OPTN Minority Affairs Committee (MAC) and Kidney Transplantation Committee Reassess Race in eGFR Calculation Workgroup Meeting Summary October 5, 2021 Conference Call

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Introduction

The Reassess Race in eGFR Calculation Workgroup (the Workgroup) met via Citrix GoToMeeting teleconference on 10/05/2021 to discuss the following agenda items:

1. Public Comment Feedback Review
2. National Kidney Foundation (NKF) – American Society of Nephrology (ASN) Task Force Recommendations: *Reassessing the Inclusion of Race in Diagnosing Kidney Disease*
3. Reassess Race in eGFR Calculation: January 2022

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

1. Public Comment Feedback Review

The Workgroup reviewed feedback collected during the Summer 2021 Public Comment period with the Workgroup's request for information.

Data summary:

Feedback collected during public comment was gathered from the OPTN Public Comment website, OPTN Committee discussions, and 11 OPTN Regional Meetings.

Regional meeting highlights:

- Questions regarding current OPTN policy on formulas without Black race coefficient, use of cystatin C, race neutral formula's potential impact on qualified Black living donors, origins of Black race coefficient inclusion, backdating existing candidate wait time, and specific race neutral eGFR formula endorsement
- Comments that removing Black race coefficient is not difficult for institutions
- Support for removal of the Black race coefficient
- Need for reliable formulas without reference to race

OPTN Public Comment submission highlights:

- Support for removing race from eGFR calculation
- Significant recognition of the disadvantage posed to Black patients by the use of race-based eGFR formula

OPTN Committee feedback:

- Transplant Administrators Committee commented that the OPTN could consider providing reports to transplant programs regarding patients with close to qualifying eGFRs
- Ethics Committee noted that transparency impacts patient autonomy, encouraged endorsement of specific race-neutral eGFR formulas to promote consistency, and recommended education included in implementation for referring nephrologists
- Patient Affairs Committee strongly supported the urgent removal of the Black race coefficient, expressed concern about lack of transparency about formula use and impeded patient autonomy, and noted that pediatric eGFR estimation does not consider race. The application of race once a patient turns 18 is additionally discriminatory.
- Transplant Coordinators Committee (TCC) commented that the binary nature of race-based calculations isn't aligned with the diverse population of patients, and supported finding a better way to estimate eGFR while taking care not to disadvantage any population. The TCC also asked about how the OPTN planned to monitor the use of a race neutral formula and supported patient education as part of related implementation plans

Society and Association feedback:

- North American Transplant Coordinators Organization (NATCO) – "it will be very important that patients understand the rationale for race neutral eGFR, particularly if this is implemented before labs stop publishing results with race distinction"
- American Society of Transplantation (AST) – "We suggest that the MAC consider a policy that prohibits the use of race-based methods rather than mandating a specific method or equation for eGFR"
- American Society of Transplant Surgeons – "We anticipate the use of a race neutral eGFR would increase listing, improve access, encourage earlier evaluations, and reduce wait times for black and minority patients"
- Associations of Organ Procurement Organizations (AOPO) – "While there are several methods of measuring a patient's GFR, the test utilized should not provide results influenced by the potential recipient's ethnicity"

Summary of discussion:

A Workgroup Chair pointed out that, along with constructive feedback, there was overwhelming support for discontinuing the use of race-based eGFR formulas. Another Workgroup Chair agreed, adding that the timing of the request for information allows the Workgroup to consider the recent recommendations released by the NKF and ASN Task Force (the Task Force). The Chair continued that the Workgroup will need to decide whether to recommend or require a specific race-neutral equation, or else require only that race is not a variable in the eGFR calculation used. The Chair concluded, commenting that race should not be taken into account in organ allocation.

One Workgroup member expressed support for aligning policy and Workgroup recommendations with the formula recommended by the ASN and NKF, particularly as the NKF and ASN's ultimate goal is for this formula to be utilized by all laboratories across the United States (US). Another member responded, pointing out that many more race-free equations may still be developed in the future, which could potentially be more accurate. It is a matter of leaving it open and require equations without race, or requiring a 2021 equation while there's panels of race-free markers being evaluated. A member agreed, adding that codifying a specific equation that may need to be changed down the line, particularly given how extensive the policy change process is. The Chair pointed out that all the race neutral

recommendations are very similar, with relatively small variations that would prevent any population from being disadvantaged.

A Scientific Registry of Transplant Recipients (SRTR) representative suggesting including a recommendation for greater standardization in the process of being waitlisted in the future. The SRTR representative continued, noting that the lack of standardization is contributing to equity problems. A Chair agreed.

2. National Kidney Foundation (NKF) – American Society of Nephrology (ASN) Task Force Recommendations: *Reassessing the Inclusion of Race in Diagnosing Kidney Disease*

The Workgroup reviewed the recommendations put forth by the NKF-ASN Reassessing the Inclusion of Race in Diagnosing Kidney Disease Task Force.

Data summary:

The NKF-ASN Task Force utilized expert testimonials from hundreds of individuals well versed in patient assays, race, ancestry, and population health, as well as international experts and patient populations. The Task Force considered more than 25 approaches, and evaluated 7 equations.

Estimated GFR equations have only a certain level of accuracy. These equations are evaluated with a p30 statistic, which refers to the percentage of eGFR estimates that fall within 30 percent of the actual measured eGFR. For example, the Chronic Kidney Disease (CKD) Epidemiology Collaboration (CKD-EPI) equation performed better than the Modification of Diet in Renal Disease (MDRD) equation, with a p30 of 84.1 percent compared to 80.6%. There is a considerable margin of error around eGFR equations, and these equations generally perform better at higher GFR levels than lower GFR levels, where most clinical decisions are made.

The New England Journal Study's New Creatinine- and Cystatin C-Based Equations to Estimate GFR without Race[1] aimed to evaluate the accuracy of current guideline-recommended GFR equations and compare them with new equations that do not use race. This study recognizes that race is a social and not a biological construct, and further that the inclusion of race in GFR estimating equations ignores diversity within and among racial groups. This study pooled data from previous participants in the CKD-EPI 2009, CKD-EPI 2012 (development), and CKD-EPI 2012/2021 (validation) studies where GFR was measured. The seven equations assessed included:

- Current CKD-EPI 2009 Creatinine equation with race
- Current CKD-EPI 2012 cystatin-C equation (race not applicable)
- Current CKD-EPI 2012 creatinine-cystatin C equation with race
- Current CKD-EPI 2009 equation (applying the non-Black race to all participants)
- Current CKD-EPI 2009 creatinine-cystatin C equation (applying the non-Black race to all partipicants)
- New CKD-EPI 2021 creatinine equation (refit without race)
- New CKD-EPI 2021 creatinine-cystatin C equation (refit without race)

31.5 percent of participants in the 2009 CKD-EPI study were Black, and 39.7 percent of the 2012 CKD-EPI development study participants were Black. 14.3 percent of the participants in the CKD-EPI 2021 validation data were Black.

[1] https://www.nejm.org/doi/full/10.1056/NEJMoa2102953

The 2009 CKD-EPI-Creatinine equation has a race multiplier of 1.159. The 2012 CKD-EPI Creatinine-Cystatin-C Combination equation has a race coefficient of 1.08, lower than that of creatinine alone. The new approaches, looking at the non-Black coefficient for everyone sets a race coefficient of 1, to equalize. The equations that were refit without race do not have race-based coefficients.

These equations can be evaluated in looking at bias, or the median difference between measured and estimated eGFR. Negative bias is overestimating, and positive bias is underestimating. Incorrect classification refers to how often the eGFR matched the measured GFR staging category.

- The current creatinine equation doesn't have a have a high difference between the curves for Black and non-Black participants.
- Utilizing the non-Black race coefficient for everyone in the current equation, Black participants have positive bias (GFR is underestimated) and non-Black participants have negative bias (GFR is overestimated). However, the p30 is quite good for this equation
- The new creatinine equation refit without race underestimates GFR for Black participants and overestimates for non-Black participants, with slight change in bias for Black participants. The p30 is quite high here as well.
- The current cystatin-C equation has minimal difference between racial groups
- The current combined creatinine cystatin-C performs much better than creatinine or cystatin C alone, with a very high p30 for Black and non-Black participants. There are similar metrics for this equation when applying the non-Black race coefficient to everyone, with similarly high p30.
- The new creatinine-cystatin C equation has less underestimation among Black participants and overestimation for non-Black participants.

The new creatinine equations may introduce inaccuracies for racial groups. However, the p30 is adequately high for clinical decision making. Utilizing the new equations will result in estimates of CKD burden and eGFR stages will change within and between racial groups, which is to be expected. The new creatinine-cystatin C combination equations performed better than creatinine equations alone, specifically the equation refit without race. The combined creatinine-cystatin C equations minimized inaccuracies for both racial groups and minimized differences in estimated CKD prevalence between racial groups.

The Task Force recommends immediate implementation of the 2021 CKD-EPI equation (refit without race), as well as national efforts to facilitate increased, routine, and timely use of cystatin C, especially to confirm eGFR in adults who are at risk for or have CKD. The Task Force also recommends research on GFR estimation with new endogenous filtration markers and on interventions to eliminate race and ethnic disparities in kidney disease to be encouraged and funded.

Summary of discussion:

A Workgroup Chair asked how prevalent, accessible, and affordable Cystatin C measurements are. A member responded that cost depends on a number of factors, including who an institution has contracted out, and the volume ordered. The member added that they have heard differentials ranging from 3-10-1 to 10-to-1.

A Workgroup Chair asked what the optimal p30 score was, and the presenting member clarified that 80-90 is an acceptable range, with a higher p30 levels preferable. An SRTR representative noted that relying on p30 is reflective of the relative inaccuracy of these equations, otherwise a 910 could be used.

A member noted that removing the race coefficient makes minimal difference in terms of the performance of these equations. The member added that the NKF is working on building an implementation toolkit for institutions to transition away from race-based eGFR formulas.

3. Reassess Race in eGFR Calculation: January 2022

The Workgroup discussed and voted on proposed policy language to recommend to the Kidney Transplantation and Minority Affairs Committee.

Data summary:

Glomerular Filtration Rate (GFR): A measure of filtering capacity of the kidneys. GFR can be measured directly or estimated (eGFR) using various Formulae.[2] Formulae used to calculate eGFR must not use a race based variable.

Summary of discussion:

The Workgroup voted unanimously to recommend the removal of the Black race coefficient in eGFR calculation from OPTN policy.

Upcoming Meeting

- November 1, 2021

[2] KDOQI Clinical Practice Guidelines for Chronic Kidney Disease: Evaluation, Classification, and Stratification. American Journal of Kidney Diseases, Vol 39, No 2, Suppl 1 (February), 2002: pp 576-5110.

Attendance

- **Workgroup Members**
  - Paulo Martins
  - Martha Pavlakis
  - Alejandro Diez
  - Amaka Eneanya
  - Beatrice Concepcion
  - Denise Alveranga
  - Irene Kim
  - Oyedolamu Olaitan
  - Precious McCowan
- **HRSA Representatives**
  - Adriana Martinez
  - Jim Bowman
  - Raelene Skerda
  - Vanessa Arriola
- **SRTR Staff**
  - Bryn Thompson
  - Jonathan Miller
  - Monica Colvin
  - Peter Stock
- **UNOS Staff**
  - Joann White
  - Lindsay Larkin
  - Kelley Poff
  - Kayla Temple
  - Kelsi Linblad
  - Lauren Motley
  - Leah Slife
  - Matthew Prentice
  - Ross Walton
  - Sara Moriarty
  - Chelsea Haynes