decision support provides little guidance about how to calculate the patient's eGFR if she is biracial, refuses to answer the question about race, or self-identifies with a race that is different than that recorded in the medical record.

Estimated GFR equations have major clinical consequences. Many essential medications including antibiotics are withheld from patients with a low eGFR or are administered at reduced doses. The authoritative Kidney Disease: Improving Global Outcomes (KDIGO) guidelines recommend nephrology referral if a patient's eGFR is less than 30 mL/min/1.73 m^2. If the patient in the above example were considered to be black, her eGFR would be 33 mL/min/1.73 m^2, but if she were considered to be white, her eGFR would be 28 mL/min/1.73 m^2 with the CKD-EPI equation (ie, below the threshold for referral). In addition, clinical trials commonly exclude patients with reduced kidney function. If this patient were considered to be black, she could enter some trials that would exclude her if she were considered to be white.

Perhaps the most concerning implication of race in eGFR is that it has the potential to reduce access to kidney transplantation, for which racial disparities are substantial. In the United States, being wait-listed for a kidney transplant requires an eGFR of less than

Figure. Relationship Between Racial Categories and Estimation of Kidney Function Across the Spectrum of Chronic Kidney Disease



Circles indicate how much higher estimated glomerular filtration rate (eGFR) is for patients when assigned black race instead of nonblack race. eGFR was calculated twice for self-identified black adults, first by assigning them black race and then assigning them nonblack race. Patients must have kidney function lower than (ie, to the left of) the solid orange line to be eligible for the kidney transplant waiting list. The Kidney Disease: Improving Global Outcomes (KDIGO) guidelines recommend nephrology referral for all patients with kidney function lower than (left of) the dashed blue line. Data are from 534 adult participants in the Chronic Renal Insufficiency Cohort who underwent urinary ^{125}I-iothalamate clearance testing, a gold-standard measurement of kidney filtration function. Estimated GFR was calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation.

20 mL/min/1.73 m^2. If this hypothetical patient were encountered 5 years later and she had a creatinine level of 2.8 mg/dL, her eGFR would be 18 mL/min/1.73 m^2 if she were white and would be 21 mL/min/1.73 m^2 if she were black, and she would qualify for wait-listing if considered white but would be ineligible for wait-listing at that time if considered black.

Supporters of the status quo may affirm that taking account of race enables more precise estimation of kidney function and is thereby worthwhile, but historical mistreatment of racial minority groups suggests that race-based treatment prescriptions need very strong justification.[6] Using race to guide clinical care is justified only if (1) the use confers substantial benefit; (2) the benefit cannot be achieved through other feasible approaches; (3) patients who reject race categorization are accommodated fairly; and (4) the use of race is transparent.

Kidney function equations fail this test. As a result, investigators should develop new eGFR equations that substitute objective data such as height and weight for race. The **Figure** illustrates how much higher eGFR would be if patients were assigned black race and emphasizes thresholds at which key clinical decisions are made. There may be reason for optimism in improving these equations. One study showed that the race coefficient was reduced from 20% to 3.3% when body composition variables were added to the eGFR equation.[7]

Research is also needed to quantify the benefits and harms of abandoning race in GFR estimation. If race is excluded, black patients might have enhanced access to transplantation but also might receive inappropriately low antibiotic dosing. If race is excluded, more black patients could also be falsely labeled as having kidney disease or having a more advanced stage of disease, potentially leading to anxiety or unnecessary treatment. In addition, clinicians should take opportunities to discuss how race is used with their patients to more effectively engage in shared decision-making.

For nearly 20 years, eGFR equations have helped clinicians screen for kidney disease and care for patients. The problems of racial classification related to eGFR have not been closely examined. The value of racial labels should be measured and alternatives to using this variable should be carefully considered before committing to the same algorithms in the future.

ARTICLE INFORMATION

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