



PRESS RELEASE

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HOW WOULD ELIMINATING RACE-BASED ADJUSTMENTS IN ESTIMATES OF KIDNEY FUNCTION IMPACT CLINICAL TRIALS?

Such adjustments may affect the inclusion of participants in kidney disease trials, as well as the trials' results.

Highlights

- In an analysis of data from a recent clinical trial, researchers found that removing a race-based adjustment in the estimation of individuals' kidney function had a small but potentially important impact on the inclusion of participants, with differing effects on Black and non-Black participants.
- Removal of the race-based adjustment also influenced inclusion parameters such as participants' severity of kidney function impairment at baseline as well as their risk of developing cardiovascular- and kidney-related outcomes.

Washington, DC (January 21, 2022) — Considerable controversy surrounds race-based algorithms in medicine—such as an adjustment for Black race in equations that estimate individuals' kidney function. A new study in *CJASN* has examined the impact of changes to these equations on the inclusion of Black participants in kidney disease-related clinical trials, and on the results of such trials.

Current methods for estimating an individual's kidney function—what's known as a patient's estimated glomerular filtration rate (eGFR)—are derived from serum creatinine levels. The most commonly used eGFR equation—the 2009 CKD-Epi equation—includes an adjustment for Black vs. non-Black race, resulting in higher eGFR values for a Black patient compared with a non-Black patient. Because race is a social and not a biological construct, however, several healthcare institutions no longer report eGFR with an adjustment for Black race, and ASN and the National Kidney Foundation have endorsed the idea that race modifiers should not be included in equations to estimate kidney function.

“Two solutions have been suggested. The first was the use of 2009 CKD-Epi equation without the race coefficient. More recently ASN recommended use of a new completely

recalculated equation, the 2021 CKD-Epi creatinine equation, that does not include race and that redistributes the coefficients to more equitably distribute any inequalities in the accuracy of estimates across racial categories,” said lead author David Charytan, MD, MSc, of NYU Grossman School of Medicine.

Dr. Charytan and his colleagues designed a study to evaluate the impact of including vs. excluding race in eGFR equations on screening, recruitment, and outcomes of clinical trials. The team evaluated the inclusion and outcomes of participants in the CREDENCE trial, which randomized individuals with type 2 diabetes and chronic kidney disease to canagliflozin or placebo, after calculating eGFR using the 2009 CKD-Epi with and without a race-specific coefficient or the 2021 CKD-Epi equation that contains parameters for age, sex, and serum creatinine, but does not contain a coefficient for race.

Among the major findings:

- Among randomized participants, recalculation of screening eGFR using the 2009 CKD-Epi equation without a race-specific coefficient had no impact on the likelihood of non-Black participants meeting inclusion criteria to enroll in the trial but would have excluded 10% of randomized Black participants for low eGFR.
- Use of the 2021 CKD-Epi equation would have excluded 4% of Black participants for low and 0.4% for high eGFR, as well as 0.7% and 7% of non-Black participants for low and high eGFR, respectively.
- A high proportion of trial endpoints (cardiovascular- and kidney-related outcomes) in Black participants occurred in individuals who would have been excluded following recalculation using the race-free 2009 CKD-Epi equation but not with the 2021 CKD-Epi equation.
- Cardiovascular and kidney treatment effects remained consistent across eGFR categories following recalculation with either equation.

“Our analysis of CREDENCE demonstrates that removing the race-specific coefficient in the estimation of eGFR has a small but potentially important impact on the inclusion of participants in kidney disease trials. We also found that there were small effects on the severity of kidney function impairment at baseline and the risk of developing cardiovascular and kidney outcomes among enrolled participants after eGFR recalculation,” said Dr. Charytan. “These effects should be considered in terms of interpretation and design of clinical trials as we move to wider implementation of the new equation.”

Study authors include David M. Charytan, MD, MSc, Jie Yu, MD, PhD, Meg J. Jardine, MBBS, PhD, Christopher P. Cannon, MD, Rajiv Agarwal, MD, George Bakris, MD, Tom Greene, PhD, Adeera Levin, MD, Carol Pollock, MBBS, PhD, Neil R. Powe, MD, MPH, MBA, Clare Arnott, MBBS(Hons), PhD, and Kenneth W. Mahaffey, MD.

Disclosures:

D. Charytan has personal fees or fees paid by Janssen Pharmaceuticals to the Baim Institute for work on the CREDENCE trial steering committee. He has received consulting fees from Amgen, Eli Lilly, Fresenius, Gilead, Medtronic/Covidien, Merck, Novo Nordisk, Zoll, AstraZeneca, Merck, PLC Medical and Allena Pharmaceuticals, and has received research support from Medtronic and Amgen.

J. Yu is an employee of the George Institute.

M.J.Jardine is supported by a Medical Research Future Fund Next Generation Clinical Researchers Program Career Development Fellowship; is responsible for research projects that have received unrestricted funding from Amgen, Baxter, CSL, Eli Lilly, Gambro, and MSD; has served on advisory boards sponsored by Akebia, Astra Zeneca, Baxter, Bayer, Boehringer Ingelheim, MSD and Vifor; serves on Steering Committee for trials sponsored by CSL and Janssen; serves on a Steering Committee for an investigator-initiated trial with funding support from Dimerix, spoken at scientific meetings sponsored by Janssen, Amgen, Roche and Vifor; with any consultancy, honoraria or travel support paid to her institution.

C.P. Cannon has received research grants from Amgen, Boehringer Ingelheim, Bristol-Myers Squibb, Daiichi Sankyo, Merck, Janssen, and Takeda; and has received consulting fees from Aegerion, Alnylam, Amarin, Amgen, AstraZeneca, Boehringer Ingelheim, Bristol-Myers Squibb, Corvidia, GlaxoSmithKline, Innovent, Eisai, Eli Lilly, Kowa, Merck, Pfizer, Regeneron, and Sanofi.

R. Agarwal was a member of the CREDENCE study steering committee and chair of its adjudication committee; is a member of the Steering committees of FIDELIO/FIGARO (Bayer); INNOVATE/PROTECT (Akebia); AMBER (Relypsa/Vifor) and chairs a data safety monitoring board (Chinook). He also serves as a consultant for AstraZeneca, Bayer, Boehringer Ingelheim, DiaMedica, Janssen, Merck, Reata, Relypsa, and Sanofi.

G. Bakris works for The University of Chicago Medicine. He is a Consultant for Merck, Bayer, Vascular Dynamics, KBP Biosciences, Ionis, Alnylam, and Astra Zeneca. He has research support and is on the Steering committee of trials for Bayer and Vascular Dynamics. He is the Editor of the American Journal of Nephrology.

T. Greene has received consulting fees from Janssen, Durect, and Pfizer; and research support from AstraZeneca and Boehringer Ingelheim.

A. Levin serves as a scientific advisor to Boehringer Ingelheim, AstraZeneca, and the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK); is on the data safety and monitoring board for NIDDK, Kidney Precision Medicine, University of Washington Kidney Research Institute Scientific Advisory Committee; and is funded by the Canadian Institute of Health Research and Kidney Foundation of Canada. She has received fees for time as CREDENCE National Coordinator from Janssen, directed to her academic team.

C. Pollock has received honoraria for serving on advisory boards and as a speaker for Merck Sharp & Dohme, AstraZeneca, and Boehringer Ingelheim/Eli Lilly.

N.R. Powe reports receiving honoraria from the Patient Centered Outcomes Research Institute, Robert Wood Johnson Foundation, University of Washington, Yale University, and Vanderbilt University; and serving as a scientific advisor for the Patient Centered Outcomes Research Institute, Robert Wood Johnson Foundation, University of Washington, Vanderbilt University, and Yale University. He is co-Chair of the NKF- ASN Task Force on Reassessing the Inclusion of Race in Diagnosing Kidney Diseases. C. Arnott is supported by a NSW Health EMCR Grant and a NHMRC/MRFF Priority Investigator Grant. She is an employee of the George Institute. Kenneth W. Mahaffey's financial disclosures can be viewed at <http://med.stanford.edu/profiles/kenneth-mahaffey>.

The article, titled "Potential Effects of Elimination of the Black Race Coefficient in eGFR Calculations in the CREDENCE Trial," will appear online at <http://cjasn.asnjournals.org/> on January 21, 2022, doi: 10.2215/CJN.08980621.

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