

Briefing to the OPTN Board of Directors on

Establish OPTN Requirement for Race-Neutral Estimated Glomerular Filtration Rate (eGFR) Calculations

OPTN Minority Affairs and Kidney Transplantation Committees

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Contents

Executive Summary	2
Purpose	4
Background	4
Proposal for Board Consideration	8
Overall Sentiment from Public Comment	13
Compliance Analysis	16
Implementation Considerations	17
Post-implementation Monitoring	20
Conclusion	21
Policy Language	22

Establish OPTN Requirement for Race-Neutral Estimated Glomerular Filtration Rate (eGFR) Calculations

Affected Policies:

1.2: Definitions

3.6.B.i: Non-function of a Transplanted Kidney

8.4.A: Waiting Time for Candidates Registered at Age 18 Years or Older

8.5.G: Prioritization for Liver Recipients on the Kidney Waiting List

9.5.H: Requirements for Primary Hyperoxaluria MELD or PELD Score Exceptions

9.9.B: Liver-Kidney Candidate Eligibility for Candidates 18 Years or Older

13.7.G: OPTN KPD Waiting Time Reinstatement

Sponsoring Committees:

Minority Affairs and Kidney Transplantation

Public Comment Period:

January 27, 2022 – March 23, 2022

Board of Directors Meeting:

June 27, 2022

Executive Summary

Current OPTN policy is not prescriptive as to what methods of GFR measurement or estimation programs should or should not be used when registering kidney candidates.¹ There are several widely used estimated GFR (eGFR) formulas with varying compositions that sometimes include a Black race coefficient. Because current OPTN policy is not prescriptive, equations that include and exclude the race coefficient are currently permitted for OPTN use. Overestimated eGFR values resulting from race adjustments have the potential to delay referral for kidney transplantation and the initiation of qualifying waiting time.² Research has shown that the use of race adjustments in the calculation of eGFR has the potential to exacerbate existing disparities and negatively impact patient outcomes.³

Community feedback received on the *Reassess Inclusion of Race in Estimated Glomerular Filtration Rate (eGFR) Equation Request for Feedback (RFF)* in summer 2021 was used to develop this proposal to prohibit the use of eGFR calculations that include a race-based variable in OPTN policy.⁴ This proposal defines GFR within *OPTN Policy 1.2: Definitions* so that any eGFR calculation used must not contain a race-based coefficient.⁵ This requirement for race-neutral calculations intends to more accurately estimate Black kidney candidates' GFR values. National stakeholders, such as the National Kidney

¹ OPTN Policy 8.4.A: Waiting Time for Candidates Registered at Age 18 or Older

² Eneanya ND, Yang W, Reese PP. Reconsidering the Consequences of Using Race to Estimate Kidney Function. *American Medical Association*. 2019. 322(2):113-114.

³ Reese PP, Sumit M, King KL, Williams WW, Potluri VS, Harhay MN, Eneanya ND. Racial disparities in preemptive waitlisting and deceased donor kidney transplantation: Ethics and solutions. *The American Journal of Transplant*. 2020. 21:958–967. <https://doi.org/10.1111/ajt.16392>.

⁴ OPTN, Establish OPTN Requirement for Race-Neutral Estimated Glomerular Filtration Rate (eGFR) Calculations, https://optn.transplant.hrsa.gov/media/f2gqujia/establish-optn-requirement-for-race-neutral-egfr-calculations_winter-2022-ppc.pdf (accessed April 19, 2022)

⁵ Ibid.

Foundation (NKF) and American Society of Nephrology (ASN) along with well-known laboratories, such as LabCorp have already recommended and implemented use of estimated GFR calculations that do not include race-based variables.⁶ Prohibiting the use of race-based variables in estimated GFR calculations aims to update OPTN policy to align with current research and national trends.⁷

⁶ Delgado C, Baweja M, Crews DC, Nwamaka ED, Gadegbeku CA, Inker LA, Mendu ML, Miller WG, Moxey-Mims MM, Glenda RV, St. Peter WL, Warfield C, Powe NR. A Unifying Approach for GFR Estimation: Recommendations of the NKF-ASN Task Force on Reassessing the Inclusion of Race in Diagnosing Kidney Disease. *Journal of the American Society of Nephrology*. 2021. <https://doi.org/10.1681/ASN.2021070988>

⁷ OPTN Public Comment, Establish OPTN Requirement for Race-Neutral eGFR Calculations, <https://optn.transplant.hrsa.gov/policies-bylaws/public-comment/establish-optn-requirement-for-race-neutral-egfr-calculations/> (accessed April 19, 2021).

Purpose

The proposal's purpose is to prohibit the use of eGFR calculations that include a race-based variable in OPTN policy. It defines GFR within *OPTN Policy 1.2: Definitions* so that any eGFR calculation used must not contain a race-based variable.⁸ This requirement for race-neutral calculations intends to increase equity in access to transplantation for Black kidney candidates by more accurately estimating their GFR values. If the Black race coefficient is prohibited from use in eGFR calculations within OPTN policy, Black kidney candidates' eGFR values will be more reflective of their actual kidney function.

Background

Use of eGFR in OPTN Policy

GFR values are used as qualifying measures throughout OPTN policy. *Policy 8.4.A: Waiting Time for Candidates Registered at Age 18 or Older* requires one of the following to initiate candidate waiting time accrual:⁹

1. The candidate's registration date with a measured or calculated creatinine clearance or GFR less than or equal to 20 mL/min.
2. The date after registration that a candidate's measured or calculated creatinine clearance or GFR becomes less than or equal to 20 mL/min.
3. The date that the candidate began regularly administered dialysis as an End Stage Renal Disease (ESRD) patient in a hospital based, independent non-hospital based, or home setting.

These eGFR and dialysis criteria are used for initiation of wait time accrual and are not required for kidney candidate registration. A transplant program may register a kidney transplant candidate with any GFR value, but the candidate will not accrue waiting time until one of the criteria listed in *Policy 8.4.A: Waiting Time for Candidates Registered at Age 18 or Older* is met.¹⁰ Waiting time plays a significant role in the prioritization of kidney offers. Generally, the earlier a candidate qualifies to accrue waiting time, the sooner they will receive access to a transplant.¹¹ Unlike adult kidney candidates, pediatric kidney candidates' initiation of wait time accrual is based on the date that the candidate registered on the waiting list regardless of clinical criteria. Pediatric candidates may also qualify with the date they began regularly administered dialysis as an ESRD patient.¹²

Current OPTN policy is not prescriptive as to what methods of GFR measurement or estimation programs should or should not be using when registering kidney candidates.¹³ There are several widely used eGFR formulas with varying compositions that sometimes include a Black race coefficient. Because current OPTN policy is not prescriptive, equations that include and exclude the race coefficient are currently permitted for OPTN use.

⁸ OPTN, Establish OPTN Requirement for Race-Neutral Estimated Glomerular Filtration Rate (eGFR) Calculations, https://optn.transplant.hrsa.gov/media/f2qpujia/establish-optn-requirement-for-race-neutral-egfr-calculations_winter-2022-pc.pdf (accessed April 19, 2022)

⁹ OPTN Policy 8.4.A: Waiting Time for Candidates Registered at Age 18 or Older

¹⁰ Organ Procurement and Transplantation Network (2014). The New Kidney Allocation System (KAS) Frequently Asked Questions. https://optn.transplant.hrsa.gov/media/1235/kas_faqs.pdf

¹¹ OPTN Policy 8.3: Kidney Allocation Score

¹² OPTN Policy 8.4.B: Waiting Time for Candidates Registered prior to Age 18

¹³ OPTN Policy 8.4.A: Waiting Time for Candidates Registered at Age 18 or Older

The OPTN uses GFR thresholds as qualifying criteria in several policies. One of two qualifying criteria in *OPTN Policy 3.6.B.i: Non-function of a Transplanted Kidney* uses a GFR threshold to determine if a candidate's waiting time will be reinstated after kidney graft failure.¹⁴ Similarly, two of three qualifying criteria in *OPTN Policy 8.4.A: Waiting Time for Candidates Registered at Age 18 Years or Older* use such thresholds to determine when a candidate will begin to accrue waiting time.¹⁵ One of two qualifying criteria in *OPTN Policy 8.5.G: Prioritization for Liver Recipients on the Kidney Waiting List* uses a GFR threshold to determine if a candidate will be classified as a prior liver recipient and receive additional kidney priority, often referred to as the safety net.¹⁶ One of three qualifying criteria in *OPTN Policy: 9.5.H: Requirements for Primary Hyperoxaluria Model for End-Stage Liver Disease (MELD) or Pediatric End- Stage Liver Disease (PELD) Score Exceptions* uses GFR thresholds to determine if a candidate qualifies to receive a MELD or PELD score exception for primary hyperoxaluria.¹⁷ Current OPTN policy requires the eGFR values in 9.5.H to be estimated by the Modification of Diet in Renal Disease (MDRD) 6 formula which includes a race-based variable.

Use of Black race in eGFR

Modification of Diet in Renal Disease (MDRD) Study

In 1999, the MDRD study developed an equation to improve prediction of GFR from serum creatinine concentration. Included in the results of this study were findings that suggested Black race was associated with higher serum creatinine levels at the same measured GFR than for White race.¹⁸ Twelve percent of the study's participants were Black (n = 197) and 88% (n= 1,304) participants were White.¹⁹ This study resulted in assignment of a multiplication factor for Black patients' eGFR values.

Chronic Kidney Disease Epidemiology Collaboration (CKD- EPI)

In 2009, researchers developed the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation as a more accurate method for estimating GFR.²⁰ This equation aimed to calibrate and standardize traditional serum creatinine–based measures of kidney function and is currently one of the most widely used formulas.²¹ It was developed through analysis of a number of independent studies and combined data from thousands of individuals. Results observed similar racial differences in serum creatinine levels as in the MDRD study. Recent research has found that the Black race coefficient in the CKD- EPI equation increases estimated GFR values by as much as 16% for Black individuals.²²

¹⁴ *OPTN Policy 3.6. B. i: Non-function of a Transplanted Kidney*

¹⁵ *OPTN Policy 8.4.A: Waiting Time for Candidates Registered at Age 18 or Older*

¹⁶ *OPTN Policy 8.5.G: Prioritization for Liver Recipients on the Kidney Waiting List*

¹⁷ *OPTN Policy: 9.5.H: Requirements for Primary Hyperoxaluria MELD or PELD Score Exceptions*

¹⁸ Levey AS, Bosch JP, Lewis JB, Green T, Rogers N, Roth D. A More Accurate Method To Estimate Glomerular Filtration Rate from Serum Creatinine: A New Prediction Equation. *Annals of Internal Medicine*. 1999. 130(6): 461-470

¹⁹ *Ibid.*

²⁰ Levey AS, Stevens LA, Schmid CH, Zhang YP, Castro III AF, Feldman HI, Kusek JW, Eggers P, Van Lente F, Greene T, Coresh J. A New Equation to Estimate Glomerular Filtration Rate. *Annals of Internal Medicine*. 2009. 150(9): 604–612

²¹ *Ibid.*

²² Eneanya ND, Yang W, Reese PP. Reconsidering the Consequences of Using Race to Estimate Kidney Function. *American Medical Association*. 2019. 322(2):113-114

Limitations of the original and subsequent study

Recent research suggests that the design of the studies that resulted in development of the Black race coefficient have considerable limitations. Both the MDRD and CKD-EPI studies used Black study populations that were not representative of the Black population as a whole. Additionally, researchers used incomplete data that excluded participants' sociodemographic characteristics, diet, clinical conditions, and medications, all of which can affect creatinine levels.^{23,24} At the conclusion of the CKD-EPI study, Levey et al. advised that further research would be necessary to improve GFR estimation.²⁵ As a result of limited representation of other minority groups in this study population, minority groups other than Black were not included in large enough numbers to draw conclusions on racial differences in serum creatinine levels of kidney function.²⁶

Issues with binary distinction on race

Currently when the Black race coefficient is used in formulas, eGFR calculators only offer two response options: Black or Not Black. These options do not include a designation for mixed race or multiracial individuals and do not account for the existing genetic diversity within the Black population.²⁷ The concept of race is a social construct and an unreliable proxy for genetic differences, therefore not a biological marker or clinical measure.²⁸ It is important to note that these issues with the binary distinction of race do not discount the evidence in the following sections that describe the effect of using a race-based coefficient and the broad national efforts that support eliminating it.

Effect of using eGFR

A recent study examined the impact of the race multiplier for the Black population in the CKD-EPI equation on CKD classification and care delivery by hypothetically removing the Black race coefficient from the eGFR formula. Results found:²⁹

- 16% increase in the total number of Black patients classified as having CKD in this study's registry
- 33.4% of Black participants who were already diagnosed with CKD would have been reclassified to a more severe stage
- 3% or 64 patients were reclassified from an eGFR greater than 20 ml/min to an eGFR equal to or less than 20 ml/min

²³ Eneanya ND, Yang W, Reese PP. Reconsidering the Consequences of Using Race to Estimate Kidney Function. *American Medical Association*. 2019. 322(2):113-114

²⁴ Schmidt IM, Waikar SS. Separate and Unequal: Race-Based Algorithms and Implications for Nephrology. *Journal of the American Society of Nephrology*. 2021. 32(3): 529-533.

²⁵ Eneanya ND, Yang W, Reese PP. Reconsidering the Consequences of Using Race to Estimate Kidney Function. *American Medical Association*. 2019. 322(2):113-114

²⁶ Delgado C, Baweja M, Rios Burros N, Crews DC, Eneanya ND, Gadegbeku CA, Inker LA, Mendu ML, Miller WG, Moxey-Mims MM, Roberts GV, St. Peter WL, Warfield C, Powe NR. Reassessing the Inclusion of Race in Diagnosing Kidney Diseases: An Interim Report from the NKF-ASN Task Force. *Journal of the American Society of Nephrology*. 2021. 32: 1305- 1317.

²⁷ Eneanya ND, Yang W, Reese PP. Reconsidering the Consequences of Using Race to Estimate Kidney Function. *American Medical Association*. 2019. 322(2):113-114

²⁸ Vyas DA, Einstein LG, Jones DS. Hidden in Plain Sight — Reconsidering the Use of Race Correction in Clinical Algorithms. *The New England Journal of Medicine*. 2020. 383(9): 874-882.

²⁹ Ahmed S, Nutt CT, Eneanya ND, Reese PR, Sivashanker K, Morse M, Sequist T, Mendu ML. Examining the Potential Impact of Race Multiplier Utilization in Estimated Glomerular Filtration Rate Calculation on African-American Care Outcomes. *Journal of General Internal Medicine*. 2020. 36(2):464–71DOI: 10.1007/s11606-020-06280-5

Overestimated eGFR values resulting from race adjustments have the potential to delay referral for kidney transplantation and the initiation of qualifying waiting time.³⁰ Black patients with CKD have worse outcomes and an increased rate of ESRD when compared with other racial groups.³¹ They are also less likely to be added to the transplant waiting list and receive a transplant.³² The use of race adjustments in the calculation of eGFR has the potential to exacerbate existing disparities and negatively impact patient outcomes. Timely assessment and intervention is critical for outcomes of CKD patients, as the disease can progress quickly towards kidney failure. Earlier detection of CKD could improve efforts to prevent progression.³³

National efforts

In November 2020, the United States House of Representatives Ways and Means Committee invited a number of professional organizations, societies, and community stakeholders to comment on a Request for Information (RFI) pertaining to racial bias in clinical tools. This communication specifically highlighted the connection between race adjusted eGFR calculations and the racial health inequities in kidney transplantation. This RFI posed questions regarding the organization's plans for reevaluating the use of race in clinical algorithms and ensuring improved access to transplant for the impacted population. Responses from a number of these professional organizations are available on the Ways and Means Committee's website.

In July 2020, the use of the Black race coefficient in eGFR calculations gained the attention of the NKF and ASN. These organizations collaborated to form the NKF and ASN Task Force on Reassessing the Inclusion of Race in Diagnosing Kidney Diseases (the Task Force). The Task Force examined the inclusion of race in estimation of GFR and its implications for diagnosis and subsequent management of patients with, or at risk for, kidney disease.

In March 2021, leaders at both ASN and NKF released a statement asserting that:³⁴

Race modifiers should not be included in equations to estimate kidney function and current race-based equations should be replaced by a suitable approach that is accurate, inclusive, and standardized in every laboratory in the United States. Any such approach must not differentially introduce bias, inaccuracy, or inequalities.

In September 2021, the Task Force released their final recommendations which included the following statement:³⁵

³⁰ Eneanya ND, Yang W, Reese PP. Reconsidering the Consequences of Using Race to Estimate Kidney Function. American Medical Association. 2019. 322(2):113-114

³¹ Ahmed S, Nutt CT, Eneanya ND, Reese PR, Sivashanker K, Morse M, Sequist T, Mendu ML. Examining the Potential Impact of Race Multiplier Utilization in Estimated Glomerular Filtration Rate Calculation on African-American Care Outcomes. Journal of General Internal Medicine. 2020. 36(2):464–71DOI: 10.1007/s11606-020-06280-5

³² Zelnick LR, Leca N, Young B, Bansal N. Association of the Estimated Glomerular Filtration Rate With vs Without a Coefficient for Race with Time to Eligibility for Kidney Transplant. The Journal of the American Medical Association. 2021;4(1):e2034004. doi:10.1001/jamanetworkopen.2020.34004

³³ Reese PP, Sumit M, King KL, Williams WW, Potluri VS, Harhay MN, Eneanya ND. Racial disparities in preemptive waitlisting and deceased donor kidney transplantation: Ethics and solutions. The American Journal of Transplant. 2020. 21:958–967. <https://doi.org/10.1111/ajt.16392>

³⁴ National Kidney Foundation. (2021, March 9). Removing Race from Estimates of Kidney Function. <https://www.kidney.org/news/removing-race-estimates-kidney-function>

³⁵ Ibid.

The Task Force recommends immediate implementation of the CKD-EPI creatinine equation refit without the race variable in all laboratories because the calculation does not include race, it included diversity in its development, its potential adverse consequences do not disproportionately affect any one group, and it is immediately available to all laboratories.

The Task Force also recommended national efforts to increase the availability of cystatin C testing and continued research on GFR estimation that aims to eliminate racial and ethnic disparities.^{36, 37}

Development Process

In March 2021, the OPTN Reassess Race in eGFR Calculation Workgroup (the Workgroup) was formed to evaluate the use of the Black race coefficient in eGFR calculations. The Workgroup included members from the OPTN Minority Affairs and Kidney Transplantation Committees (the Committees) as well as subject matter experts, such as nephrologists, epidemiologists, and patients.

In August 2021, the Committees released the Reassess Inclusion of Race in Estimated Glomerular Filtration Rate (eGFR) Equation Request for Feedback (RFF) to solicit community input on potential changes to OPTN policy to restrict the use of the Black race coefficient in eGFR calculations.³⁸ The vast majority of community feedback was supportive of establishing an OPTN requirement for race-neutral eGFR calculations.³⁹ This feedback was used to develop this proposal for Board consideration.

In January 2022, the OPTN Workgroup garnered support from the NKF/ASN Task Force. These groups met virtually to discuss best practices for amplifying the message of the potential OPTN policy change to reach a wider circle of referring nephrologists and their patients. The NKF and ASN each submitted public comments in support of the proposal.⁴⁰

Proposal for Board Consideration

The Committees propose an update to OPTN policy that requires eGFR calculations be race-neutral. This proposal defines GFR within *OPTN Policy 1.2: Definitions* so that any eGFR calculation must not include a race-based variable.⁴¹

³⁶ Inker, L. A., M.D., Eneanya, N. D., Coresh, J., Tighiouart, H., Wang, D., Sang, Y., Crews, D. C., Doria, A., Estrella, M. M., Froissart, M., Grams, M. E., Greene, T., et al., for the Chronic Kidney Disease Epidemiology Collaboration. New Creatinine- and Cystatin C–Based Equations to Estimate GFR without Race. *The New England Journal of Medicine*. 2021. 385:1737-1749. <https://doi.org/10.1056/NEJMoa2102953>

³⁷ Delgado C, Baweja M, Crews DC, Nwamaka ED, Gadegbeku CA, Inker LA, Mendu ML, Miller WG, Moxey-Mims MM, Glenda RV, St. Peter WL, Warfield C, Powe NR. A Unifying Approach for GFR Estimation: Recommendations of the NKF-ASN Task Force on Reassessing the Inclusion of Race in Diagnosing Kidney Disease. *Journal of the American Society of Nephrology*. 2021. <https://doi.org/10.1681/ASN.2021070988>

³⁸ OPTN, Establish OPTN Requirement for Race-Neutral Estimated Glomerular Filtration Rate (eGFR) Calculations, https://optn.transplant.hrsa.gov/media/f2qpjia/establish-optn-requirement-for-race-neutral-egfr-calculations_winter-2022-pc.pdf (accessed April 19, 2022)

³⁹ Ibid.

⁴⁰ OPTN Public Comment, Establish OPTN Requirement for Race-Neutral eGFR Calculations, <https://optn.transplant.hrsa.gov/policies-bylaws/public-comment/establish-optn-requirement-for-race-neutral-egfr-calculations/> (accessed April 19, 2021)

⁴¹ OPTN, Establish OPTN Requirement for Race-Neutral Estimated Glomerular Filtration Rate (eGFR) Calculations, https://optn.transplant.hrsa.gov/media/f2qpjia/establish-optn-requirement-for-race-neutral-egfr-calculations_winter-2022-

Developing a Policy Solution

The Workgroup considered two policy solutions:

1. Selection of one universal eGFR calculation for use by all transplant programs
2. Allow transplant programs to use any eGFR calculation that excludes race

The Workgroup discussed that the selection of one universal eGFR calculation would better align with ASN/NKF recommendations, but may be overly prescriptive at this time.⁴² The Workgroup also considered the rapid evolution of the nephrology field and ongoing advancements regarding the estimation of kidney function. After learning that additional and potentially more accurate race-neutral eGFR calculations are already under development, the Workgroup determined that they would recommend the less prescriptive of the two policy solutions.^{43,44} As additional advancements are made in this field, the Committees will continue to assess whether the selected policy solution remains appropriate or if one universal eGFR formula should be required.

One of the Task Force's final recommendations calls for:⁴⁵

Research on GFR estimation with new endogenous filtration markers and on interventions to eliminate race and ethnic disparities should be encouraged and funded. An investment in science is needed for newer approaches that generate accurate, unbiased, and precise GFR measurement and estimation without the inclusion of race, and that promote health equity and do not generate disparate care.

Proposing a less prescriptive policy which allows any eGFR calculation that does not include a race variable to be used places OPTN members in position to utilize the most modern race-neutral eGFR calculations as research on the topic continues to advance.⁴⁶

The vast majority of community feedback was supportive of the Workgroup's determined policy solution that allows transplant programs to use any eGFR calculation that excludes race.⁴⁷ A few members of the OPTN Ethics Committee and OPTN Transplant Coordinators Committee recommended that for the sake

pc.pdf (accessed April 19, 2022)

⁴² See Reassess Race in eGFR Calculation Workgroup Meeting Summary, October 5, 2021. Available at <https://optn.transplant.hrsa.gov/>

⁴³ Delgado C, Baweja M, Crews DC, Nwamaka ED, Gadegbeku CA, Inker LA, Mendu ML, Miller WG, Moxey-Mims MM, Glenda RV, St. Peter WL, Warfield C, Powe NR. A Unifying Approach for GFR Estimation: Recommendations of the NKF-ASN Task Force on Reassessing the Inclusion of Race in Diagnosing Kidney Disease. *Journal of the American Society of Nephrology*. 2021. <https://doi.org/10.1681/ASN.2021070988>

⁴⁴ See Reassess Race in eGFR Calculation Workgroup Meeting Summary, October 5, 2021. Available at <https://optn.transplant.hrsa.gov/>

⁴⁵ Delgado C, Baweja M, Crews DC, Nwamaka ED, Gadegbeku CA, Inker LA, Mendu ML, Miller WG, Moxey-Mims MM, Glenda RV, St. Peter WL, Warfield C, Powe NR. A Unifying Approach for GFR Estimation: Recommendations of the NKF-ASN Task Force on Reassessing the Inclusion of Race in Diagnosing Kidney Disease. *Journal of the American Society of Nephrology*. 2021. <https://doi.org/10.1681/ASN.2021070988>

⁴⁶ See Reassess Race in eGFR Calculation Workgroup Meeting Summary, October 5, 2021. Available at <https://optn.transplant.hrsa.gov/>

⁴⁷ OPTN Public Comment, Establish OPTN Requirement for Race-Neutral eGFR Calculations, <https://optn.transplant.hrsa.gov/policies-bylaws/public-comment/establish-optn-requirement-for-race-neutral-egfr-calculations/> (accessed April 19, 2021)

of consistency, the OPTN should recommend one universal eGFR calculation or develop an eGFR calculator tool.⁴⁸ The minority of feedback supported the use of one universal eGFR calculation and the majority supported allowing transplant programs to choose any estimated GFR calculation that does not include race.

Race-Neutral eGFR Calculations in OPTN Policy

Defining GFR

The Workgroup proposes adding the following definition to *OPTN Policy 1.2: Definitions*:⁴⁹

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

The proposed definition prohibits use of formulae used to calculate eGFR that include a race-based variable and would apply throughout OPTN policy, affecting all policies that include eGFR. To comply with this proposed policy, formulae used to estimate GFR are required to be race-neutral.⁵⁰ Several clerical language changes are proposed in the affected policies to align with the addition of the GFR definition.

Impact on Waiting Time and Prioritization Policies

The addition of GFR to *OPTN Policy 1.2: Definitions* would require that race-neutral eGFR calculations are used for the following policies regarding waiting time and prioritization:^{51 52 53}

- *Policy 3.6.B.i: Non-function of a Transplanted Kidney*
- *Policy 8.4.A: Waiting Time for Candidates Registered at Age 18 Years or Older*
- *Policy 8.5.G: Prioritization for Liver Recipients on the Kidney Waiting List*

Each of these OPTN policies use eGFR thresholds as qualifying criteria. The proposed changes to OPTN policy intend to increase GFR estimation accuracy and access to transplantation for Black kidney candidates, as more of these candidates should meet the qualifying thresholds in a timelier manner.

Impact on OPTN Policy 9.5.H: Requirements for Primary Hyperoxaluria MELD or PELD Score Exceptions

One of the three qualifying criteria in *OPTN Policy 9.5.H: Requirements for Primary Hyperoxaluria MELD or PELD Score Exceptions* currently includes a requirement for an eGFR of six variable MDRD6 or GFR measured by iothalamate or iohexol, less than or equal to 25 mL/min on 2 occasions at least 42 days apart.⁵⁴ The MDRD6 eGFR formula includes a race-based variable. In order to align with this proposal for

⁴⁸ Ibid.

⁴⁹ OPTN, Establish OPTN Requirement for Race-Neutral Estimated Glomerular Filtration Rate (eGFR) Calculations, https://optn.transplant.hrsa.gov/media/f2qpujia/establish-optn-requirement-for-race-neutral-egfr-calculations_winter-2022-pc.pdf (accessed April 19, 2022)

⁵⁰ Ibid.

⁵¹ OPTN Policy 3.6. B. i: Non-function of a Transplanted Kidney

⁵² OPTN Policy 8.4.A: Waiting Time for Candidates Registered at Age 18 or Older

⁵³ OPTN Policy 8.5.G: Prioritization for Liver Recipients on the Kidney Waiting List

⁵⁴ OPTN Policy 9.5.H: Requirements for Primary Hyperoxaluria MELD or PELD Score Exceptions

race-neutral eGFR calculations, MDRD6 would be removed so that any eGFR calculation may be used, as long as it does not include a race-based variable. The OPTN Liver and Intestinal Organ Transplantation Committee was consulted and agreed on this change. The Committees determined current language stating that measured GFR should be done with iothalamate or iohexol should be removed because it is unnecessary.

Support for OPTN policy change

Respondents discussed rationale for why formulae used to calculate an eGFR should not use a race-based variable.⁵⁵ Much of this rationale referenced race as a social construct that is not appropriate for use in clinical decision making. These respondents encouraged the continued development of biological markers that can be used to identify genetic difference. Feedback also expressed support for the removal the Black race coefficient on the basis of improved equity and access to transplantation for patients who have been historically disadvantaged. Other comments stated that the binary nature of the “Black/Not Black” response options currently used in race-inclusive eGFR calculators may perpetuate racial disparities in healthcare. Feedback also indicated that these limited response options provide no distinction for mixed race or multi-racial individuals.

Considering Potential Unintended Consequences

Decrease in qualifying potential Black living donors

During the RFF’s time in public comment, the first and most frequently expressed concern was that removal of the Black race coefficient from eGFR could inappropriately exclude potential Black living kidney donors and overall decrease the size of the Black living kidney donor pool.⁵⁶ The Workgroup understood this as a concern, as living kidney donation is considered optimal treatment for candidates with CKD and is linked to improved patient outcomes.⁵⁷ Historically, the Black population has had limited access to living donor organs. In 2019, the Black population represented 31.5% of the kidney transplant waiting list but only 13.1% of living donor kidney transplant recipients. Conversely, White patients represented 37.9 % of the transplant waiting list and 63.9% of living donor kidney transplant recipients.⁵⁸

Workgroup members noted that measurement of GFR by isotopic method or a creatinine clearance calculated from a 24-hour urine collection, not an estimation of GFR, is the listed requirement in *OPTN Policy 14.4.B: Additional Requirements for the Medical Evaluation of Living Kidney Donors*.^{59, 73} Even so,

⁵⁵ OPTN Public Comment, Establish OPTN Requirement for Race-Neutral eGFR Calculations, <https://optn.transplant.hrsa.gov/policies-bylaws/public-comment/establish-optn-requirement-for-race-neutral-egfr-calculations/> (accessed April 19, 2022)

⁵⁶ Reassess Inclusion of Race in Estimated Glomerular Filtration Rate (eGFR) Equation, OPTN Minority Affairs and Kidney Transplantation Committees, August 2021, https://optn.transplant.hrsa.gov/media/4782/2021august_-reassess-race-in-egfr_request-for-feedback.pdf (accessed November 12, 2021)

⁵⁷ Kuppachi, S., Norman, S. P., Lentine, K. L., Axelrod, D. A. Using race to estimate glomerular filtration and its impact in kidney transplantation. *Clinical Transplant*. 2020. <https://doi.org/10/1111/ctr.14136>

⁵⁸ Organ Procurement and Transplantation Network (OPTN) and Scientific Registry of Transplant Recipients (SRTR). OPTN/SRTR 2019 Annual Data Report. Rockville: Department of Health and Human Services, Health Resources and Services Administration; 2021. Accessed September 29, 2021. <https://srtr.transplant.hrsa.gov>

⁵⁹ OPTN Public Comment. Reassess Inclusion of Race in Estimated Glomerular Filtration Rate (eGFR) Equation, OPTN Minority Affairs and Kidney Transplantation Committees, August 2021 <https://optn.transplant.hrsa.gov/governance/public-comment/reassess-inclusion-of-race-in-estimated-glomerular-filtration-rate-egfr-equation/> (accessed November 12)

the Workgroup acknowledged that some transplant programs may use eGFR to screen potential living kidney donors. In this case, higher eGFR values are associated with decreased risk to potential living donors and lower eGFR values are associated with increased risk to potential living donors.⁶⁰ A prospective Black living kidney donor whose status changes from qualifying to not qualifying based upon the use of a race-neutral eGFR calculation should not be considered inappropriately excluded, as their previously qualifying eGFR value was likely near the low end of the program's acceptable risk threshold.⁶¹ For these reasons, the Committees found accurate estimation of GFR crucial for the safety of potential Black living kidney donors.

Underestimation of GFR

During the RFF's time in public comment, a minority of community members also voiced concern that the removal of the race coefficient could underestimate Black patient's eGFRs. These respondents suggested the impacts of underestimation could include over diagnosis of CKD, premature dialysis initiation, and promotion of unnecessary transplants.⁶² While research has shown that the removal of the Black race coefficient may reclassify Black patients to a more severe stage of CKD, the Workgroup noted that this population has higher rates of end-stage kidney disease and death due to kidney failure when compared with the overall population.^{63, 64} Because the inclusion of the Black race coefficient overestimates Black patients' eGFR and does not accurately recognize the severity of their illness, Black patients may not receive timely CKD intervention. The Workgroup discussed that the removal of the Black race coefficient could improve timing of CKD treatment, prevent disease progression, and contribute to better patient outcomes.⁶⁵

This public comment proposal received comments similar to those previously expressed by the community regarding potential consequences.⁶⁶ Some respondents suggested that if eGFR is used to screen potential living donors, fewer Black donors may qualify and this may aggravate already existing disparities. The minority of respondents expressed that removal of the Black race coefficient could underestimate GFR for all Black patients and increase CKD burden for this population. Overall, feedback recommended the OPTN monitor the impacts of this policy on the Black kidney candidate population and assess outcomes to identify any unintended consequences.

⁶⁰ OPTN Policy 14.4.B: Additional Requirements for the Medical Evaluation of Living Kidney Donors

⁶¹ OPTN Public Comment. Reassess Inclusion of Race in Estimated Glomerular Filtration Rate (eGFR) Equation, OPTN Minority Affairs and Kidney Transplantation Committees, August 2021 <https://optn.transplant.hrsa.gov/governance/public-comment/reassess-inclusion-of-race-in-estimated-glomerular-filtration-rate-egfr-equation/> (accessed November 12, 2021)

⁶² OPTN Public Comment. Reassess Inclusion of Race in Estimated Glomerular Filtration Rate (eGFR) Equation, OPTN Minority Affairs and Kidney Transplantation Committees, August 2021 <https://optn.transplant.hrsa.gov/governance/public-comment/reassess-inclusion-of-race-in-estimated-glomerular-filtration-rate-egfr-equation/> (accessed November 12, 2021)

⁶³ Ahmed S, Nutt CT, Eneanya ND, Reese PR, Sivashanker K, Morse M, Sequist T, Mendu ML. Examining the Potential Impact of Race Multiplier Utilization in Estimated Glomerular Filtration Rate Calculation on African-American Care Outcomes. *Journal of General Internal Medicine*. 2020. 36(2):464–71DOI: 10.1007/s11606-020-06280-5

⁶⁴ Vyas DA, Einstein LG, Jones DS. Hidden in Plain Sight — Reconsidering the Use of Race Correction in Clinical Algorithms. *The New England Journal of Medicine*. 2020. 383(9): 874-882.

⁶⁵ Ibid.

⁶⁶ OPTN Public Comment, Establish OPTN Requirement for Race-Neutral eGFR Calculations, <https://optn.transplant.hrsa.gov/policies-bylaws/public-comment/establish-optn-requirement-for-race-neutral-egfr-calculations/> (accessed April 19, 2022)

The Committees reviewed and discussed the results of public comment, including feedback on potential unintended consequences. They concluded that the public sentiment supports sending the proposal to the Board. The Committees also supported non-substantive, clarifying changes to the policy language.⁶⁷

Overall Sentiment from Public Comment

The Committees solicited feedback on this proposal from January 27, 2022 to March 23, 2022. These specific questions were posed to the community:⁶⁸

- Do community members agree with the Committees' proposed policy solution? Why or why not?
- If approved, what changes would transplant programs need to make to align with this policy?
- What kind of educational resources would assist in facilitating a smooth transition for your program?
- What impact would this proposal have on patients?
- Should the OPTN considering developing a pathway for transplant centers to modify waiting time for kidney candidates who could have begun accruing waiting time at an earlier date if a race-neutral eGFR calculation was used? If yes, how could this be done?
- Do community members believe that the potential positive impact of this proposal outweighs the potential unintended consequences? Why or why not?

Themes

Community responses to the questions above were generally supportive of the proposal as presented during public comment. Feedback included the following themes:⁶⁹

- Equity
- Unintended consequences
- Concerns with binary distinction on race
- Education
- Waiting time modifications
- Reconsidering the use of race in other OPTN policy

Equity

Equity was the most commonly cited theme during public comment. The majority of respondents expressed their support for the removal of the Black race coefficient to increase equity in access to transplantation for Black kidney candidates. Members also acknowledged race as a social and economic construct that should not be used as a proxy for genetic difference or to make clinical judgments.⁷⁰

⁶⁷ See Reassess Race in eGFR Calculation Workgroup Meeting Summary, May 3, 2022. Available at <https://optn.transplant.hrsa.gov/>

⁶⁸ OPTN, Establish OPTN Requirement for Race-Neutral Estimated Glomerular Filtration Rate (eGFR) Calculations, https://optn.transplant.hrsa.gov/media/f2qpuija/establish-optn-requirement-for-race-neutral-egfr-calculations_winter-2022-pc.pdf (accessed April 19, 2022)

⁶⁹ OPTN Public Comment, Establish OPTN Requirement for Race-Neutral eGFR Calculations, <https://optn.transplant.hrsa.gov/policies-bylaws/public-comment/establish-optn-requirement-for-race-neutral-egfr-calculations/> (accessed April 19, 2022)

⁷⁰ Ibid.

Unintended consequences

As previously mentioned, there are two potential unintended consequences expressed by the community. The first is that the requirement for race-neutral eGFR calculations could interfere with the number of eligible Black living donors. Sometimes eGFR is used to screen potential living donors, although measurement of GFR by isotopic method or a creatinine clearance calculated from a 24-hour urine collection is listed as a requirement in *OPTN Policy 14.4.B: Additional Requirements for the Medical Evaluation of Living Kidney Donors*. The second unintended consequence is the requirement for race-neutral eGFR calculations could underestimate GFR values of Black kidney candidates, which would provide these candidates with an unfair advantage and generally increase CKD burden. Feedback recommended the OPTN monitor and evaluate the policy's impact on the Black kidney candidate and potential Black living donor populations.⁷¹

Concerns with binary distinction on race

Similar to feedback received on the *Reassess Inclusion of Race in Estimated Glomerular Filtration Rate (eGFR) Equation Request for Feedback*, community input indicated concern with the binary race options offered by race- inclusive eGFR calculators. Respondents noted that these “Black” and “Not Black” response options perpetuate racial disparities in health care. Additionally, feedback highlighted that the current options do not account for those of mixed race or the growing population of multi-racial individuals.⁷²

Education

Feedback expressed the community's desire for guidance regarding the implementation of this policy. Respondents who identified as transplant hospitals requested education for nephrology staff on listing referrals and for coordinators on the transition to race-neutral eGFR equations. It was also noted that outside labs that collaborate with transplant hospitals would need to be informed of any policy changes impacting eGFR testing.⁷³

The OPTN has been informed that LabCorp adopted the Task Force recommended eGFR 2021 CKD EPI creatinine equation that estimates kidney function without a race variable in February 2022 and Quest labs will make a similar transition in July 2022.⁷⁴

Waiting Time Modifications

The proposal received some feedback regarding waiting time modifications for patients who have been impacted by race- inclusive eGFR calculations. The majority of these respondents recommended the OPTN consider developing a pathway for Black patients whose eGFRs were impacted by a race-inclusive calculations to regain lost waiting time. One comment recommended the policy be implemented prospectively, as converting race- inclusive eGFR values to race exclusive eGFR values could be challenging for transplant programs with large waiting lists.⁷⁵

⁷¹ OPTN Public Comment, Establish OPTN Requirement for Race-Neutral eGFR Calculations, <https://optn.transplant.hrsa.gov/policies-bylaws/public-comment/establish-optn-requirement-for-race-neutral-egfr-calculations/> (accessed April 19, 2022)

⁷² Ibid.

⁷³ Ibid.

⁷⁴ Ibid.

⁷⁵ Ibid.

Reconsidering the use of race in other transplant tools

A few respondents encouraged the OPTN’s continued assessment of race-based policies and tools. Feedback expressed that race-neutrality should be extended to Kidney donor Profile Index (KDPI), which currently includes race as a variable when assessing deceased donor kidney quality.⁷⁶

Sentiment

The proposal received a total of 240 sentiment responses, including 47 substantive, written comments. This includes 4 comments from OPTN committees and 8 comments from organizations and societies. The proposal was on the non- discussion agenda, but received substantive comments from 9 of the 11 regions through the sentiment polling software.

Figure 1 shows sentiment received from all respondents (regional meeting, online, and email) by their stated region. 10 of the 11 regions indicated neutral, supportive, or strongly supportive sentiment on the proposal. Region 5 submitted one opposing sentiment response.

Figure 1: Sentiment by Region, Establish OPTN Requirement for Race Neutral eGFR Calculations⁷⁷

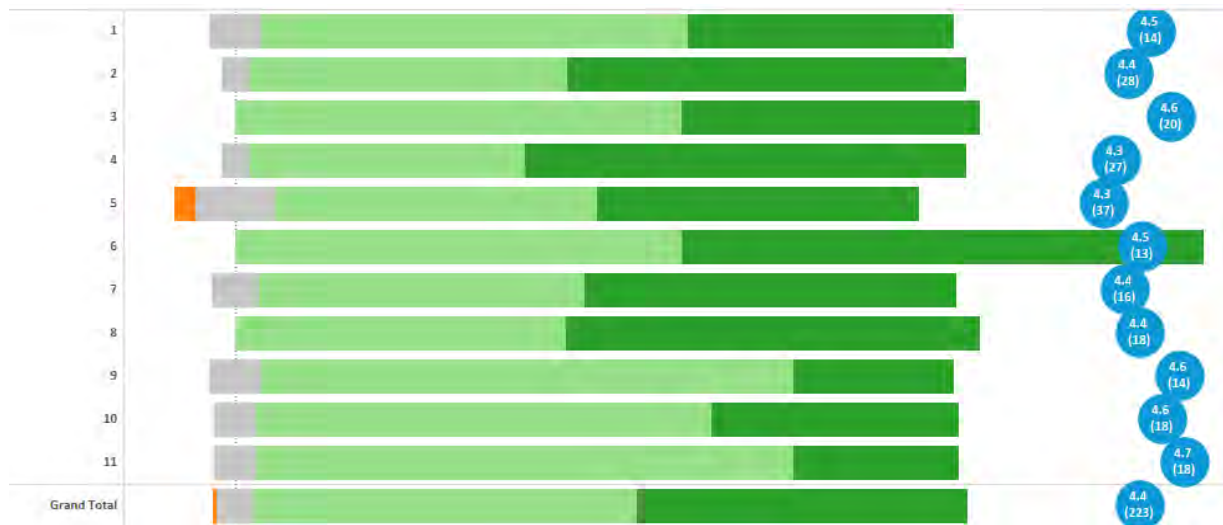
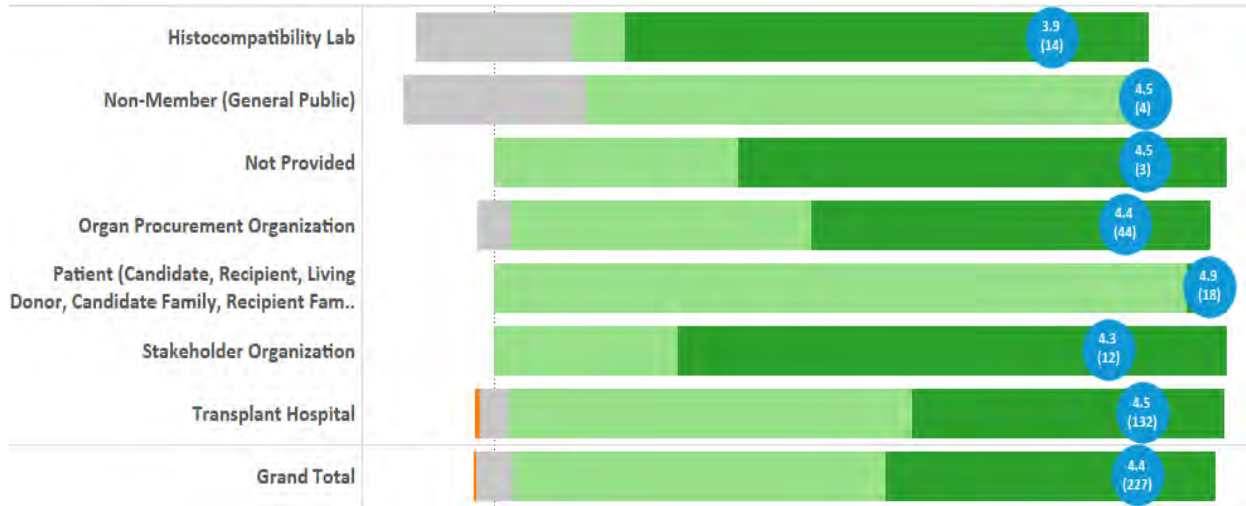


Figure 2 shows sentiment received from all respondents (regional meeting, online, and email) by their stated member type. The majority of responses were submitted by transplant hospitals. 6 of the 7 member types indicated neutral, supportive, or strongly supportive sentiment on the proposal. A transplant hospital submitted one opposing sentiment response.

⁷⁶ OPTN Public Comment, Establish OPTN Requirement for Race-Neutral eGFR Calculations, <https://optn.transplant.hrsa.gov/policies-bylaws/public-comment/establish-optn-requirement-for-race-neutral-egfr-calculations/> (accessed April 19, 2022)

⁷⁷This chart shows the sentiment for the public comment proposal. Sentiment is reported by the participant using a 5-point Likert scale (1-5 representing Strongly Oppose to Strongly Support). The circles after each bar indicate the average sentiment score and the number of participants in is in the parentheses

Figure 2: Sentiment by Member Type, Establish OPTN Requirement for Race Neutral eGFR Calculations⁷⁸



Compliance Analysis

NOTA and OPTN Final Rule

The OPTN Minority Affairs and Kidney Transplantation Committees submit the following project for consideration under the authority of NOTA, which requires the OPTN to “establish...medical criteria for allocating organs and provide to members of the public an opportunity to comment with respect to such criteria,”⁷⁹ and the OPTN Final Rule, which states the OPTN shall develop “Policies for the equitable allocation of cadaveric organs in accordance with §121.8.”⁸⁰ This proposal impacts allocation of organs because using a Black race coefficient overestimates eGFR values, which can delay the accrual of wait time, which could impact a candidate’s placement on the match run.

The Final Rule requires that when developing policies for the equitable allocation of cadaveric organs, such policies must be developed “in accordance with §121.8,” which requires that allocation policies “(1) Shall be based on sound medical judgment; (2) Shall seek to achieve the best use of donated organs; (3) Shall preserve the ability of a transplant program to decline an offer of an organ or not to use the organ for the potential recipient in accordance with §121.7(b)(4)(d) and (e); (4) Shall be specific for each organ type or combination of organ types to be transplanted into a transplant candidate; (5) Shall be designed to avoid wasting organs, to avoid futile transplants, to promote patient access to transplantation, and to promote the efficient management of organ placement;...(8) Shall not be based on the candidate’s place of residence or place of listing, except to the extent required by paragraphs (a)(1)-(5) of this section.”⁸¹

⁷⁸This chart shows the sentiment for the public comment proposal. Sentiment is reported by the participant using a 5-point Likert scale (1-5 representing Strongly Oppose to Strongly Support). The circles after each bar indicate the average sentiment score and the number of participants in is in the parentheses

⁷⁹ 42 U.S.C. §274(b)(2)(B)

⁸⁰ 42 CFR §121.4(a) (1).

⁸¹ 42 C.F.R. §121.8(a)

This proposal:

- **Is based on sound medical judgment⁸².** The proposed changes to OPTN policy are supported by data and literature showing that inclusion of the Black race coefficient in eGFR calculations overestimates Black kidney candidates eGFR values.⁸³ The data and literature show that if race-neutral eGFR calculations are required the severity of Black kidney candidates' illness will be recognized and support timely referral for kidney transplantation and the initiation of qualifying waiting time.⁸⁴
- **Seeks to achieve the best use of donated organs⁸⁵ by** ensuring organs are allocated and transplanted according to medical urgency. Requiring race-neutral eGFR calculations will more accurately estimate Black kidney candidate's kidney function and therefore provide a more accurate assessment of their medical urgency.
- **Is designed to...promote patient access to transplantation⁸⁶ by** giving similarly situated candidates equitable opportunities to receive an organ offer. Requiring race-neutral eGFR calculations will allow kidney candidates with similar degrees of medical urgency to have equitable opportunities to be registered on the waiting list and to receive an organ offer, independent of candidates' race.
- **Is not based on the candidate's place of residence or place of listing.**

Although the proposal outlined in this briefing paper addresses certain aspects of the Final Rule listed above, the Committee does not expect impacts on the following aspects of the Final Rule:

- Is designed to avoid futile transplants
- Is designed to avoid wasting organs
- Promotes the efficient management of organ placement

OPTN Strategic Plan

Improve equity in access to transplants:

This proposal intends to improve equity in access to transplants by addressing equity for Black kidney transplant candidates. This proposed policy change prohibits the use of eGFR calculations that include a race-based variable in OPTN policy. This change intends to improve accuracy in estimation of GFR for Black kidney transplant candidates and make their eGFR values more reflective of actual kidney function.

Implementation Considerations

Member and OPTN Operations

Operations affecting the OPTN

The OPTN will implement the proposed changes to policy in the OPTN Computer System. There will be limited changes to the OPTN Waiting List system, including modifications to data field labels on the

⁸² 42 CFR §121.8(a) (1).

⁸³ Ahmed S, Nutt CT, Eneanya ND, Reese PR, Sivashanker K, Morse M, Sequist T, Mendu ML. Examining the Potential Impact of Race Multiplier Utilization in Estimated Glomerular Filtration Rate Calculation on African-American Care Outcomes. *Journal of Should I General Internal Medicine*. 2020. 36(2):464–71DOI: 10.1007/s11606-020-06280-5

⁸⁴ Ibid.

⁸⁵ 42 CFR §121.8(a)(2).

⁸⁶ Id.

kidney and kidney-pancreas candidate records as well as the simultaneous liver-kidney section of the liver candidate record. Additionally, appropriate modifications will be made to update MELD/PELD exception forms with GFR references.

Operations affecting Transplant Hospitals

This proposal is anticipated to affect the operations of transplant hospitals. Upon implementation, transplant hospitals will not be permitted to use eGFR calculations that include race for purposes of the OPTN. Transplant hospitals that have not already transitioned to the use of race-neutral eGFR calculations will need to do so at this time. The transition process could include program-wide notification of this policy change and training for staff. Transplant hospitals may also have to update their EMRs and work with lab partners to modify eGFR calculation and reporting for purposes of the OPTN.

Operations affecting Histocompatibility Laboratories

This proposal is not anticipated to affect the operations of Histocompatibility Laboratories.

Operations affecting Organ Procurement Organizations

This proposal is not anticipated to affect the operations of Organ Procurement Organizations.

Potential Impact on Select Patient Populations

The Final Rule requires the OPTN to “consider whether to adopt transition procedures that would treat people on the waiting list and awaiting transplantation prior to the adoption or effective date of the revised policies no less favorably than they would have been treated under the previous policies.”⁸⁷ If approved, this policy could improve access to transplantation for Black kidney candidates by appropriately prioritizing them amongst all other candidates awaiting kidney transplantation.

The Committees discussed the need for transition procedures upon the policy’s implementation. They considered that in any instance when an allocation change is made, some populations will experience increased access and others decreased access. The Committee did not identify any populations that may be treated “less favorably than they would have been treated under the previous policies” because this policy change aims to correct an existing disadvantage to access for Black patients.⁸⁸ Nevertheless, the Committee has identified one immediate measure to mitigate the transition to the new policy, and is also contemplating a future change.

The OPTN plans to make transplant hospitals aware of actions they can take immediately to benefit a select population of candidates impacted by race-inclusive eGFR calculations. *OPTN Policy 8.4.A: Waiting Time for Candidates Registered at Age 18 or Older* states that one way to qualify to accrue waiting time is the date after registration that a candidate’s measured or calculated creatinine clearance or GFR becomes less than or equal to 20 mL/min. This policy does not allow qualified waiting time to be calculated based on a date prior to the candidate’s listing date. When a candidate’s qualifying eGFR is updated in the computer system, they will gain any waiting time back up until the listing date.

⁸⁷ 42 C.F.R. § 121.8(d).

⁸⁸ See Reassess Race in eGFR Calculation Workgroup Meeting Summary, November 1, 2021. Available at <https://optn.transplant.hrsa.gov/>

Current transplant hospital purview for modifying candidate eGFR waiting time is described below:
If a transplant hospital:

- Registered a candidate to the waiting list without a qualifying eGFR value and at a later date used a race-inclusive eGFR calculation to qualify the candidate to begin accruing waiting time

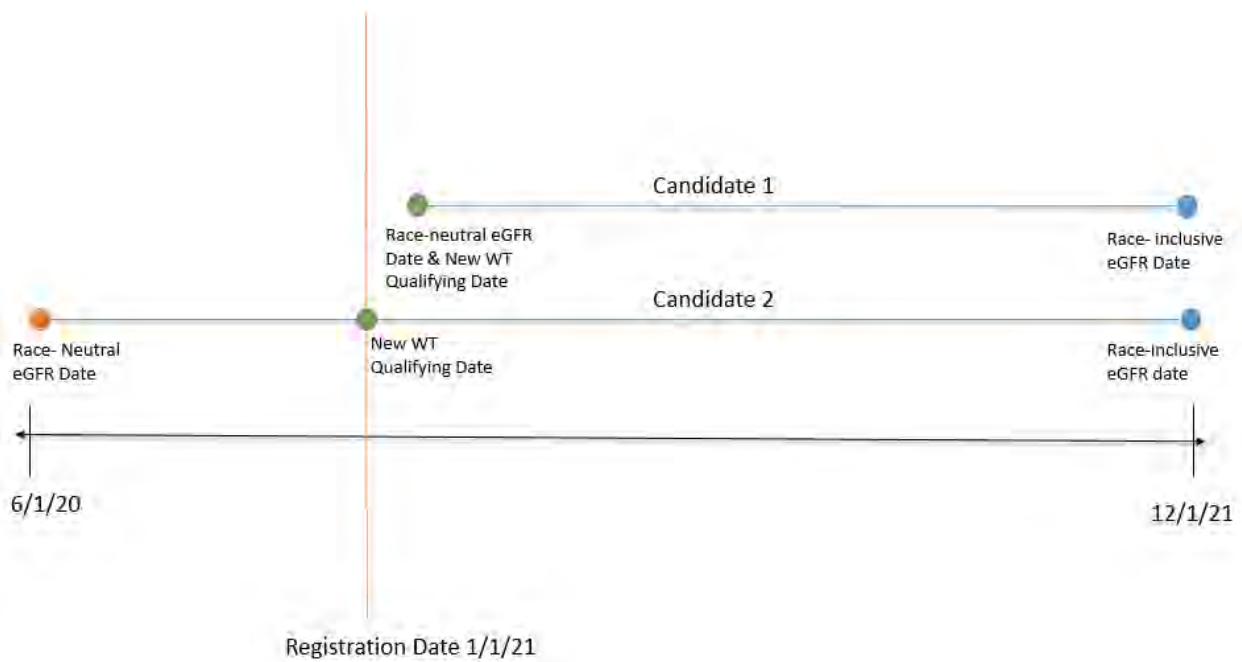
Then the transplant hospital may:

- Recalculate the candidate's eGFR using a race-neutral calculation and update the candidate's qualifying eGFR date in the OPTN Computer system

Transplant hospitals will be responsible for the identification of candidates who qualify for immediate eGFR waiting time modification on their transplant waiting lists, as the OPTN does not collect information on which eGFR calculation was used or if the calculation included a race-based variable.

Figure 3: Current Transplant Hospital Purview for Modifying eGFR Waiting Time displays two candidates who qualify for immediate waiting time modification. Both Candidate 1 and Candidate 2 were registered on January 1, 2021 and qualified to begin accruing waiting time on December 1, 2021 with race-inclusive eGFR calculations. When a race-neutral eGFR calculation was used, Candidate 1 would have qualified to begin accruing waiting time soon after their time of registration. Candidate 1's recalculated race-neutral eGFR date does not pre-date the registration date, so the race-neutral eGFR date will be considered their new waiting time qualifying date and Candidate 1 will regain this time. For Candidate 2, the race-neutral eGFR calculation gives them a qualifying date that falls before their registration date. OPTN Policy 8.4.A: Waiting Time for Candidates Registered at Age 18 or Older does not allow a qualifying eGFR date to predate a candidates' registration date. Therefore, the Candidate 2's waiting time will backdate to their registration date of January 1, 2021.

Figure 3: Current Transplant Hospital Purview for Modifying eGFR Waiting Time



Addressing listed candidates impacted by race-inclusive eGFR Calculations

Additionally, the Committees have reconvened the Workgroup to discuss the development of a proposal that aims to address all listed kidney candidates who may have been impacted by race- inclusive eGFR calculations. This project would consider providing transplant hospitals with the opportunity to identify and apply for modification of waiting time for candidates who were registered and began their waiting time using a race-inclusive eGFR calculation, but have a new qualifying eGFR date that pre-dates their registration when a race- neutral calculation is used. If approved, these candidates' listing dates could be moved back to match the qualifying eGFR date, increasing their waiting time. There is a level of complexity in the operationalization of modifying waiting time for candidates based upon the use of race-inclusive estimated GFR calculations. Any potential changes regarding this topic will be developed by the Workgroup and Committees and proposed during a future public comment period.

Projected Fiscal Impact

This proposal is expected to have a fiscal impact on the OPTN and transplant hospitals, but does not have a fiscal impact on organ procurement organizations or histocompatibility laboratories.

Projected Impact on the OPTN

This project is expected to have a small impact on the OPTN, primarily related to the data field label changes associated with the kidney, kidney-pancreas, and simultaneous liver- kidney candidate forms in addition to appropriate updates to the MELD/PELD exception forms in the OPTN Computer System.

Projected Impact on Transplant Hospitals

Transplant hospitals could incur minor operational costs, but the extent of this cost depends upon which race-neutral formula the transplant hospital elects to use. Additionally, there could be costs associated with staff training and new education process efforts, as well as changes to contractual agreements if the transplant hospital is outsourcing eGFR testing. There could be an ongoing fiscal impact for transplant hospitals due to the increased number of candidates that could be listed after the proposal is implemented.

Projected Impact on Histocompatibility Laboratories

No Impact.

Projected Impact on Organ Procurement Organizations

No Impact.

Post-implementation Monitoring

Member Compliance

The Final Rule requires that allocation policies “include appropriate procedures to promote and review compliance including, to the extent appropriate, prospective and retrospective reviews of each transplant program's application of the policies to patients listed or proposed to be listed at the program.”

The OPTN will continue to monitor GFR values entered into the OPTN Computer System, and provide additional individual member instruction and validation of transition to race-neutral eGFR calculation post board approval.

Policy Evaluation

The Final Rule requires that allocation policies “be reviewed periodically and revised as appropriate.”⁸⁹

The OPTN Minority Affairs and Kidney Transplantation Committees considers the number of Black kidney candidates listed pre-dialysis, the number of kidney transplants to Black candidates, and the amount of time waiting until transplant for Black kidney candidates the key metrics to assess the outcome of the proposed change to eGFR requirements. All metrics will be compared pre- to post-implementation and will be provided both overall and stratified by ethnicity, with particular attention paid to the impact on Black candidates.

Metrics to be evaluated include:

- Count and percent of Black kidney candidates listed pre-dialysis
- Number of kidney transplants to Black candidates, broken out by transplants performed pre-dialysis versus post-dialysis
- eGFR at listing for Black kidney candidates qualifying by eGFR
- Waiting list mortality for Black kidney candidates
- Time waiting from listing until transplant for Black kidney candidates
- Probability of transplant within one year for Black kidney candidates

These metrics will be reviewed at approximately six months, one year, and two years post-implementation. Waiting list mortality, time waiting to transplant, and probability of transplant within one year for Black kidney candidates will be provided only at one and two years post-implementation.

Conclusion

Current OPTN policy is not prescriptive as to which eGFR calculation must be used. This proposal’s purpose is to prohibit the use of eGFR calculations that include a race-based variable. This policy change intends to increase equity in access to transplantation for Black kidney candidates by more accurately estimating their GFR values. By requiring the use of race-neutral eGFR calculations, Black kidney candidates’ eGFR values will be more reflective of their actual kidney function.

⁸⁹ 42 CFR §121.8(a)(6).

Policy Language

Proposed new language is underlined (example) and language that is proposed for removal is struck through (~~example~~). Heading numbers, table and figure captions, and cross-references affected by the numbering of these policies will be updated as necessary.

1 1.2 Definitions

2 The definitions that follow are used to define terms specific to the OPTN Policies.

3

4 **Glomerular Filtration Rate (GFR)**

5 A measure of filtering capacity of the kidneys. GFR can be measured directly or estimated (eGFR) using
6 various formulae. Formulae used to calculate an eGFR must not use a race-based variable.

7

8 **3.6.B.i Non-function of a Transplanted Kidney**

9 Immediate and permanent non-function of a transplanted kidney is defined as *either*:

- 10
- 11 • Kidney graft removal within the first 90 days of transplant documented by an operative report of the removal of the transplanted kidney.
 - 12 • Kidney graft failure within the first 90 days of transplant with documentation that
 - 13 the candidate is either on dialysis or has a glomerular filtration rate (GFR) or
 - 14 measured or estimated creatinine clearance (CrCl) ~~or calculated glomerular filtration~~
 - 15 ~~rate (GFR)~~ less than or equal to 20 mL/min within 90 days after the candidate's
 - 16 kidney transplant.

17 Kidney waiting time will be reinstated when the OPTN receives a completed *Renal Waiting Time*
18 *Reinstatement Form* and the supporting documentation required above. The Estimated Post Transplant
19 Survival (EPTS) score will also be calculated without interruption. The OPTN will send a notice of waiting
20 time reinstatement to the transplant hospital involved.

21 **8.4.A Waiting Time for Candidates Registered at Age 18 Years or Older**

22 If a kidney candidate is 18 years or older on the date the candidate is registered for a kidney,
23 then the candidate's waiting time is based on the earliest of the following:

24

- 25 1. The candidate's registration date with a glomerular filtration rate (GFR) or measured or
26 calculated-estimated creatinine clearance (CrCl) ~~or glomerular filtration rate (GFR)~~ less than
27 or equal to 20 mL/min.
- 28 2. The date after registration that a candidate's GFR or measured or ~~calculated-estimated~~
29 ~~creatinine clearance CrCl or GFR~~ becomes less than or equal to 20 mL/min.
- 30 3. The date that the candidate began regularly administered dialysis as an End Stage Renal
31 Disease (ESRD) patient in a hospital based, independent non-hospital based, or home
32 setting.

33

34 **8.5.G Prioritization for Liver Recipients on the Kidney Waiting List**

35 If a kidney candidate received a liver transplant, but not a liver and kidney transplant from the
 36 same deceased donor, the candidate will be classified as a prior liver recipient. This classification
 37 gives priority to a kidney candidate if *both* of the following criteria are met:
 38

- 39 1. The candidate is registered on the kidney waiting list prior to the one-year anniversary of
 40 the candidate's most recent liver transplant date
- 41 2. On a date that is at least 60 days but not more than 365 days after the candidate's liver
 42 transplant date, at least *one* of the following criteria is met:
 - 43 • The candidate has a GFR or measured or ~~calculated~~ estimated creatinine clearance
 44 (CrCl) or glomerular filtration rate (GFR) less than or equal to 20 mL/min.
 - 45 • The candidate is on dialysis.

46
 47 When the transplant program reports that the candidate meets the criteria for this
 48 classification, the candidate will remain at this classification for 30 days from the date of the
 49 qualifying test or treatment. If the transplant program reports additional qualifying tests or
 50 treatments, then the candidate will remain at this classification for 30 days from the most
 51 recent date of the test or treatment. If the transplant program reports that the candidate meets
 52 the criteria for 90 consecutive days, the candidate will remain at this classification until the
 53 candidate is removed from the kidney waiting list. If the candidate transfers kidney waiting time
 54 according to *Policy 3.6.C: Individual Waiting Time Transfers* and has met the criteria for 90
 55 consecutive days, then the candidate's classification will be included in the transfer.
 56

57 If a liver recipient receives a kidney using this priority classification and returns to the kidney
 58 waiting list after the most recent kidney transplant, the candidate must again meet the criteria
 59 for this classification, unless the candidate qualifies for kidney waiting time reinstatement
 60 according to *Policy 3.6.B.i: Non-function of a Transplanted Kidney*. If the candidate qualifies for
 61 kidney waiting time reinstatement, the candidate will be classified as qualifying for the
 62 classification.
 63

64 If a kidney candidate received a liver and kidney transplant from the same deceased donor, the
 65 candidate will only qualify for this classification if the candidate qualifies for kidney waiting time
 66 reinstatement according to *Policy 3.6.B.i: Non-function of a Transplanted Kidney*
 67

68 **9.5.H Requirements for Primary Hyperoxaluria MELD or PELD Score Exceptions**

69 A candidate will receive a MELD or PELD score exception for primary hyperoxaluria if the
 70 candidate's transplant hospital submits evidence of all of the following:
 71

- 72 1. The liver candidate is registered on the waiting list for a kidney transplant at that transplant
 73 hospital.
- 74 2. Alanine glyoxylate aminotransferase (AGT) deficiency proven by liver biopsy using sample
 75 analysis or genetic analysis.

76 3. ~~Estimated~~ Glomerular filtration rate (GFR) by six-variable Modification of Diet in Renal
 77 Disease formula (MDRD6), or glomerular filtration rate (GFR) measured by iothalamate or
 78 iohexol, is less than or equal to 25 mL/min on 2 occasions at least 42 days apart.

79
 80 **9.9.B Liver-Kidney Candidate Eligibility for Candidates 18 Years or Older**

81 Candidates who are 18 years or older when registered on the liver waiting list are
 82 eligible to receive both a liver and a kidney from the same deceased donor when the
 83 candidate is registered on the waiting list for both organs and meets at least *one* of the
 84 criteria according to *Table 9-17*.

85 **Table 9-17: Medical Eligibility Criteria for Liver-Kidney Allocation**

If the candidate’s transplant nephrologist confirms a diagnosis of:	Then the transplant program must report to the OPTN and document in the candidate’s medical record:
Chronic kidney disease (CKD) with a measured or calculated estimated <u>glomerular filtration rate (GFR)</u> less than or equal to 60 mL/min for greater than 90 consecutive days	At least <i>one</i> of the following: <ul style="list-style-type: none"> ● That the candidate has begun regularly administered dialysis as an end-stage renal disease (ESRD) patient in a hospital based, independent non-hospital based, or home setting. ● At the time of registration on the kidney waiting list, that the candidate’s most recent <u>GFR or measured or calculated estimated creatinine clearance (CrCl) or GFR</u> is less than or equal to 30 mL/min. ● On a date after registration on the kidney waiting list, that the candidate’s <u>GFR or measured or calculated estimated CrCl or GFR</u> is less than or equal to 30 mL/min.
Sustained acute kidney injury	At least <i>one</i> of the following, or a combination of <i>both</i> of the following, for the last 6 weeks: <ul style="list-style-type: none"> ● That the candidate has been on dialysis at least once every 7 days. ● That the candidate has a <u>GFR or measured or calculated estimated CrCl or GFR</u> less than or equal to 25 mL/min at least once every 7 days. If the candidate’s eligibility is not confirmed at least once every seven days for the last 6 weeks, the candidate is not eligible to receive a liver and a kidney from the same donor.

If the candidate’s transplant nephrologist confirms a diagnosis of:	Then the transplant program must report to the OPTN and document in the candidate’s medical record:
Metabolic disease	A diagnosis of at least <i>one</i> of the following: <ul style="list-style-type: none"> ● Hyperoxaluria ● Atypical hemolytic uremic syndrome (HUS) from mutations in factor H or factor I ● Familial non-neuropathic systemic amyloidosis ● Methylmalonic aciduria

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88 **13.7.G OPTN KPD Waiting Time Reinstatement**

89 KPD waiting time begins on the day the candidate’s transplant hospital registers the candidate in
 90 the OPTN KPD program. Candidates accrue 0.07 points per day from the date the candidate is
 91 registered in the OPTN KPD program. A candidate will accrue KPD waiting time at both active
 92 and inactive status in the OPTN KPD program.

93 The OPTN Contractor will reinstate OPTN KPD waiting time to recipients, without interruption, if
 94 the OPTN KPD candidate experiences immediate and permanent non-function of any
 95 transplanted kidney and the KPD candidate is re-registered in the OPTN KPD program with
 96 another living donor. Immediate and permanent non-function of a transplanted kidney is
 97 defined as *either*:

- 98 1. Kidney graft removal within the first 90 days of transplant documented by a report of the
 99 removal of the transplanted kidney.
- 100 2. Kidney graft failure within the first 90 days of transplant with documentation that the
 101 candidate is either on dialysis or has a glomerular filtration rate (GFR) or measured or
 102 estimated creatinine clearance (CrCl) ~~or calculated glomerular filtration rate (GFR)~~ less than
 103 or equal to 20 mL/min within 90 days of the kidney transplant.

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