Commentary ◧ Health services

Elimination of race in estimates of kidney function to provide unbiased clinical management in Canada

Rulan S. Parekh MD MS, Jeffrey Perl MD SM, Bourne Auguste MD MSc, Manish M. Sood MD MSc

For many years, the universally used equation for estimating risk of kidney disease (the kidney function estimate, Chronic Kidney Disease Epidemiology Collaboration [CKD-EPI] equation), included an adjustment for Black race that led to an upward correction in estimated glomerular filtration rate (eGFR). In 2021, new equations that omit race but include other factors were developed and found to be more accurate in estimating eGFR,[1] and the US National Kidney Foundation, American Society of Nephrology Task Force on Reassessing the Inclusion of Race in Diagnosing Kidney Diseases and the UK National Institute for Health and Care Excellence recommended the removal of race from the calculation of eGFR.[2,3] We discuss why the inclusion of race in kidney function estimates is biased and harmful, and why swift adoption of calculations that omit race is important in clinical care in Canada.

In the United States and Canada, Black people have a higher incidence of chronic kidney disease (CKD), have more rapid kidney disease progression, are referred later for kidney care, are less likely to receive home-based dialysis or a kidney transplant, and have higher mortality after kidney transplantation.[4,5] Calculations of eGFR using the Black "race correction," which have been widely used in Canada, can falsely increase eGFR up to 10%, which can lead to delayed diagnosis and thus poorer outcomes.[1]

The global prevalence of kidney disease is 8%–16%.[6] Early disease is often asymptomatic and, therefore, missed, which is why methods were developed to improve screening, to identify people at risk earlier and to allow referral for appropriate care to prevent disease advancement. Application and widespread use of equations to estimate kidney function were a major advance in addressing kidney disease in clinical practice. The eGFR is automatically calculated with serum creatinine and reported by many laboratories throughout Canada. The widespread adoption of eGFR reporting in Ontario and British Columbia led to a 2%–6% increase in use of medications that slow the progression of CKD.[7] In tandem, rates of referral to nephrology rose to 24%, the equivalent of 23 new

Key points

- For many years, the universally used Chronic Kidney Disease Epidemiology Collaboration equation (CKD-EPI) for estimating kidney disease function has included an adjustment for Black race that resulted in an upward correction in estimated glomerular filtration rate (eGFR).

- In 2021, new equations that omit race but include other factors were developed and found to be more accurate in estimating eGFR.

- In Canada, Black people are at elevated risk of developing kidney disease, have more rapid progression of kidney disease, are referred later for kidney care, are less likely to receive home-based dialysis or a kidney transplant, and have higher mortality after kidney transplantation.

- Widespread implementation in clinical practice of new equations for eGFR that omit a correction for race would be an important first step toward equitable delivery of kidney care for Black people in Canada.

consults per nephrologist per year in Ontario.[8] Automatic reporting of kidney function enables clinical interpretation while raising awareness of kidney disease for both patients and providers.

Serum creatinine is a constituent of muscle protein metabolism, linked to protein intake, intrinsic muscle mass and kidney function. Serum creatinine estimates were widely believed to be less accurate in people of Black race and were hypothesized to be due to higher muscle mass on average. Whether or not this is true remains controversial.[9] Estimating equations of kidney function using serum creatinine were developed and incorporated a correction factor for Black race with the goal of improving scientific measurement and accuracy. As data on race are not routinely collected by health systems in Canada, laboratories have reported kidney function estimates without race correction, and the decision to apply the race adjustment was left to the judgment of clinicians.

As race adjustment inflates the CKD-EPI eGFR measurements in Black people, delays in referral could occur at 3 crucial time points according to expert consensus across Canada (https://www.ckdpathway.ca/): at referral to a nephrologist by a primary care practitioner (recommended for patients with an eGFR < 30 mL/min/1.73 m²); at referral to specialized multidisciplinary clinics for advanced kidney disease care for those with high-risk CKD (eGFR < 15 mL/min/1.73 m² or estimated 2-year risk of end-stage kidney disease [ESKD] ≥ 10% based on a formula with eGFR); and at referral for kidney transplant evaluation (eGFR < 15 mL/min/1.73 m² or estimated 2-year risk of ESKD ≥ 25%). The Ontario Renal Network and Trillium Gift of Life Network manage provincial services for patients with CKD and for transplantation, respectively, and both groups recently stopped the use of race-correction estimates of kidney function to ensure equity in access to kidney care such as dialysis and transplantation for Black people in Ontario.[10] Other provincial kidney organizations should consider similar actions to address local practice. Black people who have CKD or who are receiving dialysis account for 7.4% of the prevalence of kidney disease in Canada even though Black people make up only 4.1% of the population of Canada.[5,11,12] Earlier access to and delivery of care may reduce inequity; however, other systemic barriers need to be addressed.[11]

Biased estimates of kidney function may also limit Black patients' access to newer therapies that have the potential to reduce long-term cardiovascular and diabetic morbidity and mortality. Evaluation of the race-corrected eGFR equation has found a differential bias of 3.2 mL/min/1.73 m² (95% confidence interval 1.3–5) between Black people and those who are not.[1] Although a small differential, it can be critical in those with borderline kidney function in which thresholds are used for specific drug eligibility. If physicians are concerned that a single measurement of kidney function may preclude access to care or medications, serial measurements will improve precision and guide clinical management better. Using the new race-free CKD-EPI equation, however, will remove any bias. A second new equation that includes an alternative biomarker (cystatin C), which is independent of muscle mass and more accurate, should also be recommended for widespread implementation in Canada.

During the COVID-19 pandemic, it became clear that data on self-ascribed race or ethnicity were lacking, and yet necessary and important to ensure the delivery of equitable care in Canada. However, the application of a race correction for estimating kidney function is problematic because race is a social construct and provider perception can introduce bias. A genetic locus containing the *APOL1* variants is strongly associated with African ancestry and CKD, but the frequency of risk variants for kidney disease differs substantially across Black populations globally.[2] Use of ancestry to improve estimates of kidney function was suggested among Hispanic people.[13] However, the 2021 multicentre observational Chronic Renal Insufficiency Cohort study reported that the incorporation of African genetic ancestry did not improve estimates of kidney function among Black people.[14] In addition, the clinical application of the race term by clinicians is inconsistent, which consequently raises the question of validity and utility of racial classification that is not self-ascribed.[2]

Inclusion of race in estimates of kidney function is implicitly biased as it relies on clinicians' assessment of people of colour to adjust for race. Statistical bias in estimating equations leads to overestimation of kidney function if Black race is used as a factor. This may preclude the provision of timely kidney care. The science supports the need to abandon the correction factor for Black race in estimates of kidney function in Canada. Furthermore, optimizing screening is critical for Black people, who are disproportionately affected by CKD, to prevent subsequent health morbidity and ensure equity in kidney care.

References

1. Inker LA, Eneanya ND, Coresh J, et al.; Chronic Kidney Disease Epidemiology Collaboration. New creatinine- and cystatin C-based equations to estimate GFR without race. *N Engl J Med* 2021;385:1737-49.

2. Delgado C, Baweja M, Crews DC, et al. A unifying approach for GFR estimation: recommendations of the NKF-ASN task force on reassessing the inclusion of race in diagnosing kidney disease. *J Am Soc Nephrol* 2021;32:2994-3015.

3. Gama RM, Kalyesubula R, Fabian J, et al. NICE takes ethnicity out of estimating kidney function. *BMJ* 2021;374.

4. Trinh E, Na Y, Sood MM, et al. Racial differences in home dialysis utilization and outcomes in Canada. *Clin J Am Soc Nephrol* 2017;12:1841-51.

5. Yeates KE, Schaubel DE, Cass A, et al. Access to renal transplantation for minority patients with ESRD in Canada. *Am J Kidney Dis* 2004;44:1083-9.

6. GBD Chronic Kidney Disease Collaboration. Global, regional, and national burden of chronic kidney disease, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet* 2020;395:709-33.

7. Jain AK, Cuerden MS, McLeod I, et al. Reporting of the estimated glomerular filtration rate was associated with increased use of angiotensin-converting enzyme inhibitors and angiotensin-II receptor blockers in CKD. *Kidney Int* 2012;81:1248-53.

8. Jain AK, McLeod I, Huo C, et al. When laboratories report estimated glomerular filtration rates in addition to serum creatinines, nephrology consults increase. *Kidney Int* 2009;76:318-23.

9. Hsu J, Johansen KL, Hsu C-Y, et al. Higher serum creatinine concentrations in black patients with chronic kidney disease: beyond nutritional status and body composition. *Clin J Am Soc Nephrol* 2008;3:992-7.

10. Brimble KS, Treleaven D, Cooper R, et al. Removal of eGFR adjustment for race in Ontario [letter]. *CMAJ* 2021 Apr. 6. Available: https://www.cmaj.ca/content/193/2/E55/tab-e-letters#removal-of-egfr-adjustment-for-race-in-ontario (accessed 2022 Feb. 9).

11. Perl J, McArthur E, Tan VS, et al. ESRD among immigrants to Ontario, Canada: a population-based study. *J Am Soc Nephrol* 2018;29:1948-59.

12. Dryden O, Nnorom O. Time to dismantle systemic anti-Black racism in medicine in Canada. *CMAJ* 2021;193:E55-7.

13. Horimoto ARVR, Xue D, Cai J, et al. Genome-wide admixture mapping of estimated glomerular filtration rate and chronic kidney disease identify European and African ancestry-of-origin loci in Hispanic and Latino individuals in the United States. *J Am Soc Nephrol* 2022;33:77-87.

14. Hsu C-Y, Yang W, Parikh RV, et al.; CRIC Study Investigators. Race, genetic ancestry, and estimating kidney function in CKD. *N Engl J Med* 2021; 385:1750-60.

Affiliations: Department of Medicine (Parekh, Perl, Auguste), University of Toronto; Division of Nephrology (Parekh), Women's College Hospital; Department of Pediatrics (Parekh), The Hospital for Sick Children, University of Toronto; Division of Nephrology (Perl), St. Michael's Hospital, Unity Health; Division of Nephrology (Auguste), Sunnybrook Health Sciences Centre, Toronto, Ont.; Department of Medicine and the Ottawa Hospital Research Institute (Sood), The Ottawa Hospital, Ottawa, Ont.