Race and eGFR: Lessons Learned and Future Directions

Amaka Eneanya, MD MPH, FASN
Adjunct Associate Professor of Medicine
University of Pennsylvania

Financial Disclosures

- None

Life Disclosures

- Black nephrologist
- Nigerian American
- Family history of kidney disease
- Studied Black sociology in college (Cornell University – go Big Red!)
- Received medical education from a Historically Black College/University (Meharry Medical College)
- Health equity researcher

Objectives

- Discuss racial/ethnic disparities in chronic kidney disease
- Review history of using race in estimating glomerular filtration rate equations and the pitfalls of this approach
- Describe national changes in standards and policies surrounding the use of eGFR in the management of kidney disease

Racial and ethnic disparities in chronic kidney disease

Racial disparities in CKD prevalence

Figure 2.1 Prevalence of CKD overall and by stage in older adult Medicare FFS beneficiaries, 2010-2020

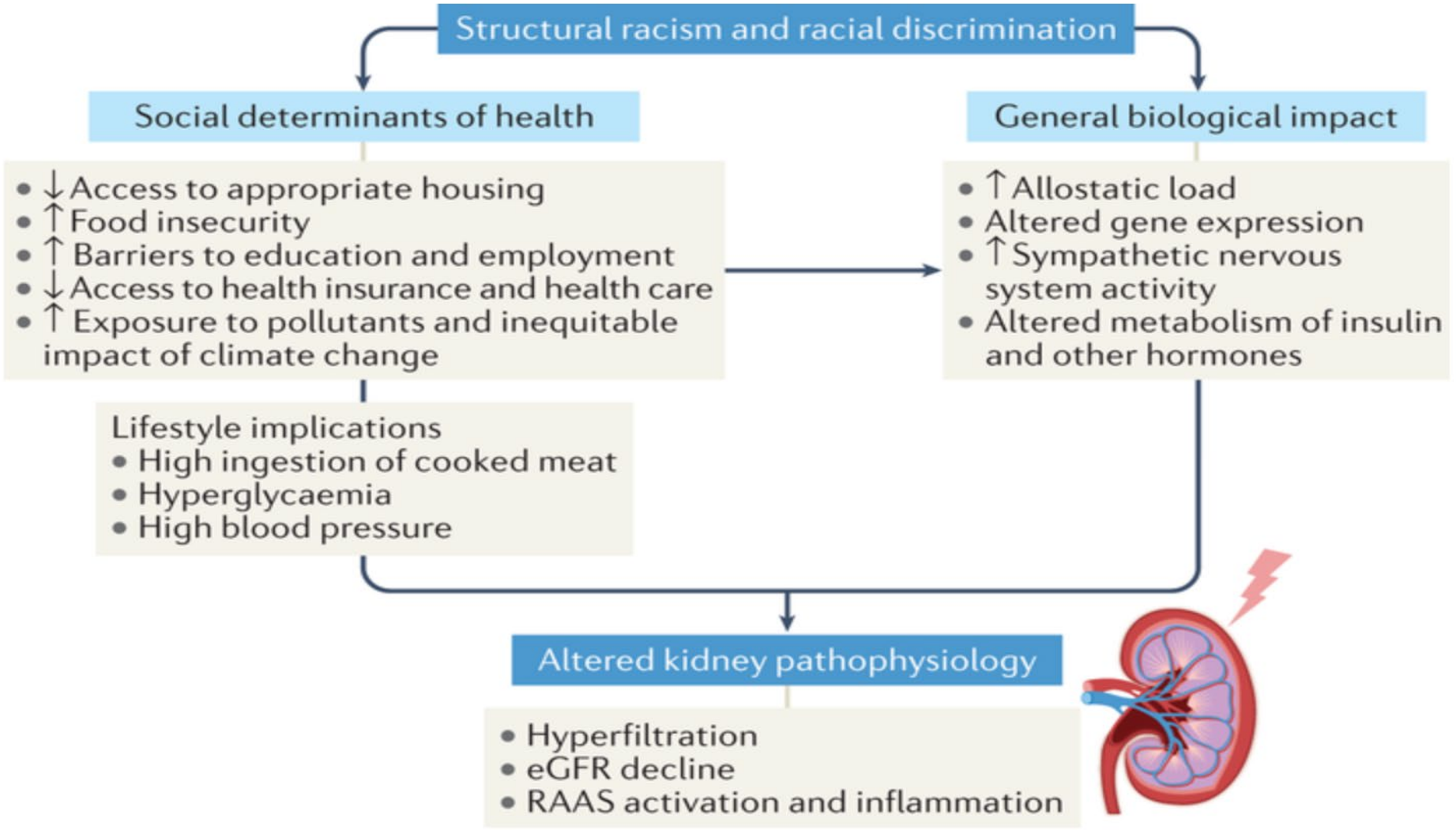
Data Source: 2022 United States Renal Data System Annual Data Report

Racial/ethnic disparities in CKD risk factors and outcomes

- The prevalence of diabetes is highest among Black individuals compared to other racial groups
  - Black and Hispanic individuals are diagnosed at younger ages compared to White individuals
- Black individuals have significantly higher rates of hypertension compared to White individuals
  - Hypertension control is less among Black and Hispanic individuals compared to White individuals
- Black individuals are less likely to receive nephrology care prior to starting dialysis compared to other racial groups
- Risk of developing kidney failure that requires dialysis or kidney transplantation
  - 4-fold higher in Black versus White individuals
  - 1.3-fold higher in Hispanic versus White individuals
- Black individuals are less likely to receive kidney transplantation compared to other racial groups

Eneanya ND et al. *Nature Rev Neph.* 2021; USRDS 2022

Racism and potential effects on kidney pathophysiology



Eneanya ND et al. *Nature Rev Neph.* 2021

History of eGFR equations

Race, eGFR, and clinical presentations

Black person

- 65 years old
- Male
- Serum Cr – 1.7 mg/dL
- CKD-EPI 2009 eGFR – 47 ml/min/1.73 m^2

Non-Black person

- 65 years old
- Male
- Serum Cr – 1.7 mg/dL
- CKD EPI 2009 eGFR – 41 ml/min/1.73 m^2

History of estimated glomerular filtration rate (eGFR)

- Racial differences in relationship between creatinine and measured GFR

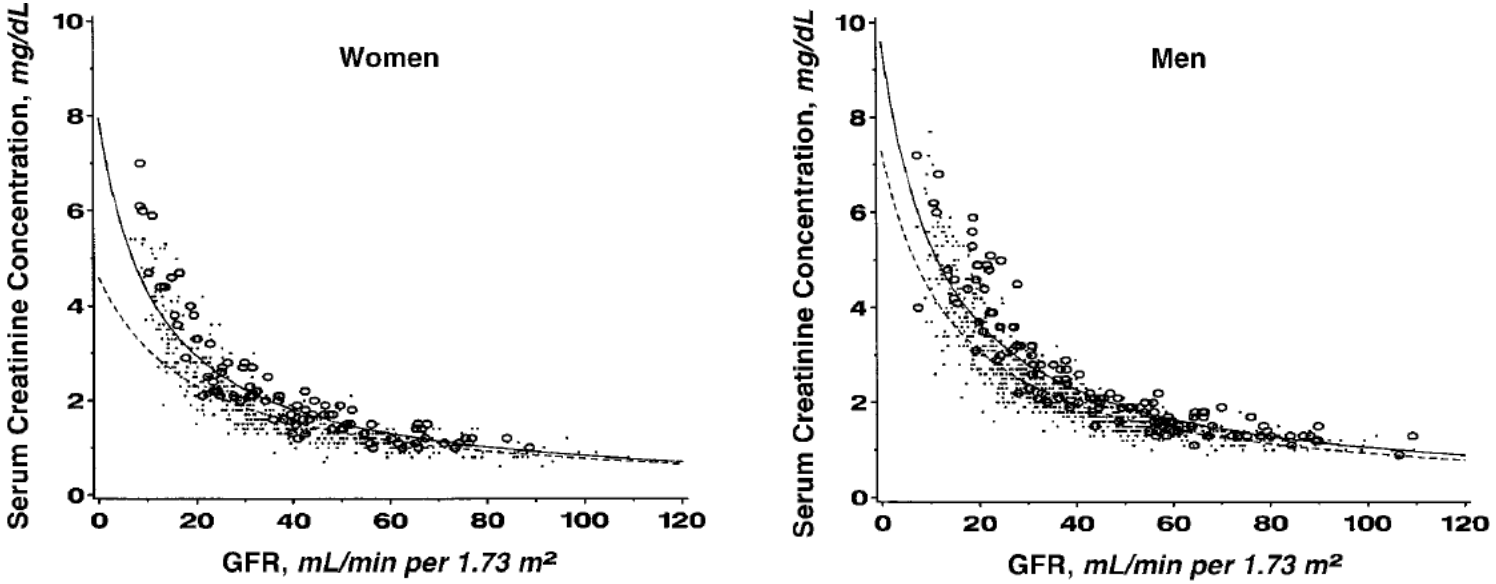


Figure 1. Relation of serum creatinine concentration to measured glomerular filtration rate (*GFR*). Each point represents the baseline measurement for one patient during the MDRD Study. Glomerular filtration rate was measured as the renal clearance of ^{125}I-iothalamate. Serum creatinine concentration (P_{cr}) was measured by using a kinetic alkaline picrate assay. Values are shown separately for men ($n = 915$) and women ($n = 586$) by ethnicity (white persons [*dashed lines and dots*] and black persons [*solid lines and circles*]). Regression lines were computed from the relation $1/P_{cr}$

Levey AS et al. *Ann Int Med*. 1999

Pitfalls of using race in eGFR equations

- Delay in referral to nephrology specialty care
  - Current KDIGO guidelines recommend referral once GFR < 30 ml/min/1.73m^2
- Delay in kidney transplantation evaluation
  - Kidney transplant waitlist time occurs once GFR ≤ 20 ml/min/1.73m^2
- Delay in referral for kidney failure care
  - Patient education
  - Vascular access creation
- Improper dosing of pharmacologic treatments
- No accommodation for patients of mixed race and ethnicity
- Lack of transparency with patients during shared decision-making

Eneanya ND et al. *JAMA*. 2019; KDIGO 2012

Bias in nephrology

- Race and eGFR equations
  - Clinicians are left to judge patient's physical characteristics to determine which eGFR calculation to use (explicit bias)
  - **Unclear how false beliefs regarding biological differences influences clinical care (implicit bias)**

Eneanya ND et al. *JAMA*. 2019

National changes in eGFR reporting standards and policies

ASN-NKF Task Force

NKF and ASN Form Joint Task Force to Focus on Use of Race in eGFR

August 24, 2020

In August of 2020, the National Kidney Foundation (NKF) and the American Society of Nephrology (ASN) formed a joint task force to focus on the use of race to estimate GFR. For more information, please read the joint NKF-ASN statement on "Establishing a Task Force to Reassess the Inclusion of Race in Diagnosing Kidney Diseases."

The NKF-ASN Task Force on Reassessing the Inclusion of Race in Diagnosing Kidney Disease, in consultation with an eGFR Advisory Board, plans to provide its initial recommendations in 2020. ASN and NKF leaders are very grateful to all those who are working on this effort, dedicating their time and expertise to ensure optimum patient care.

Co-chaired by Cynthia Delgado, MD, FASN, and Neil R. Powe, MD, FASN, the task force includes members with broad expertise, including (but not limited to) health and health care disparities, epidemiology and health services research, genetic ancestry, clinical chemistry, patient safety and performance improvement, pharmacology, and social sciences. The task force also includes two patients.

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

- Cynthia Delgado, MD, FASN, Cochair
- Neil R. Powe, MD, FASN, Cochair
- Mukta Baweja, MD
- Nilka Rios Burrows, MPH, MT
- Deidra C. Crews, MD, FASN
- Nwamaka D. Eneanya, MD , MPH, FASN
- Crystal A. Gadegbeku, MD, FASN
- Lesley Inker, MD
- Mallika L. Mendu, MD, MBA
- W. Greg Miller, PhD

ASN-NKF Task Force Update

- On September 23, 2021, “In the final report, the task force recommends:
  - Immediate implementation of the “2021 CKD-EPI equation” (refit without race)
  - National efforts to facilitate increased, routine, and timely use of cystatin C, especially to confirm eGFR in adults who are at risk for or have chronic kidney disease
  - Research on GFR estimation with new endogenous filtration markers and on interventions to eliminate race and ethnic disparities in kidney disease be encouraged and funded

Delgado C et al. *JASN*. 2021. Inker L et al. *NEJM* 2021.

New United Network of Organ Sharing (UNOS) Transplant Policies

- June 2022 – All US transplant centers are **prohibited** from using any race-based eGFR equation for kidney transplant listing

- January 2023 – All US transplant centers are **required** to review all Black patients on the kidney transplant waitlist and modify their waitlist time if a race-based eGFR equation was used for listing

The NEW ENGLAND JOURNAL of MEDICINE

MEDICINE AND SOCIETY

Debra Malina, Ph.D., *Editor*

Race Correction and the X-Ray Machine — The Controversy over Increased Radiation Doses for Black Americans in 1968

Itai Bavli, Ph.D., and David S. Jones, M.D., Ph.D.

On May 23, 1968, Howard Goldman, director of the New York Bureau of X-Ray Technology, acknowledged that x-ray technicians routinely exposed Black patients to doses of radiation that were higher than those White patients received.[1] This practice, which adhered to guidelines from

ingful biologic concept.[21] Despite this consensus, and despite recent attempts to mitigate the harmful effects of racial biases in medicine, race-based beliefs and practices, especially the use of racial categories, remain widespread.[8] The history of race adjustment for x-ray dosing reveals

Summary

- The prevalence of health inequities in nephrology is longstanding and driven by systemic factors in the healthcare system
- The misuse of race in science and clinical practice can lead to false beliefs about racialized biology and promote bias and disparate health outcomes
- New clinical guidelines and policies that center health equity are key to ensuring sustainable change in care

Contact

- Email: amakaeneanya@gmail.com
- Twitter: @AmakaEMD
- Instagram: @AmakaEMD

Race and eGFR: Implementation of race-free equations

Paul M. Palevsky, MD

Professor of Medicine, Critical Care Medicine and Clinical & Translational Science, University of Pittsburgh

Deputy Executive Director, VHA Kidney Medicine Program

Chief, Kidney Medicine, VA Pittsburgh Healthcare System

Disclosures

- Consultant: Janssen R&D, LLC
- Grant support: NIH/NIDDK; VA CSP
- Non-financial: Past-president and BOD member, National Kidney Foundation

NKF-ASN Task Force Recommendations

1. Immediate implementation of 2021 CKD-EPI eGFRcr equation refit without race
2. National efforts to facilitate increased, routine, and timely use of cystatin C
3. Research on GFR estimation with new endogenous filtration markers and on interventions to eliminate race and ethnic disparities should be encouraged and funded

Am J Kidney Dis. 2021; 78:103-115.

Getting from Recommendation to Action

Laboratory Engagement

CKD intercept

CKDIntercept: LABORATORY ENGAGEMENT PLAN

Leading the way to advance early diagnosis of chronic kidney disease

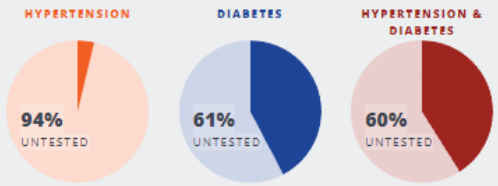
National Kidney Foundation, American Society for Clinical Pathology, Leading Laboratories and Clinical Laboratory Societies Unite to Diagnose Chronic Kidney Disease

This collaboration is believed to be the first to combine the resources and talents of leading clinical laboratory societies, multiple laboratory providers, and a patient advocacy group to advance improvements in CKD laboratory testing.

Many people with high blood pressure (hypertension) and diabetes are not receiving both tests necessary to detect and assess chronic kidney disease as recommended by clinical practice guidelines, despite these being the top two risk factors for developing chronic kidney disease.

The goal of this collaboration is to help standardize the tests used to detect CKD, improve comparison of test results between laboratories, increase early recognition of the disease and promote patient awareness of the condition.

LOW RATES OF ALBUMIN-CREATININE RATIO TESTING FOR CKD



Hypertension and diabetes are the top two risk factors for developing CKD, but many people with these conditions are not receiving recommended testing.

SOURCE: United States Renal Data System. 2016 USRDS annual data report: Epidemiology of kidney disease in the United States. National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, MD, 2016

Pathology Societies

STRONGERTOGETHER
AACC
ACLA American Clinical Laboratory Association
CLMA
NILA
Association of Pathology Chairs

Commercial Laboratories

ARUP LABORATORIES
Memorial Sloan Kettering Cancer Center
BioReference LABORATORIES
Quest Diagnostics
Enzo
SONIC HEALTHCARE
Sonora Quest Laboratories
LabCorp
MAYO CLINIC Mayo Medical Laboratories
TRICORE REFERENCE LABORATORIES
WESTPAC LABS

Health System Laboratories

VCU
BalladHealth
Henry Ford HEALTH SYSTEM
THE University of Vermont MEDICAL CENTER
Health Care
UVAHealth
U.S. Department of Veterans Affairs
Tufts UNIVERSITY

NATIONAL KIDNEY FOUNDATION®

Logical Observation Identifiers Names and Codes (LOINC codes)

LOINC

LOINC CODE
98979-8

LOINC STATUS
Prerelease

Special Use

This Special Use code has been developed in response to an urgent or emergent situation. This code is based on the most up to date information available at the time of its creation. It has undergone the normal QA terminology process. LOINC supports its use in the unique situation that resulted in its rapid creation. However, be aware that downstream users may not be ready to handle prerelease codes until they are published in an official release.

Long Common Name

Glomerular filtration rate/1.73 sq M.predicted [Volume Rate/Area] in Serum, Plasma or Blood by Creatinine-based formula (CKD-EPI 2021)

Term Description

Glomerular filtration rate (GFR) is considered the best overall index of kidney function; however measured GFR is not practical in the routine clinical setting. Estimated glomerular filtration rate (eGFR) is a suitable alternative and can be calculated for adults >= 18 years using an equation incorporating the patient's age, gender, and measured serum/plasma/blood creatinine only (eGFRcr) (this term) or both serum/plasma/blood creatinine and serum/plasma cystatin C (eGFRcr-cys) [LOINC: 98980-6]. The serum/plasma/blood creatinine value is based on a measurement procedure that is traceable to the isotope dilution mass spectrometry (IDMS) reference measurement procedure for creatinine. The 2021 CKD-EPI equations used for eGFRcr and eGFRcr-cys do not have a race term as does the older estimating equations that they replace. [https://www.nejm.org/doi/pdf/10.1056/NEJMoa2102953]

https://loinc.org/98979-8/

LOINC

LOINC CODE
98980-6

LOINC STATUS
Prerelease

Special Use

This Special Use code has been developed in response to an urgent or emergent situation. This code is based on the most up to date information available at the time of its creation. It has undergone the normal QA terminology process. LOINC supports its use in the unique situation that resulted in its rapid creation. However, be aware that downstream users may not be ready to handle prerelease codes until they are published in an official release.

Long Common Name

Glomerular filtration rate/1.73 sq M.predicted [Volume Rate/Area] in Serum, Plasma or Blood by Creatinine and Cystatin C-based formula (CKD-EPI 2021)

Term Description

Glomerular filtration rate (GFR) is considered the best overall index of kidney function; however measured GFR is not practical in the routine clinical setting. Estimated glomerular filtration rate (eGFR) is a suitable alternative and can be calculated for adults >= 18 years using an equation incorporating the patient's age, gender, and measured serum/plasma/blood creatinine only (eGFRcr) [LOINC: 98979-8] or both serum/plasma/blood creatinine and serum/plasma cystatin C (eGFRcr-cys) (this term). The serum/plasma/blood creatinine value is based on a measurement procedure that is traceable to the isotope dilution mass spectrometry (IDMS) reference measurement procedure for creatinine, and the serum/plasma/blood cystatin C value is based on a measurement procedure that is traceable to the certified reference material ERM-DA471/IFCC from the Joint Research Center of the European Commission. The 2021 CKD-EPI equations used for eGFRcr and eGFRcr-cys do not have a race term as does the older estimating equations that they replace. [https://www.nejm.org/doi/pdf/10.1056/NEJMoa2102953]

https://loinc.org/98980-6/

Laboratory Engagement

Laboratory Implementation of the NKF-ASN Task Force Reassessing the Inclusion of Race in Diagnosing Kidney Diseases

The National Kidney Foundation (NKF) and the American Society of Nephrology (ASN) Task Force on Reassessing the Inclusion of Race in Diagnosing Kidney Diseases has released its final report which outlines a new race-free way to diagnose this life-threatening illness. The report recommends the adoption of the eGFR 2021 CKD EPI creatinine equation that estimates kidney function without a race variable. The task force also recommended increased use of cystatin C combined with creatinine as a confirmatory assessment of kidney function.

We urge all laboratories nationwide to adopt this newly modified equation to estimate GFR so that we can move towards more a consistent method of diagnosing kidney diseases.

The NKF would like to thank its Laboratory Engagement Initiative Workgroup for their efforts to develop tools to support laboratories implementing this new approach to calculating eGFR.

1. Position Statement: U.S Pathology & Laboratory Society Leadership Endorse Use of CKD-EPI 2021 Race-free Equations for eGFR
2. eGFR summary for ordering clinicians
3. Not by Muscle, Race or Ethnicity: Practical use of Cystatin C to estimate GFR
4. eGFR Results Messages
5. eGFR 2021 CKD EPI creatinine equation that estimates kidney function without a race variable in NEJM paper
6. NKF-ASN Task Force final report
7. FAQs About GFR Estimates
8. Laboratory guidance for implementing CKD-EPI 2021 race-free eGFR equations
9. Patient information about kidney disease and eGFR testing

The Laboratory Engagement Initiative, which is comprised of the National Kidney Foundation in collaboration with the American Society for Clinical Pathology, the laboratory community, and clinical laboratory societies, has developed content and tools that are aimed at advancing earlier diagnosis of chronic kidney disease as well as improvements in CKD laboratory testing.

https://www.kidney.org/content/laboratory-implementation-nkf-asn-task-force-reassessing-inclusion-race-diagnosing-kidney

NATIONAL KIDNEY FOUNDATION®

Clinical Chemistry 68:4
511–520 (2022)

Special Report

National Kidney Foundation Laboratory Engagement Working Group Recommendations for Implementing the CKD-EPI 2021 Race-Free Equations for Estimated Glomerular Filtration Rate: Practical Guidance for Clinical Laboratories

W. Greg Miller,[a,*] Harvey W. Kaufman,[b] Andrew S. Levey,[c] Joely A. Straseski,[d] Kelly W. Wilhelms,[e] Hoi-Ying (Elsie) Yu,[f] J. Stacey Klutts,[g] Lee H. Hilborne,[b] Gary L. Horowitz,[c] John Lieske,[h] Jennifer L. Ennis,[i] James L. Bowling,[j] Mary Jane Lewis,[k] Elizabeth Montgomery,[k] Joseph A. Vassalotti,[l] and Lesley A. Inker[c]

Recognizing that race is a social and not a biological construct, healthcare professionals and the public have called for removal of race in clinical algorithms. In response, the National Kidney Foundation and the American Society of Nephrology created the Task Force on Reassessing the Inclusion of Race in Diagnosing Kidney Diseases to examine the issue and provide recommendations.

The final report from the Task Force recommends calculating estimated glomerular filtration rate (eGFR) without a race coefficient using the recently published CKD-EPI 2021 creatinine (cr) and creatinine-cystatin C (cr-cys) equations. The Task Force recommends immediately replacing older $eGFR_{cr}$ equations (MDRD Study and CKD-EPI 2009) with the new CKD-EPI 2021 equation.

Introduction

Glomerular filtration rate (GFR) is essential to many aspects of medical care, public health, and research. Clinical laboratories provide an important role in the assessment of GFR and diagnosis of kidney disease. Measuring serum creatinine along with an estimated glomerular filtration rate ($eGFR_{cr}$) is recommended as the first step in GFR evaluation by current clinical practice guidelines (1, 2). Confirmatory tests include serum cystatin C for calculation of eGFR alone or with creatinine ($eGFR_{cys}$ or $eGFR_{cr\text{-}cys}$, respectively) or measured clearances of creatinine or exogenous filtration markers (1, 2).

Serum creatinine may be ordered alone but most frequently it is ordered as part of the basic and compre-

SPECIAL REPORT

AACC/NKF Guidance Document on Improving Equity in Chronic Kidney Disease Care

Christina C. Pierre [a,b] Mark A. Marzinke,[c] Sofia B. Ahmed,[d] David Collister,[e,f] Jessica M. Colón-Franco,[g] Melanie P. Hoenig,[h,i] Thomas Lorey [j] Paul M. Palevsky,[k,l,m] Octavia Peck Palmer [n] Sylvia E. Rosas,[m,o,p] Joseph Vassalotti,[m,q] Cameron T. Whitley,[r] and Dina N. Greene [s,t,*]

Background: Kidney disease (KD) is an important health equity issue with Black, Hispanic, and socioeconomically disadvantaged individuals experiencing a disproportionate disease burden. Prior to 2021, the commonly used estimated glomerular filtration rate (eGFR) equations incorporated coefficients for Black race that conferred higher GFR estimates for Black individuals compared to non-Black individuals of the same sex, age, and blood creatinine concentration. With a recognition that race does not delineate distinct biological categories, a joint task force of the National Kidney Foundation and the American Society of Nephrology recommended the adoption of the CKD-EPI 2021 race-agnostic equations.

Content: This document provides guidance on implementation of the CKD-EPI 2021 equations. It describes recommendations for KD biomarker testing, and opportunities for collaboration between clinical laboratories and providers to improve KD detection in high-risk populations. Further, the document provides guidance on the use of cystatin C, and eGFR reporting and interpretation in gender-diverse populations.

Summary: Implementation of the CKD-EPI 2021 eGFR equations represents progress toward health equity in the management of KD. Ongoing efforts by multidisciplinary teams, including clinical laboratorians, should focus on improved disease detection in clinically and socially high-risk populations. Routine use of cystatin C is recommended to improve the accuracy of eGFR, particularly in patients whose blood creatinine concentrations

J Appl Lab Med epub 28 June 2023

March 2022 CAP Survey

Table 2. Results of US Laboratory Respondents by Type of Laboratory

Question	US laboratories, No. (%)	Results by type of laboratory, No. (%)			
		Hospital/medical center (academic)	Hospital/medical center (nonacademic)	Nonhospital laboratory	Physician office laboratory/clinic
1. Is your laboratory aware of the 2021 CKD-EPI equations for eGFR that do not include race adjustment factors?[a]					
Yes	2859 (76.9)	603 (80.1)	1503 (76.8)	554 (76.9)	199 (68.9)
No	859 (23.1)	150 (19.9)	453 (23.2)	166 (23.1)	90 (31.1)
Total	3718	753	1956	720	289
2. Has your laboratory adopted the 2021 CKD-EPI creatinine equation for eGFR reporting?[b]					
Yes	1124 (30.3)	241 (32.1)	568 (29.1)	248 (34.6)	67 (23.2)
No	2059 (55.5)	415 (55.3)	1116 (57.2)	356 (49.7)	172 (59.5)
Unsure	525 (14.2)	95 (12.6)	268 (13.7)	112 (15.6)	50 (17.3)
Total	3708	751	1952	716	289
3. When does your laboratory plan to adopt the 2021 CKD-EPI creatinine equation for eGFR reporting?[c]					
Before July 1, 2022	440 (21.6)	96 (23.6)	256 (23.2)	53 (15.0)	35 (20.7)
Between July 1 and December 31, 2022	218 (10.7)	47 (11.5)	125 (11.3)	36 (10.2)	10 (5.9)
2023 or later	45 (2.2)	10 (2.5)	23 (2.1)	9 (2.5)	3 (1.8)
Unsure	1187 (58.4)	227 (55.8)	644 (58.3)	219 (62.0)	97 (57.4)
Not applicable; do not plan to implement this equation	144 (7.1)	27 (6.6)	57 (5.2)	36 (10.2)	24 (14.2)
Total	2034	407	1105	353	169

Genzen JR, et al. JAMA 2022; 328: 2060-2062

2021 CKD-EPI eGFRcr
Adoption in Large National Laboratories

Lab	Date of Adoption
LabCorp	28 February 2022
Quest Diagnostics	11 July 2022
ARUP Labs	15 August 2022
Mayo Clinic Labs	23 August 2022

VA adopts race-free test to determine kidney health

Kidney disease is a silent killer, but with early detection and treatment, kidney failure can be prevented and lives can be saved. In 2020, the National Kidney Medicine Program for the Veterans Health Administration issued a national strategic plan to prevent kidney failure in Veterans by using a race-free kidney health screening test and best treatment practices.

Two screening tests are used to determine kidney health. One is a simple urine test and the other a blood test. The blood test is used to calculate how well the kidneys are cleaning or filtering waste products from the blood and is called the "eGFR," short for estimated glomerular filtration rate.

Past math formulas to calculate eGFR from blood tests required adjustment for race, but today's broadened understanding of race suggests benefits to using a race-free math formula instead.

All VA laboratories now use race-free formula

In early 2021, the VA Kidney Medicine Program and the Pathology & Laboratory Program established the plan for all VA laboratories to use the race-free eGFR formula.

The formula was developed by a panel of experts assembled by the American Society of Nephrology and the National Kidney Foundation, and was published in late 2021.

The requirement for all VA locations to be using the VA approved 2021 race-free eGFR formula by April 1, 2022, is in keeping with the VA Kidney Medicine Program's national strategic plan to improve the kidney health of all Veterans.

As the largest integrated national provider of kidney care in the United States, VA is also leading the way in meeting the goal of the Executive Order "Advancing American Kidney Health" (AAKH).

By Susan T Crowley is executive director for VA Kidney Medicine Program, Professor of Medicine (Nephrology), Yale University

Appears in:

Health

Topics in this story

Early detection kidney disease

Share this story

Published on Feb. 22, 2022
Estimated reading time is 1.3 min.
Views to date: 1,015

Summary

- Removal of race from the estimation of eGFR required a carefully organized implementation strategy
- Key components included:
  - Early engagement of the laboratory medicine community
  - Rapid release of new LOINC codes to allow use of the updated equation in EHRs
  - Multidisciplinary education
  - Patient education