

**Reassess Race in Estimated Glomerular Filtration Rate (eGFR) Calculation Workgroup  
OPTN Minority Affairs Committee (MAC) and OPTN Kidney Transplantation Committee  
Meeting Summary  
March 29, 2021  
Conference Call**

**Irene Kim, MD, MAC Chair  
Paulo Martins, MD, PhD, MAC Vice Chair  
Martha Pavlakis, MD, Kidney Committee Vice Chair**

## **Introduction**

The Reassess Race in eGFR Calculation Workgroup (the Workgroup) met via Citrix GoToMeeting teleconference on 3/29/2021 to discuss the following agenda items:

1. Project Overview
2. Controversies in Nephrology: Reconsidering Race and eGFR

The following is a summary of the Committee's discussions.

### **1. Project Overview**

The Workgroup reviewed the purpose, proposal, and scope of the project, including the current goal of determining if and what kind of policy should be developed to exclude the Black race coefficient from the eGFR calculation as it is used to qualify a kidney candidate to accumulate wait time.

#### Summary of discussion:

A Workgroup Chair remarked that the OPTN Minority Affairs Committee noted at a recent meeting that many clinical algorithms utilized race adjustments. Pulmonary function tests can account for race and are often used in assigning the lung allocation score (LAS). The kidney donor paired index (KDPI) used to rate donor kidney quality also utilizes a race component.

Staff confirmed that the Workgroup's focus is to reassess the use of the Black race coefficient in the eGFR calculations used to qualify for kidney waiting time.

### **2. Overview of eGFR in OPTN Policy**

A Workgroup member presented on the history, use, and consequences of the race coefficient in eGFR equations.

#### Data summary:

Estimated GFR equations allow for indirect assessment of the GFR using endogenous filtration biomarkers without the need for clearance measurements such as creatinine and cystatin-C.

- eGFR equations are predictive multi-variable regression models relating measured GFR to observed concentrations of filtration markers and accounting for the demographic and clinical variables that can impact these markers

The Modification of Diet in Renal Disease (MDRD) study by Levey et al<sup>1</sup> at Tufts was a prospective trial, for which all participants had measured I-iothalamate, an exogenous filtration marker. The study utilized a stepwise multiple regression model to determine a set of variables that jointly predicted GFR.

- The study identified 6 variables that together best predicted measured GFR: serum creatinine, age, serum urea nitrogen, albumin, sex, and ethnicity.
  - The MDRD group found that black men and women had higher concentrations of serum creatinine compared to white individuals at any measured GFR, with a black race coefficient of 1.181. All else equal, a black individual's eGFR would be approximately 18 percent higher than any other racial group.
- However, the MDRD study had little racial diversity. Out of about 1600 participants, only 197 – about 12 percent – were Black
- The MDRD study implied the independent association of Black race with higher GFRs at the same serum creatinine level was due to differences in measured GFR, rather than the current recognition that these differences relate to serum creatinine levels
  - The association justified differences in GFR with few supporting references from three small, older studies looking at body composition finding that Black individuals, on average, have greater muscle mass than white persons.

Since the MDRD study, several other studies have sought to develop predictive eGFR equations, including:

- The Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) had significantly more Black patients, and found a Black race coefficient of 1.16
- The CKD-EPI Cystatin-C study utilized Cystatin-C instead of creatinine, and found no significant Black race coefficient
- The CKD-EPI creatinine-cystatin-c combined both creatinine and cystatin-c, and was the most accurate predictor of GFR. This study found a significant Black race coefficient of 1.08
- Most other studies still lack significant diversity, both between and within racial groups

Statistical measures evaluating the proportion of eGFR measures within 30 percent of the true GFR find a margin of error around both the MDRD and CKD-EPI equations. The margin of error increases at lower GFRs, where most clinical decisions are made.

- When the Black race coefficient is removed, the margin of error is not significantly altered

There are a number of consequences to utilizing race coefficients in eGFR equations, including:

- Disparity in Black patients starting dialysis without ever consulting a nephrologist
- Delayed referral for dialysis care, patient education, and vascular access creation
- Improper pharmacological dosing
- No accommodation for patients of mixed race and ethnicity
- Lack of transparency with patients during shared decision making

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<sup>1</sup> Levey AS, Bosch JP, Lewis JB, Greene T, Rogers N, Roth D. A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. Modification of Diet in Renal Disease Study Group. *Ann Intern Med.* 1999 Mar 16;130(6):461-70. doi: 10.7326/0003-4819-130-6-199903160-00002. PMID: 10075613.

- Barriers in racial disparities involved in preemptive wait-listing and deceased donor kidney transplant

Implicit and explicit bias can play a role in disparities for black patients, from conscious controlled decisions used to determine which eGFR calculation to use to false biological beliefs taught in schools influencing clinical care.

The study Impact of eGFR Race Correction on Care Delivery<sup>2</sup> sought to find out how many Black patients with CKD would be reclassified into a more severe stage of CKD without race correction, and how care delivery would change.

- 4 percent of the 2225 participant cohort was black, of which 33.4 percent would change to a more severe stage of CKD
- 64 individuals, or 3.1 percent were reclassified to a wait-time qualifying eGFR of less than 20 mL/min
- With race correction, Black individuals were more likely to be referred for transplant than white individuals, which could speak to rapidity of CKD progression in black patients
- No significant racial differences in dialysis access placement

Counter arguments to the removal of race corrections for kidney function predicting equations include:

- Black patients may have an over-diagnosis of CKD
- Black patients could receive treatments such as dialysis and transplant when not indicated
- Black patients could receive inappropriately low dosing of pharmacologic medications
- Black patients could lose access to crucial medications
- Black patients could become ineligible to donate kidneys

Confirmatory testing for kidney function and the use of eGFR trends to evaluate render most of these arguments weak, with the exception of loss of access to medications.

Norris et al. showed that removing the race coefficient from eGFR equations could result in up to 1 million Black individuals with new diagnoses of CKD.<sup>3</sup> Previous studies have shown that Black CKD patients are more likely to progress quickly and need kidney failure or transplant. Earlier intervention could be critical for those patients, and could close the disparity for Black patients with advanced kidney disease.

Eneanya et al. publication “Reconsidering the use of race”<sup>4</sup> found that the use of race to guide clinical care is only justified if:

- It confers substantial benefit,
- The benefit cannot be achieved through other feasible approaches,
- Patients who reject race categorization are accommodated fairly,
- And the use of race is transparent

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<sup>2</sup> Ahmed, S., Nutt, C.T., Eneanya, N.D. et al. Examining the Potential Impact of Race Multiplier Utilization in Estimated Glomerular Filtration Rate Calculation on African-American Care Outcomes. *J GEN INTERN MED* 36, 464–471 (2021). <https://doi.org/10.1007/s11606-020-06280-5>

<sup>3</sup> Norris KC, Eneanya ND, Boulware LE. Removal of Race From Estimates of Kidney Function: First, Do No Harm. *JAMA*. 2021;325(2):135–137. doi:10.1001/jama.2020.23373

<sup>4</sup> Eneanya ND, Yang W, Reese PP. Reconsidering the Consequences of Using Race to Estimate Kidney Function. *JAMA*. 2019;322(2):113–114. doi:10.1001/jama.2019.5774

Future approaches to defining kidney function without race include:

- Rigorous research to investigate previously accepted notions of racial differences in eGFR equations
- Determine association of ancestry with GFR
- Use alternative eGFR equations or measures of kidney function not using race
- Develop novel filtration markers not relying on race
- Transparency in discussing eGFR determination with patients

Summary of discussion:

A Workgroup Chair agreed that the use of race in clinical equations cannot be justified if it disadvantages patients, and noted that the removal of the Black race coefficient is a just and timely effort.

A Workgroup Chair remarked that eliminating race correction in eGFR calculation could be a cost-effective effort, as earlier intervention for chronic kidney disease patients could increase the use of prevention measures that would preclude the need for dialysis or kidney transplant. The Workgroup Chair inquired if there were any initiatives, national or international, to perform larger and higher quality studies to produce more reliable and predictive eGFR algorithms. A member noted that true clinical measures of GFR, such as urinary clearance of iothalamate, are very difficult to collect, and that this is a large barrier in recruiting large cohorts and study populations. The member continued that the Black race coefficient has not contributed to statistical accuracy among international patients, and as a result is not used in many countries, including Brazil, Ghana, and South Africa.

One Workgroup Chair wondered if online medical record systems take into account race variables and report the eGFR without identifying if it's race-rated, and the degree variability in reporting for eGFR. A Workgroup member agreed that eGFR reporting often varies even within hospital systems, noting that some report back a standard, non-race corrected eGFR, annotated with instruction to multiply by a certain coefficient, depending upon which equation is being used to calculate eGFR. The Workgroup Chair remarked that some report both the Black and non-Black eGFR, while others give a range between the two, described as dependent on a number of variables. The Workgroup Chair added that lack of standardization in reporting can contribute to confusion, but refocused the discussion to the goal of determining appropriate changes to policy to address the disadvantages experienced by Black patients through widespread use of the race coefficient in eGFR calculations used to waitlist. Another Workgroup Chair agreed, noting that the OPTN does not prescribe which eGFR calculation must be used, resulting in transplant center discretion in the use of race coefficients. The Workgroup will need to discuss if the use of the Black race coefficient in eGFR calculation should be decided at a local level or addressed in national policy.

A staff member remarked that amount of time on the waitlist, rather than eGFR, determines an individual patient's access to pre-emptive transplant, including listing date, start of dialysis, and rate of disease progression. Staff continued, asking if removing the Black race coefficient risks inadvertently accelerating black patients' decision to begin dialysis, to the extent that decision is influenced by eGFR. A Workgroup Chair briefly described the history of dialysis initiation, noting that eGFR is not the only consideration in dialysis decisions, pointing particularly to the severity of symptoms, bicarbonate in the blood, potassium, and fluids. The Workgroup Chair concluded that removing the race coefficient from eGFR calculations would not likely cause patients to begin dialysis earlier than would be clinically appropriate. The staff member mentioned studies that show African Americans begin dialysis at higher eGFRs than other ethnic populations. One Workgroup Chair noted those eGFRs were likely race-corrected. Another member shared that their conservative management clinics have patients with single

digit GFRs that don't experience symptoms requiring dialysis. While it is possible some medical professionals would become concerned about lower eGFRs and begin patients on dialysis, many wait for their patients to experience symptoms or a refractory response to medical treatment. The staff member expressed concern that level of sophisticated care is not widely available or accessible, and increased early dialysis could result from use of non-race-corrected eGFR calculations.

A staff member wondered if increasing the eGFR wait time threshold was appropriate, particularly if some race-corrected eGFR calculations can be acknowledged as more accurate and predictive of true GFR than non-race-corrected equations. A Workgroup Chair responded that altering the eGFR wait time threshold would not address disparities caused by the use of the race-corrected eGFR calculations. Another Workgroup Chair agreed, pointing out that the race coefficient will always overestimate GFR by 16 percent, no matter where the wait time accumulation threshold is. The Chair continued, citing a publication by Reese et al. that found twice as many white patients as Black patients have access to pre-emptive transplant.<sup>5</sup> Though Black patients are much more likely to have chronic kidney disease, they are under-represented in pre-emptive kidney transplant and experience longer wait times.

A Workgroup Chair remarked that the counter arguments of the removal of race coefficients from eGFR calculations are relatively weak, and benefits far outweigh any disadvantage. The Chair continued that the OPTN Final Rule requires allocation to be equitable, and the current use of race-corrected GFR calculations preclude equity in allocation and access. Another Workgroup Chair agreed, and re-centered the Workgroup's focus to OPTN kidney listing and wait time accumulation policy. Concerns about when patients begin dialysis are outside of the purview of the current project.

A member remarked that the Workgroup will need to address a number of interlocking issues in kidney listing and wait time accumulation policy in addressing concerns about race-corrected eGFR calculation. The member pointed to the requirement of a single eGFR to begin accumulating wait time as one way in which those privileged with better access to care can be pre-emptively listed. A Workgroup Chair agreed, remarking that any national conversation about eGFR and listing would need to address these issues. Another Workgroup Chair confirmed that most of the opposition to the removal of the Black race coefficient was individual, and no other workgroup members knew of any organizations or institutions lobbying against the removal of the Black race co-efficient. The Workgroup Chair continued that many other professional organizations such as the National Kidney Foundation and the American Society of Nephrology (ASN) have released statements in support of the removal of the race coefficient.

#### Next Steps:

The OPTN Executive Committee will review this project for approval. Staff will send out follow-up questions for consideration and discussion as the Workgroup begins the evidence gathering phase.

#### **Upcoming Meeting**

- May 3, 2021 (Teleconference)

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<sup>5</sup> Reese PP, Mohan S, King KL, Williams WW, Potluri VS, Harhay MN, Eneanya ND, Racial disparities in preemptive waitlisting and deceased donor kidney transplantation: Ethics and solutions. American Journal of Transplantation. 2020;. doi:10.1111/ajt.16392

## Attendance

- **Workgroup Members**
  - Paulo Martins
  - Martha Pavlakis
  - Amaka Eneanya
  - Arpita Basu
  - Beatrice Concepcion
  - Precious McCowan
  - Denise Alveranga
  - Jim Kim
  - Oscar Serrano
  - Peter Reese
- **SRTR Representatives**
  - Christian Folken
  - Jonathan Miller
  - Nick Salkowski
  - Peter Stock
- **HRSA Representatives**
  - Jim Bowman
- **UNOS Staff**
  - Lindsay Larkin
  - Joanne White
  - Kelley Poff
  - Kayla Temple
  - Ross Walton
  - Tina Rhoades
  - Leah Slife
  - Anne Zehner
  - David Klassen