What should we know about the last eGFR equations without “race”?

Pierre Delanaye, MD, PhD

Nephrology Dialysis and Transplantation

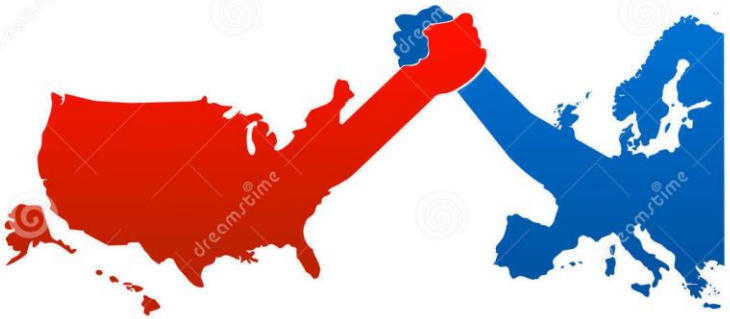
University of Liège

CHU Sart Tilman

Liège

BELGIUM

- Thanks for the invitation…
- But this is a very touchy topic, not because it is about "race"
- This is not only science
- Difference of perception between USA and Europe

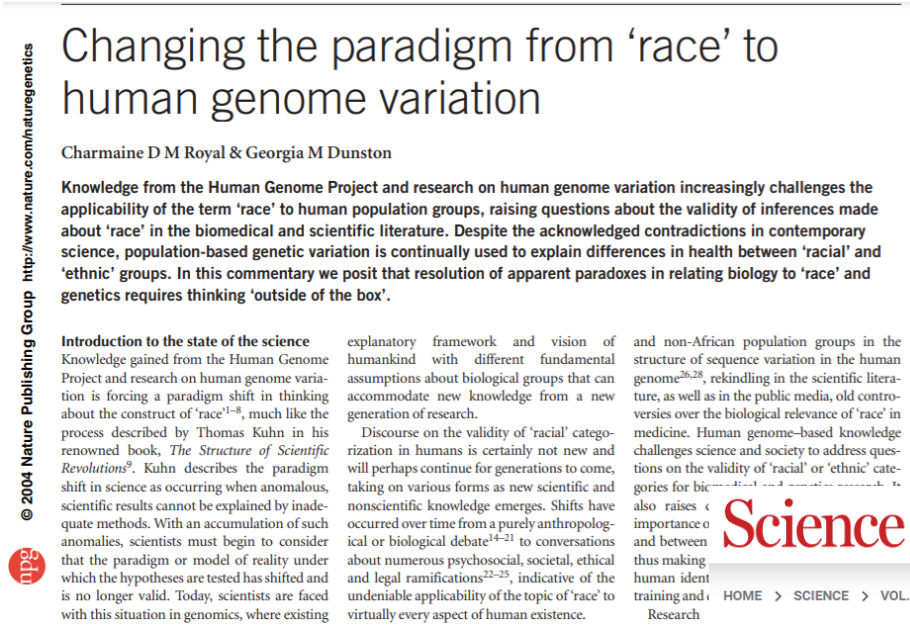


Not only science

- History
- Sociology
- Philosophy
- Politics
- Communication (politically correct, wokism, tokenism)

The word RACE

We all agree that race, from a scientific (genetic) point of view does not exist : we are all *Homo Sapiens*



Changing the paradigm from 'race' to human genome variation

Charmaine D M Royal & Georgia M Dunston

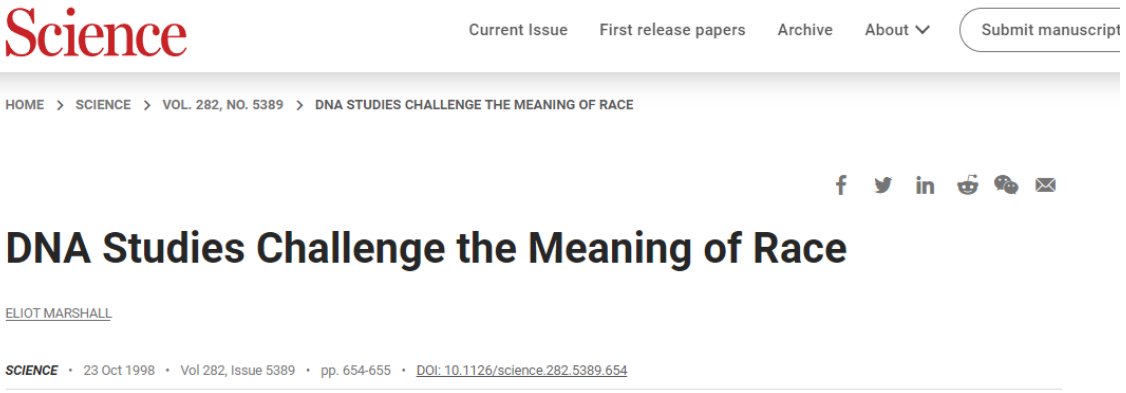
Knowledge from the Human Genome Project and research on human genome variation increasingly challenges the applicability of the term 'race' to human population groups, raising questions about the validity of inferences made about 'race' in the biomedical and scientific literature. Despite the acknowledged contradictions in contemporary science, population-based genetic variation is continually used to explain differences in health between 'racial' and 'ethnic' groups. In this commentary we posit that resolution of apparent paradoxes in relating biology to 'race' and genetics requires thinking 'outside of the box'.

Introduction to the state of the science

Knowledge gained from the Human Genome Project and research on human genome variation is forcing a paradigm shift in thinking about the construct of 'race'[1–8], much like the process described by Thomas Kuhn in his renowned book, *The Structure of Scientific Revolutions*[9]. Kuhn describes the paradigm shift in science as occurring when anomalous, scientific results cannot be explained by inadequate methods. With an accumulation of such anomalies, scientists must begin to consider that the paradigm or model of reality under which the hypotheses are tested has shifted and is no longer valid. Today, scientists are faced with this situation in genomics, where existing explanatory framework and vision of humankind with different fundamental assumptions about biological groups that can accommodate new knowledge from a new generation of research.

Discourse on the validity of 'racial' categorization in humans is certainly not new and will perhaps continue for generations to come, taking on various forms as new scientific and nonscientific knowledge emerges. Shifts have occurred over time from a purely anthropological or biological debate[14–21] to conversations about numerous psychosocial, societal, ethical and legal ramifications[22–25], indicative of the undeniable applicability of the topic of 'race' to virtually every aspect of human existence.

and non-African population groups in the structure of sequence variation in the human genome[26,28], rekindling in the scientific literature, as well as in the public media, old controversies over the biological relevance of 'race' in medicine. Human genome–based knowledge challenges science and society to address questions on the validity of 'racial' or 'ethnic' categories for bio
also raises
importance o
and between
thus making
human ident
training and
Research



Science

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HOME > SCIENCE > VOL. 282, NO. 5389 > DNA STUDIES CHALLENGE THE MEANING OF RACE

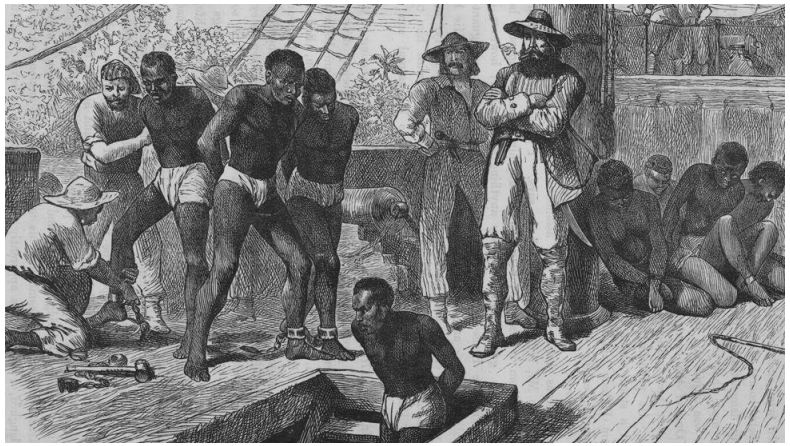
DNA Studies Challenge the Meaning of Race

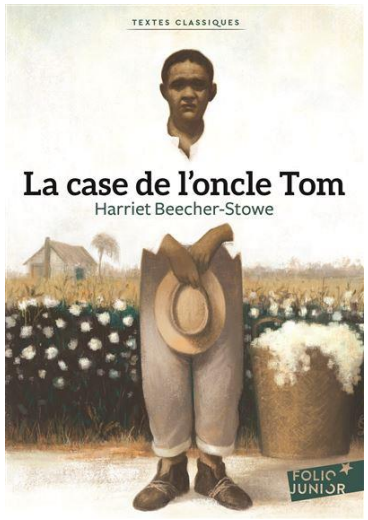
ELIOT MARSHALL

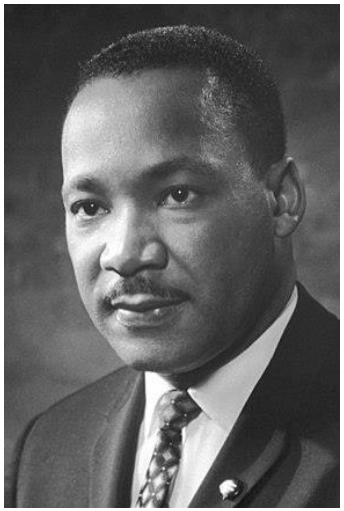
SCIENCE • 23 Oct 1998 • Vol 282, Issue 5389 • pp. 654-655 • DOI: 10.1126/science.282.5389.654

- In Europe, even using the word “race” in a scientific article could be considered as “racist”
- (but which alternative is semantically the best: ethnicity? ancestry?)
- In USA, this is a social categorization and the word “race” is used without restriction

Racism does exist in Europe and USA but it is not the same story







MDRD	$GFR = 175 \times (S_{Cr})^{-1.154} \times (Age)^{-0.203} \times (0.742 \text{ if female}) \times (1.212 \text{ if African American})$	+21%
CKD-EPI	$GFR = 141 \times \min(S_{Cr}/\kappa, 1)^{\alpha} \times \max(S_{Cr}/\kappa, 1)^{-1.209} \times 0.993^{Age} \times (1.018 \text{ if female}) \times (1.159 \text{ if African American})$	+16%

*S_{cr} is serum creatinine in mg/dL
κ is 0.7 for females and 0.9 for males
α is -0.329 for females and -0.411 for males
min indicates the minimum of S_{cr}/κ or 1
max indicates the maximum of S_{cr}/κ or 1

eGFR

VIEWPOINT

Reconsidering the Consequences of Using Race to Estimate Kidney Function

Nwamaka Denise Eneanya, MD, MPH
Renal-Electrolyte and Hypertension Division, Perelman School of Medicine, University of Pennsylvania, Philadelphia; and Palliative and Advanced Illness Research Center, Perelman School of Medicine, University of Pennsylvania, Philadelphia.

Estimated GFR equations are distinct because they assert that existing organ function is different between individuals who are identical except for race.

JAMA Published online June 6, 2019

- Race is a social construct rather than a biological one
- How is race defined?
- Problem of mixed people (Brazil)
- A 40 years old woman with creatinine at 3.0 mg/dL

CKD-EPI: 19 mL/min/1.73m² if non-Black vs 22 mL/min/1.73m² if Black => difference in referral to nephrologists, to be included in RCT, and to be wait-listed **for a kidney transplant (20 mL/min/1,73m²)**

REVIEWS

FEBRUARY 2022 | VOLUME 18

Check for updates

Health inequities and the inappropriate use of race in nephrology

Nwamaka D. Eneanya[1] ✉, L. Ebony Boulware[2], Jennifer Tsai[3], Marino A. Bruce[4], Chandra L. Ford[5], Christina Harris[6], Leo S. Morales[7], Michael J. Ryan[7], Peter P. Reese[1,8], Roland J. Thorpe Jr.[9], Michelle Morse[10], Valencia Walker[11], Fatiu A. Arogundade[12], Antonio A. Lopes[13] and Keith C. Norris[6]

Table 1 | **Potential implications of the removal of race from the 2009 CKD-EPI eGFR equation**

Clinical implication	eGFR threshold (ml/min/1.73 m²)	Estimated impact[a]	Additional considerations	Warranted future research
CKD diagnosis	<60	~ 1 million Black adults will be newly diagnosed with CKD	Potential for closer monitoring for CKD progression in a high-risk group	Racial disparities in early CKD diagnosis among Black adults
Referral to nephrologist	<30	An additional ~68,000 Black patients will have increased specialty evaluation	More aggressive control of cardiac and kidney failure risk factors	Time to referral for Black adults before and after removing the race coefficient
Eligibility for kidney transplant waiting list	≤20	An additional ~37,000 Black patients will have timely access to transplant evaluation	Timely access to optimal treatment for a high-risk population	Trends in proportion of transplants received among Black adults with kidney failure before and after removal of the race coefficient Time to transplant listing for Black adults before and after removal of the race coefficient

In-Depth Review

Are the Creatinine-Based Equations Accurate to Estimate Glomerular Filtration Rate in African American Populations?

Pierre Delanaye, Christophe Mariat,† Nicolas Maillard,† Jean-Marie Krzesinski,* and Etienne Cavalier‡*

Summary

Regarding the high prevalence of African American patients with ESRD, it is important to estimate the prevalence of early stages of chronic kidney disease in this specific population. Because serum creatinine concentration is dependent on muscular mass, an ethnic factor has to be applied to creatinine-based equations. Such ethnic factors have been proposed in the Modification of Diet in Renal Disease (MDRD) study equation and in the more recent Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equations. This review analyzes how these correction factors have been developed and how they have, or have not, been validated in external populations. It will be demonstrated that the African American factor in the MDRD study equation is accurate in African American chronic kidney disease (CKD) patients. However, it will be shown that this factor is probably too high for subjects with a GFR of ≥60 ml/min per 1.73 m^2, leading to an underestimation of the prevalence of CKD in the global African American population. It will also be confirmed that this ethnic factor is not accurate in African (non-American) subjects. Lastly, the lack of true external validation of the new CKD-EPI equations will be discussed. Additional trials seem necessary in American African and African populations to better estimate GFR and apprehend the true prevalence of CKD in this population with a high renal risk.

Clin J Am Soc Nephrol 6: 906–912, 2011. doi: 10.2215/CJN.10931210

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Removing Race from Estimates of Kidney Function

March 9, 2021 - A joint statement from the presidents of the American Society of Nephrology and the National Kidney Foundation

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BMJ: first published as 1

EDITORIALS

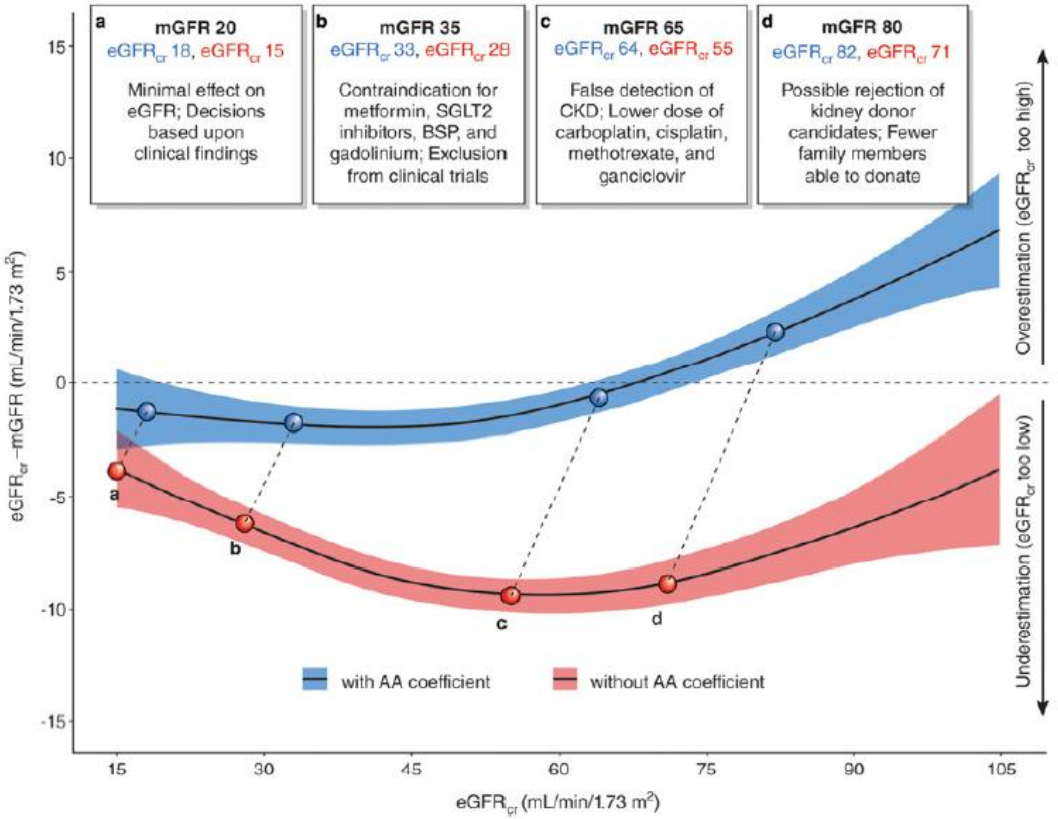
NICE takes ethnicity out of estimating kidney function

A welcome step with the potential to reduce health inequalities

Estimation of Glomerular Filtration Rate With vs Without Including Patient Race

Andrew S. Levey, MD
Hocine Tighiouart, MS
Silvia M. Titan, MD, PhD
Lesley A. Inker, MD, MS

JAMA Internal Medicine May 2020 Volume 180, Number 5



- 8254 and 2601 (31.5%) were African American
- Without race coefficient, worse results in Black Americans

REVIEW

The « race » correction in estimating glomerular filtration rate: an European point of view

Pierre Delanaye[a,b], *Christophe Mariat*[c], *Etienne Cavalier*[d], *Richard J. Glassock*[e], *François Gemenne*[f,g], *and Hans Pottel*[h]

Curr Opin Nephrol Hypertens 2021, 30:525–530

Is mGFR different between Black and White populations (USA)?

Geriatrics. May-Jun 1946;1:232-9.

Kidney function tests in aged males

N W SHOCK

PMID: 20989676

'Average values on a group of 10 colored subjects aged 18 to 41 years...did not vary significantly from average results on young white males, published in the literature' [41].

Is mGFR different between Black and White population (USA)?

http://www.kidney-international.org original article

see commentary on page 1001
see original article on page 1071

Demographic and clinical characteristics associated with glomerular filtration rates in living kidney donors

Emilio D. Poggio[1], Andrew D. Rule[2], Roberto Tanchanco[1], Susana Arrigain[3], Robert S. Butler[1], Titte Srinivas[1], Brian R. Stephany[1], Kathryn H. Meyer[3], Saul Nurko[1], Richard A. Fatica[1], Daniel A. Shoskes[4], Venkatesh Krishnamurthi[4], David A. Goldfarb[4], Inderbir Gill[4] and Martin J. Schreiber Jr[1]

[1]Department of Nephrology and Hypertension, Glickman Urological and Kidney Institute, Cleveland, Ohio, USA; [2]Division of Nephrology and Hypertension, Mayo Clinic, Rochester, Minnesota, USA; [3]Department of Quantitative Health Sciences, Cleveland Clinic, Cleveland, Ohio, USA and [4]Department of Urology, Glickman Urological and Kidney Institute, Cleveland, Ohio, USA

Table 3 | 'Expected' adjusted GFR by ^{125}I-iothalamate urinary clearances (and re-expressed MDRD equation) in prospective living kidney donors derived from the actual or observed GFR values presented in Table 2[a]

	^{125}I-Iothalamate GFR (re-expressed MDRD study equation) (ml/min per 1.73 m^2)		
Age (years)	Expected 5th percentile	Mean expected value	Expected 95th percentile
Women			
20	89 (76)	116 (102)	144 (128)
25	87 (73)	114 (99)	142 (125)
30	85 (70)	113 (96)	140 (122)
35	83 (67)	111 (93)	138 (119)
40	81 (64)	109 (90)	136 (116)
45	79 (61)	107 (87)	134 (113)
50	74 (58)	101 (84)	129 (110)
55	69 (55)	96 (81)	124 (107)
60	64 (52)	91 (78)	119 (104)
Men			
20	86 (79)	113 (105)	141 (131)
25	84 (76)	111 (102)	139 (127)
30	82 (73)	109 (99)	137 (124)
35	80 (70)	107 (96)	135 (121)
40	78 (67)	105 (93)	133 (118)
45	76 (64)	103 (90)	131 (115)
50	71 (61)	98 (86)	126 (112)
55	66 (57)	93 (83)	121 (109)
60	60 (54)	88 (80)	116 (106)

GFR, glomerular filtration rate; MDRD, Modification of Diet in Renal Disease.
[a]For mGFR, all living kidney donors (n=1057), for MDRD all living kidney donors from 1996 to 2005 with measured serum creatinine (n=545).

N=1057 prospective living kidney donors
113 African Americans

Data are scarce in Black American individuals

Is mGFR different between Black and White population (Europe)?

Int Urol Nephrol (2015) 47:201–208
DOI 10.1007/s11255-014-0859-y

NEPHROLOGY - ORIGINAL PAPER

Comparison of estimated GFR and measured GFR in prospective living kidney donors

Thakshyanee Bhuvanakrishna · Glen M. Blake · Rachel Hilton · Lisa Burnapp · Christopher Sibley-Allen · David Goldsmith

mGFR in 508 living kidney donors (398 Caucasians and 50 Afro-Carribeans): no difference in mGFR

Is mGFR different between Black and White population (Africa)?

www.kidney-international.org

**Performance of cr
equations to estir
rate in sub-Sahara**

Justine B. Bukabau[1,7], Eric Ya
Etienne Cavalier[5], Aliocha Nl
Nazaire M. Nseka[1], Jean-Mar

*[1]Renal Unit, Department of Internal
Congo; [2]Département de Biochimie,
Coast; [3]Département de Néphrologie,
Public Health and Primary Care, KU L
(ULg CHU), University of Liège, Liège
University of Liège, Liège, Belgium*

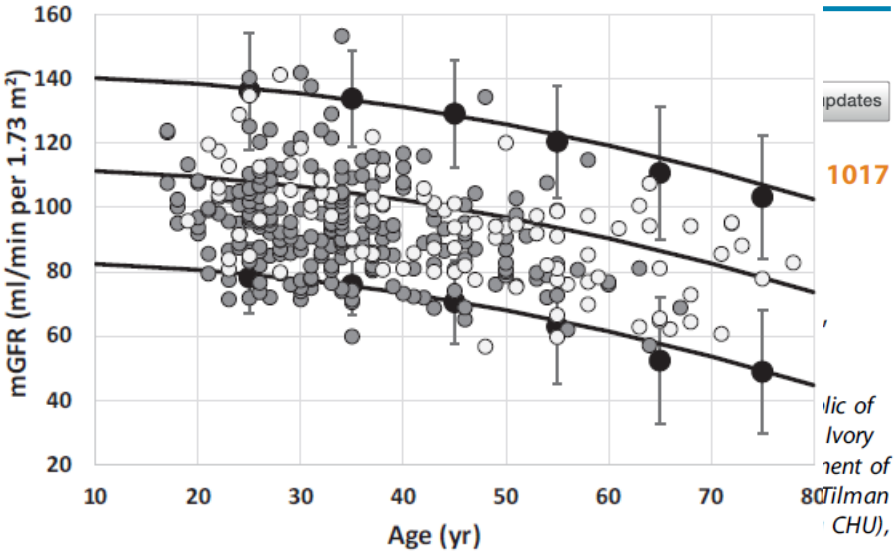


Figure 2| Comparison of measured glomerular filtration rate (mGFR) values in healthy Whites, Congolese, and Ivorian subjects. Solid gray circles represent mGFR results and solid black lines represent 2.5th percentile (Pct), 50th Pct, and 97.5th Pct for mGFR in the Ivorian population (n = 237).[18] Solid black circles with error bars represent upper and lower reference limits obtained from the meta-analysis including 633 White potential living kidney donors.[26] Added white circles represent Congolese healthy subjects (n = 95).

Is serum creatinine different between Black and White populations?

Is serum creatinine different between Black and White populations (USA)?

http://www.kidney-international.org original article

see commentary on page 1001
see original article on page 1071

Demographic and clinical characteristics associated with glomerular filtration rates in living kidney donors

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N=1057 prospective living kidney donors
113 African Americans

Serum creatinine in AA: 0,96±0,22 mg/dL
Serum creatinine in non-AA: 0,90±0,22 mg/dL

Is serum different between Black and White population (USA)?

Serum Creatinine Levels in the US Population: Third National Health and Nutrition Examination Survey

Camille A. Jones, MD, MPH, Geraldine M. McQuillan, PhD, John W. Kusek, PhD, Mark S. Eberhardt, PhD, William H. Herman, MD, MPH, Josef Coresh, MD, PhD, Marcel Salive, MD, MPH, Camara P. Jones, MD, PhD, and Lawrence Y. Agodoa, MD

American Journal of Kidney Diseases, Vol 32, No 6 (December), 1998: pp 992-999

Is serum different between Black and White population (USA)?

Table 2. Mean Serum Creatinine Values in the US Population Without Hypertension or a History of Diabetes and the Hypertensive US Population by Ethnicity, Age Group, and Sex NHANES III, 1988-1994

Ethnicity	Age (yr)	Men		Women	
		Healthy	HTN	Healthy	HTN
Total US	Total	1.13 (<0.01)	1.23 (0.01)	0.93 (<0.01)	1.04 (0.01)
	12-19	1.00 (0.01)	0.99 (0.03)	0.88 (0.01)	0.89 (0.01)
	20-39	1.14 (<0.01)	1.17 (0.02)	0.92 (0.01)	0.94 (0.01)
	40-59	1.17 (0.01)	1.18 (0.01)	0.95 (<0.01)	1.00 (0.01)
	60+	1.24 (0.01)	1.33 (0.01)	1.02 (0.01)	1.10 (0.01)
Non-Hispanic white	Total	1.13 (<0.01)	1.21 (0.01)	0.94 (<0.01)	1.03 (0.01)
	12-19	0.99 (0.01)	0.99 (0.06)	0.88 (0.01)	0.89 (0.02)
	20-39	1.14 (0.01)	1.15 (0.01)	0.93 (0.01)	0.93 (0.02)
	40-59	1.17 (0.01)	1.16 (0.01)	0.96 (0.01)	0.99 (0.01)
	60+	1.23 (0.01)	1.31 (0.01)	1.01 (0.01)	1.09 (0.01)
Non-Hispanic black	Total	1.20 (0.01)	1.37 (0.03)	0.95 (0.01)	1.13 (0.03)
	12-19	1.06 (0.01)	1.07 (0.03)	0.90 (0.01)	0.91 (0.01)
	20-39	1.24 (0.01)	1.31 (0.07)	0.96 (0.01)	1.05 (0.04)
	40-59	1.23 (0.01)	1.34 (0.05)	0.98 (0.01)	1.10 (0.06)
	60+	1.47 (0.16)	1.49 (0.04)	1.10 (0.02)	1.24 (0.03)
Mexican-American	Total	1.06 (0.01)	1.11 (0.01)	0.85 (<0.01)	0.91 (0.02)
	12-19	0.96 (0.01)	0.93 (0.05)	0.81 (0.01)	0.84 (0.03)
	20-39	1.08 (0.01)	1.09 (0.01)	0.85 (0.01)	0.86 (0.02)
	40-59	1.11 (0.01)	1.12 (0.02)	0.89 (0.01)	0.88 (0.01)
	60+	1.18 (0.03)	1.23 (0.02)	0.91 (0.01)	1.03 (0.04)

NOTE. Values expressed as mean (standard error). The healthy population excludes those persons with a history of hypertension or diabetes, and those who have an average measured blood pressure ≥140/90 mm Hg. HTN designates the hypertensive population, and total US indicates participants of all ethnic groups, including "other."

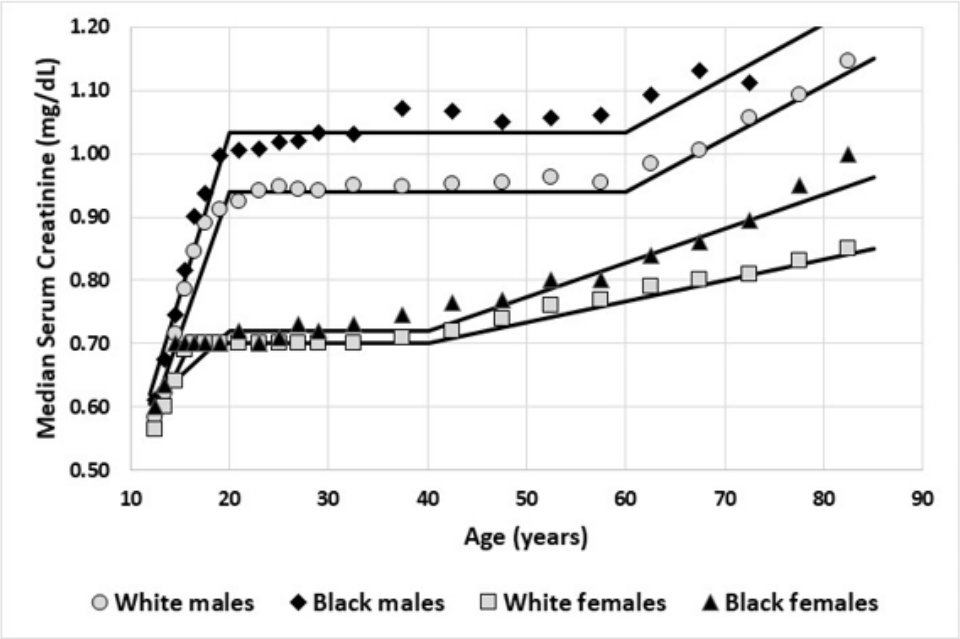


Figure 1- Legend

Figure 1. Median serum creatinine (of 1-year (12-18 year), 2-year (18-30 year) and 5-year (> 30 years) age-groups) are plotted against age for White and Black American males and females (from National Health and Nutrition Examination Survey trial). The medians are then modelled with three linear splines. The middle spline is horizontal and corresponds to Q = 0.94 mg/dL for White American males, Q = 1.03 mg/dL for Black American males, Q = 0.70 mg/dL for White American females and Q = 0.72 mg/dL for Black American females.

Is serum different between Black and White population (USA)?

Clinica Chimica Acta 520 (2021) 16–22

Contents lists available at ScienceDirect

Clinica Chimica Acta

journal homepage: www.elsevier.com/locate/cca

Calculating estimated glomerular filtration rate without the race correction factor: Observations at a large academic medical system

Junyan Shi [a], Edwin G. Lindo [b], Geoffrey S. Baird [a], Bessie Young [c], Michael Ryan [d], J. Ashley Jefferson [d], Rajnish Mehrotra [c], Patrick C. Mathias [e], Andrew N. Hoofnagle [f,*]

[a] Department of Laboratory Medicine and Pathology; University of Washington, School of Medicine, United States
[b] Department of Family Medicine; Department of Bioethics & Humanities; Office of Healthcare Equity; University of Washington, School of Medicine, United States
[c] Kidney Research Institute, Division of Nephrology, Department of Medicine; University of Washington, School of Medicine, United States
[d] Division of Nephrology, Department of Medicine; University of Washington, School of Medicine, United States
[e] Department of Laboratory Medicine and Pathology; Department of Biomedical Informatics and Medical Education; University of Washington, School of Medicine, United States
[f] Department of Laboratory Medicine and Pathology; Kidney Research Institute; Division of Metabolism, Endocrinology, and Nutrition, Department of Medicine; University of Washington, School of Medicine, United States

Information was extracted from the laboratory data warehouse for all UW Medicine outpatients, inpatients, and emergency room patients over a 20.5-month period and totaled 1,059,002 creatinine results.

Is serum different between Black and White population (USA)?

	Male median of creatinine (N)	Female median of creatinine (N)
Non-Black & Non-Asian	0.93 (97255)	0.73 (98720)
Black	1.00 (10865)	0.73 (9849)
Asian	0.93 (11119)	0.67 (13952)

Supplementary Table S2. Creatinine in different patient populations.

	Serum creatinine concentration at different percentiles of patients (mg/dL)				
	10%	25%	50%	75%	90%
Non-Black	0.61	0.71	0.83	0.99	1.19
Black	0.59	0.71	0.88	1.08	1.35
Asian	0.56	0.65	0.78	0.95	1.17

MDRD

$$GFR = 175 \times (S_{Cr})^{-1.154} \times (Age)^{-0.203} \times (0.742 \text{ if female}) \times (1.212 \text{ if African American})$$

+21%

CKD-EPI

$$GFR = 141 \times \min(S_{Cr}/\kappa, 1)^{\alpha} \times \max(S_{Cr}/\kappa, 1)^{-1.209} \times 0.993^{Age} \times (1.018 \text{ if female}) \times (1.159 \text{ if African American})$$

+16%

*S_{cr} is serum creatinine in mg/dL
κ is 0.7 for females and 0.9 for males
α is -0.329 for females and -0.411 for males
min indicates the minimum of S_{cr}/κ or 1
max indicates the maximum of S_{cr}/κ or 1

CORRECTION FOR RACE AT THE GFR LEVEL !
AND THE SAME for MALES and FEMALES

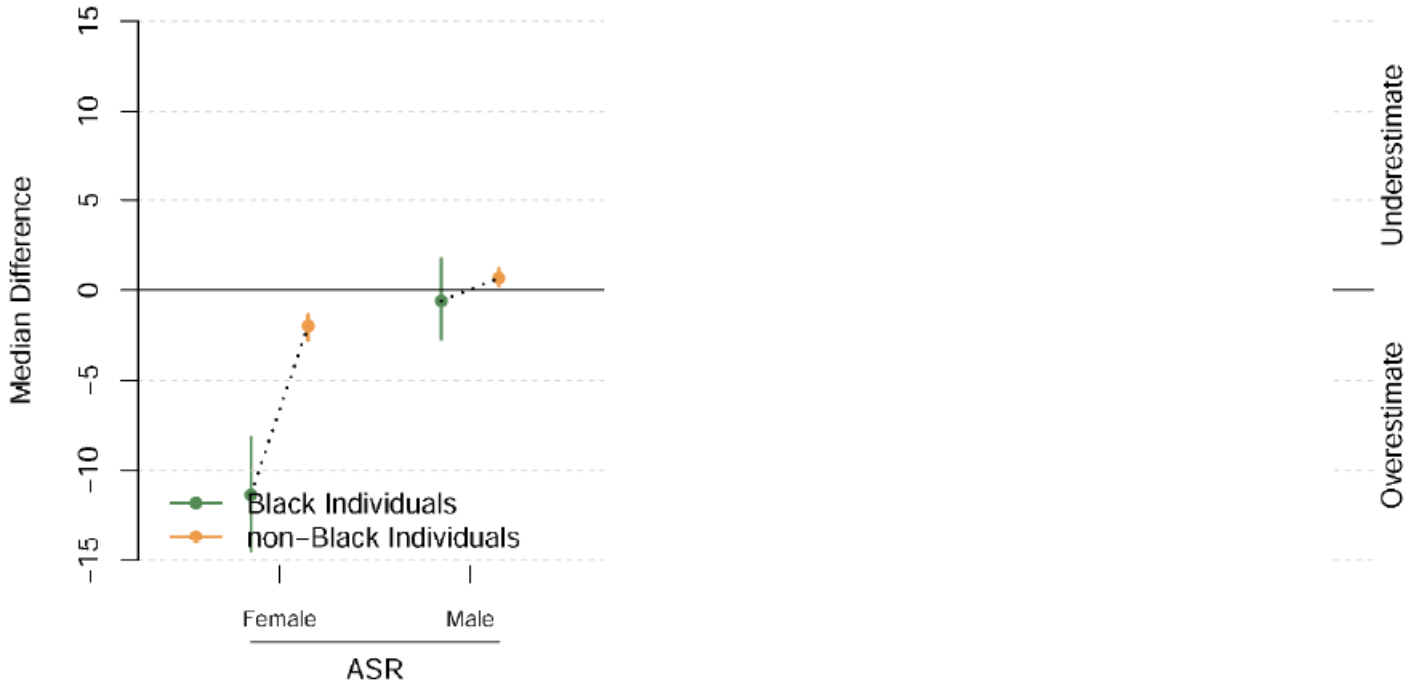
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

New Creatinine- and Cystatin C–Based Equations to Estimate GFR without Race

L.A. Inker, N.D. Eneanya, J. Coresh, H. Tighiouart, D. Wang, Y. Sang, D.C. Crews, A. Doria, M.M. Estrella, M. Froissart, M.E. Grams, T. Greene, A. Grubb, V. Gudnason, O.M. Gutiérrez, R. Kalil, A.B. Karger, M. Mauer, G. Navis, R.G. Nelson, E.D. Poggio, R. Rodby, P. Rossing, A.D. Rule, E. Selvin, J.C. Seegmiller, M.G. Shlipak, V.E. Torres, W. Yang, S.H. Ballew, S.J. Couture, N.R. Powe, and A.S. Levey, for the Chronic Kidney Disease Epidemiology Collaboration*

j. Performance of eGFR creatinine by sex subgroups in 2021 external validation



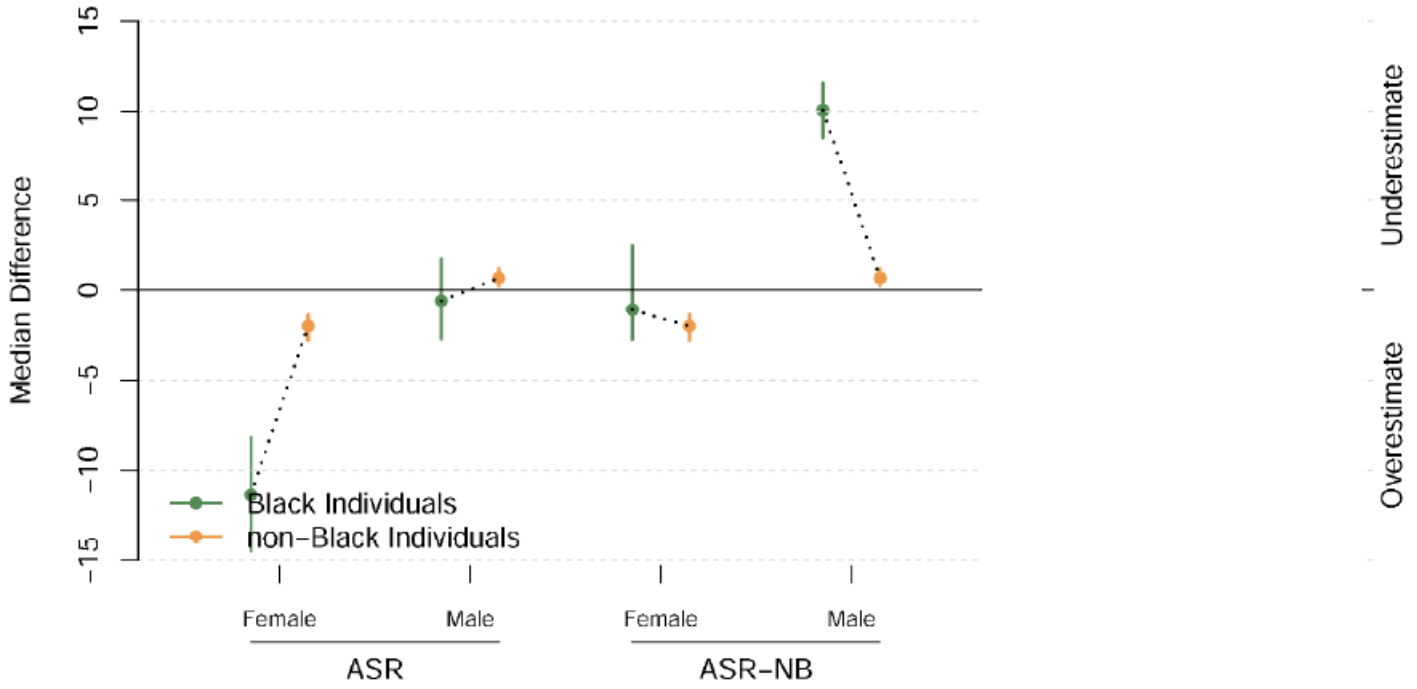
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

New Creatinine- and Cystatin C–Based Equations to Estimate GFR without Race

L.A. Inker, N.D. Eneanya, J. Coresh, H. Tighiouart, D. Wang, Y. Sang, D.C. Crews, A. Doria, M.M. Estrella, M. Froissart, M.E. Grams, T. Greene, A. Grubb, V. Gudnason, O.M. Gutiérrez, R. Kalil, A.B. Karger, M. Mauer, G. Navis, R.G. Nelson, E.D. Poggio, R. Rodby, P. Rossing, A.D. Rule, E. Selvin, J.C. Seegmiller, M.G. Shlipak, V.E. Torres, W. Yang, S.H. Ballew, S.J. Couture, N.R. Powe, and A.S. Levey, for the Chronic Kidney Disease Epidemiology Collaboration*

j. Performance of eGFR creatinine by sex subgroups in 2021 external validation



Unplished (submitted) data from Europe and Africa

Performance of creatinine-based equations to estimate glomerular filtration rate in White and Black populations in Europe, Brazil, and Africa

Pierre Delanaye[1,2*], Emmanuelle Vidal-Petiot[3*], Jonas Björk[4,5],Natalie Ebert[6], Björn O. Eriksen[7], Laurence Dubourg[8], Anders Grubb[9], Magnus Hansson[10], Edmund J. Lamb[11], Karin Littmann[12], Christophe Mariat[13], Toralf Melsom[7], Elke Schaeffner[6], Per-Ola Sundin[14], Arend Bökenkamp[15], Ulla B. Berg[16], Kajsa Åsling-Monemi[16], Anna Åkesson[4,5], Anders Larsson[17], Etienne Cavalier[18], R. Neil Dalton[19], Marie Courbebaisse[20], Lionel Couzi[21], Francois Gaillard[22], Cyril Garrouste[23], Lola Jacquemont[24], Nassim Kamar[25] Christophe Legendre[26], Lionel Rostaing[27], Thomas Stehlé[28,29], Jean-Philippe Haymann[30], Luciano da Silva Selistre[31], Jorge P. Strogoff-de-Matos[32], Justine B. Bukabau[33], Ernest K. Sumaili[33], Eric Yayo[34], Dagui Monnet[34], Ulf Nyman[35], Hans Pottel[36], Martin Flamant[37**]**

Table S3: Method and patients characteristics

Mean and SD of age and measured glomerular filtration

Center	Country	Cohort	n	Method	Exogenous marker	Age	mGFR (mL/min/1.73m²)	% of female
White populations								
Amsterdam	The Netherlands	CAPA-study[5] + referrals	48	Plasma clearance	Inulin	18.7±0.9	93.7±27.9	25.0
Berlin	Germany	BIS-Study[6]	657	Plasma clearance	Iohexol	78.4±6.1	60.3±21.5	41.7
France	France	Kidney Donor Study[7]	2,572	Plasma/renal clearance	Iohexol/^{51}Cr-EDTA/inulin	50.4±11.8	100.1±22.2	61.9
Kent	UK	GFR in old adults[8]	394	Plasma clearance	Iohexol	80.4±4.6	55.3±20.5	52.0
Leuven	Belgium	Referrals	21	Plasma clearance	^{51}Cr-EDTA	19.1±1.2	78.2±23.1	47.6
Lund	Sweden	CAPA-study[5]	2,847	Plasma clearance	Iohexol	60.1±16.5	62.5±34.1	48.5
Lyon	France	Referrals	2,435	Plasma/renal clearance	Iohexol/inulin	31.3±16.7	84.5±32.7	46.8
Örebro	Sweden	Referrals	2,051	Plasma clearance	Iohexol	56.5±16.3	64.3±36.0	41.7
Saint-Etienne	France	HIV-study[9]	203	Plasma clearance	Iohexol	48.7±10.3	100.3±27.3	48.7
Stockholm	Sweden	Referrals	856	Plasma clearance	Iohexol	72.9±14.1	48.7±27.6	44.2
Tromsø	Norway	RENIS-T6 study[10]	1,627	Plasma clearance	Iohexol	58.1±3.8	101.5±19.9	50.8
Kinshasa/ Abidjan	DRC/Côte d'Ivoire	African Study[11]	508	Plasma clearance	Iohexol	41.8±14.3	80.5±28.9	46.7
Rio de Janeiro	Brazil	Brazilian study[12]	39	Plasma clearance	^{51}Cr-EDTA	60.0±13.5	41.9±23.4	59.0
Paris	France	Referrals	4429	Plasma clearance	^{51}Cr-EDTA	52.4±14.8	61.3±26.6	41.1
Black population								
Kinshasa/ Abidjan	DRC/Côte d'Ivoire	African Study[11]	508	Plasma clearance	Iohexol	41.8±14.3	80.5±28.9	46.7
Rio de Janeiro	Brazil	Brazilian study[12]	61	Plasma clearance	^{51}Cr-EDTA	55.9±13.8	49.8±32.2	50.8
Paris	France	Referrals	964	Plasma clearance	^{51}Cr-EDTA	50.4±13.8	61.1±24.6	41.1

*Referrals = referred for plasma or renal clearance measurement on clinical grounds. Results mean±SD

EKFC
17321
White Europeans (Paris)
4429
Black Europeans (Paris)
964
Africans
508

- mGFR seems not different
- Serum creatinine is not different between race
- …but serum creatinine is different between populations
- Nothing to do with race nor skin colour
- Difference in muscle mass ?
- Difference in creatinine tubular secretion ?
- Difference in diet?
- Difference in creatine turnover?
- Genetic? (no proof)
- Differences could be explained indirectly by racism (muscle mass, diet)

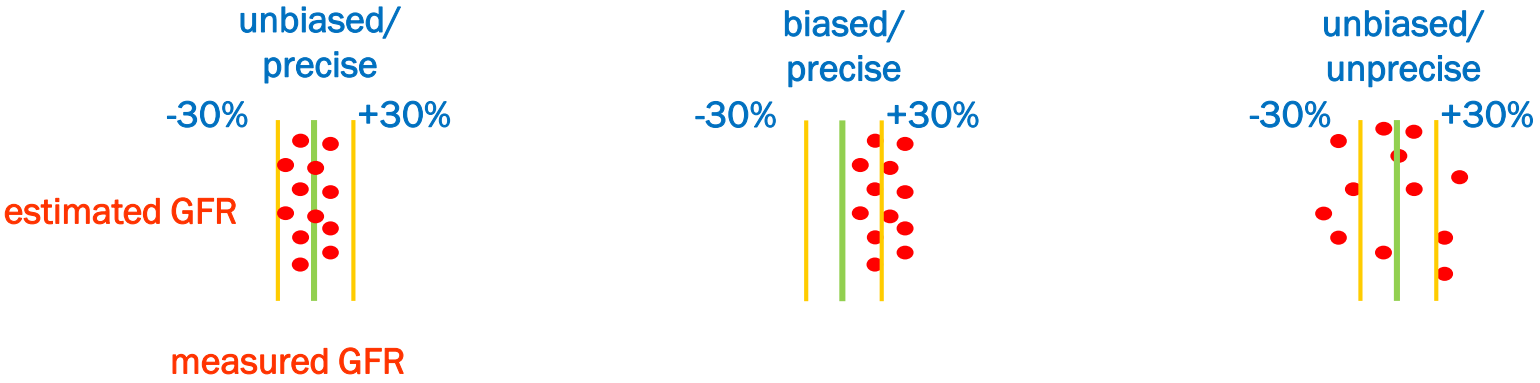
We use serum creatinine for one century, and we still don't know why serum creatinine is different in some populations

Solutions?

- Cystatin C
- A new creatinine-based CKD-EPI equation
- A new creatinine-based equation

Statistics

- Good correlation: a "*sine qua non*" condition but insufficient
- Bias: mean difference between two values = the systematic error
- Precision: SD around the bias = the random error
- Accuracy 30% = % of eGFR between ± 30% of measured GFR



Cystatin C

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Estimating Glomerular Filtration Rate from Serum Creatinine and Cystatin C

Lesley A. Inker, M.D., Christopher H. Schmid, Ph.D., Hocine Tighiouart, M.S., John H. Eckfeldt, M.D., Ph.D., Harold I. Feldman, M.D., Tom Greene, Ph.D., John W. Kusek, Ph.D., Jane Manzi, Ph.D., Frederick Van Lente, Ph.D., Yaping Lucy Zhang, M.S., Josef Coresh, M.D., Ph.D., and Andrew S. Levey, M.D., for the CKD-EPI Investigators*

N Engl J Med 2012;367:20-9.

Table 2. Creatinine Equation (CKD-EPI 2009), Cystatin C Equation (CKD-EPI 2012), and Creatinine–Cystatin C Equation (CKD-EPI 2012) for Estimating GFR, Expressed for Specified Sex, Serum Creatinine Level, and Serum Cystatin C Level.*

Basis of Equation and Sex	Serum Creatinine†	Serum Cystatin C	Equation for Estimating GFR
	mg/dl	*mg/liter*	
CKD-EPI creatinine equation‡			
Female	≤0.7		$144 \times (\text{Scr}/0.7)^{-0.329} \times 0.993^{\text{Age}}$ [× 1.159 if black]
Female	>0.7		$144 \times (\text{Scr}/0.7)^{-1.209} \times 0.993^{\text{Age}}$ [× 1.159 if black]
Male	≤0.9		$141 \times (\text{Scr}/0.9)^{-0.411} \times 0.993^{\text{Age}}$ [× 1.159 if black]
Male	>0.9		$141 \times (\text{Scr}/0.9)^{-1.209} \times 0.993^{\text{Age}}$ [× 1.159 if black]
CKD-EPI cystatin C equation§			
Female or male		≤0.8	$133 \times (\text{Scys}/0.8)^{-0.499} \times 0.996^{\text{Age}}$ [× 0.932 if female]
Female or male		>0.8	$133 \times (\text{Scys}/0.8)^{-1.328} \times 0.996^{\text{Age}}$ [× 0.932 if female]
CKD-EPI creatinine–cystatin C equation¶			
Female	≤0.7	≤0.8	$130 \times (\text{Scr}/0.7)^{-0.248} \times (\text{Scys}/0.8)^{-0.375} \times 0.995^{\text{Age}}$ [× 1.08 if black]
		>0.8	$130 \times (\text{Scr}/0.7)^{-0.248} \times (\text{Scys}/0.8)^{-0.711} \times 0.995^{\text{Age}}$ [× 1.08 if black]
Female	>0.7	≤0.8	$130 \times (\text{Scr}/0.7)^{-0.601} \times (\text{Scys}/0.8)^{-0.375} \times 0.995^{\text{Age}}$ [× 1.08 if black]
		>0.8	$130 \times (\text{Scr}/0.7)^{-0.601} \times (\text{Scys}/0.8)^{-0.711} \times 0.995^{\text{Age}}$ [× 1.08 if black]
Male	≤0.9	≤0.8	$135 \times (\text{Scr}/0.9)^{-0.207} \times (\text{Scys}/0.8)^{-0.375} \times 0.995^{\text{Age}}$ [× 1.08 if black]
		>0.8	$135 \times (\text{Scr}/0.9)^{-0.207} \times (\text{Scys}/0.8)^{-0.711} \times 0.995^{\text{Age}}$ [× 1.08 if black]
Male	>0.9	≤0.8	$135 \times (\text{Scr}/0.9)^{-0.601} \times (\text{Scys}/0.8)^{-0.375} \times 0.995^{\text{Age}}$ [× 1.08 if black]
		>0.8	$135 \times (\text{Scr}/0.9)^{-0.601} \times (\text{Scys}/0.8)^{-0.711} \times 0.995^{\text{Age}}$ [× 1.08 if black]

Table 3. Use of the CKD-EPI Creatinine Equation (2009), CKD-EPI Cystatin C Equation (2012), and CKD-EPI Creatinine–Cystatin C Equations (2012) in the External-Validation Data Set Comprising 1119 Participants.*

Variable	Estimated GFR			
	Overall	<60	60–89	≥90
	ml/min/1.73 m² of body-surface area			
Bias — median difference (95% CI)				
Creatinine equation	3.7 (2.8 to 4.6)	1.8 (1.1 to 2.5)	6.6 (3.5 to 9.2)	11.1 (8.0 to 12.5)
Cystatin C equation	3.4 (2.3 to 4.4)	0.4 (–0.5 to 1.4)	6.0 (4.6 to 8.5)	8.5 (6.5 to 11.2)
Creatinine–cystatin C equation	3.9 (3.2 to 4.5)	1.3 (0.5 to 1.8)	6.9 (5.0 to 8.9)	10.6 (9.5 to 12.7)
Average of creatinine and cystatin C†	3.5 (2.8 to 4.1)	0.4 (–0.3 to 0.8)	6.5 (4.6 to 8.4)	11.9 (9.9 to 13.9)
Precision — IQR of the difference (95% CI)				
Creatinine equation	15.4 (14.3 to 16.5)	10.0 (8.9 to 11.0)	19.6 (17.3 to 23.2)	25.0 (21.6 to 28.1)
Cystatin C equation	16.4 (14.8 to 17.8)	11.0 (10.0 to 12.4)	19.6 (16.1 to 23.1)	22.6 (18.8 to 26.3)
Creatinine–cystatin C equation	13.4 (12.3 to 14.5)	8.1 (7.3 to 9.1)	15.9 (13.9 to 18.1)	18.8 (16.8 to 22.5)
Average of creatinine and cystatin C equations†	13.9 (12.9 to 14.7)	7.9 (7.1 to 9.0)	15.8 (13.9 to 17.7)	18.6 (16.1 to 22.2)
Accuracy — % (95% CI)‡				
$1-P_{30}$				
Creatinine equation	12.8 (10.9 to 14.7)	16.6 (13.6 to 19.7)	10.2 (6.4 to 14.2)	7.8 (5.1 to 11.0)
Cystatin C equation	14.1 (12.2 to 16.2)	21.4 (18.2 to 24.9)	12.7 (8.5 to 17.4)	2.2 (0.6 to 3.9)
Creatinine–cystatin C equation	8.5 (7.0 to 10.2)	13.3 (10.7 to 16.1)	5.3 (2.7 to 8.2)	2.3 (0.9 to 4.2)
Average of creatinine and cystatin C equations†	8.2 (6.7 to 9.9)	12.1 (9.5 to 14.8)	6.4 (3.6 to 9.7)	2.9 (1.3 to 4.9)
$1-P_{20}$				
Creatinine equation	32.9 (30.1 to 35.7)	37.2 (33.1 to 41.2)	31.1 (25.1 to 37.4)	26.5 (21.7 to 31.4)
Cystatin C equation	33.0 (30.3 to 35.7)	42.1 (38.2 to 46.1)	29.3 (23.6 to 35.4)	19.4 (15.4 to 23.7)
Creatinine–cystatin C equation	22.8 (20.4 to 25.2)	28.6 (25.1 to 32.4)	17.8 (13.3 to 22.9)	16.2 (12.4 to 20.5)
Average of creatinine and cystatin C equations†	23.7 (21.3 to 26.1)	29.1 (25.7 to 32.8)	17.6 (13.2 to 22.4)	18.8 (14.6 to 23.2)

A new creatinine-based CKD-EPI equation

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

New Creatinine- and Cystatin C–Based Equations to Estimate GFR without Race

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N Engl J Med. 2021 Nov 4;385(19):1737-1749.

Table 2. Current and New Equations to Estimate GFR.*

Model; Name of Equation†	Intercept μ (95% CI)	Coefficients for Creatinine (95% CI)‡		Coefficients for Cystatin C (95% CI)§		Coefficient c for Age (95% CI)	Coefficient d for Female Sex (95% CI)	Coefficient e for Black Race (95% CI)
		a_1	a_2	b_1	b_2			
2009 CKD-EPI creatinine[2]; eGFRcr(ASR), current	141 (139 to 144)	F: −0.329 (−0.428 to −0.230); M: −0.411 (−0.508 to −0.314)	−1.209 (−1.220 to −1.198)	—	—	0.9929 (0.9925 to 0.9933)	1.018 (1.007 to 1.029)	1.159 (1.144 to 1.170)
2009 CKD-EPI creatinine[2]; eGFRcr(ASR-NB), new	141 (139 to 144)	F: −0.329 (−0.428 to −0.230); M: −0.411 (−0.508 to −0.314)	−1.209 (−1.220 to −1.198)	—	—	0.9929 (0.9925 to 0.9933)	1.018 (1.007 to 1.029)	1
2021 CKD-EPI creatinine (2009 CKD-EPI creatinine fit without race); eGFRcr(AS), new	142 (139 to 144)	F: −0.241 (−0.344 to −0.138); M: −0.302 (−0.403 to −0.202)	−1.200 (−1.211 to −1.189)	—	—	0.9938 (0.9935 to 0.9942)	1.012 (1.000 to 1.023)	—
2012 CKD-EPI cystatin C[3]; eGFRcys(AS), current	133 (130 to 136)	—	—	−0.499 (−0.610 to −0.388)	−1.328 (−1.344 to −1.312)	0.9962 (0.9957 to 0.9966)	0.932 (0.921 to 0.944)	—
2012 CKD-EPI creatinine–cystatin C[4]; eGFRcr-cys(ASR), current	135 (132 to 137)	F: −0.248 (−0.364 to −0.132); M: −0.207 (−0.308 to −0.107)	−0.601 (−0.630 to −0.571)	−0.375 (−0.477 to −0.274)	−0.711 (−0.744 to −0.678)	0.9952 (0.9948 to 0.9957)	0.969 (0.958 to 0.980)	1.080 (1.067 to 1.093)
2012 CKD-EPI creatinine–cystatin C[3]; eGFRcr-cys(ASR-NB), new	135 (132 to 137)	F: −0.248 (−0.364 to −0.132); M: −0.207 (−0.308 to −0.107)	−0.601 (−0.630 to −0.571)	−0.375 (−0.477 to −0.274)	−0.711 (−0.744 to −0.678)	0.9952 (0.9948 to 0.9957)	0.969 (0.958 to 0.980)	1
2021 CKD-EPI creatinine–cystatin C (2012 CKD-EPI creatinine–cystatin C fit without race); eGFRcr-cys(AS), new	135 (132 to 137)	F: −0.219 (−0.336 to −0.101); M: −0.144 (−0.245 to −0.042)	−0.544 (−0.572 to −0.515)	−0.323 (−0.426 to −0.220)	−0.778 (−0.809 to −0.746)	0.9961 (0.9957 to 0.9965)	0.963 (0.952 to 0.974)	—

* The cells show coefficients to use in the following formula: $eGFR = \mu \times \min(Scr/\kappa, 1)^{a} \times \max(Scr/\kappa, 1)^{-a} \times \min(Scys/0.8, 1)^{b} \times \max(Scys/0.8, 1)^{-b} \times c^{Age} \times d[\text{if female}] \times e[\text{if Black}]$. Here, κ is 0.7 for female participants and 0.9 for male participants, min indicates the minimum of Scr/κ and 1, and max indicates the maximum of Scr/κ and 1. The 2009 and 2012 models were developed previously. Sex differences for eGFRcr and eGFRcr-cys equations are modeled as sex-specific creatinine coefficients as well as female sex coefficients. CKD-EPI denotes Chronic Kidney Disease Epidemiology Collaboration, F female, and M male.

† The equations are referred to by the filtration marker or markers (creatinine [eGFRcr], cystatin C [eGFRcys], or creatinine–cystatin C [eGFRcr-cys]) and the demographic factors (age, sex, and race [ASR] or age and sex [AS]) that were used in their development. Non-Black (NB) refers to equations in which the Black race coefficient was omitted in computation of the eGFR value.

‡ The coefficient a_1 is used for levels of creatinine less than or equal to 0.7 mg per deciliter for male participants and 0.9 mg per deciliter for female participants. The coefficient a_2 is used for levels of creatinine greater than 0.7 mg per deciliter for male participants and 0.9 mg per deciliter for female participants.

§ The coefficient b_1 is used for levels of cystatin C less than or equal to 0.8 mg per liter, and the coefficient b_2 is used for levels greater than 0.8 mg per liter.

Table 3. Accuracy of Current and New Approaches for GFR Estimation as Compared with Measured GFR in the Validation Data Set.

Filtration Marker and Equation*	Black Participants	Non-Black Participants	Difference between Black Participants and Non-Black Participants (95% CI)†
	Bias: Median Difference between Measured GFR and eGFR (95% CI)‡		
	milliliters per minute per 1.73 square meters		
Creatinine			
eGFRcr(ASR), current	−3.7 (−5.4 to −1.8)	−0.5 (−0.9 to 0.0)	−3.2 (−5.0 to −1.3)
eGFRcr(ASR-NB), new	7.1 (5.9 to 8.8)	−0.5 (−0.9 to 0.0)	7.6 (6.1 to 9.0)
eGFRcr(AS), new	3.6 (1.8 to 5.5)	−3.9 (−4.4 to −3.4)	7.6 (5.6 to 9.5)
Creatinine			
eGFRcr(ASR), current	85.1 (82.2 to 87.9)	89.5 (88.5 to 90.4)	−4.4 (−7.6 to −1.2)
eGFRcr(ASR-NB), new	86.4 (83.4 to 89.1)	89.5 (88.5 to 90.4)	−3.1 (−6.2 to 0)
eGFRcr(AS), new	87.2 (84.5 to 90.0)	86.5 (85.4 to 87.6)	0.7 (−2.4 to 3.8)

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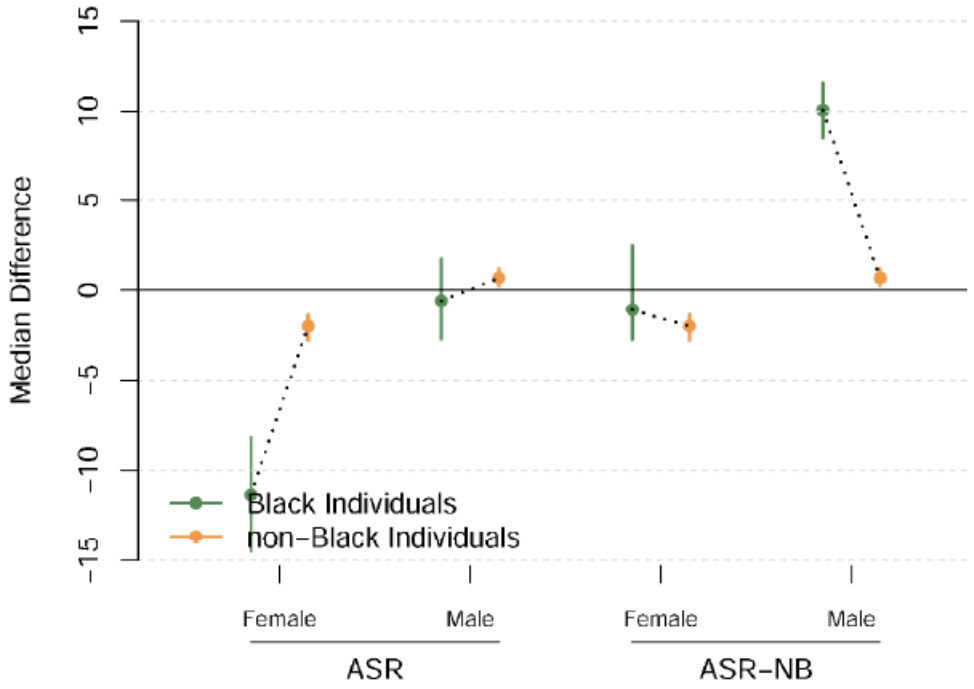

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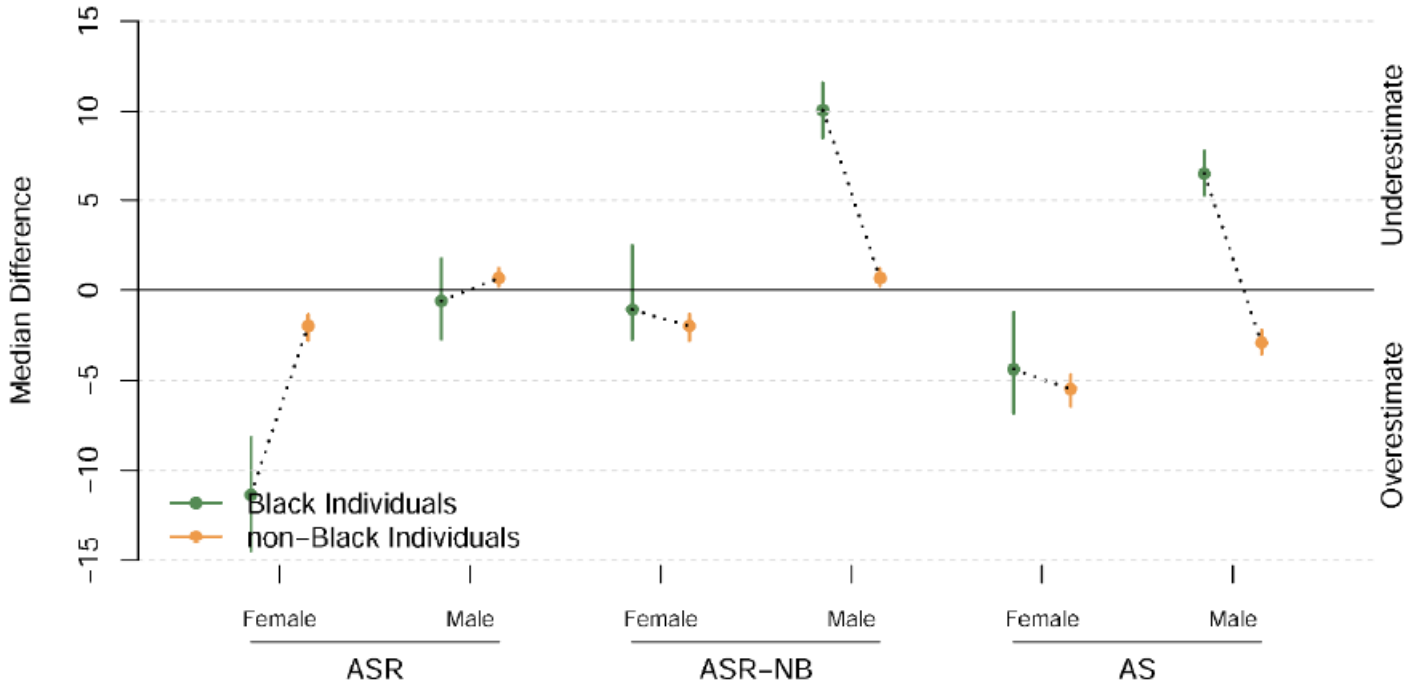

This article was published on September 23, 2021, at NEJM.org.

NKF and ASN Release New Way to Diagnose Kidney Diseases

Both Organizations Recommend Race-Free Approach to Estimate GFR

Sept. 23, 2021, New York, NY – Today, 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 approach to diagnose kidney disease. In the report, the NKF-ASN Task Force recommends the adoption of the new **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 serum (blood) creatinine, as a confirmatory assessment of GFR or kidney function.** The final report, published today online in the *American Journal*

The impact on CKD prevalence in Europe

Research Letter

Effect of the Refitted Race-Free eGFR Formula on the CKD Prevalence and Mortality in the Danish Population

Søren Viborg Vestergaard,[1,2] Uffe Heide-Jørgensen,[1,2] Henrik Birn,[3,4] and Christian Fynbo Christiansen[1,2]

CJASN 17: 426–428, 2022. doi: https://doi.org/10.2215/CJN.14491121

- Danish population-based laboratory data (creatinine from 2016-2018)
- N=4,768,234

Table 1. Prevalence of CKD in Denmark at January 1, 2019, overall and by stage, when using two different formulas to calculate eGFR on the basis of plasma creatinine

Covariate	eGFRcr(ASR-NB) (original)					eGFRcr(AS) (refitted)				
	Cohort					Cohort				
	Any CKD (stages 3–5)	CKD Stage 3a	CKD Stage 3b	CKD Stage 4	CKD Stage 5	Any CKD (stages 3–5)	CKD Stage 3a	CKD Stage 3b	CKD Stage 4	CKD Stage 5
~~Individuals, n~~	~~261,625~~	~~168,889~~	~~67,771~~	~~20,511~~	~~4254~~	~~199,367~~	~~126,679~~	~~51,513~~	~~15,502~~	~~4673~~
Prevalence, %	5.49	3.53	1.42	0.43	0.11	4.16	2.66	1.08	0.33	0.10
~~1-year mortality, %~~	~~7.9~~	~~5.7~~	~~10.3~~	~~16.1~~	~~17.7~~	~~8.9~~	~~6.7~~	~~11.2~~	~~16.5~~	~~17.6~~
Male sex, %	44	43	44	46	60	44	43	43	47	61
Median age, yrs	78	77	80	81	70	78	78	81	80	69
Age category										
18–49	1.8	1.4	1.5	2.7	14.2	2.0	1.4	1.8	3.2	15.6
50–69	18.0	20.2	12.6	13.8	33.4	16.8	18.0	12.7	15.4	34.9
70–89	70.8	71.4	72.2	67.4	48.0	70.8	72.1	71.1	66.5	46.0
90+	9.4	6.9	13.7	16.1	4.4	10.4	8.5	14.4	14.9	3.5
Comorbidity <20 yrs before index, %										
Diabetes	24.3	20.1	29.3	38.8	38.4	26.5	22.3	31.7	39.7	37.7
Liver disease	2.0	1.8	2.2	2.5	3.6	2.1	1.9	2.3	2.6	3.7
Chronic pulmonary disease	14.3	12.9	16.3	19.1	15.7	15.1	13.8	17.2	18.8	15.7
Connective tissue disease	7.8	7.3	8.4	8.8	9.7	8.0	7.6	8.4	9.0	9.7
Heart failure	1.0	0.6	1.3	2.6	4.9	1.2	0.7	1.6	2.8	5.1
Thromboembolic disease	31.6	27.9	36.8	41.9	43.3	33.6	30.2	38.3	42.2	43.5
Cancer	20.9	20.1	22.5	22.7	20.3	21.4	20.8	22.6	22.7	20.1

eGFRcr(ASR-NB), eGFR creatinine (age+sex+race-non-Black); eGFRcr(AS), eGFR creatinine (age+sex).

-25%

THE WORLD ACCORDING TO AMERICANS

Clinical Chemistry 54:7
1197–1202 (2008)

Estimating Glomerular Filtration Rate in Black South Africans by Use of the Modification of Diet in Renal Disease and Cockcroft-Gault Equations

Hendrick E. van Deventer,[1*] Jaya A. George,[1] Janice E. Paiker,[1] Piet J. Becker,[2] and Ivor J. Katz[3]

Table 1. Performance of equations.[a]

eGFR	n	Median bias, mL/min/1.73 m² (95% CI)	Median percentage bias, %	IQR, mL/min/1.73 m²	RMSE, mL/min/1.73 m²	P_{30}, %
4-v MDRD with ethnicity factor of 1.212						
eGFR <30 mL/min/1.73 m²	20	1.7 (−1.7 to 4.4)	10.0	7.0	7.2	55
eGFR 30–60 mL/min/1.73 m²	15	8.8 (−2.2 to 14.8)	23.8	15.7	18.0	53
eGFR >60 mL/min/1.73 m²	65	20.4 (17.6 to 28)	28.8	28.6	35.1	51
Overall	100	13.1 (5.5 to 18.3)	27.0	25.2	28.5	52
4-v MDRD without ethnicity factor						
eGFR <30 mL/min/1.73 m²	21	−1.4 (−4.0 to 2.2)	−6.7	7.0	7.2	67
eGFR 30–60 mL/min/1.73 m²	24	0.4 (−6.4 to 5.1)	1.4	11.8	11.8	75
eGFR >60 mL/min/1.73 m²	55	5.1 (−0.3 to 17.0)	8.8	26.3	26.8	76
Overall	100	1.9 (−0.8 to 4.5)	4.8	16.4	16.6	74

Hindawi
International Journal of Nephrology
Volume 2020, Article ID 2141038, 9 pages
https://doi.org/10.1155/2020/2141038

Research Article

No Race-Ethnicity Adjustment in CKD-EPI Equations Is Required for Estimating Glomerular Filtration Rate in the Brazilian Population

Amanda D. Rocha,[1] Suzane Garcia,[2] Andressa B. Santos,[3] José C. C. Eduardo,[3] Claudio T. Mesquita,[2,4] Jocemir R. Lugon,[1,3] and Jorge P. Strogoff-de-Matos[1,3]

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[3]*Nephrology Division, Department of Medicine, Fluminense Federal University (UFF), Niterói, Rio de Janeiro, Brazil*
[4]*Nuclear Medicine Division, EBESERH/Hospital Antonio Pedro, Fluminense Federal University (UFF), Niterói, Rio de Janeiro, Brazil*

Table 5: Performance of the equations for estimation of GFR.

	$eGFR_{Cr}$ (no race adjustment)	$eGFR_{Cr}$ (with race adjustment)	$eGFR_{Cr\text{-}Cys}$ (no race adjustment)	$eGFR_{Cr\text{-}Cys}$ (with race adjustment)
Bias (mL/min/1.73 m^2)				
All participants N=100	0.1 (−6.5–7.1)	2.8 (−1.9–11.0)[a]	−0.1 (−6.2–4.0)	1.6 (−3.7–5.5)[b]
White	0.7 (−5.6–7.8)	—	0.4 (−5.6–4.8)	—
African Brazilian N=61	−0.5 (−8.1–5.9)	3.2 (−0.5–14.3)[a]	−0.2 (−7.1–3.0)	2.4 (−2.2–5.8)[b]
Precision (mL/min/1.73 m^2)				
All participants	6.8 (3.2–11.9)	6.3 (2.2–12.2)	5.1 (2.0–10.7)[c]	4.5 (2.3–10.3)[d]
White	6.3 (3.5–11.1)	—	4.8 (2.1–8.4)	—
African Brazilian	7.4 (3.0–13.3)	5.5 (2.0–14.3)	5.5 (2.0–11.4)	4.3 (2.4–11.8)
Accuracy (P30)				
All participants	79.0 (70.0–85.9)	74.0 (64.6–81.6)	83.0 (74.3–89.2)	82.0 (73.2–88.4)
White	84.6 (69.9–93.1)	—	87.2 (72.8–94.9)	—
African Brazilian	75.4 (63.2–84.6)	67.2 (54.7–77.7)	80.3 (68.5–88.5)	78.7 (66.7–87.2)

eGFR: estimated glomerular filtration rate; Cr: creatinine; Cys: cystatin C. Bias and precision are expressed as median (interquartile range), and accuracy as percentage (95% confidence interval). [a]$P < 0.0001$ vs. $eGFR_{Cr}$ without race adjustment and $eGFR_{Cr\text{-}Cys}$ without race adjustment; [b]$P < 0.0001$ vs. $eGFR_{Cr\text{-}Cys}$ without race adjustment; [c]$P = 0.013$ vs. $eGFR_{Cr}$ without race adjustment; [d]$P = 0.005$ vs. $eGFR_{Cr}$ with race adjustment.

Data from Africa

www.kidney-international.org clinical investigation

Performance of creatinine- or cystatin C–based equations to estimate glomerular filtration rate in sub-Saharan African populations

see commentary on page 1017

Justine B. Bukabau[1,7], Eric Yayo[2,7], Appolinaire Gnionsahé[3], Dagui Monnet[2], Hans Pottel[4], Etienne Cavalier[5], Aliocha Nkodila[1], Jean Robert R. Makulo[1], Vieux M. Mokoli[1], François B. Lepira[1], Nazaire M. Nseka[1], Jean-Marie Krzesinski[6], Ernest K. Sumaili[1,7] and Pierre Delanaye[6,7]

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Table 3 | Performance of equations in the whole cohort (N = 494)

Equation	Absolute bias (95% CI)	Absolute SD	Accuracy within 30% (95% CI)
CKD-EPI	0.0 (−1.6 to 1.6)	18.1	77.7 (74.1 to 81.4)
CKD-EPI ef	13.3 (11.4 to 15.2)	21.3	64.6 (60.3 to 68.8)

editorial www.kidney-international.org

Pierre Delanaye[1,2], Hans Pottel[3] and Richard J. Glassock[4]
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Americentrism in estimation of glomerular filtration rate equations

Kidney International (2022) **101,** 856–858; https://doi.org/10.1016/j.kint.2022.02.022

KEYWORDS: glomerular filtration rate; race; serum creatinine

- Arguments can be posited in favor of using the previous CKD-EPI creatinine equation in Europe, Africa and Brazil **without any race correction**
- Should these countries use a new equation, developed in America to remedy a specific issue of structural racism relating to the Black Americans population, for a problem that may not be relevant in their own country?
- Especially if the performance characteristics of the new equation are poorer than the current equation when used **without any race variable**?

A new creatinine-based equation

Ann Intern Med. 2021;174:183-191.

Annals of Internal Medicine ORIGINAL RESEARCH

Development and Validation of a Modified Full Age Spectrum Creatinine-Based Equation to Estimate Glomerular Filtration Rate

A Cross-sectional Analysis of Pooled Data

Hans Pottel, PhD*; Jonas Björk, PhD*; Marie Courbebaisse, MD, PhD; Lionel Couzi, MD, PhD; Natalie Ebert, MD, MPH; Björn O. Eriksen, MD, PhD; R. Neil Dalton, PhD; Laurence Dubourg, MD, PhD; François Gaillard, MD, PhD; Cyril Garrouste, MD; Anders Grubb, MD, PhD; Lola Jacquemont, MD, PhD; Magnus Hansson, MD, PhD; Nassim Kamar, MD, PhD; Edmund J. Lamb, PhD; Christophe Legendre, MD; Karin Littmann, MD; Christophe Mariat, MD, PhD; Toralf Melsom, MD, PhD; Lionel Rostaing, MD, PhD; Andrew D. Rule, MD; Elke Schaeffner, MD, PhD, MSc; Per-Ola Sundin, MD, PhD; Stephen Turner, MD, PhD; Arend Bökenkamp, MD; Ulla Berg, MD, PhD; Kajsa Åsling-Monemi, MD, PhD; Luciano Selistre, MD, PhD; Anna Åkesson, BSc; Anders Larsson, MD, PhD; Ulf Nyman, MD, PhD†; and Pierre Delanaye, MD, PhD†

- Subjects with measured GFR and standardized creatinine
- 11,251 development and internal validation
- 8,378 external validation
- 1,254 aged between 2 to 18 years
- 7 + 6 cohorts
- Only White people

Figure 1. The new EKFC equation.

Age	SCr/Q	Equation
2–40 y	<1	$107.3 \times (SCr/Q)^{-0.322}$
	≥1	$107.3 \times (SCr/Q)^{-1.132}$
>40 y	<1	$107.3 \times (SCr/Q)^{-0.322} \times 0.990^{(Age - 40)}$
	≥1	$107.3 \times (SCr/Q)^{-1.132} \times 0.990^{(Age - 40)}$

Q Values

For ages 2–25 y:

Males:

$$\ln(Q) = 3.200 + 0.259 \times Age - 0.543 \times \ln(Age) - 0.00763 \times Age^2 + 0.0000790 \times Age^3$$

Females:

$$\ln(Q) = 3.080 + 0.177 \times Age - 0.223 \times \ln(Age) - 0.00596 \times Age^2 + 0.0000686 \times Age^3$$

For ages >25 y:

Males:

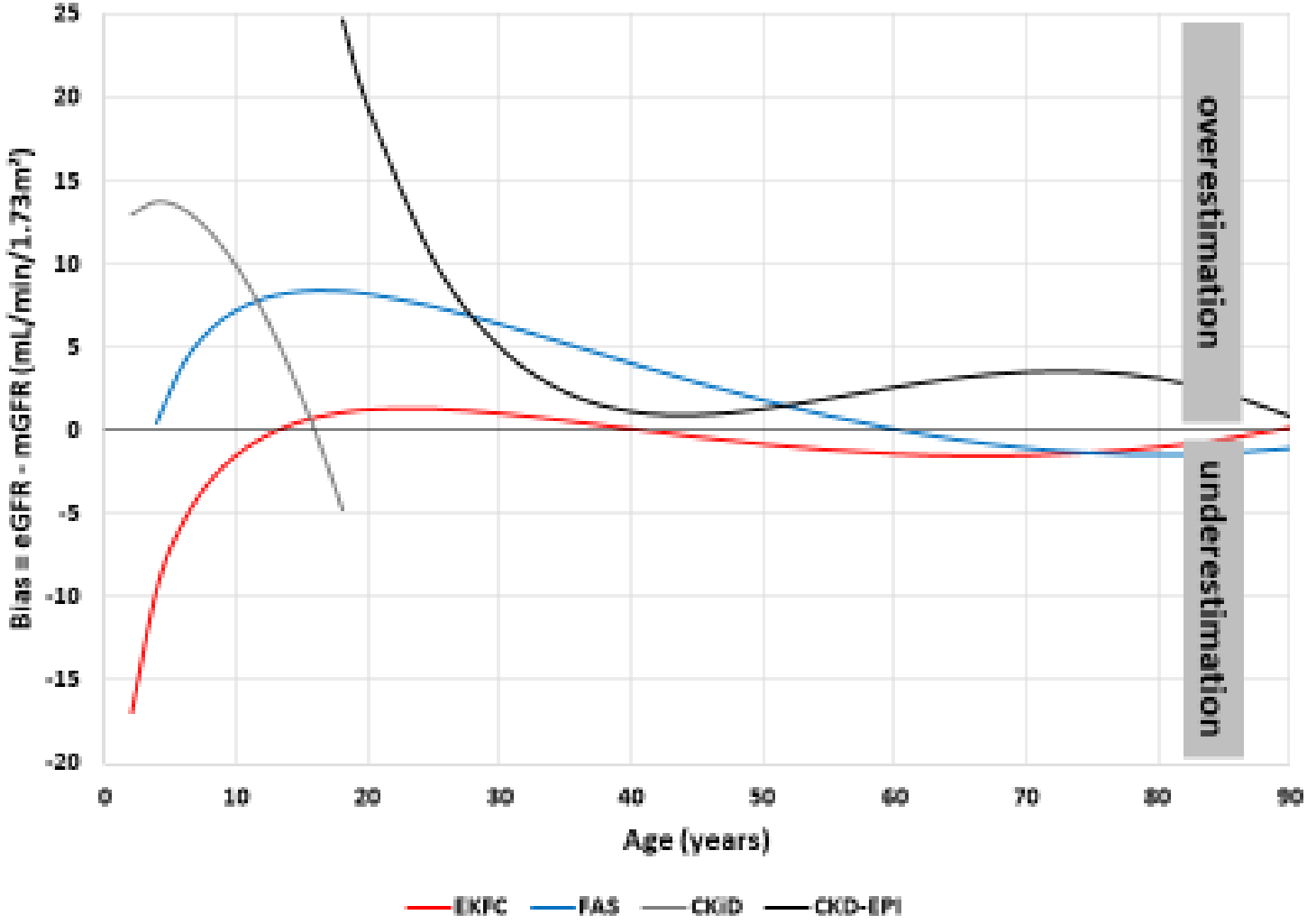
$Q = 80$ µmol/L (0.90 mg/dL)

Females:

$Q = 62$ µmol/L (0.70 mg/dL)

SCr and Q in µmol/L (to convert to mg/dL, divide by 88.4)

Q values (in µmol/L or mg/dL) correspond to the median SCr values for the age- and sex-specific populations. EKFC = European Kidney Function Consortium; SCr = serum creatinine.


Bias = eGFR - mGFR (mL/min/1.73m²)
25
20
15
10
5
0
-5
-10
-15
-20
0
10
20
30
40
50
60
70
80
90
Age (years)
overestimation
underestimation
EKFC
FAS
CKiD
CKD-EPI

Unpublished (submitted) data from Europe and Africa

Performance of creatinine-based equations to estimate glomerular filtration rate in White and Black populations in Europe, Brazil, and Africa

Pierre Delanaye[1,2*], Emmanuelle Vidal-Petiot[3*], Jonas Björk[4,5],Natalie Ebert[6], Björn O. Eriksen[7], Laurence Dubourg[8], Anders Grubb[9], Magnus Hansson[10], Edmund J. Lamb[11], Karin Littmann[12], Christophe Mariat[13], Toralf Melsom[7], Elke Schaeffner[6], Per-Ola Sundin[14], Arend Bökenkamp[15], Ulla B. Berg[16], Kajsa Åsling-Monemi[16], Anna Åkesson[4,5], Anders Larsson[17], Etienne Cavalier[18], R. Neil Dalton[19], Marie Courbebaisse[20], Lionel Couzi[21], Francois Gaillard[22], Cyril Garrouste[23], Lola Jacquemont[24], Nassim Kamar[25] Christophe Legendre[26], Lionel Rostaing[27], Thomas Stehlé[28,29], Jean-Philippe Haymann[30], Luciano da Silva Selistre[31], Jorge P. Strogoff-de-Matos[32], Justine B. Bukabau[33], Ernest K. Sumaili[33], Eric Yayo[34], Dagui Monnet[34], Ulf Nyman[35], Hans Pottel[36], Martin Flamant[37**]**

Table S3: Method and patients characteristics

Mean and SD of age and measured glomerular filtration

Center	Country	Cohort	n	Method	Exogenous marker	Age	mGFR (mL/min/1.73m²)	% of female
White populations								
Amsterdam	The Netherlands	CAPA-study[5] + referrals	48	Plasma clearance	Inulin	18.7±0.9	93.7±27.9	25.0
Berlin	Germany	BIS-Study[6]	657	Plasma clearance	Iohexol	78.4±6.1	60.3±21.5	41.7
France	France	Kidney Donor Study[7]	2,572	Plasma/renal clearance	Iohexol/^{51}Cr-EDTA/inulin	50.4±11.8	100.1±22.2	61.9
Kent	UK	GFR in old adults[8]	394	Plasma clearance	Iohexol	80.4±4.6	55.3±20.5	52.0
Leuven	Belgium	Referrals	21	Plasma clearance	^{51}Cr-EDTA	19.1±1.2	78.2±23.1	47.6
Lund	Sweden	CAPA-study[5]	2,847	Plasma clearance	Iohexol	60.1±16.5	62.5±34.1	48.5
Lyon	France	Referrals	2,435	Plasma/renal clearance	Iohexol/inulin	31.3±16.7	84.5±32.7	46.8
Örebro	Sweden	Referrals	2,051	Plasma clearance	Iohexol	56.5±16.3	64.3±36.0	41.7
Saint-Etienne	France	HIV-study[9]	203	Plasma clearance	Iohexol	48.7±10.3	100.3±27.3	48.7
Stockholm	Sweden	Referrals	856	Plasma clearance	Iohexol	72.9±14.1	48.7±27.6	44.2
Tromsø	Norway	RENIS-T6 study[10]	1,627	Plasma clearance	Iohexol	58.1±3.8	101.5±19.9	50.8
Kinshasa/ Abidjan	DRC/Côte d'Ivoire	African Study[11]	508	Plasma clearance	Iohexol	41.8±14.3	80.5±28.9	46.7
Rio de Janeiro	Brazil	Brazilian study[12]	39	Plasma clearance	^{51}Cr-EDTA	60.0±13.5	41.9±23.4	59.0
Paris	France	Referrals	4429	Plasma clearance	^{51}Cr-EDTA	52.4±14.8	61.3±26.6	41.1
Black population								
Kinshasa/ Abidjan	DRC/Côte d'Ivoire	African Study[11]	508	Plasma clearance	Iohexol	41.8±14.3	80.5±28.9	46.7
Rio de Janeiro	Brazil	Brazilian study[12]	61	Plasma clearance	^{51}Cr-EDTA	55.9±13.8	49.8±32.2	50.8
Paris	France	Referrals	964	Plasma clearance	^{51}Cr-EDTA	50.4±13.8	61.1±24.6	41.1

*Referrals = referred for plasma or renal clearance measurement on clinical grounds. Results mean±SD

EKFC
17321
White Europeans (Paris)
4429
Black Europeans (Paris)
964
Africans
508

Having said that….

Annals of Internal Medicine

EDITORIAL

Eliminating Racial Inequities in Kidney Health: Much More Than Revising Estimating Equations

Editorials | 11 January 2022

Akinlolu Ojo, MD, PhD, MBA
University of Kansas Medical Center, Kansas City, Kansas

Ann Intern Med. doi:10.7326/M21-4875

These enduring kidney health inequities in Black persons have been with us for decades, and the effortful tokenism of revisions to GFR estimating equations will have no materially significant effect on kidney health inequities experienced by Black patients with CKD today, tomorrow, or a decade from now even with universal adoption of the new CKD-EPI creatinine equation refit. The solutions and productive target of efforts to achieve racial equity in kidney health lie in improving our health care and public health systems, not fine-tuning the estimating equations for GFR or validating KFRE scoring with or without the CKD-EPI equation refit.

Having said that…

- All equations remain "estimation"…relatively good at the population level, but large imprecision at the individual level

White Europeans (EKFC+Paris) n = 17,321	CKD-EPI$_{ASR}$	CKD-EPI$_{ASR-NB}$	CKD-EPI$_{AS}$	LMREV	EKFC
Bias	3.0 [2.7; 3.2]	3.0 [2.7; 3.2]	6.0 [5.8; 6.3]	-3.2 [-3.4; -3.0]	-0.3 [-0.5; -0.1]
IQR [Pct25; Pct75]	16.8 [-4.4; 12.3]	16.8 [-4.4; 12.3]	17.2 [-1.5; 15.7]	15.5 [-11.3; 4.2]	15.1 [-7.7; 7.4]
P20	66.9 [66.2; 67.6]	66.9 [66.2; 67.6]	63.0 [62.3; 63.7]	71.0 [70.3; 71.7]	72.4 [71.8; 73.1]
P30	82.5 [82.0; 83.1]	82.5 [82.0; 83.1]	78.5 [77.9; 79.1]	87.3 [86.8; 87.8]	86.6 [86.1; 87.1]
P10	39,7	39,7	36,2	39,4	39,6

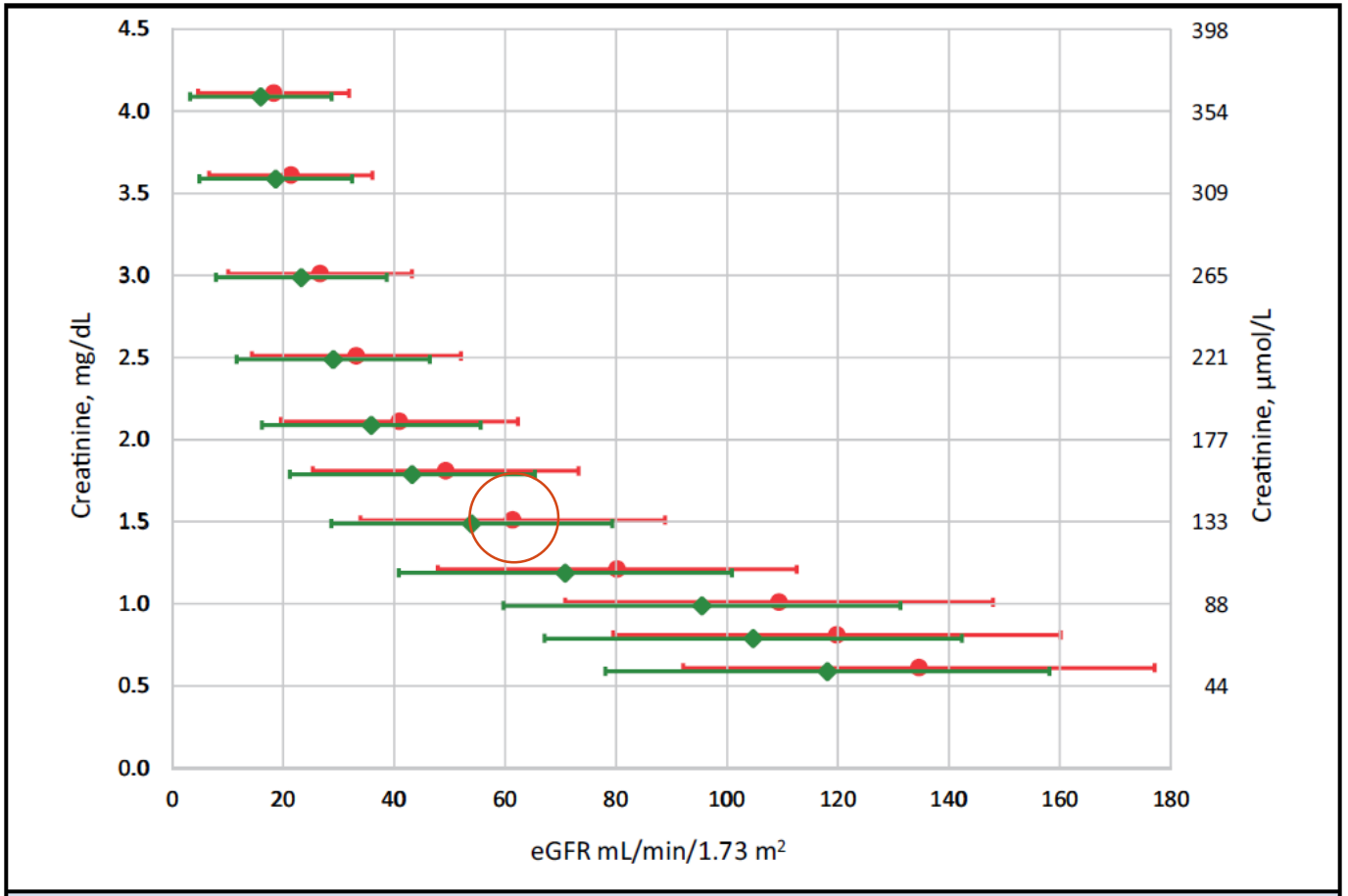
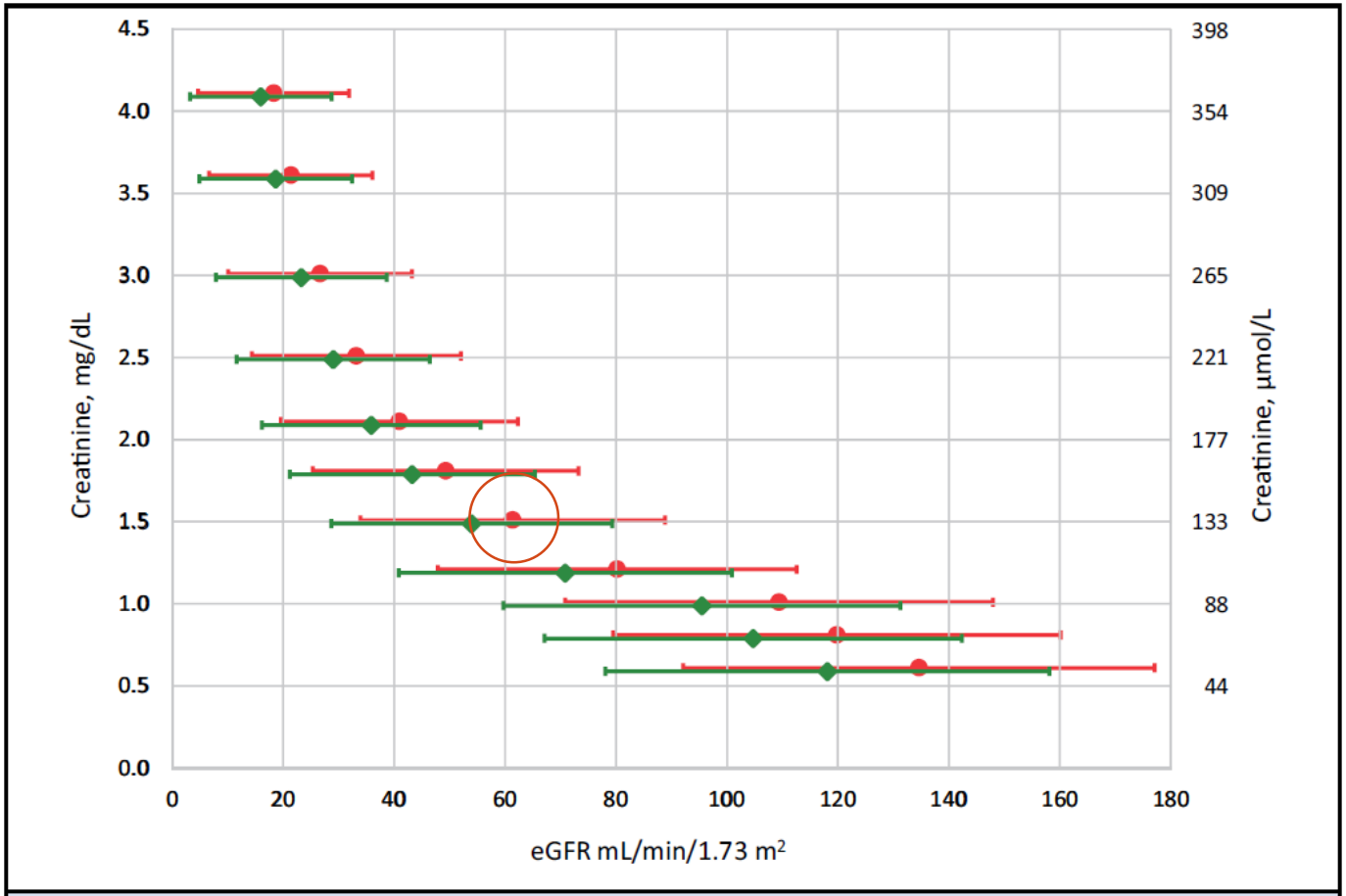


Fig. 1. Uncertainty of eGFR calculated using the CKD-EPI equations for African-Americans and non-African-Americans at various creatinine concentrations for a 50-year-old male. Circles (red, larger values) indicate African-American and diamonds (green, lower values) indicate non-African-American equations. Plot symbols are the eGFR values and error bars represent the 95% CI for each eGFR value.

eGFR = 60,25 ml/min/1.73m²

Miller WG, Clin Chem, 2021, p693 and p820



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eGFR ~~= 60,25 ml/min/1.73m²~~

= 60 ml/min/1.73m² (CI 95%: 33-87)

Miller WG, Clin Chem, 2021, p693 and p820

Having said that…

- All equations remain "estimation"…relatively good at the population level, but large imprecision at the individual level

White Europeans (EKFC+Paris) n = 17,321	CKD-EPI$_{ASR}$	CKD-EPI$_{ASR-NB}$	CKD-EPI$_{AS}$	LMREV	EKFC
Bias	3.0 [2.7; 3.2]	3.0 [2.7; 3.2]	6.0 [5.8; 6.3]	-3.2 [-3.4; -3.0]	-0.3 [-0.5; -0.1]
IQR [Pct25; Pct75]	16.8 [-4.4; 12.3]	16.8 [-4.4; 12.3]	17.2 [-1.5; 15.7]	15.5 [-11.3; 4.2]	15.1 [-7.7; 7.4]
P20	66.9 [66.2; 67.6]	66.9 [66.2; 67.6]	63.0 [62.3; 63.7]	71.0 [70.3; 71.7]	72.4 [71.8; 73.1]
P30	82.5 [82.0; 83.1]	82.5 [82.0; 83.1]	78.5 [77.9; 79.1]	87.3 [86.8; 87.8]	86.6 [86.1; 87.1]
P10	39,7	39,7	36,2	39,4	39,6

- Measuring GFR is sometimes important

Conclusions

- The game is over in USA
- In White Europeans, the new equation performs worse than the previous one, and not better in Black Africans (without race coefficient)
- There are difference in serum creatinine between *populations*
- We don't know why (and it is a pity)
- The correction should be at the creatinine level (for race and sex)
- This is done in the EKFC equation with dedicated (not race-adapted but population-specifically developed) Q values
- « Population » should be self-identified (might be large or not)
- Cystatin C is another solution
- Measured GFR is precision medicine

Thank you !

Questions?