



March 9, 2023

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Dear Dr. Umschield:

The National Kidney Foundation (NKF) and the American Society of Nephrology (ASN) thank the Agency for Healthcare Research and Quality (AHRQ) for its commitment to eliminating racial and ethnic disparities in health and healthcare. NKF and ASN also appreciate the opportunity to provide comments on AHRQ's report on the "Impact of Healthcare Algorithms on Racial and Ethnic Disparities in Health and Healthcare."

NKF and ASN Joint Task Force on Reassessing the Inclusion of Race in Diagnosing Kidney Diseases

NKF and ASN created a joint Task Force on Reassessing the Inclusion of Race in Diagnosing Kidney Diseases in July of 2020, recognizing the potential for race in the calculation of the estimated glomerular filtration rate (eGFR) to perpetuate healthcare disparities. The NKF-ASN Task Force released its final report on September 23, 2021, recommending a race-free approach, including the recommendation to utilize a new creatinine-based race-free "refit" Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation for first line use and additional use of cystatin-C to confirm estimate kidney function. (The task force also recommended increased funding for research in this arena.)

The Task Force chose a data- and value-driven process to assess eGFR estimation approaches. To do so, the NKF-ASN Task Force organized its work into three phases: 1) clarify the problem and evidence regarding eGFR equations in the United States; 2) evaluate different approaches to estimate kidney function examining clinical, systemic and societal consequences and the impact on health care delivery of each approach; and 3) provide recommendations. The group identified 26 approaches for the estimation of GFR and narrowed their focus by consensus to five approaches. Inclusive processes that were used in this yearlong work engaged relevant experts and perspectives including patients; trainees; nephrologists; researchers in genetics, race theory, estimating equations, body composition and population science; laboratory medicine experts; transplantation; pharmacists; public health professionals; and government stakeholders.

In its final report, the NKF-ASN Task Force recommended the adoption of a recently published eGFR 2021 CKD-EPI creatinine equation that estimates kidney function

without a race variable. This equation was chosen using an iterative process of review. The approach balanced equation precision across racial groups removing the need for a race variable, while also mitigating the risk for amplification of existing disparities or creation of new disparities based on data presented to the Task Force and simulation analysis completed by the Task Force using data from the National Health and Nutrition Examination Survey (NHANES). The Task Force also recommended increased use of serum (blood) cystatin C and creatinine measurement in a combined eGFR equation, as a confirmatory assessment of kidney function. The final report was published in both the [American Journal of Kidney Diseases \(AJKD\)](#) and the [Journal of the American Society of Nephrology \(JASN\)](#) and was drafted with considerable input from hundreds of stakeholders to achieve consensus for an unbiased and reasonably accurate estimation of GFR so that laboratories, clinicians, patients, and public health officials can make informed decisions to advance equity and personalized care for patients with kidney diseases.

Comments on AHRQ's Impact of Healthcare Algorithms on Racial and Ethnic Disparities in Health and Healthcare Draft Report

NKF and ASN agree that removal of the eGFR Black race coefficient may reduce racial disparities, such as more timely transplant evaluation, while also potentially increasing other disparities, such as reducing access to medications that are contraindicated in advanced CKD. Both NKF and ASN applaud AHRQ for its excellent synthesis of this key literature.

The kidney community has made great progress and serves as a national example of deploying strategies to mitigate racial and ethnic bias associated with algorithms (Key Question 2). In addition, NKF and ASN have been engaged in dissemination of the task force findings via national conferences and publication of online calculators. The Task Force recommendations have been endorsed by other professional societies, and implementation strategies are being considered by large health systems and laboratories. Efforts are also underway to derive more accurate equations that are less dependent on social factors. Implementation efforts on the currently recommended approach are also well underway under the guidance of NKF. Finally, as discussed below, the Health Resources and Services Agency's (HRSA's) Organ Procurement and Transplantation Network (OPTN) recently decided to modify kidney transplant wait times for Black individuals affected by the race-based kidney function estimating equation and "back-date" waitlist time for those impacted by race-based eGFR.

In pursuit towards a consistent method of diagnosing kidney diseases that is independent of race and ensuring racial bias does not affect subsequent treatment, NKF published an online [eGFR Calculator](#) for both adult and pediatric patients based on the joint NKF-ASN Taskforce recommendations. The calculator takes the input of a patient's serum creatinine and cystatin C concentration and provides a GFR estimate utilizing three race neutral equations (CKD-EPI creatinine equation (2021), CKD-EPI

creatinine-cystatin equation (2021), and CKD-EPI cystatin C equation (2012)) for optimal clinical decision making. The calculator further aids in the evaluation and prognosis of CKD by eGFR and urinary albumin-creatinine ratio (uACR) categories.

To support the laboratory community in its implementation of the recommendations from the NKF-ASN Task Force reassessing the inclusion of race in diagnosing kidney diseases, NKF partnered with the American Society for Clinical Pathology and other leading laboratories and large health systems across the country in a Laboratory Engagement Initiative. This collaboration developed the “Kidney Profile,” combining the eGFR and uACR to simplify test ordering for screening and diagnosis of kidney diseases that align with the NKF-ASN Task force recommendations. Additional resources developed for the laboratory community included technical summaries of the tests for ordering clinicians, validation tables for implementation of eGFR 2021 CKD EPI creatinine equation, and suggested results report messaging. National implementation efforts across the clinical laboratory community were further augmented by the official endorsement of the new race-free equation by the US Pathology and Laboratory Society Leadership. Lastly, the NKF Laboratory Working Group published practical guidance for U.S. clinical laboratories to implement the recommendations of the NKF-ASN Task Force in Clinical Chemistry. Hyperlink:

<https://academic.oup.com/clinchem/article/68/4/511/6463626> These efforts will ultimately improve comparison of test results between laboratories, increase early recognition of the disease, and promote patient awareness of the condition.

NKF and ASN agree with AHRQ's list of mitigation strategies and pursued the "removing race or ethnicity input variable from the algorithm" option. Further, NKF and ASN look forward to collaborating with additional medical associations, specialty societies, and patient groups to promote stakeholder awareness, especially patients, of potential risk associated with race algorithms.

Future Directions: Kidney Donor Risk Index/ Kidney Donor Profile Index and Cystatin C Implementation

Building on the work of the NKF-ASN Task Force, in December 2022, the HRSA OPTN, which is operated by the United Network for Organ Sharing (UNOS), finalized a policy to modify kidney transplant waitlist waiting times for Black transplant candidates affected by the race-based eGFR calculation.ⁱ NKF and ASN requested this important change and welcomed its announcement as a crucial step towards ensuring equity in access to kidney transplant. As described by Mohottige et al, this “restorative process was expressly intended to repair damage done by historical race-based practices.”ⁱⁱ

More urgent work remains to remove the inappropriate use of race throughout kidney medicine, particularly regarding kidney transplantation. The Kidney Donor Risk Index (KDRI) is an estimate of the relative risk of post-transplant kidney graft failure (in an average, adult recipient) from a particular deceased donor compared to a reference

donor and is used to predict deceased donor organ quality. Problematically, one of the 10 factors used to calculate KDRI, and a related measure—the Kidney Donor Profile Index (KDPI)—is race/ethnicity: KDRI and KDPI downgrade the estimated quality of a kidney if the donor was Black.ⁱⁱⁱ

KDPI is one of the core components OPTN uses to guide kidney allocation nationwide, and transplant professionals use it to guide their decision-making when considering organs offered on behalf of their wait-listed patients.^{iv} (Kidneys with a low KDPI score are offered to patients with the longest expected survival. However, as many as 60% of kidneys assigned a high KDPI score go unused even though data indicate that patients on dialysis would have better outcomes if those higher KDPI kidneys were accepted on their behalf.^v

Thus, the continued use of race in KDPI has significant negative implications for all wait-listed kidney patients: the race-based equation erroneously devalues the quality of organs from Black patients, making them less likely to be accepted by a surgical team and transplanted into patients who would benefit (as well as unnecessarily contributing to overall organ nonuse). Such practices may discourage individuals from participating in a kidney donation program.

The misuse of race in KDPI has even more profound implications for Black patients who are on the kidney wait list. Black patients are more likely to match with kidneys from Black deceased donors due to ABO blood group and HLA compatibility factors. Correcting (and appropriately increasing) the KDPI scores for kidneys from Black donors should increase the overall transplant rate for Black patients.^{vi} This goal is tremendously important, since Black patients are currently transplanted at a significantly lower rate than patients from other racial/ethnic groups despite being 3 times more likely to experience end stage kidney disease.^{vii}

Since 2021, ASN and NKF have requested that OPTN remove race from KDRI as expeditiously as possible, reiterating the task force’s conclusion that race has no place in clinical algorithms and offering to support this critical, time-sensitive effort in any way.^{viii}, ^{ix} Hyperlink: <https://www.asn-online.org/policy/webdocs/23.2.23ASN-NKFKDRIOPTNLetter.pdf> NKF and ASN encourage AHRQ to support HRSA and OPTN in any possible way in this important effort, including to help ensure the removal of race from KDRI/KDPI happens as expeditiously as possible. This challenge has received increasing attention from leading researchers and policymakers, such as the co-authors of several recent articles in the *Journal of the American Medical Association*, who assert that “KDPI in its current form is not fit to guide kidney allocation,” and the US House of Representatives Committee on Ways and Means Subcommittee on Health, which found that KDRI “could unnecessarily diminish Black kidney donors.”^x, ^{xi}, ^{xii}

The Ways and Means Subcommittee on Health issued this comment as part of a final majority staff report titled *Fact Versus Fiction: Clinical Decision Support Tools and the*

(Mis)Use of Race, which was the culmination of a monthslong investigation into the use of numerous race-based algorithms and specialty societies' efforts to address them. The subcommittee requested that ASN address the use of race in eGFR; the society's complete response to the committee is available at <https://www.asn-online.org/policy/webdocs/20.9.25ASNResponsetoChairmanNealreRaceandeGFR.pdf>. Moreover, in meetings with subcommittee staff leading the investigation, ASN also surfaced the problematic use of race in the KDRI/KDPI formulas, highlighting the need to tackle this instance of inappropriate use next.

Gratified to see the OPTN Minority Affairs Committee (MAC) consider the issue of the misuse of race in KDRI during its February 2023 meeting, NKF and ASN were pleased to have the opportunity to sit in on the meeting. OPTN leadership have signaled a commitment to addressing this issue through the OPTN policymaking process, a move that our two organizations celebrate and support. NKF and ASN will continue to make every possible effort to bolster and help expedite OPTN's work to address race in KDRI, including by sharing insights and lessons learned from NKF and ASN's own efforts to remove race from the eGFR equation.

Conclusion: Work to Be Done

A limitation that currently impedes progress in more widespread implementation of the CKD EPI combined is the availability of cystatin C measurement in laboratories. This challenge is a compounded effect from lower rates of utility by nephrologists due to lack of availability, and subsequently the cystatin C assays are more expensive, a circumstance that could be alleviated with higher rates of usage. To mitigate this problem further, education for nephrologists and primary care physicians is needed to avoid further delays in adoption, as well as to mitigate variation in clinical outcomes and impacts on care delivery.

At this time, the kidney community has begun work on the impact of healthcare algorithms on racial and ethnic disparities that affect people with and at risk for kidney diseases. The algorithms themselves are not the sole contributor to health inequities, and NKF and ASN are both committed to furthering efforts to achieving equity and justice in healthcare. NKF and ASN acknowledge that many simultaneous changes to the current kidney health ecosystem must occur urgently to achieve the goal of health equity for all patients. It is incumbent upon our organizations, other patient and health professional groups, policymakers, and other entities with a role in kidney health to relentlessly highlight opportunities for improvement in health equity and work as expeditiously as possible to achieve them.

NKF and ASN stand ready to work with AHRQ on this important mission. If you have questions, please contact NKF Quality and Regulatory Affairs Director Ivory Harding at ivory.harding@kidney.org and ASN Regulatory and Quality Officer David L. White at dwhite@asn-online.org.

Sincerely,



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ⁱ <https://optn.transplant.hrsa.gov/policies-bylaws/a-closer-look/waiting-time-modifications-for-candidates-affected-by-race-inclusive-egfr-calculations/for-professionals-faqs-about-egfr-waiting-time-modifications/>

ⁱⁱ https://jamanetwork.com/journals/jama/fullarticle/2802100?guestAccessKey=0dfe2458-b5f9-4453-88ca-918e1321c8e0&utm_source=silverchair&utm_medium=email&utm_campaign=article_alert-jama&utm_content=olf&utm_term=022723

ⁱⁱⁱ https://optn.transplant.hrsa.gov/media/1512/guide_to_calculating_interpreting_kdpi.pdf

^{iv} Ibid.

^v Massie AB, Luo X, Chow EK, Alejo JL, Desai NM, Segev DL. Survival benefit of primary deceased donor transplantation with high-KDPI kidneys. *Am J Transplant.* 2014;14(10):2310-2316. doi:10.1111/ajt.12830

^{vi} https://jamanetwork.com/journals/jama/fullarticle/2802101?guestAccessKey=10e49e49-c4b6-4812-ae3f-472a1a70f4ec&utm_source=silverchair&utm_medium=email&utm_campaign=article_alert-jama&utm_content=olf&utm_term=022723

^{vii} *JAMA Netw Open.* 2021;4(1):e2034630. doi:10.1001/jamanetworkopen.2020.34630

^{viii} *JASN* 32: 2987–2989, 2021. doi: <https://doi.org/10.1681/ASN.2021091284>

^{ix} <https://unos.org/wp-content/uploads/UNOSGR-2022.06.23-NKF-and-ASN-Letter-Thanking-OPTN-eGFR.pdf>

^x https://jamanetwork.com/journals/jama/fullarticle/2802101?guestAccessKey=10e49e49-c4b6-4812-ae3f-472a1a70f4ec&utm_source=silverchair&utm_medium=email&utm_campaign=article_alert-jama&utm_content=olf&utm_term=022723

^{xi} https://jamanetwork.com/journals/jama/fullarticle/2802100?guestAccessKey=0dfe2458-b5f9-4453-88ca-918e1321c8e0&utm_source=silverchair&utm_medium=email&utm_campaign=article_alert-jama&utm_content=olf&utm_term=022723

^{xii} Fact Versus Fiction: Clinical Decision Support Tools and the (Mis)Use of Race. House Committee on Ways and Means Majority Staff Report. October 2021. <https://democrats-waysandmeans.house.gov/sites/democrats.waysandmeans.house.gov/files/documents/Fact%20Versus%20Fiction%20Clinical%20Decision%20Support%20Tools%20and%20the%20%28Mis%29Use%20of%20Race%20%282%29.pdf>