33rd EUROPEAN MEETING ON HYPERTENSION AND CARDIOVASCULAR PROTECTION

BERLIN

MAY 31 - JUNE 3, 2024

www.eshannualmeetings.eu

Delanaye Pierre

Department of Nephrology, Dialysis, Transplantationn, University of Liège, Belgium

Pitfall in GFR estimation

Category	Disclosure Information
Employer	Nothing to disclose.
Ownership Interest	Nothing to disclose.
Consultancy	IDS; Nephrolyx; Alentis Therapeutics; ARK Bioscience; Astellas
Research Funding	Nothing to disclose.
Honoraria	IDS; Fresenius Kabi; Fresenius Medical Care; Nephrolyx; Alentis Therapeutics; ARK Bioscience; AstraZeneca; Bayer
Patents or Royalties	Nothing to disclose.
Advisory or Leadership Role	Nothing to disclose.
Speakers Bureau	Nothing to disclose.
Other Interests or Relationships	Nothing to disclose.

The Glomerular Filtration Rate is usually the best parameter to assess the global kidney function.

Homer William Smith (January 2, 1895 – March 25, 1962)

Table 4 | Use of GFR and albuminuria

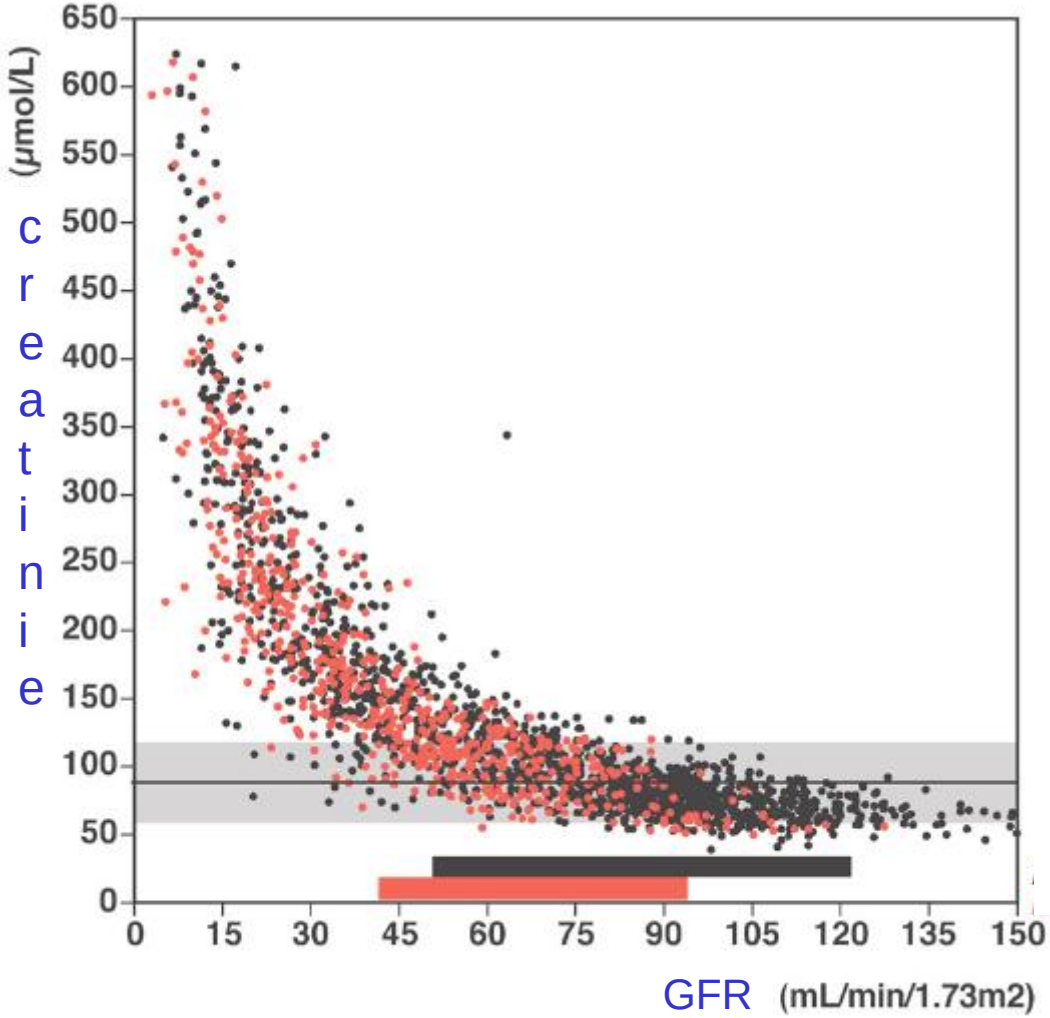
	Current level		
Clinical decisions	**GFR**	**Albuminuria**	**Change in the level of GFR**
Diagnosis and staging	• Detection of CKD • Evaluation for kidney donation	• Detection of CKD	• Detection of AKI and AKD • Detection of CKD progression
Treatment	• Referral to nephrologists • Patient and family education about CKD and benefit of lifestyle changes • Monitor progression of GFR decline • Referral for kidney transplantation • Placement of dialysis access • Dosage and monitoring for medications cleared by the kidney • Determine safety of diagnostic tests or procedures • Eligibility for clinical trials	• Referral to nephrologists • Patient and family education about CKD and benefit of lifestyle changes • Monitor progression of GFR decline • Eligibility for clinical trials	• Treatment of AKI • Monitoring drug toxicity • Re-evaluate CKD treatment strategies
Risk assessment	• Risk of CKD complications • Risk for CKD progression • Risk of CVD • Risk for medication errors • Risk for perioperative complications • Risk for mortality • Fertility and risk of complications of pregnancy	• Risk for CKD progression • Risk for CVD • Risk for mortality • Fertility and risk of complications of pregnancy	• Risk for kidney failure • Risk for CVD, HF, and mortality • Risk for adverse pregnancy outcome

AKD, acute kidney disease; AKI, acute kidney injury; CKD, chronic kidney disease; CVD, cardiovascular disease; GFR, glomerular filtration rate; HF, heart failure.

GFR is estimated with biomarkers

Serum creatinine is one the most prescribed analysis

The most important is probably to know the limitations…



NephroTest Cohort (France)
Which GFR for patients with serum creatinine measured at 80 µmol/L (0.9 mg/dL)?

CI 95% for subjects<65 years old
CI 95% for subjects>65 years old

S. Creatinine lab normality range

Analytical

Jaffe methods

Enzymatic methods

Jaffe and enzymatic methods gives slightly different results

Pseudochromogen: glucose, fructose, ascorbate, proteins, urate, acetoacetate, acetone, pyruvate => false positive

Bilirubins: false negative

Physiological: Tubular secretion

10 to 40%

Increase with decreased GFR

Unpredictable at the individual level !

Physiological: Muscular mass

Production (relatively) constant but muscular production => serum creatinine is dependent of muscualr mass, not only GFR (age? sex/gender? race/population?)

Extra-renal production

Creatinine clearance

Not recommended (first line)

Creatinine tubular secretion

Lack of precision:

errors in urine collection

22 to 27% for « trained » patients

50 to 70 % for others

large intra-individual variability for creatinine excretion

KDIGO, Kidney Int, 2024
Perrone RD, Clin Chem, 1992, 38, 1933

Which one?

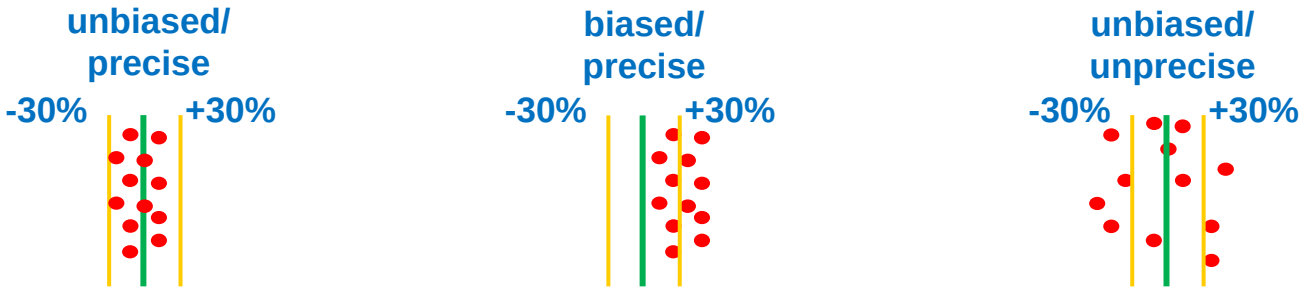
Cockcroft

CKD-EPI

EKFC

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



Bland JM, Altman DG, Lancet, 1986, 8476, 307
Delanaye P, Nephrol Dial Transplant, 2013, 28, 1396

Which one?

~~Cockcroft~~

CKD-EPI

EKFC

OFFICIAL JOURNAL OF THE INTERNATIONAL SOCIETY OF NEPHROLOGY

ISN INTERNATIONAL SOCIETY OF NEPHROLOGY

SUPPLEMENT TO

kidney INTERNATIONAL

KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease

Table 14 | Validated GFR estimating equations

Marker	Equation name and year	Age	Variables	Development populations
Creatinine	CKD-EPI 2009[238]	≥18; modification CKD-EPI 40 for pediatric available	Developed using A, S, R but reported not using the Black race coefficient, A, S, R (NB)	8254 Black and NB individuals from 10 studies in the United States and Europe[a]
	CKiD U25 2021[239]	1–25	A, S, height	928 children with CKD in the United States and Canada
	CKD-EPI 2021[147]	≥18	A, S	8254 Black and NB individuals from 10 studies in the United States and Europe[a]
	EKFC 2021[240]	2–100	A, S, European Black and NB specific Q-value; separate Q-values for Africa vs. Europe	mGFR vs. SCr (11,251 participants in 7 studies in Europe and 1 study from the United States) Normal GFR from 5482 participants in 12 studies of kidney donor candidates (100% Caucasian) European NB Q from 83,157 laboratory samples (age 2–40 years) in 3 European hospital clinical laboratories; European Black Q-value (N = 90 living kidney donors from Paris); African Black Q-value (N = 470 healthy individuals from République Démocratique de Congo); All Q-values developed in cohorts independent for EKFC development and validation
	Lund Malmö Revised 2014[241]		A, S	3495 GFR examinations from 2847 adults from Sweden referred for measurement of GFR
	CKD-EPI 2009 Modified for China 2014[b,242]	≥18	A, S	589 people with diabetes from the Third Affiliated Hospital of Sun Yat-sen University, China
	CKD-EPI 2009 Modified for Japan 2016[b,83]	≥18	A, S	413 hospitalized Japanese people in 80 medical centers
	CKD-EPI 2009 Modified for Pakistan 2013[b,235]	≥18	A, S	542 randomly selected low- to middle-income communities in Karachi and 39 people from the kidney clinic
Cystatin C	CKD-EPI 2012[148]	≥18	A, S	5352 Black and NB individuals from 13 studies in the United States and Europe
	EKFC 2023[91]	18–100	A	mGFR vs. SCys (assumed to be the same as mGFR vs. SCr) Normal GFR (same as for the SCr equation) Q from laboratory samples from 227,643 (42% female) laboratory samples from Uppsala University Hospital, Sweden
	CAPA 2014[243]		A, S	4690 individuals within large subpopulations of children and Asian and Caucasian adults
Creatinine-cystatin C	CKD-EPI 2012[148]	≥18	Developed using A, S, R but reported not using the Black race coefficient, A, S, R (NB)	5352 Black and NB individuals from 13 studies in the United States and Europe
	CKD-EPI 2021[147]	≥18	A, S	5352 Black and NB individuals from 13 studies in the United States and Europe
	Average of EKFC cr and cys[240]	≥2	A, S, European race specific Q-value; separate Q-values for Africa vs. Europe	See above for EKFC creatinine and cystatin C

ARTICLE | Annals of Internal Medicine

A New Equation to Estimate Glomerular Filtration Rate

Andrew S. Levey, MD; Lesley A. Stevens, MD, MS; Christopher H. Schmid, PhD; Yaping (Lucy) Zhang, MS; Alejandro F. Castro III, MPH; Harold I. Feldman, MD, MSCE; John W. Kusek, PhD; Paul Eggers, PhD; Frederick Van Lente, PhD; Tom Greene, PhD; and Josef Coresh, MD, PhD, MHS, for the CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration)*

Table 2. The CKD-EPI Equation for Estimating GFR on the Natural Scale*

Race and Sex	Serum Creatinine Level, μmol/L (mg/dL)	Equation
Black		
Female	≤62 (≤0.7)	$GFR = 166 \times (Scr/0.7)^{-0.329} \times (0.993)^{Age}$
	>62 (>0.7)	$GFR = 166 \times (Scr/0.7)^{-1.209} \times (0.993)^{Age}$
Male	≤80 (≤0.9)	$GFR = 163 \times (Scr/0.9)^{-0.411} \times (0.993)^{Age}$
	>80 (>0.9)	$GFR = 163 \times (Scr/0.9)^{-1.209} \times (0.993)^{Age}$
White or other		
Female	≤62 (≤0.7)	$GFR = 144 \times (Scr/0.7)^{-0.329} \times (0.993)^{Age}$
	>62 (>0.7)	$GFR = 144 \times (Scr/0.7)^{-1.209} \times (0.993)^{Age}$
Male	≤80 (≤0.9)	$GFR = 141 \times (Scr/0.9)^{-0.411} \times (0.993)^{Age}$
	>80 (>0.9)	$GFR = 141 \times (Scr/0.9)^{-1.209} \times (0.993)^{Age}$

Ann Intern Med. 2009;150:604-612.

Debate on the race factor in USA

Semantic remark

Serum creatinine is different between Black and non-Black people in USA
(and we don't know why!)

(normal) mGFR is not different

The race coefficient in the CKD-EPI$_{2009}$ was considered as a source of discrimination

Eneanya N, Nat Rev Nephrol, 2022, 18, p84
Hsu CY, N Engl J med, 2021, p1750

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*

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

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)

NO !

RESEARCH LETTER

Performance of GFR Estimating Equations in African Europeans: Basis for a Lower Race-Ethnicity Factor Than in African Americans

Am J Kidney Dis, 2013, 62, p179

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

Hindawi

Research Article

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

PLOS ONE

RESEARCH ARTICLE

Performance of glomerular filtration rate estimation equations in Congolese healthy adults: The inopportunity of the ethnic correction

Justine B. Bukabau[1]*, Ernest K. Sumaili[1], Etienne Cavalier[2], Hans Pottel[3], Bejos Kifakiou[1], Aliocha Nkodila[1], Jean Robert R. Makulo[1], Vieux M. Mokoli[1], Chantal V. Zinga[1], Augustin L. Longo[1], Yannick M. Engole[1], Yannick M. Nlandu[1], François B. Lepira[1], Nazaire M. Nseka[1], Jean Marie Krzesinski[4], Pierre Delanaye[4]

1 Renal Unit, Department of Internal medicine, Kinshasa University Hospital, University of Kinshasa, Kinshasa, Democratic Republic of the Congo, 2 Division of Clinical Chemistry, CHU Sart Tilman (ULg CHU), University of Liège, Liège, Belgium, 3 Division of Public Health and Primary Care, KU Leuven Campus Kulak Kortrijk, Kortrijk, Belgium, 4 Division of Nephrology-Dialysis-Transplantation, CHU Sart Tilman (ULg CHU), University of Liège, Liège, Belgium

* justinebuk@yahoo.fr

Check for updates

ARTICLE IN PRESS

www.kidney-international.org clinical investigation

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

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]

[1]Renal Unit, Department of Internal Medicine, Kinshasa University Hospital, University of Kinshasa, Kinshasa, Democratic Republic of Congo; [2]Département de Biochimie, UFR Sciences Pharmaceutiques et Biologiques, Université Felix Houphouet Boigny, Abidjan, Ivory Coast; [3]Département de Néphrologie, UFR Sciences Médicales, Université Felix Houphouet Boigny, Abidjan, Ivory Coast; [4]Department of Public Health and Primary Care, KU Leuven Campus Kulak Kortrijk, Kortrijk, Belgium; [5]Division of Clinical Chemistry, CHU Sart Tilman (ULg CHU), University of Liège, Liège, Belgium; and [6]Division of Nephrology-Dialysis-Transplantation, CHU Sart Tilman (ULg CHU), University of Liège, Liège, Belgium

Yayo ES, Nephrol Ther, 2016 , 12 , p454
Flamant M, Am J Kidney Dis, 2013, 62, p179
Bukabau JB, Plos One, 2018, 13, e0193384
Bukabau JB, Kidney Int, 2019, 95, p1181

editorial

www.kidney-international.org

Americentrism in estimation of glomerular filtration rate equations

Pierre Delanaye[1,2], Hans Pottel[3] and Richard J. Glassock[4]

[1]*Department of Nephrology-Dialysis-Transplantation, University of Liège, Centre Hospitalier Universitaire Sart Tilman, Liège, Belgium;* [2]*Department of Nephrology-Dialysis-Apheresis, Hôpital Universitaire Carémeau, Nîmes, France;* [3]*Department of Public Health and Primary Care, Katholieke Universiteit Leuven Campus Kulak Kortrijk, Kortrijk, Belgium; and* [4]*Department of Medicine, Geffen School of Medicine, University of California, Los Angeles, California, USA*

Correspondence: *Pierre Delanaye, Service de Dialyse, Centre Hospitalier Universitaire Sart Tilman, 4000 Liège, Belgium. E-mail: pierre_delanaye@yahoo.fr*

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

KEYWORDS: glomerular filtration rate; race; serum creatinine

Ann Intern Med. 2021;174:183-191. doi:10.7326/M20-4366

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†

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.

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:

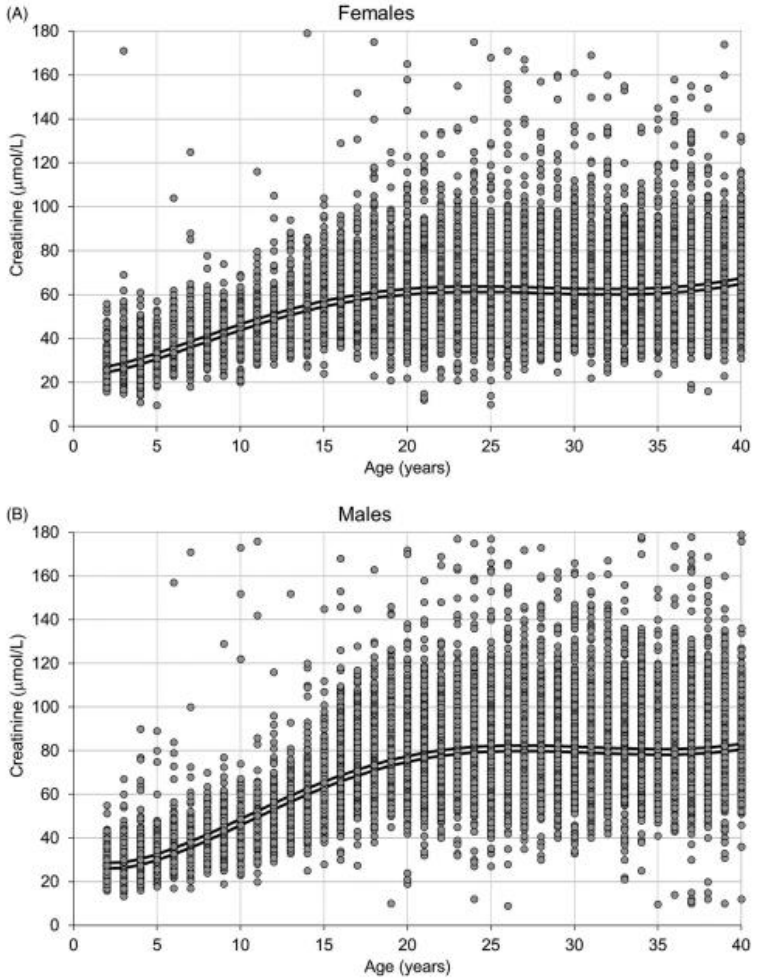
$Q = 80$ µmol/L (0.90 mg/dL)

Females:

$Q = 62$ µmol/L (0.70 mg/dL)

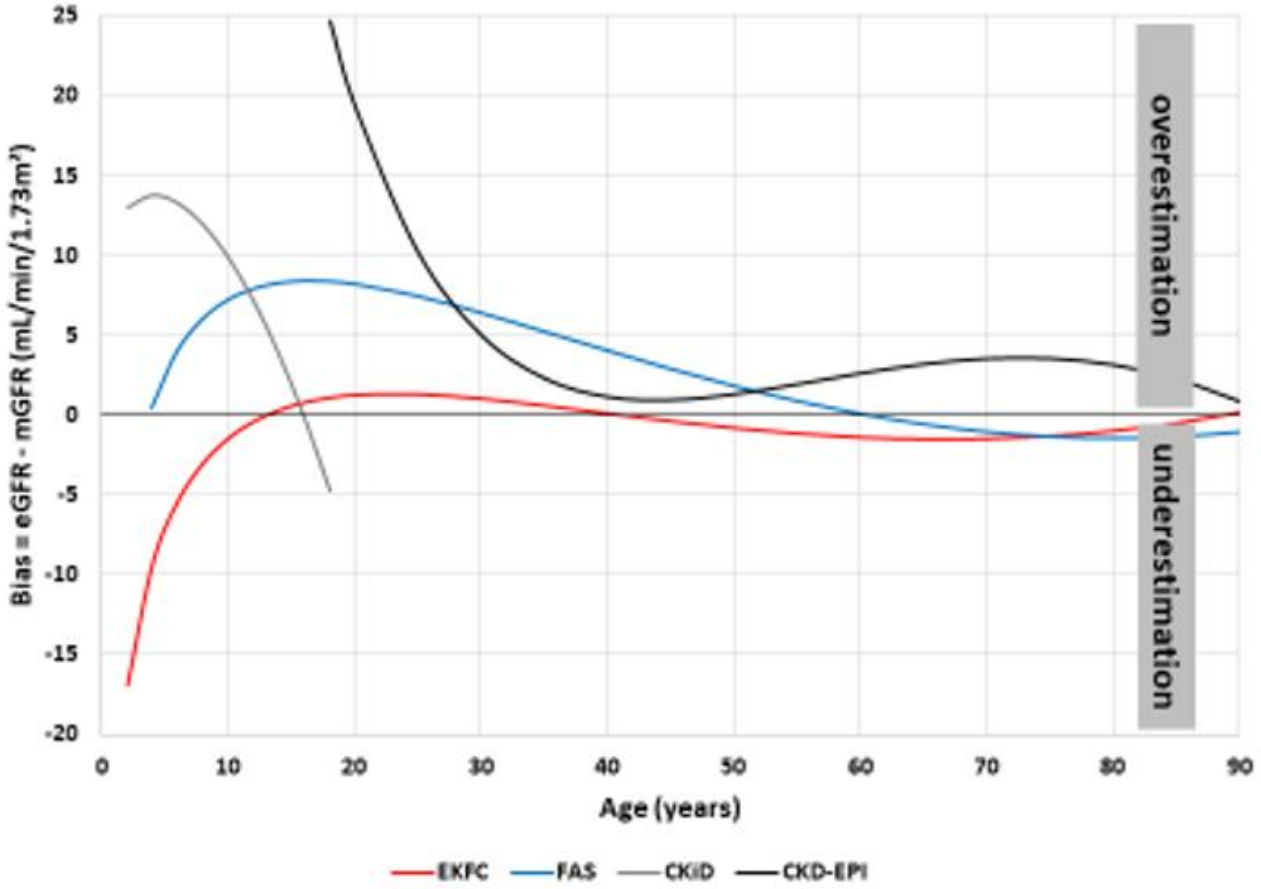
SCr and Q in µmol/L (to convert to mg/dL, divide by 88.4)

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.



N=83,257 from three labs (Sweden, Belgium)

Björk J, Scand J Clin Lab Invest, 2020, 80, p456


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

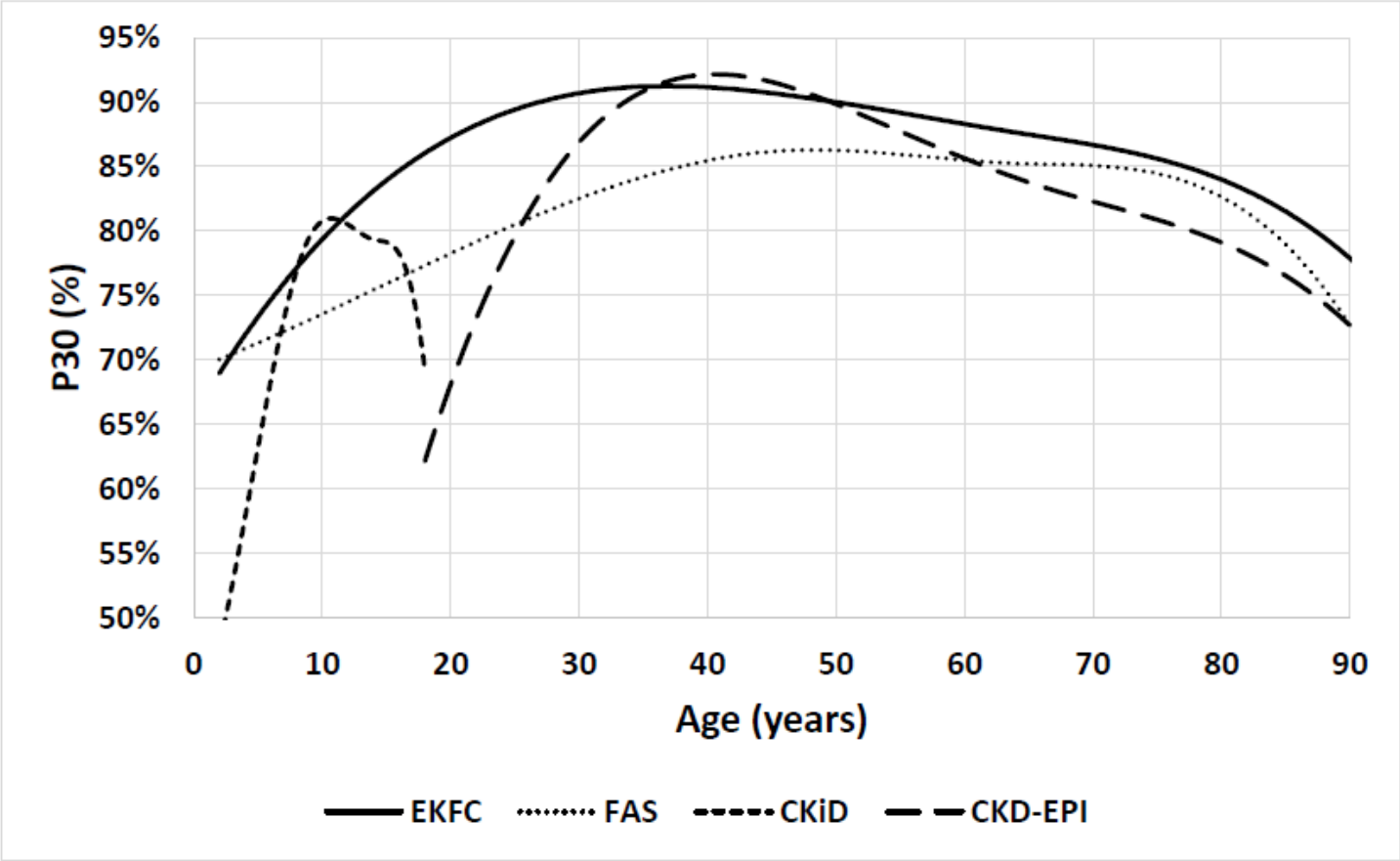


Figure S8. P30-accuracy against age for the EKFC, FAS, CKiD and CKD-EPI equation in the external validation dataset. P30 (%) was graphically presented across the age spectrum using cubic splines with two free knots and using 3rd degree polynomials.

EKFC: added value(s)

Better performance (not more expensive)

More « physiological»: correction at the serum creatinine level (sex, race) and age better conceptualized

Valid from 2y to old ages

No implausible jump at transition adolescence/young adults

Children: no need for height

Flexible! Q adapted to populations or race-free

www.kidney-international.org clinical investigation

Performance of the European Kidney Function Consortium (EKFC) creatinine-based equation in United States cohorts

see commentary on page 445

Pierre Delanaye[1,2,16], Andrew D. Rule[3,16], Elke Schaeffner[4,16], Etienne Cavalier[5,16], Junyan Shi[6,7], Andrew N. Hoofnagle[7,8,9,10], Ulf Nyman[11,16], Jonas Björk[12,13,15,16] and Hans Pottel[14,15,16]

[1]Department of Nephrology-Dialysis-Transplantation, University of Liège, CHU Sart Tilman, Liège, Belgium; [2]Department of Nephrology-Dialysis-Apheresis, Hôpital Universitaire Carémeau, Nîmes, France; [3]Division of Nephrology and Hypertension, Mayo Clinic, Rochester, Minnesota, USA; [4]Institute of Public Health, Charité – Universitätsmedizin Berlin, Berlin, Germany; [5]Department of Clinical Chemistry, University of Liège, CHU Sart Tilman, Liège, Belgium; [6]Department of Pathology and Laboratory Medicine, University of British Columbia, Vancouver, British Columbia, Canada; [7]Department of Laboratory Medicine and Pathology, University of Washington, Seattle, Washington, USA; [8]Kidney Research Institute, Department of Medicine, University of Washington, Seattle, Washington, USA; [9]Division of Metabolism, Endocrinology, and Nutrition, University of Washington, Seattle, Washington, USA; [10]Department of Medicine, University of Washington, Seattle, Washington, USA; [11]Department of Translational Medicine, Division of Medical Radiology, Lund University, Malmö, Sweden; [12]Division of Occupational and Environmental Medicine, Lund University, Lund, Sweden; [13]Clinical Studies Sweden, Forum South, Skåne University Hospital, Lund, Sweden; and [14]Department of Public Health and Primary Care, KU Leuven Campus Kulak Kortrijk, Kortrijk, Belgium

Kidney International (2024) **105**, 629–637;

Validation of EKFC in US populations

Cohorts	Sample Size	Age (years)	Measured GFR (mL/min/1.73m²)	% of women	% of Black subjects	Proportion of individuals with urinary clearance data available
All	*12,854*	*56.0 [22.1]*	*57 [46]*	*44.3*	*21.7*	*93.2*
AASK	1,844	54.5 [16.0]	57 [35]	35.9	100	100
ALTOLD	381	43.3 [19.0]	97 [18]	65.1	1.8	0
CRIC	1,194	59.0 [17.7]	48 [28]	44.4	44.7	100
CRISP	217	34.0 [13.0]	93 [34]	59.0	11.1	100
DCCT/EDIC	809	31.0 [9.0]	119 [25]	47.8	1.4	100
GENOA/ECAC	1,093	66.1 [12.1]	80 [27]	56.6	0	100
Mayo Clinic	5,069	59.0 [21.0]	50 [40]	44.6	2.0	100
MDRD	1,756	51.0 [21.0]	36 [29]	39.5	12.4	100
PERL	491	52.0 [15.0]	70 [25]	33.6	10.8	0

Results are expressed in % or Median [interquartile range].
GFR: glomerular filtration rate

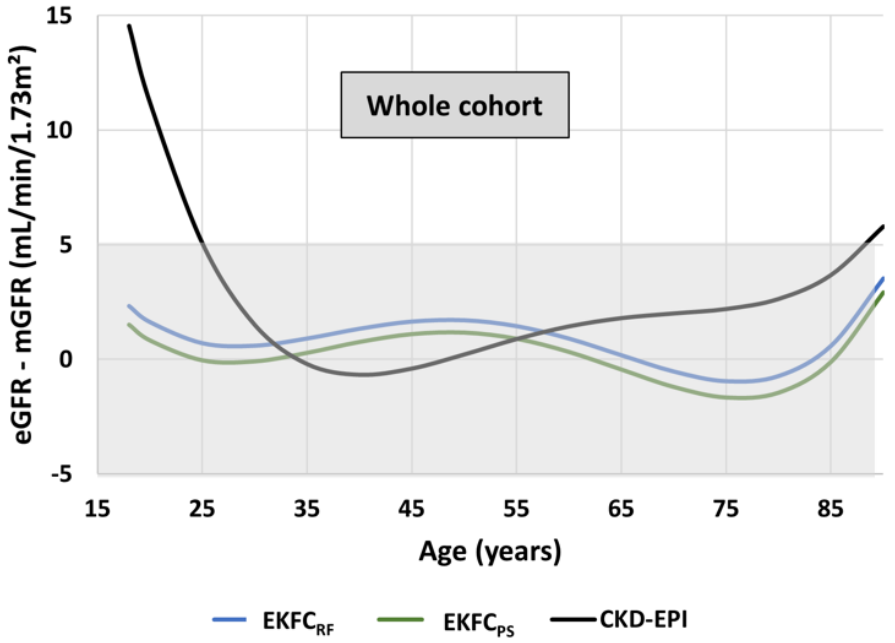
Q-values could be population specific

Q-values determined in different populations

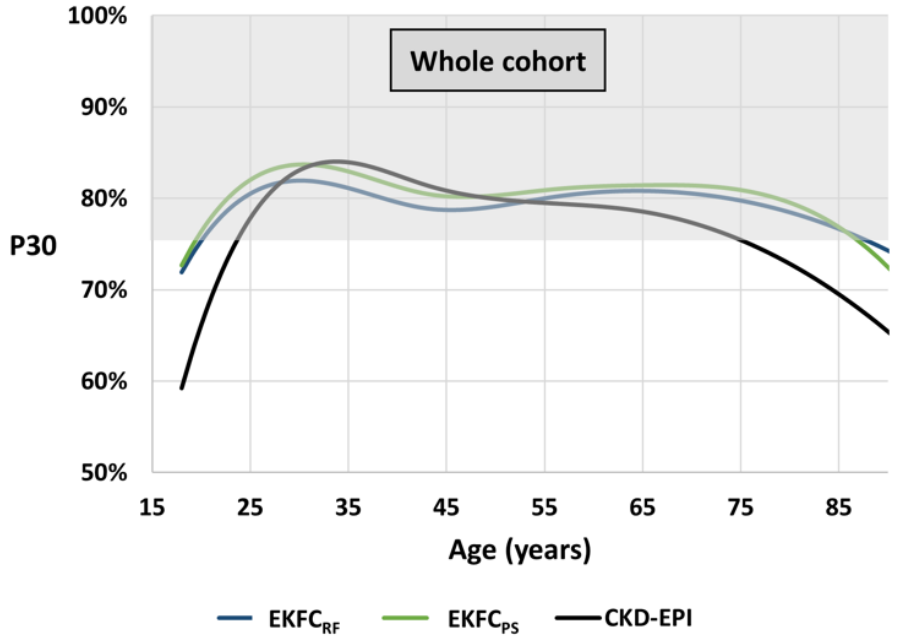
	Q value in women	Q value in men	Origine
White European	0.70	0.90	Large data from laboratories in Sweden and Belgium
Black European	0.74	1.02	Living kidney donors in Paris
Black Africans (Central Africa)	0.72	0.96	Healthy people in Congo
White US population-specific	0.73	0.93	Large data from laboratories from University of Washington Medicine System
Black US population-specific	0.73	1.00	Large data from laboratories from University of Washington Medicine System
White US population-specific	0.70	0.94	National Health and Nutrition Examination Survey
Black US population-specific	0.72	1.03	National Health and Nutrition Examination Survey
US race-free	0.73	0.97	Large data from laboratories from University of Washington Medicine System
China	0.62	0.88	[illegible] people

All results are expressed in mg/dL

A


eGFR - mGFR (mL/min/1.73m²)
15
10
5
0
-5
Whole cohort
15
25
35
45
55
65
75
85
Age (years)
EKFC$_{RF}$
EKFC$_{PS}$
CKD-EPI

B


P30
100%
90%
80%
70%
60%
50%
Whole cohort
15
25
35
45
55
65
75
85
Age (years)
EKFC$_{RF}$
EKFC$_{PS}$
CKD-EPI

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)

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Cystatin C–Based Equation to Estimate GFR without the Inclusion of Race and Sex

H. Pottel, J. Björk, A.D. Rule, N. Ebert, B.O. Eriksen, L. Dubourg, E. Vidal-Petiot, A. Grubb, M. Hansson, E.J. Lamb, K. Littmann, C. Mariat, T. Melsom, E. Schaeffner, P.-O. Sundin, A. Åkesson, A. Larsson, E. Cavalier, J.B. Bukabau, E.K. Sumaili, E. Yayo, D. Monnet, M. Flamant, U. Nyman, and P. Delanaye

ABSTRACT

N Engl J Med 2023;388:333-43.

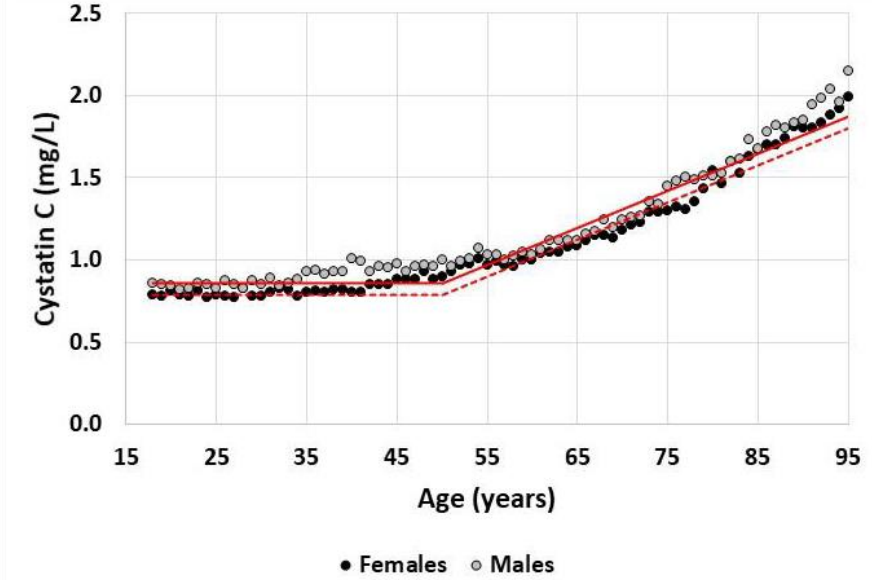
Measured GFR, IDMS traceable creatinine, calibrated cystatin C
N=12,832

11 cohorts
White Europeans: n=7,727
White Europeans from Paris: n=2,646
White US: n=1,093
Black Europeans from Paris: n=858
Black Africans: n=508

$$\text{EKFC} - \text{eGFR} = 107.3/[\text{Biomarker}/Q]^{\alpha} \times [0.990^{(\text{Age}-40)} \text{ if age } >40 \text{ years}],$$

with $\alpha = 0.322$ when biomarker/Q is less than 1
and $\alpha = 1.132$ when biomarker/Q is 1 or more.

Figure S4. Median plasma cystatin C in one-year intervals against age for men and women. A mathematical model to define Q'-values is proposed (red solid line): for adults Q' = 0.79 mg/L (women, dashed line) and 0.86 mg/L (men, solid line) until 50 years and a linear increasing model thereafter.



Q' = 0.83 mg/L until 50 years
Q' = 0.83 + 0.005 x (Age – 50)

Laboratory data from Sweden
N=227,643

Table 1. Performance of Single Biomarker (Serum Creatinine or Cystatin C)–Based Equations to Estimate the Glomerular Filtration Rate.*

Variable	Serum Creatinine–Based Equations		
	CKD-EPI eGFRcr(ASR)	CKD-EPI eGFRcr(AS)	EKFC eGFRcr
EKFC cohort, 7727 White patients			
Median bias (95% CI) — ml/min/1.73 m²†	3.96 (3.67 to 4.32)	7.40 (7.02 to 7.76)	0.58 (0.32 to 0.86)
IQR of estimated GFR– measured GFR— ml/min/1.73 m²‡	15.5 (–3.0 to 12.5)	16.3 (0.0 to 16.3)	14.5 (–6.5 to 8.0)
Root-mean-square error (95% CI) — ml/min/1.73 m²§	14.8 (14.4 to 15.2)	16.3 (15.9 to 16.6)	13.1 (12.8 to 13.4)
P_{10} — % (95% CI)¶	40.3 (39.2 to 41.4)	34.7 (33.6 to 35.8)	43.3 (42.2 to 44.4)
P_{30} — % (95% CI)‖	81.6 (80.8 to 82.5)	75.7 (74.8 to 76.7)	85.8 (85.0 to 86.5)

7.40 (7.02 to 7.76) 0.58 (0.32 to 0.86)
16.3 (0.0 to 16.3) 14.5 (–6.5 to 8.0)
16.3 (15.9 to 16.6) 13.1 (12.8 to 13.4)
34.7 (33.6 to 35.8) 43.3 (42.2 to 44.4)
75.7 (74.8 to 76.7) 85.8 (85.0 to 86.5)

Table 1. Performance of Single Biomarker (Serum Creatinine or Cystatin C)–Based Equations to Estimate the Glomerular Filtration Rate.*

Variable	Cystatin C–Based Equations	
	CKD-EPI eGFRcys	EKFC eGFRcys without Sex
EKFC cohort, 7727 White patients		
Median bias (95% CI) — ml/min/1.73 m²†	0.28 (–0.02 to 0.64)	0.00 (–0.37 to 0.27)
IQR of estimated GFR– measured GFR— ml/min/1.73 m²‡	19.1 (–7.9 to 11.2)	14.4 (–7.9 to 6.5)
Root-mean-square error (95% CI) — ml/min/1.73 m²§	15.8 (15.5 to 16.1)	13.5 (12.9 to 14.1)
P_{10} — % (95% CI)¶	32.0 (31.0 to 33.0)	41.7 (40.6 to 42.8)
P_{30} — % (95% CI)‖	80.8 (79.9 to 81.7)	86.2 (85.4 to 87.0)

Cystatin C–Based Equations

CKD-EPI eGFRcys | EKFC eGFRcys without Sex

0.28 (–0.02 to 0.64) | 0.00 (–0.37 to 0.27)
19.1 (–7.9 to 11.2) | 14.4 (–7.9 to 6.5)
15.8 (15.5 to 16.1) | 13.5 (12.9 to 14.1)
32.0 (31.0 to 33.0) | 41.7 (40.6 to 42.8)
80.8 (79.9 to 81.7) | 86.2 (85.4 to 87.0)

Table 2. Performance of Combined Serum Creatinine– and Cystatin C–Based Equations to Estimate GFR.*

Variable	CKD-EPI eGFRcr-cys(ASR)	CKD-EPI eGFRcr-cys(AS)	EKFC eGFRcr-cys without Sex
EKFC cohort, 7727 White patients			
Median bias (95% CI) — ml/min/1.73 m²†	2.50 (2.17 to 2.76)	5.04 (4.69 to 5.36)	0.37 (0.14 to 0.66)
IQR of estimated GFR – measured GFR — ml/min/1.73 m²‡	14.8 (–3.6 to 11.2)	16.7 (–1.8 to 14.9)	12.0 (–5.9 to 6.1)
Root-mean-square error (95% CI) — ml/min/1.73 m²§	13.1 (12.8 to 13.4)	14.7 (14.4 to 15.0)	11.3 (11.0 to 11.6)
P_{10} — % (95% CI)¶	41.5 (40.4 to 42.6)	37.2 (36.2 to 38.3)	48.9 (47.8 to 50.0)
P_{30} — % (95% CI)‖	88.3 (87.6 to 89.0)	84.2 (83.4 to 85.0)	90.4 (89.8 to 91.1)
Paris cohort, 2646 White patients			
Median bias (95% CI) — ml/min/1.73 m²†	–1.35 (–1.82 to –0.97)	0.64 (0.16 to 1.15)	–0.65 (–1.06 to –0.23)
IQR of estimated GFR – measured GFR — ml/min/1.73 m²‡	13.4 (–7.5 to 5.8)	14.1 (–5.8 to 8.3)	12.4 (–6.8 to 5.6)
Root-mean-square error (95% CI) — ml/min/1.73 m²§	12.1 (11.6 to 12.7)	12.6 (12.0 to 13.1)	11.8 (11.2 to 12.4)
P_{10} — % (95% CI)¶	43.9 (42.0 to 45.8)	42.3 (40.4 to 44.1)	45.8 (43.9 to 47.7)
P_{30} — % (95% CI)‖	89.7 (88.5 to 90.8)	89.2 (88.0 to 90.4)	92.1 (91.1 to 93.1)
U.S. cohort, 1093 White patients			
Median bias (95% CI) — ml/min/1.73 m²†	9.23 (8.45 to 10.10)	13.9 (13.1 to 14.9)	0.97 (0.01 to 2.12)
IQR of estimated GFR – measured GFR — ml/min/1.73 m²‡	18.4 (0.5 to 18.8)	18.1 (5.1 to 23.3)	17.4 (–8.2 to 9.2)
Root-mean-square error (95% CI) — ml/min/1.73 m²§	18.1 (17.1 to 19.1)	21.0 (20.1 to 22.0)	15.5 (14.3 to 16.7)
P_{10} — % (95% CI)¶	37.1 (34.3 to 40.0)	28.1 (25.4 to 30.8)	45.7 (42.7 to 48.6)
P_{30} — % (95% CI)‖	79.5 (77.1 to 81.9)	72.1 (69.4 to 74.8)	88.7 (86.9 to 90.6)
Paris cohort, 858 Black patients			
Median bias (95% CI) — ml/min/1.73 m²†	–0.37 (–1.06 to 0.57)	–2.08 (–2.71 to –1.32)	–0.65 (–1.23 to 0.11)
IQR of estimated GFR – measured GFR — ml/min/1.73 m²‡	15.2 (–6.4 to 8.8)	14.0 (–7.9 to 6.1)	12.4 (–6.2 to 6.2)
Root-mean-square error (95% CI) — ml/min/1.73 m²§	13.3 (11.9 to 14.6)	12.6 (11.2 to 13.9)	11.6 (10.0 to 13.0)
P_{10} — % (95% CI)¶	38.7 (35.4 to 42.0)	38.9 (35.7 to 42.2)	48.3 (44.9 to 51.6)
P_{30} — % (95% CI)‖	87.9 (85.7 to 90.1)	89.0 (87.0 to 91.1)	92.0 (90.1 to 93.8)
African cohort, 508 Black patients			
Median bias (95% CI) — ml/min/1.73 m²†	8.55 (6.87 to 10.30)	4.08 (2.37 to 5.78)	0.42 (–1.03 to 1.51)
IQR of estimated GFR – measured GFR — ml/min/1.73 m²‡	24.7 (–4.5 to 20.1)	22.0 (–7.4 to 14.7)	17.1 (–7.2 to 10.0)
Root-mean-square error (95% CI) — ml/min/1.73 m²§	19.7 (18.2 to 21.1)	17.2 (15.8 to 18.5)	14.7 (13.3 to 16.0)
P_{10} — % (95% CI)¶	28.7 (24.8 to 32.7)	34.3 (30.1 to 38.4)	43.5 (39.2 to 47.8)
P_{30} — % (95% CI)‖	75.0 (71.2 to 78.8)	77.6 (73.9 to 81.2)	84.3 (81.1 to 87.4)

Cystatin C allows an eGFR without race nor sex

EKFC is mathematically the same as EKFC creatinine, only Q is changing

EKFC equations are better than corresponding CKD-EPI equations
=> good alternative to CKD-Epi in Europe and Africa

Equations based on cystatin C are not better than equations based on creatinine

Combined equations are better (P30 +5-10%)

Standardisation

More costly

How to manage discrepant results?

https://ekfccalculator.pages.dev/

Limitations of equations = creatinine

Specific populations:
Equations are not magic!
Keep our clinical feeling!!

Anorexia Nervosa (Delanaye P, Clin Nephrol, 2009, 71, 482)

Cirrhosis (Skluzacek PA, Am J Kidney Dis, 2003, 42, 1169)

ICU (Delanaye P, BMC Nephrology, 2014, 15, 9)

Hospitalized (Poggio ED, Am J Kidney Dis, 2005, 46, 242)

Heart Transplanted (Delanaye P, Clin Transplant, 2006, 20, 596)

Kidney Transplanted (Masson I, Transplantation, 2013, 95, 1211)

Obesity (Bouquegneau A, NDT, 2013, 28, iv122)

Do not over-interpet an eGFR result…

All equations remain estimation…

Good at the population level

Lack of precision at the individual level

Variable	CKD-EPI eGFRcr-cys(ASR)	CKD-EPI eGFRcr-cys(AS)	EKFC eGFRcr-cys without Sex
EKFC cohort, 7727 White patients			
Median bias (95% CI) — ml/min/1.73 m²†	2.50 (2.17 to 2.76)	5.04 (4.69 to 5.36)	0.37 (0.14 to 0.66)
IQR of estimated GFR – measured GFR — ml/min/1.73 m²‡	14.8 (–3.6 to 11.2)	16.7 (–1.8 to 14.9)	12.0 (–5.9 to 6.1)
Root-mean-square error (95% CI) — ml/min/1.73 m²§	13.1 (12.8 to 13.4)	14.7 (14.4 to 15.0)	11.3 (11.0 to 11.6)
P_{10} — % (95% CI)¶	41.5 (40.4 to 42.6)	37.2 (36.2 to 38.3)	48.9 (47.8 to 50.0)
P_{30} — % (95% CI)‖	88.3 (87.6 to 89.0)	84.2 (83.4 to 85.0)	90.4 (89.8 to 91.1)

REVIEWS

The applicability of eGFR equations to different populations

Pierre Delanaye and Christophe Mariat

GO BACK to MEASURED GFR

Delanaye P, Nature Rev Nephrol, 2013, 9, p513
Ebert N, Clin Kidney J, 2021, 14, p1861
Agarwal R, Nephrol Dial Transplant, 2019, 34, p2001
Shafi T, Ann Intern Med, 2022, 175, p1073

CLINICAL KIDNEY JOURNAL

ckj OXFORD

Clinical Kidney Journal, 2016, vol. 9, no. 5, 682–699

doi: 10.1093/ckj/sfw070
Advance Access Publication Date: 23 August 2016
CKJ Review

CKJ REVIEW

Iohexol plasma clearance for measuring glomerular filtration rate in clinical practice and research: a review. Part 1: How to measure glomerular filtration rate with iohexol?

Pierre Delanaye[1], Natalie Ebert[2], Toralf Melsom[3,4], Flavio Gaspari[5], Christophe Mariat[6], Etienne Cavalier[7], Jonas Björk[8], Anders Christensson[9], Ulf Nyman[10], Esteban Porrini[11], Giuseppe Remuzzi[12,13], Piero Ruggenenti[12,13], Elke Schaeffner[2], Inga Soveri[14], Gunnar Sterner[15], Bjørn Odvar Eriksen[3,4] and Sten-Erik Bäck[16]

Iohexol plasma clearance

Not so cumbersome
Not so costly

CLINICAL KIDNEY JOURNAL

ckj OXFORD

Clinical Kidney Journal, 2016, vol. 9, no. 5, 700–704

doi: 10.1093/ckj/sfw071
Advance Access Publication Date: 9 September 2016
CKJ Review

CKJ REVIEW

Iohexol plasma clearance for measuring glomerular filtration rate in clinical practice and research: a review. Part 2: Why to measure glomerular filtration rate with iohexol?

Pierre Delanaye[1], Toralf Melsom[2], Natalie Ebert[3], Sten-Erik Bäck[4], Christophe Mariat[5], Etienne Cavalier[6], Jonas Björk[7], Anders Christensson[8], Ulf Nyman[9], Esteban Porrini[10], Giuseppe Remuzzi[11,12], Piero Ruggenenti[11,12], Elke Schaeffner[3], Inga Soveri[13], Gunnar Sterner[14], Bjørn Odvar Eriksen[2] and Flavio Gaspari[15]

[1]Department of Nephrology, Dialysis and Transplantation, University of Liège Hospital (ULg CHU), 4000 Liège, Belgium, [2]Metabolic and Renal Research Group, UiT The Arctic University of Norway and Section of Nephrology, University Hospital of North Norway, Tromsø, Norway, [3]Charité University Medicine, Institute of Public Health, Berlin, Germany, [4]Department of Clinical Chemistry, Skåne University Hospital, Lund, Sweden, [5]Department of Nephrology, Dialysis, Transplantation and Hypertension, CHU Hôpital Nord, University Jean Monnet, PRES Université de LYON, Saint-Etienne, France, [6]Department of Clinical Chemistry, University of Liège Hospital (ULg CHU), Liège, Belgium, [7]Department of Occupational and Environmental Medicine, Lund University, Lund, Sweden, [8]Department of Nephrology, Skåne University Hospital, Lund, Sweden, [9]Department of Translational Medicine, Division of Medical Radiology, Skåne University Hospital, Malmö, Sweden, [10]University of La Laguna, CIBICAN-ITB, Faculty of Medicine, Hospital Universtario de Canarias, Tenerife, Spain, [11]Centro di Ricerche Cliniche per le Malattie Rare 'Aldo e Cele Daccò', Istituto di Ricerche Farmacologiche Mario Negri, Centro Anna Maria Astori, Science and Technology Park Kilometro Rosso, Bergamo, Italy, [12]Unit of Nephrology, Azienda Socio Sanitaria Territoriale (ASST) Ospedale Papa Giovanni XXIII, Bergamo, Italy, [13]Department of Medical Sciences, Uppsala University, Uppsala, Sweden, [14]Department of Nephrology, Skåne University Hospital, Malmö, Sweden and [15]IRCCS - Istituto di Ricerche Farmacologiche 'Mario Negri', Centro di Ricerche Cliniche per le Malattie Rare 'Aldo e Cele Daccò', Ranica, Bergamo, Italy

Correspondence and offprint requests to: Pierre Delanaye; E-mail: pierre_delanaye@yahoo.fr

Practice Point 1.2.2.2: Where more accurate ascertainment of GFR will impact treatment decisions, measure GFR using plasma or urinary clearance of an exogenous filtration marker (Table 9).

Thank for your attention

« The Cat » a Belgian Comic star…