



**Article:**

Caroline E. Franks and Mitchell G. Scott

*On the Basis of Race: The Utility of a Race Factor in Estimating Glomerular Filtration*

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**Guest:**

Dr. Franks is a clinical chemistry fellow at the Washington University School of Medicine in St. Louis in the Department of Pathology and Immunology. Dr. Scott is the Professor in the same department at Washington University and is the Co-Medical Director of Clinical Chemistry at Barnes-Jewish Hospital in St. Louis.

Randy Kaye:

Hello, and welcome to this edition of JALM Talk from *The Journal of Applied Laboratory Medicine*, a publication of the American Association for Clinical Chemistry. I'm your host, Randy Kaye.

The Glomerular Filtration Rate or GFR is a value used widely in the clinical setting to detect and monitor kidney dysfunction. GFR also serves as a prognostic tool for the staging of chronic kidney disease. GFR is commonly estimated, rather than directly measured, using estimation equations that use lab results of biomarkers such as creatinine. Equations to estimate eGFR commonly use a race multiplication factor for Black individuals. However, the evidence supporting this practice has come into question.

A review article in the January 2021 JALM special issue on Health Disparities discusses the history and evidence for race-based GFR equations and assesses the appropriateness and clinical impact of this practice. The authors of the review article are Dr. Caroline Franks and Dr. Mitchell Scott. Dr. Franks is a clinical chemistry fellow at the Washington University School of Medicine in St. Louis in the Department of Pathology and Immunology. Dr. Scott is the Professor in the same department at Washington University and is the Co-Medical Director of Clinical Chemistry at Barnes-Jewish Hospital in St. Louis. Both Doctors Franks and Scott are joining us for this podcast.

Welcome Doctors. First question is: I think we can all agree on the importance of this topic and bringing race to the forefront of healthcare discussions; What led you to write this review?

Mitchell Scott:

Well, I've been doing the renal physiology, renal testing in the clinical chemistry lab lecture for our residents and fellows for over 30 years. And I incorporated the eGFR equation to estimate GFR in around 2002 when the publications came out and everybody started using it.

But at the same time, when I include this in my sessions, I raise some of the questions about eGFR including the use of

a race factor and I make the argument that race is not binary. The best example I can give is Barack Obama. Is he Black or is he White, which factor do you use? And at the Annual Meeting in 2019, there was a session on using race factor to estimate GFR and I raised this issue again. And I'm assuming that Dina Greene, who is one of the Associate Editors of JALM, saw me and shortly thereafter invited me to write a review on the use of race in eGFR for the January 21 special issue that focuses on inequities in health care.

Well, that was July of 2019. In July of 2019 Caroline was a first-year fellow and I guess she appreciating the fact that in my lecture I was getting up on a soapbox and saying that this may not be the wisest thing to do, because again, race is not binary. She became very interested in the topic, started doing some research on her own into why this factor exists in the equations to estimate GFR, and about the same time Dina Greene gave me a call and invited me to write a review.

So I said, "Caroline, you seem intrigued by this, you want to write a review article?" From there, Caroline took it on very vigorously, did an outstanding job of writing the first draft of the review (which required very little editing on my part), and the result of that work is in the January 21 issue of JALM, and I think raises some very good questions about the use of this race factor and does it introduce inequities in healthcare based upon race.

So that's how it started and I'm going to let Caroline take it from here because she now knows more about this than I do.

Caroline Franks:

Thanks Dr. Scott. So after I attended Dr. Scott's lecture I actually dug deeper into the history of race-based medicine. And I discovered just how little is incorporated into med student, resident, and fellow education, especially in regard to healthcare inequity. And as laboratorians it's our job to ensure that we provide the most accurate test results to promote patient outcomes.

And when I looked at the history of race-based eGFR equations, I felt strongly that we were not doing this for Black patients.

And so, in addition to writing this review, I shared a grand rounds talk on this topic within our department that actually catalyzed the collaboration between lab medicine and nephrology to change the way that we report eGFR. We were able to remove race-based reporting within Barnes-Jewish Hospital, and we are currently working to remove race-based reporting on a system-wide level.

It's incredibly important to me to be able to utilize my expertise to promote healthcare equity for all, and to be able

to see the immediate impacts of our efforts has been quite rewarding.

Randye Kaye: Well, your article mentions that the first estimated GFR equation to include a race factor came from the Modification of Diet in Renal Disease or MDRD study, and this study identified race as an independent predictor of higher GFR. What was the basis of this finding?

Caroline Franks: So in the first publication of the MDRD study equation by Levey et al in 1999, the authors found that Black individuals had increased serum creatinine as compared to White individuals within their study population. The authors then go on to support this claim for the broader population of all Black individuals by stating that previous studies had shown that Black persons have greater muscle mass as compared to White persons. So as a result, you would expect to see increased serum creatinine.

However, if you take a look at the publication that the authors referenced, you'll find three articles dated from 1977 to 1990 that certainly do not provide such well-defined conclusions.

The first study, published in 1977, looked at serum electrolytes in 47 age-matched White and Black individuals and found that the Black individuals had significantly higher total body calcium, phosphorus, sodium chloride and potassium.

The second study, published in 1978, found that 99 Black children from Bogalusa, Louisiana had significantly less body fat than White children with moderately increased body densities.

And the third study, published in 1990, which sought to assess creatine kinase concentrations in 30 Black male healthy hospital workers, found that Black individuals had significantly higher creatine kinase versus age, sex, and bodyweight matched White individuals, but they found no correlation with lean body mass.

So as a take away from these three studies, which by the way had a total n of 176 individuals, or if we include the MDRD study cohort 373 individuals, do we really mean to say that all Black individuals will have increased muscle mass? This is a generalization with significant clinical consequences, and I would encourage clinicians and laboratorians to take a look at other equations and clinical algorithms that incorporate race as well, to ensure that we are not promoting racial healthcare disparities.

Randye Kaye: Thank you. So the MDRD equation as well as the more recently established CKD-EPI equation, they are commonly

used in clinical practice. In both of these equations a race factor is incorporated by characterizing patients as either Black or White/other, now how exactly is this implemented in the clinical setting?

Caroline Franks: That is a great question with an answer that's not so clear, which highlights one of the biggest challenges in implementation of race-based equations in the clinic.

For example, as Dr. Scott mentioned earlier, let's pretend for a minute that you are past President Barack Obama's nephrologist. Would you recommend the use of race factor for calculation of his eGFR? His father is Black African and his mother is White European; how do we assess the appropriateness of a race factor for Black individuals in diverse mixed patient population? And Obama is not unique in his mixed racial background. If you look at the United States census population projections from the 2010 census, you'll find that the race category of "two or more races" is projected to increase more than any other race category by over 120% over the next 50 years. So how do we accurately implement use of race factor in this patient population?

Another challenging aspect of implementing race-based equation is the inherent necessity for conversations between clinicians and patients. Perhaps a clinician understands that a conversation is necessary to validate that a patient identifies as being a Black race, but potentially a clinician assumes just by looking at skin color that a patient is Black incorrectly and then negatively impacts the care that that patient received for the duration of their time within the hospital system.

It's very tricky and subjective and you know, even when a patient is able to self-report their own race, we have to understand that race is a social construct without biological basis. Maybe sometime in the future we will be able to quantify ethnicity by genome analysis to generate personalized lab data, but unfortunately that day is not yet here.

Randy Kaye: Well, you raised some very, very important questions. Suppose a clinician decides to use the race factor for a Black individual who has low or low-to-normal muscle mass, what could be potential consequences or clinical impacts of interpreting the estimated GFR in this type of scenario?

Caroline Franks: Great question. The clinical consequences of overestimating GFR in any patient can be absolutely detrimental and sometimes even fatal. So when the clinic eGFR is used as a single value to make a number of medical decisions, this ranges from assessment of antibiotic and NSAID dosage to evaluation of radiological study safety.

So if eGFR is overestimated due to use of race factor, patients could potentially receive increased doses of medication and radiation leading to further kidney damage. Even more importantly eGFR is used to determine when patients receive access to nephrology referrals, which is recommended at eGFR is if less than 30 mils per minute, and access to transplant wait lists, which isn't recommended until eGFR is less than 20 mils per minute.

So perhaps the most sinister consequence of all is that the use of race factor may prevent Black patients from becoming eligible for transplant. And this actually brings a bigger issue to light and that is the issue of using eGFR values as a single data point to make vital clinical decisions.

In a fantastic letter written by Dr. Greg Miller, published recently in *Clinical Chemistry*, Miller quantify the uncertainty in eGFR at a given serum creatinine value based on data from the original CKD-EPI publication. And what he found was that the uncertainty in any given eGFR measurement is much greater than the 16% difference due to a race factor.

For example, in an assumed 50-year-old male patient with a serum creatinine of 1.5 mg/dL, eGFR for a non-African-American is 54 mils per minute and in an African-American is 62 mils per minute. But if you account for uncertainty the confidence intervals for each of those patients range from 28 to 79 mils per minute in non-African-Americans and 34 to 89 mils per minute in African-Americans.

So essentially in a 50-year-old male patient with a serum creatinine of 1.5 mg/dL, CKD staging could range from Stage G2 to Stage G4 each of which has vastly different prognoses and therapies.

And so in addition to questioning the race factor, we should also be asking why such an imprecise singular value is being regularly used to make critical clinical decisions.

Randye Kaye: Thank you. Wow! These are quite the issues. So considering these issues do you have recommendations as to how the estimated GFR should be reported by clinical laboratories? What current clinical guidelines recommend, and could these guidelines be changing in the future?

Mitchell Scott: Current guidelines are to estimate GFR using CKD-EPI equation and to use the race factor of 1.16 for African-Americans. However that is under very deep discussion within the nephrology community. There will be -- and in fact it's still open for public comment -- there will be a revised recommendation coming soon from the National Kidney Foundation and American Society of Nephrology. And I think

we may want to consider using alternative methods that don't depend on lean muscle mass since there is no easy way to estimate lean muscle mass other than an MRI. Cystatin C is one potential marker of GFR that is not dependent on muscle mass and is readily available; equations to estimate GFR are available with Cystatin C.

But it's far more expensive than creatinine, and creatinine is done on every sample for which a BMP (Basic Metabolic Panel or complete metabolic panel) is ordered.

So I don't think it's going to go away. Hopefully, there will be more research to see what differences may exist between different ethnicities. I mean this equation says nothing about what to do with Hispanic or Asian ethnicities.

So there's more research to be done; revised guidelines are coming soon and we'll just have to see where it goes.

Caroline Franks: So I agree with everything that Dr. Scott has said, and I just want to summarize that the key take-home is that race is not an accurate indicator of muscle mass and therefore serum creatinine. So as Dr. Scott mentioned, there certainly will be changes to clinical guidelines coming soon regarding the use of race, but what exactly those changes will be is still currently unknown.

Randye Kaye: All right. Well both of you thank you so much for your time today for joining us.

Mitchell Scott: You are welcome.

Caroline Franks: Thanks.

Randye Kaye: That was Doctors Caroline Franks and Mitchell Scott from the Washington University School of Medicine describing their JALM Review Article "On the Basis of Race: The Utility of a Race Factor in Estimating Glomerular Filtration." Thanks for tuning into this episode of JALM Talk. See you next time and don't forget to submit something for us to talk about.