Separate and Unequal: Race-Based Algorithms and Implications for Nephrology

Insa M. Schmidt and Sushrut S. Waikar

Section of Nephrology, Department of Medicine, Boston University School of Medicine, Boston Medical Center, Boston, Massachusetts

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In October 2018, the Journal of the American Medical Association published a series of articles on race and racism in medicine and the health sciences. Drawing on historical examples of the cruel and unethical clinical experimentation on enslaved women and emphasizing the misuse and often imprecise reporting of race and ethnicity in medical research, these articles remind us how medicine and the biomedical sciences have embraced and contributed to racist ideology. A recent editorial by Vyas et al. in the New England Journal of Medicine reviewed how race and ethnicity have insidiously infiltrated clinical risk prediction equations throughout internal medicine, obstetrics, pediatrics, and surgery.

A critical look at our own field of nephrology illustrates how racist thinking has permeated both clinical care and research. The terms “racist” and “racism” here refer not to overt prejudice and bigotry but rather, to “a belief that race is a fundamental determinant of human traits and capacities” and “a political or social system founded on racism” as recently redefined by the Merriam-Webster dictionary and discussed by historian Ibram X. Kendi and others. Although much of the discussion has centered on the downstream health consequences of using race and ethnicity in nephrology—as described by Powe in a recent viewpoint in the Journal of the American Medical Association—less attention has been focused on an equally important consequence: the “normalization” of using race and ethnicity among clinicians, scientists, and trainees. We would argue that nephrology practice and teaching in graduate and medical schools today continue to perpetuate an ideology that is nonscientific, misleading to students and trainees, and ultimately, corrosive to society.

The debate on the inherent racism of GFR estimating equations has rightly received much attention. Critics have highlighted how using race as a “correction factor” is a simplistic distillation of ancestry and genomics to a label on the basis of skin color alone. Others have noted that serum creatinine concentration seems to associate with genetically determined African ancestry, at least in studies conducted in the United States. Both the Chronic Kidney Disease Epidemiology Collaboration and the Modification of Diet in Renal Disease Study equations include a so-called correction factor (1.159 and 1.210, respectively) if the patient identifies as Black, resulting in higher eGFR values reported for any Black patient compared with a White patient. This is usually justified by the assumption that Black individuals have higher serum creatinine levels because of greater muscle mass or other determinants of creatinine metabolism, such as generation rate, tubular secretion, or extrarenal elimination. This assertion, however, has been criticized for relying on studies with relatively small sample sizes and questionable anthropometric measurements and also for assuming that race would be a sufficient proxy for some of the observed differences without consideration of socioeconomic, dietary, or environmental factors.

The same “correction factors” perform poorly when applied to calculate the eGFR in Black populations in Europe or Africa, and similar bias in the equation has been reported for diverse populations in Asia. This not only emphasizes the need to rethink how “White” has been imposed as the reference category for every other group, but also demonstrates another flaw of the “race” concept, which is the use of “Black” as metonymic for ethnically very heterogenous populations. Additionally, although the so-called biracial or multiracial population represents the fastest-growing group in the United States, it still remains unclear how the “correction factor” should be used if someone has, for example, one Black parent and one White parent.

The downstream consequences of higher eGFR values vary by clinical context. Increasing the eGFR by a “race correction factor” can potentially preserve eligibility for kidney donation and use of nephroprotective medications (a positive clinical consequence), but also can lead to delayed evaluation and listing for
transplantation and inaccurate kidney disease surveillance (a negative clinical consequence). Peralta et al. have shown that current race coefficients may systematically misclassify Black individuals for whom timely interventions could be particularly critical. However, the debate over the downstream effects of race-based eGFR misses an important point: the acceptance of race as a valid biologic construct in medicine and medical education. When we teach our students, colleagues, and trainees that eGFR is different in “Black” versus “non-Black” individuals, we preserve a perverse legacy of overt dehumanization of Black people.

To what extent, then, has the legitimization of race-based eGFR led to—or been paralleled by—evidence of systemic racism in nephrology? We would argue that elements of this are quite apparent. Several areas are worth reviewing from the nephrology literature.

**KIDNEY STONE RISK**

Using retrospective data from emergency department evaluations for flank pain and computed tomography (CT) scans of the abdomen, researchers developed a risk prediction equation for the likelihood of finding a kidney stone. The study was performed in Connecticut and included a prospective validation in the same state. The resulting equation, called the sex, timing, origin, nausea, and erythrocytes (STONE) score, includes Black versus non-Black race; non-Black race gets three points (of a total possible score of 13), meaning that Black patients with otherwise similar presentations would be judged less likely to have ureteral stones. Basic principles of epidemiology seem to have escaped our critical notice as a subspecialty: can we really generalize from two hospitals in Connecticut to the entire “Black race”? Might there have been dietary, social, or other factors that accounted for differences, leading to unmeasured confounding or inappropriate assignment of causality? Were Black patients in this study more or less likely to present to the emergency room or to undergo an appropriate diagnostic procedure, which could have introduced selection bias? Of interest is the fact that a subsequent validation study failed to find “non-Black” race as a risk factor for ureteral stones.

In that same validation paper, the authors also reported that Black participants were significantly more likely to present to the emergency department at later disease stages with a duration of pain >24 hours compared with White participants. The STONE equation failed to consider the many social determinants of health that may have influenced the composition of the cohorts; it also failed to consider possible conscious or unconscious bias that may have influenced physicians’ decisions to order CT abdominal scans in Black versus White patients. The STONE equation awards three points for not being Black—the same number of points as for having hematuria. The implicit message to our students, trainees, and the scientific community is unmistakable: “Black” flank pain is different than “White” flank pain, and CT scans may not be indicated in a Black patient with otherwise identical symptoms as a White patient.

**DECEASED DONOR KIDNEYS FROM BLACK VERSUS WHITE INDIVIDUALS**

Through an analysis of administrative data collected on 69,440 deceased donor kidney transplants, Rao et al. developed an equation, the Kidney Donor Risk Index (KDRI), to predict the risk of death or graft loss on the basis of the characteristics of the deceased donor. One of the variables in the equation is Black race, which makes kidneys from Black donors less acceptable for transplantation than kidneys from non-Black donors. In fact, the equation places a greater weight on Black race than it does for both hypertension and diabetes mellitus in the deceased donor. The KDRI did not consider the social or economic context of the patients included in the datasets: was it the “Blackness” of the deceased donor’s skin or the environment in which that individual lived that is pertinent? Can we extrapolate this to all deceased Black individuals? What do we do with a donor with just one Black parent?

A subsequent study that accounted for APOL1 genotype instead of race found that more precise risk assessment using genetics could better refine the risk equation and lead to a greater likelihood of transplanting kidneys from Black deceased donors. In this sense, scores such as the KDRI not only show how the derivations of equations that rely on race are ultimately imprecise, they also illustrate the adverse consequences of applying these scores to guide clinical care and decision making. Disparities between Black and White patients are already evident in almost every step in the transplant process. Black individuals are not only less likely to be identified as kidney transplant candidates, but also less likely to be referred for kidney transplantation and to get placed on the kidney transplantation waiting list. The evaluation and funding of transplant programs in the United States on the basis of their patients’ transplant outcomes further complicate the situation. Faced with this financial pressure, many programs have created overly restrictive eligibility requirements to consider only the healthiest organs for transplantation. As Black patients are more likely to receive organs from Black donors, an inaccurate assessment of graft quality that further reduces the likelihood of donation from Black people will then likely exacerbate existing racial inequalities in transplantation.

**HYPERTENSION IN BLACK AND WHITE INDIVIDUALS**

The patterns of racial disparities in hypertension and its associated cardiovascular and metabolic diseases have led to numerous research studies over the past decades. Although the contribution of genomics research to explain these disparities has thus far remained relatively small, much research is still on the
basis of the assumption that Black individuals are genetically predisposed to hypertension.36,37

In nephrology, hypertension has long been a fertile ground for ideology rooted in racist thinking. Differences in the pathobiology of hypertension and the handling of sodium or potassium loads have been ascribed to race, which in turn has led to a body of literature in physiology linking racial disparities in hypertension to underlying physiologic differences between Blacks and Whites.38–45 However, many of these studies, if not all, reiterate what L. R. Gordon46 describes as “a familiar problem in race discourse with regard to evidence: a circular logic required looking at the outcome instead of a priori considerations on what could be otherwise.” Studies are conducted on the basis of the default assumption that a genetically determined difference between Blacks and Whites causes kidney physiology to differ, without considering socioeconomic, environmental, and psychosocial factors that could account for observed differences.

Physiologists have claimed, for example, that “[e]thnic differences in proximal and distal tubular sodium reabsorption are heritable in black and white populations”47 and that “differences in blood pressure responses of white and black subjects support the concept of a genetic predisposition to salt sensitivity of blood pressure.”47 Such studies, however, reinforce a racialized view of human biology. They illustrate, at best, how race may indeed become biology, which is through the embodiment of social, economic, and environmental inequalities.48 If we substitute the terms “Jewish” and “Christian” for “Black” and “White” in the above examples, the absurdity becomes clear (“ethnic differences in proximal and distal tubular sodium reabsorption are heritable in [Jewish] and [Christian] populations”). The same obvious criticisms (that religious self-identification is complex, that there is tremendous diversity within any group identified by religious grounds, and so on) apply equally well to race but are not as apparent to us because we have been acculturated to language and thinking that is inherently racist in its genesis.

Biological anthropologists and social epidemiologists who set out to challenge racist ideologies in the biologic sciences have shown how synergistic effects of psychosocial, genetic, and environmental factors can, in fact, explain racial differences in hypertension much more adequately than race alone.48–53 Gravlee48 and Gravlee et al.51 found that in contrast to skin pigmentation (when measured by reflectometry), self-rated and culturally ascribed color were strongly associated with BP through an interaction with education and income. More recent analyses also provide evidence that BP is not associated with genetic ancestry and that variables that account for the social environment are better predictors of the observed variation.49,50,53 A study by Non et al.49 using data from 11,357 participants of the Family Blood Pressure Program study showed that the single measure of education performed better in explaining BP variation than genetic ancestry.

The use of race in nephrology needs to be questioned and reconsidered. The recent debate over “race correction” in eGFR equations suggests that after two decades of tacit acceptance, we are struggling to rethink our assumptions and consider the broader consequences of the use of race in nephrology. In epidemiology, several authors have made suggestions about the appropriate use of race in clinical studies, such as for identifying inequalities across groups or as a statistical adjustment for race/ethnicity in estimating the causal effect of another variable of interest. Inappropriate uses in epidemiologic studies include conflating race as a risk factor (which implies causality) rather than as a risk marker (which acknowledges multiple other determinants).54,55

For studies in which clinical decisions are being made on the basis of statistical models using race as a covariate, the stakes are higher, as are the obligations of physicians and scientists to get it right. For this purpose, Vyas et al.4 have suggested three questions to be considered. Is the need for “race correction” on the basis of robust evidence and statistical analysis (for example, with consideration of internal and external validity, potential confounders, and bias)? Is there a plausible causal mechanism for the racial difference that justified the “race correction”? Would implementing this “race correction” relieve or exacerbate health inequities? In our estimation, the use of race in the examples reviewed above fails with respect to at least one of these metrics.

When we use predictive equations and publish papers that claim kidneys from Black donors are more likely to fail than kidneys from White donors, that Black eGFR is different from White eGFR, that Black hypertension is different than White hypertension, or that Black flank pain is different than non-Black flank pain, we memorialize centuries of discrimination and violence into the practice of nephrology. By not questioning the use of race-based prediction equations and not objecting to small physiologic studies claiming to discover racial differences in tubules, our profession continues to be conditioned to think that race is in fact a biologic, not a social, construct—in fact, that race is so “biologic” that peer-reviewed papers, society guidelines, and everyday clinical laboratory reports attest to the “truth” of racial differences. The discussions about ancestry versus skin color, social determinants of health, and unconscious bias are not as compelling as seeing the comment in a laboratory report: “If Black, multiply by 1.12.” Instead, we should consider institutional racism, mass incarceration, housing discrimination, and our obligations as physicians to see that we affirmatively take steps toward antiracism and social justice.

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