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Brian M. Shepard
Executive Director & CEO

December 9, 2020

The Honorable Richard Neal
2309 Rayburn Office Building
Washington, DC 20515

Dear Chairman Neal:

Thank you for your November 24, 2020, inquiry regarding clinical decision support tools, like the Kidney Donor Risk Index (KDRI), that utilize racial and ethnic factors. I am pleased to have the opportunity to respond to the Committee's questions as well as share information about UNOS' ongoing work in the area of minority access to transplantation overall. This letter provides a high level overview of the use of these tools in the current kidney allocation system, as well as responses to your specific questions about the efforts underway with regard to the use of Black race in the eGFR and KDRI equations.

The impact of race and ethnicity on candidate access to transplant has been closely monitored by UNOS and the OPTN community of volunteer patients, professionals, and donor families. The 2014 implementation of today's Kidney Allocation System (KAS) vastly *improved* transplant rates for recipients across racial and ethnic groups.[1,2] Prior to 2014, access to deceased donor kidney transplants for Black waitlisted candidates was approximately 8% lower than their waitlist representation[3]; after KAS, this disadvantage disappeared entirely,[4] in part due to the inclusion of clinical factors closely correlated with reduced access to healthcare. Of course, consistent monitoring and education about the use of these factors is paramount to ensuring efforts to reduce inequities remain effective.

In addition, HRSA recently exercised an optional task in the OPTN contract to fund a feasibility and suitability assessment to explore the acquisition of third party social determinants of health (SDOH) data to better understand the impact of SDOH on access to transplantation. This means that, for the first time, UNOS as the OPTN will be able to study those factors that impact the patient's health *before* the patient is on the wait list. UNOS will submit a final report by September 2021, including a path forward for collecting, incorporating into the OPTN database, and studying the data. A manuscript highlighting how such sources of data can help us better uncover potential disparities in the transplant system will be submitted to a peer reviewed journal.

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[1] Melanson TA, Hockenberry JM, Plantinga L, Basu M, Pastan S, Mohan S, Howard DH, Patzer RE. New kidney allocation system associated with increased rates of transplants among black and Hispanic patients. Health Affairs. 2017 Jun 1;36(6):1078-85.

[2] https://unos.org/news/odds-equal-of-kidney-transplant-for-minorities/ https://optn.transplant.hrsa.gov/news/two-year-analysis-shows-effects-of-kidney-allocation-system/

[3] https://www.transplantpro.org/wp-content/uploads/sites/3/KAS_12month_analysis.pdf

[4] https://unos.org/news/odds-equal-of-kidney-transplant-for-minorities/

To further assist you in your inquiry, I also invite you to view the Organ Procurement and Transportation Network's (OPTN) *Equity in Access Dashboard* at https://optn.transplant.hrsa.gov/data/.

Thank you for your inquiry, and please do not hesitate to contact me if you have any further questions.

Sincerely,

David Mulligan

David Mulligan

Overview of Kidney Allocation Policy and Current Use of Racial/Ethnic Factors

History of use of race and ethnicity in clinical tools in OPTN Policy from 1998-present

The establishment of medical criteria for patients to qualify for waiting time in kidney allocation was instituted in 1998 specifically to improve equity in access by race/ethnicity.[5] Prior to this policy change, accrual of "waiting time" was based solely on the time a candidate was added to the waiting list, a policy recognized as potentially unfair as it may advantage socioeconomically privileged patients who are more likely to be referred early for transplant evaluation.

Most prominently, however, is the implementation of the KAS, which resulted in major successes with regard to equity in access to transplant, vastly evening out the transplant rates for recipients across racial and ethnic groups[6,7]. KAS accomplished this by further mitigating the impact of delayed referral by crediting pre-listing time on dialysis toward waiting time accrual, a policy change that boosted transplant access most notably for Black and Hispanic candidates.[8] Finally, imminent changes to kidney allocation policy to distribute kidneys more broadly are expected to both increase geographic equity and improve access for minority patients.

Overview of the current Kidney Allocation System

As mentioned, the OPTN revised the policy for allocating kidneys in 2014. A key component of this revised kidney allocation system (KAS) was the introduction of longevity matching, which allocates kidneys predicted to last the longest to post-transplant to candidates most likely to benefit the most from a long-lasting kidney. Longevity matching is consistent with the regulatory requirements for OPTN allocation policies, which include achieving the best use of donated organs and avoiding futile transplants.[9] There are two calculations integral to the allocation of kidneys under longevity matching: the Kidney Donor Profile Index (KDPI) and the Estimated Post-Transplant Survival score (EPTS).

The EPTS is a percentage score that ranges from zero to 100 percent. The score is predictive of how long the candidate will survive following a kidney transplant relative to other candidates, and is based on the candidate's age, history of diabetes, history of dialysis, and whether the candidate previously had a solid organ transplant. The KDPI score is derived directly from the Kidney Donor Risk Index (KDRI) score. The KDPI ranges from zero to 100 percent, and is the percentage of donors in the reference population that have a KDRI less than or equal to this donor's KDRI.[10] The score is associated with how long the donated kidney is likely to function when compared to other kidneys based on the following clinical factors and demographic donor factors, some of which serve as proxies of unknown or unmeasured factors that impact kidney transplant allograft survival, and contribute to the accuracy of the estimation of kidney longevity:

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[5] Report of the Kidney and Pancreas Committee to the OPTN Board of Directors. November 12-13, 1997. Available upon request.

[6] Melanson TA, Hockenberry JM, Plantinga L, Basu M, Pastan S, Mohan S, Howard DH, Patzer RE. New kidney allocation system associated with increased rates of transplants among black and Hispanic patients. Health Affairs. 2017 Jun 1;36(6):1078-85.

[7] https://unos.org/news/odds-equal-of-kidney-transplant-for-minorities/ ; https://optn.transplant.hrsa.gov/news/two-year-analysis-shows-effects-of-kidney-allocation-system/

[8] Stewart DE, Kucheryavaya AY, Klassen DK, Turgeon NA, Formica RN, Aeder MI. Changes in deceased donor kidney transplantation one year after KAS implementation. American Journal of Transplantation. 2016 Jun;16(6):1834-47.

[9] 42 C.F.R. §121.8(a)

[10] https://optn.transplant.hrsa.gov/media/1512/guide_to_calculating_interpreting_kdpi.pdf

- Age
- Height
- Weight
- Ethnicity/Race
- History of hypertension
- History of diabetes
- Cause of death
- Serum creatinine
- HCV status
- Whether donor meets donation after cardiac death (DCD) criteria

Longevity matching is used for a subset of transplant recipients. After first being offered to the most highly sensitized (hardest to match) candidates, candidates with longer estimated post-transplant longevity (those candidates with an EPTS score of 20% or less) receive priority for kidneys from donors with a KDPI of 20% or less (those kidneys expected to function the longest).

The KDPI is also used in the kidney allocation system to preferentially allocate the highest longevity kidneys to children; to determine when it is appropriate to offer two kidneys to the same patient to improve recipient outcomes; to determine for which kidneys prior liver recipients receive priority; and as a decision tool that transplant programs and patients can use to help determine whether or not to accept a particular kidney transplant.

In addition to longevity matching, the degree of sensitization, clinical factors, and waiting time also play a role in determining the rank ordering of patients when a donor kidney is to be allocated. The majority of kidney candidates added to the waiting list have begun regularly administered dialysis for End Stage Renal Disease (ESRD), and their waiting time is based on their dialysis start date. OPTN policy calculates the starting time for an adult candidate's waiting time from the earliest of:

1. The candidate's registration date with a measured or calculated creatinine clearance or glomerular filtration rate (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.[11]

GFR is a measure of kidney function. The "gold standard" GFR measurement is a nuclear medicine GFR. However, it is invasive, less widely available, and expensive. In comparison, the estimated GFR (eGFR) calculation is readily available and widely used in clinical medicine. The eGFR is calculated based on a serum creatinine value easily obtained through a standard metabolic panel.

A candidate's GFR is relevant to kidney allocation in terms of calculating the waiting time for candidates who have not yet begun regularly administered dialysis for end stage renal disease (ESRD). The starting point for waiting time of GFR of less than or equal to 20/mL/min represents

[11] OPTN Policy 8.4.A: Waiting Time for Candidates Registered at Age 18 Years or Older. https://optn.transplant.hrsa.gov/media/1200/optn_policies.pdf (Accessed on December 9, 2020).

very advanced kidney disease. It is important to note that for a non-dialysis candidate to begin accruing waiting time, OPTN policy does not require that an eGFR be used; rather, the policy provides flexibility and clinical discretion by allowing use of either a measured creatinine clearance (CrCl), a measured GFR, or an estimated GFR. If eGFR is used to qualify, policy does not prescribe a specific formula that must be used. Since eGFR is more easily obtained, allowing use of an eGFR to qualify for waiting time may remove a potential barrier, more invasive and more costly testing, for some patients.

It is also important to note that being on dialysis or having a qualifying GFR/CrCl/eGFR is not a requirement for registering a candidate in the first place. Absent a dialysis start date or a qualifying GFR/CrCl/eGFR, a candidate can still be added to the waiting list and even receive kidney offers, but waiting time will not start to accrue until the GFR is reported to be less than or equal to 20 mL/min.[12] Again, the qualifying GFR can be demonstrated by eGFR, but it is not a policy requirement.

The implementation of KAS resulted in major successes with regard to equity in access to transplant, and vastly evened out the transplant rates for recipients across racial and ethnic groups.[13,14] KAS accomplished this by further mitigating the impact of delayed referral by crediting pre-listing time on dialysis toward waiting time accrual, a policy change that boosted transplant access most notably for Black and Hispanic candidates.[15] Finally, the OPTN plans to implement changes to kidney allocation policy in December 2020 designed to distribute kidneys more broadly, increase geographic equity, and improve access for minority patients.[16]

Options for consideration

Prohibiting use of GFR as a clinical tool from kidney allocation would prevent candidates from accruing waiting time until dialysis begins. This would drastically limit opportunities for preemptive deceased donor transplants, which are considered by many providers and patients a treatment of choice. One would instead most likely require a living donor transplant in order to receive a preemptive transplant, which is another area of historic disadvantage for Black patients. Black patients experience a lower rate of living donor transplants compared to White patients, based on factors such as family history of kidney disease and other issues related to access to care.

Another alternative could be to require a measure of true GFR. However, as previously mentioned, measuring true GFR is invasive, expensive, and less widely available.

Yet another option would be to eliminate the race component of the eGFR estimating equations. This has been done by some OPTN member institutions and is acceptable for transplant waiting time purposes, as OPTN policy does not dictate the use of a specific eGFR formula. The development and use of eGFR was not done for the sole purpose of transplantation, but rather to

[12] OPTN Policy 9.9.B: Liver-Kidney Eligibility for Candidates 18 Years or Older. https://optn.transplant.hrsa.gov/media/1200/optn_policies.pdf (Accessed on December 9, 2020).
[13] Melanson TA, Hockenberry JM, Plantinga L, Basu M, Pastan S, Mohan S, Howard DH, Patzer RE. New kidney allocation system associated with increased rates of transplants among black and Hispanic patients. Health Affairs. 2017 Jun 1;36(6):1078-85.
[14] https://unos.org/news/odds-equal-of-kidney-transplant-for-minorities/ ; https://optn.transplant.hrsa.gov/news/two-year-analysis-shows-effects-of-kidney-allocation-system/
[15] Stewart DE, Kucheryavaya AY, Klassen DK, Turgeon NA, Formica RN, Aeder MI. Changes in deceased donor kidney transplantation one year after KAS implementation. American Journal of Transplantation. 2016 Jun;16(6):1834-47.
[16] https://optn.transplant.hrsa.gov/governance/public-comment/eliminate-the-use-of-dsa-and-region-in-kidney-allocation-policy/

allow a more accurate identification of patients with renal disease. This accurate identification of renal disease is especially important for minority populations and populations with less than optimal access to care. A decision to eliminate race from eGFR requires very careful consideration and has significant implications beyond transplantation for the healthcare system.[17]

We are aware that there are a number of enhancements to KDRI/KDPI that the community is interested in, beyond addressing whether and how to account for race. For example, it is anticipated that the KDRI will be improved over time to better assess pediatric donor risk; better account for HCV+ (past vs. current infection) risk; better account for acute kidney injury and other clinical scenarios; incorporates other factors such as biopsy findings, etc., and eventually, potentially removing race in favor of relevant genetic tests such as APOL-1. UNOS and the OPTN will continue to monitor policies for these factors, develop and explore alternative policies, and work with other professional organizations to further this area of study.

Responses to Chairman Neal's Questions

1. What strategies has UNOS undertaken to reevaluate the scientific basis for the use of Black race in KDRI calculation?

With respect to the inclusion of Black race in the KDRI, UNOS recognizes there is evidence that kidney function and transplant outcomes are affected by genetic factors associated with recent African ancestry and is not fully explained by social factors but is due, in part, to a real biologic impact of the recently discovered APOL-1 gene.[18] The association of the APOL-1 gene with kidney disease risk, identified by investigators at Tufts University, is one of the most important findings in kidney disease in many years. Additional research by Julian, et al, provides a pathway to revising the KDRI to replace race with this genetic marker. UNOS is partnering in a large-scale, NIH-funded study of the relevance of the APOL-1 gene in transplantation more broadly, including its use in both living and deceased donor transplantation.[19,20] UNOS was involved in the planning of this study with the National Institute of Diabetes and Digestive Kidney Diseases (NIDDK) leadership at the NIH. UNOS is actively involved every week as part of the Executive Committee managing this important study. The enrollment in this five-year study is over 1500 kidney donors with recent African ancestry and over 2000 kidney transplant recipients. We are three years into the study and we are now entering the data analysis phase.

a. How will UNOS work to support, encourage, and coordinate with other specialty organizations that are also conducting a reevaluation of the misuse of race in clinical algorithms?

[17] Levey AS, Titan SM, Powe NR, Coresh J, Inker LA. Kidney disease, race, and GFR estimation. Clinical Journal of the American Society of Nephrology. 2020 May 11.

[18] Julian BA, Gaston RS, Brown WM, Reeves-Daniel AM, Israni AK, Schladt DP, Pastan SO, Mohan S, Freedman BI, Divers J. Effect of replacing race with apolipoprotein L1 genotype in calculation of kidney donor risk index. American Journal of Transplantation. 2017 Jun;17(6):1540-8.

[19] Freedman BI, Moxey-Mims MM, Alexander AA, Astor BC, Birdwell KA, Bowden DW, Bowen G, Bromberg J, Craven TE, Dadhania DM, Divers J. APOL1 long-term kidney transplantation outcomes network (APOLLO): Design and rationale. Kidney International Reports. 2020 Mar 1;5(3):278-88.

[20] Marin EP, Cohen E, Dahl N. Clinical Applications of Genetic Discoveries in Kidney Transplantation: A Review. Kidney360. 2020 Apr 30;1(4):300-5.

Both UNOS and the OPTN regularly collaborate with and convene the transplant community on various issues of interest. Representatives from the major donation and transplantation societies serve on the Board of Directors and organ allocation policy development committees for both UNOS and the OPTN, and targeted outreach is conducted during bi-annual OPTN public comment periods to ensure these organizations have weighed in on all proposed changes to policy. UNOS is initiating its own research efforts, as will provide data and analytical support in furtherance of efforts initiated by other organizations. We are excited about the opportunity to continue to partner with other researchers to tackle these challenging issues.

2. What has UNOS done and what does it plan to do to inform clinicians of the connection between race correction in eGFR calculation and the KDRI and racial health inequities in CKD, ESRD, and kidney transplantation?

UNOS and the OPTN have published numerous educational resources related to these topics and will continue to develop these resources as this area of study advances. These articles are posted on the UNOS and OPTN websites and published in scientific literature, reaching a broad audience of transplant practitioners. A sample of relevant publications include:

- Educational Guidance on Patient Referral to Kidney Transplantation[21]
- Kidney Equity in Access Report[22]
- Kidney Donor Profile Index (KDPI) Guide for Clinicians[23]
- Kidney and Pancreas Distribution Modeling: Analysis at a Glance[24]

As OPTN policy committees and UNOS Research continues to explore these issues in more detail, they will evaluate the mechanisms for effectively communicating updated information about these issues to the community.

a. While ending the use of Black race in the KDRI could take some time to implement, what guidance can UNOS issue quickly to redirect clinical practices and communicate the problem of misuse of race in the KDRI to patients?

UNOS and the OPTN continue to participate in the study of these issues and will incorporate the results into OPTN policy as evidence accumulates and community consensus develops. The OPTN Minority Affairs Committee leads efforts to review and adjust clinical tools and allocation policy with the potential to impact minority and vulnerable populations.

3. What interventions could UNOS develop to ensure improved access to transplant for patients who have not received it because of use of Black race in the KDRI?

A recent study conducted by the UNOS Research department found that among kidney transplant recipients, the median KDRI was no different for Black (45%) compared to White (45%) recipients. This suggests that if the inclusion of race in the KDRI does indeed contribute to non-utilization of Black donor kidneys due to elevated KDRI, it may not disproportionately affect

[21] https://optn.transplant.hrsa.gov/resources/guidance/educational-guidance-on-patient-referral-to-kidney-transplantation/
[22] https://optn.transplant.hrsa.gov/news/kidney-equity-in-access-report-updated/
[23] https://optn.transplant.hrsa.gov/resources/guidance/kidney-donor-profile-index-kdpi-guide-for-clinicians/
[24] https://optn.transplant.hrsa.gov/news/kidney-and-pancreas-distribution-modeling-analysis-at-a-glance/

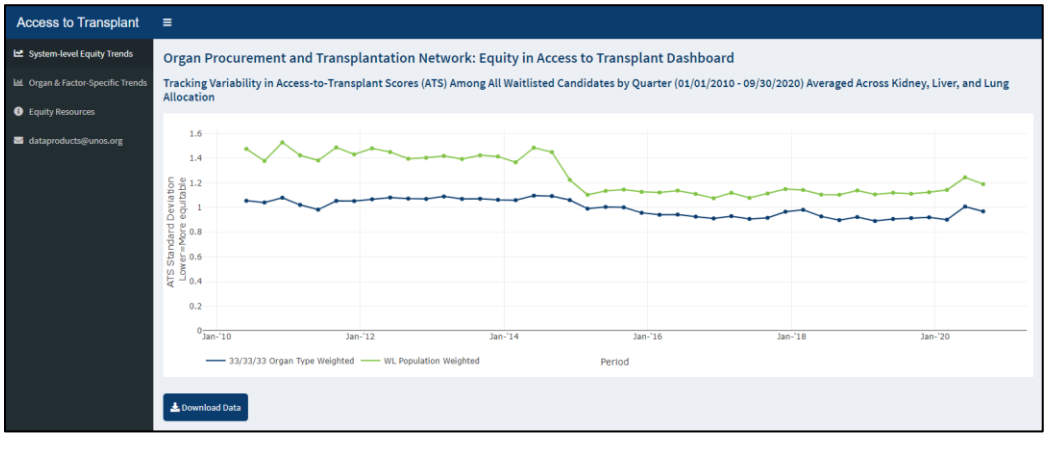
access to transplant by race. UNOS hopes to build on this research to further study issues of access to transplantation and develop evidence-based recommendations.

a. What role could the federal government play in support of this kind of initiative, if any?

We would welcome further discussion on how the government could continue to support review of this topic. Because GFR is a calculation used outside of transplant medicine, data and expertise from NIH or other relevant stakeholders about how GFR is used across the various sectors of healthcare would be key to understanding the implications of changes to the calculation on transplant and non-transplant patients alike.

b. What specific racial health equity metrics and outcomes will UNOS track and work to improve? Please provide details, including the timeframe.

In its role as the OPTN, UNOS developed[25] and published a method for measuring and monitoring equity in access to transplant[26], including by race and other kidney candidate demographic and socioeconomic factors. UNOS continuously monitors system-level health with respect to these equity in access measures, and a publicly accessible dashboard is also now available[27]. A number of enhancements to the dashboard in development, including more clearly highlighting factor-specific patterns in access by race/ethnicity and other factors. Though our equity in access methodology is focused on the OPTN's primary purview – assessing allocation policy performance (e.g., equity) with respect to candidates on the waiting list – we are also exploring expanding our analyses to include measuring and monitoring equity in access to the waiting list in the first place, particularly for kidney candidates.



OPTN Equity in Access Dashboard (8 Dec. 2020)

In addition, UNOS Research staff, also under the auspices of the OPTN, are currently conducting several studies examining the impact of COVID on disparities in access to transplant by race/ethnicity. These studies are anticipated to be presented at transplant meetings such as the American Transplant Congress (ATC) in 2021. The goal of these analyses is to determine whether

[25] https://optn.transplant.hrsa.gov/media/2842/equity_in_access_report_201611.pdf
[26] Stewart DE, Wilk AR, Toll AE, Harper AM, Lehman RR, Robinson AM, Noreen SA, Edwards EB, Klassen DK. Measuring and monitoring equity in access to deceased donor kidney transplantation. American Journal of Transplantation. 2018 Aug;18(8):1924-35.
[27] https://optn.transplant.hrsa.gov/data/ (*see* "View the Equity in Access dashboard")

racial disparities in transplant access have indeed been exacerbated during the pandemic. If so, by drawing attention to this issue, our ultimate aim would be to spur exploration of mitigation strategies during the ongoing COVID-19 pandemic, as well as possible future pandemics or related events.

HRSA recently exercised an optional task in the OPTN contract to fund a feasibility and suitability assessment to explore the acquisition of third party social determinants of health (SDOH) data to better understand the impact of SDOH on transplantation. UNOS will submit a final report by September 2021, including a path forward for collecting, incorporating into the OPTN database, and studying the data. A manuscript highlighting how such sources of data can help us better uncover potential disparities in the transplant system will be submitted to a peer reviewed journal.

Lastly, for all policy changes, in order to identify and quickly address any unintended disparities in access to transplant introduced by changes to allocation, the OPTN closely monitors the impact of policies after implementation by many factors including race/ethnicity.

4. **Black, Indigenous, and Latinx scholars have a leading and vital perspective on these issues and the proposed solutions, despite being underrepresented in medicine. How is UNOS ensuring racial diversity in the discussion and strategy development relating to health equity?**

UNOS and the OPTN are aggressively working to improve diversity in all aspects of organizational leadership, committee membership, and community engagements. We believe, as you do, that improving diversity in discussion and strategy development relating to health equity and access to care is essential to the success of our transplant and health care delivery systems.

The OPTN Board of Directors Nominating Committee oversees a robust recruitment and nominations process on an annual basis.[28] The Committee is charged with ensuring the Board and OPTN policy development committees are not only compliant with regulatory composition requirements but also reflect the diversity of the community they serve.[29] The Committee conducts a review of the entire OPTN volunteer workforce annually and makes specific, targeted recommendations in its annual Board needs assessment, including areas in which diversity may be increased in a given year. The needs assessment is shared publically and serves as the basis for the following year's call for volunteer nominations.[30] The application for a Board and committee service is open to the general public.[31]

We appreciate the opportunity to discuss these important issues with you. We look forward to continuing to collaborate with you and with other organizations engaging in this important research.

[28] https://optn.transplant.hrsa.gov/members/committees/board-of-directors-nominating-committee/
[29] 42 C.F.R. §121.3(a)
[30] More information can be found at https://optn.transplant.hrsa.gov/members/get-involved
[31] https://optn.transplant.hrsa.gov/members/get-involved/how-to-volunteer-apply/