Estimation du DFG: quelles recommandations en 2024?

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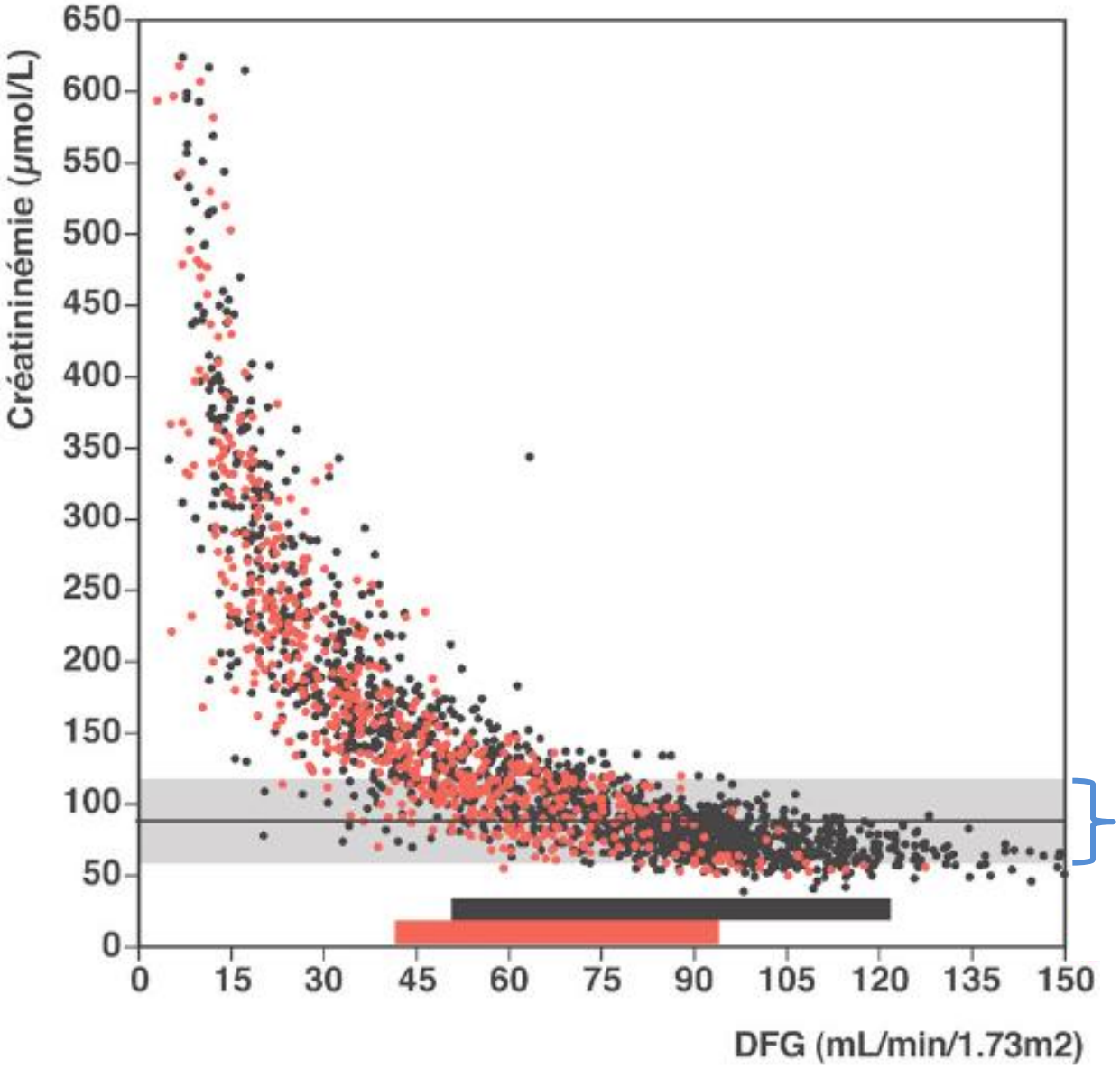
Université de Liège
Département des Sciences Cliniques
BELGIQUE

Le DFG est le paramètre le plus utilisé pour estimer la fonction globale du rein

- Le DFG est estimé avec des biomarqueurs
- La créatinine est une des analyses les plus prescrites
- Le plus important est probablement d'en connaitre les limites…



Cohorte NephroTest (France)
Quel DFG correspond à une concentration de créatinine mesurée à 0.9 mg/dL (80 µmol/L) ?

IC 95% pour sujets <65 ans
IC 95% pour sujets >65 ans

Valeurs normales de créatinine

Avec la permission de Marc Froissart

Autres Limites

Analytiques

- Méthodes de Jaffe
- Méthodes enzymatiques
- Ces deux méthodes donnent des résultats différents
- Pseudochromogènes: glucose, fructose, ascorbate, protéines, urate, acetoacetate, acétone, pyruvate => faux +
- Bilirubines: faux –
- CALIBRATION

Physiologiques: Sécrétion tubulaire

- 10 à 40%
- Augmente quand le DFG diminue
- Difficile à prédire à l'échelle individuelle

Physiologiques: Masse musculaire

- Production (relativement) constante mais production musculaire => créatinine sérique dépend de la masse musculaire, pas seulement du DFG (âge? sexe/genre? race/population?)
- Production extra-rénale

Perrone RD, Clin Chem, 1992, 38, p1933
Delanaye P, Nephron, 2017, 136, p302

Créatinine: à la poubelle?

- Bon marché! (0.04€ /Jaffe)
- Bonne spécificité
- Bon CV analytique
- Préférence pour les méthodes enzymatiques

Clairance de créatinine

- N'est recommandée par aucun guidelines
- Sécrétion tubulaire
- Manque de précision:

  erreurs dans la collecte

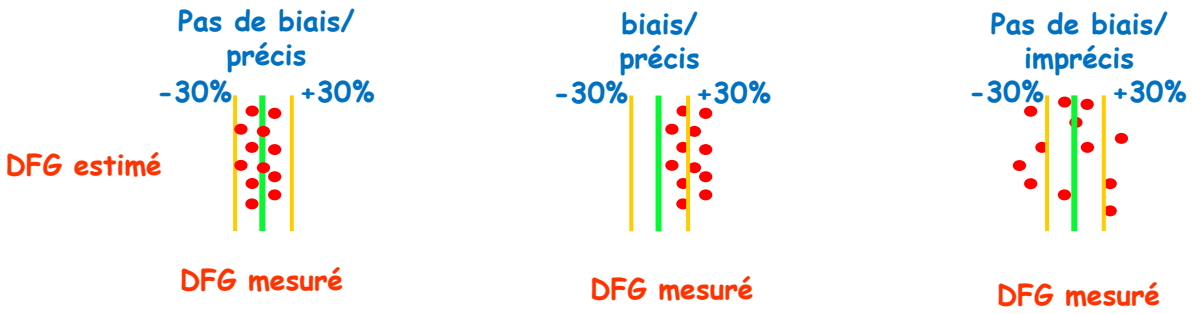
  22 à 27% chez les patients « entrainés »
  50 to 70 % pour les autres

  importante variabilité intra-individuelle de l'excrétion urinaire de créatinine

KDIGO, Kidney Int, 2012, 3
Perrone RD, Clin Chem, 1992, 38, 1933
Delanaye P, Ann Biol Clin (Paris), 2010, 68, 531

Statistiques

- Corrélation: une condition "*sine qua non*" mais insuffisante!
- Biais: différence moyenne entre 2 valeurs = erreur systématique
- Précision: SD autour de ce biais = erreur aléatoire
- Exactitude 30% = % du DFG estimée dans ± 30% du DFG mesuré



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

Quelles équations?

- Cockcroft
- CKD-EPI
- EKFC

Quelles équations?

- ~~Cockcroft~~
- CKD-EPI
- EKFC

L'équation CKD-EPI

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)*

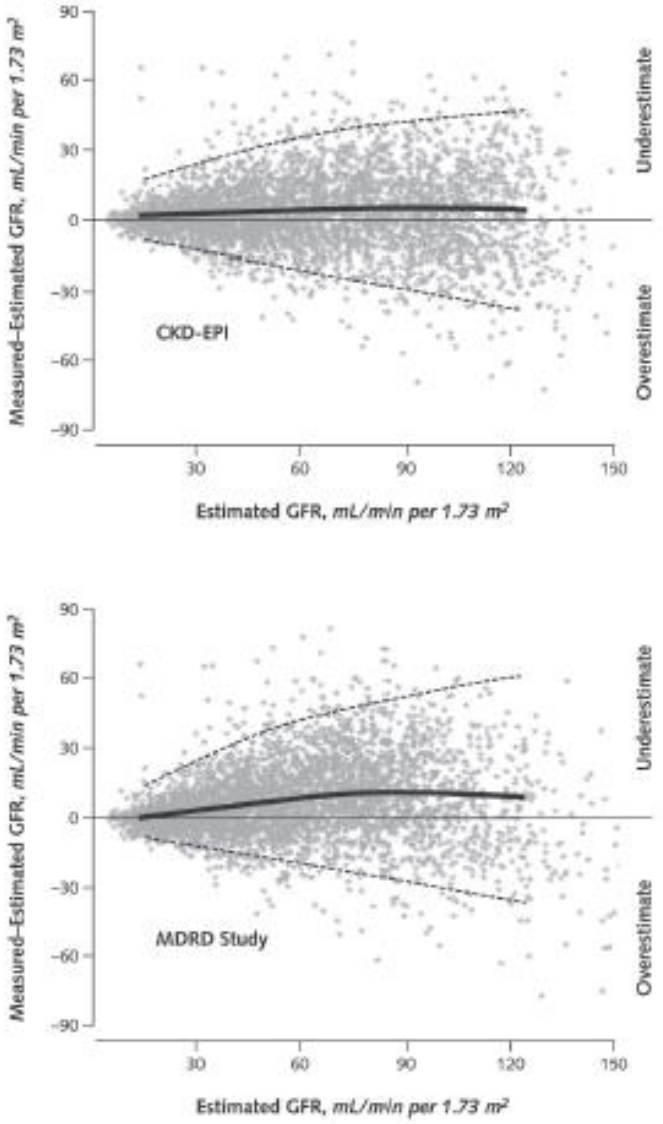
Ann Intern Med. 2009;150:604-612.

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)	$GFR = 141 \times (Scr/0.9)^{-1.209} \times (0.993)^{Age}$

- CKD-EPI
- “Development dataset”: n=5504
- “Internal validation”: n=2750
- “External validation”: n=3896
- Créatinine calibrée
- DFG médian = 68 mL/min/1.73 m²

Figure. Performance of the CKD-EPI and MDRD Study equations in estimating measured GFR in the external validation data set.



Levey AS, Ann Intern Med, 2009, p604

KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease

VOLUME 3 | ISSUE 1 | JANUARY 2013

http://www.kidney-international.org

Révisé in 2024

CKD-EPI: What else?

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†

- Sujets avec DFG mesuré et créatinine standardisée
- n=11,251 “développement et validation interne”
- n=8,378 “validation externe”
- n=1,254 âge entre 2 et 18 ans
- 7 + 6 cohortes
- « Caucasiens »

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.

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DE GRUYTER Clin Chem Lab Med 2022; 60(3): 401–407

Pierre Delanaye*, François Gaillard, Jessica van der Weijden, Geir Mjøen, Ingela Ferhman-Ekholm, Laurence Dubourg, Natalie Ebert, Elke Schaeffner, Torbjörn Åkerfeldt, Karolien Goffin, Lionel Couzi, Cyril Garrouste, Lionel Rostaing, Marie Courbebaisse, Christophe Legendre, Maryvonne Hourmant, Nassim Kamar, Etienne Cavalier, Laurent Weekers, Antoine Bouquegneau, Martin H. de Borst, Christophe Mariat, Hans Pottel and Marco van Londen

Age-adapted percentiles of measured glomerular filtration in healthy individuals: extrapolation to living kidney donors over 65 years

Avant 40 ans: DFG mesuré = 107 mL/min/1.73m²
…et cela semble assez universel

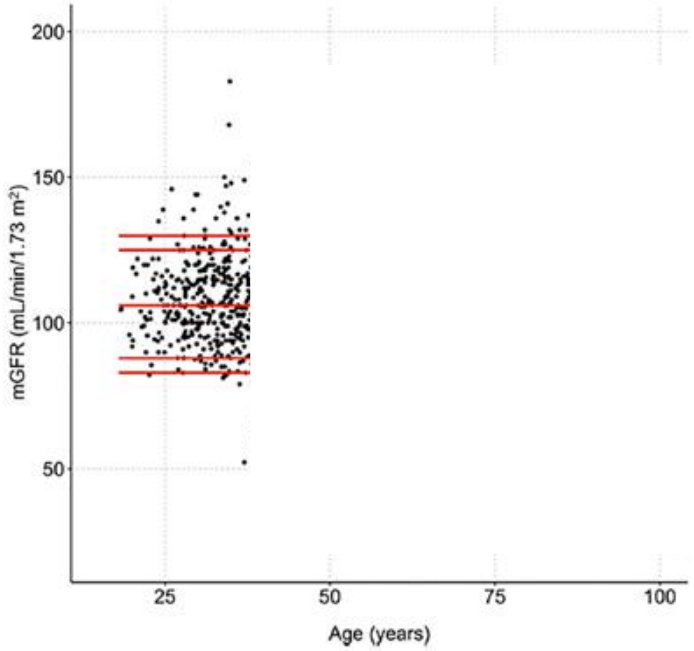

Figure 3: mGFR according to age in the development (dark dots) and external validation cohort (n=329) (gray dots). Red lines are percentiles 5, 10, 50, 90 and 95, calculated from kidney donors younger than 65 years and extrapolated for ages >65 years.

Pierre Delanaye*, François Gaillard, Jessica van der Weijden, Geir Mjøen, Ingela Ferhman-Ekholm, Laurence Dubourg, Natalie Ebert, Elke Schaeffner, Torbjörn Åkerfeldt, Karolien Goffin, Lionel Couzi, Cyril Garrouste, Lionel Rostaing, Marie Courbebaisse, Christophe Legendre, Maryvonne Hourmant, Nassim Kamar, Etienne Cavalier, Laurent Weekers, Antoine Bouquegneau, Martin H. de Borst, Christophe Mariat, Hans Pottel and Marco van Londen

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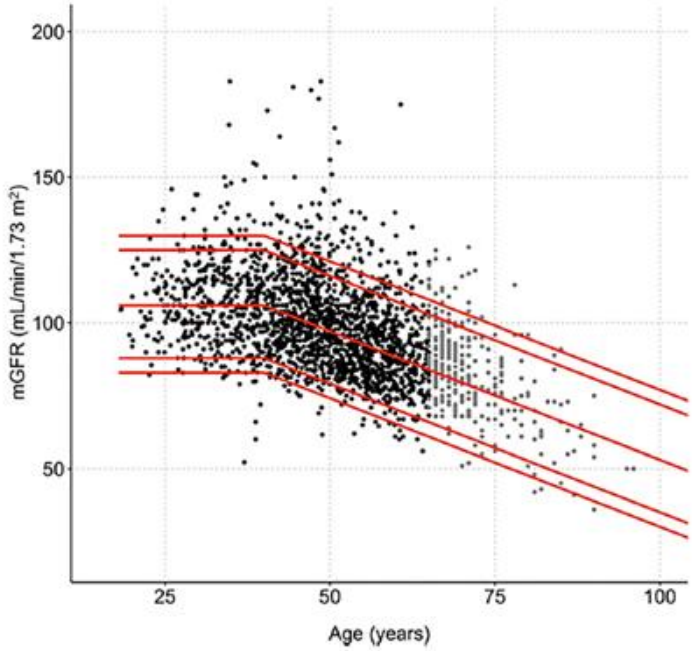

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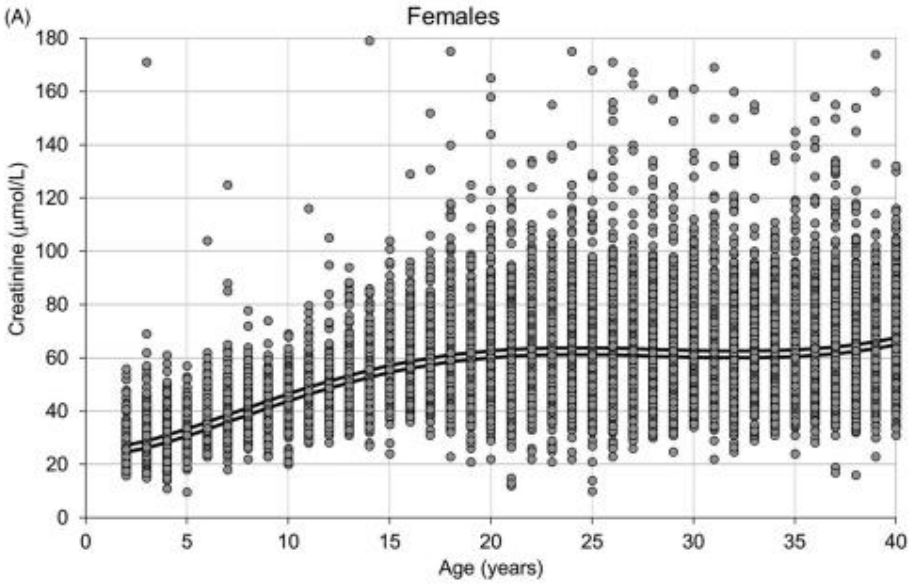
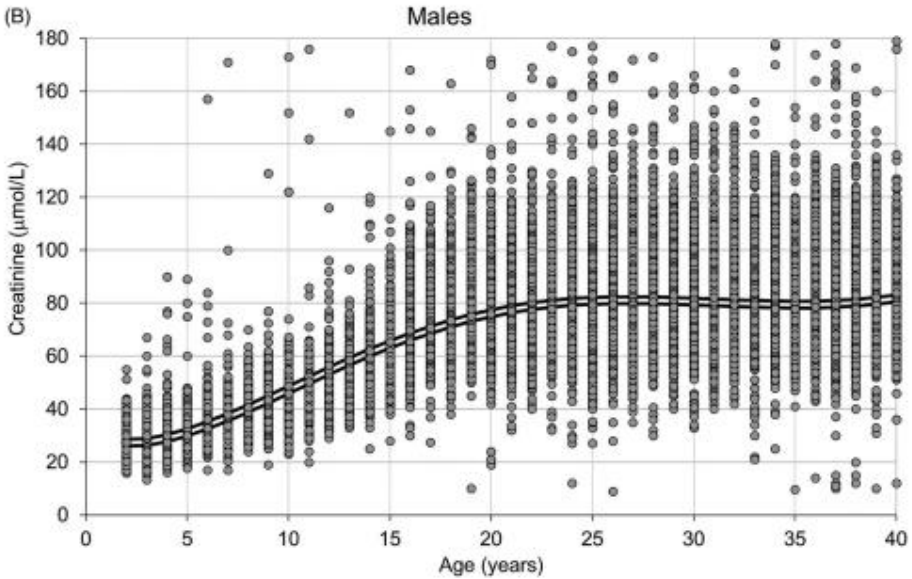


N=83,257 de 3 laboratoires (Suède, Belgique)

62 µmol/L= 0,70 mg/dL



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

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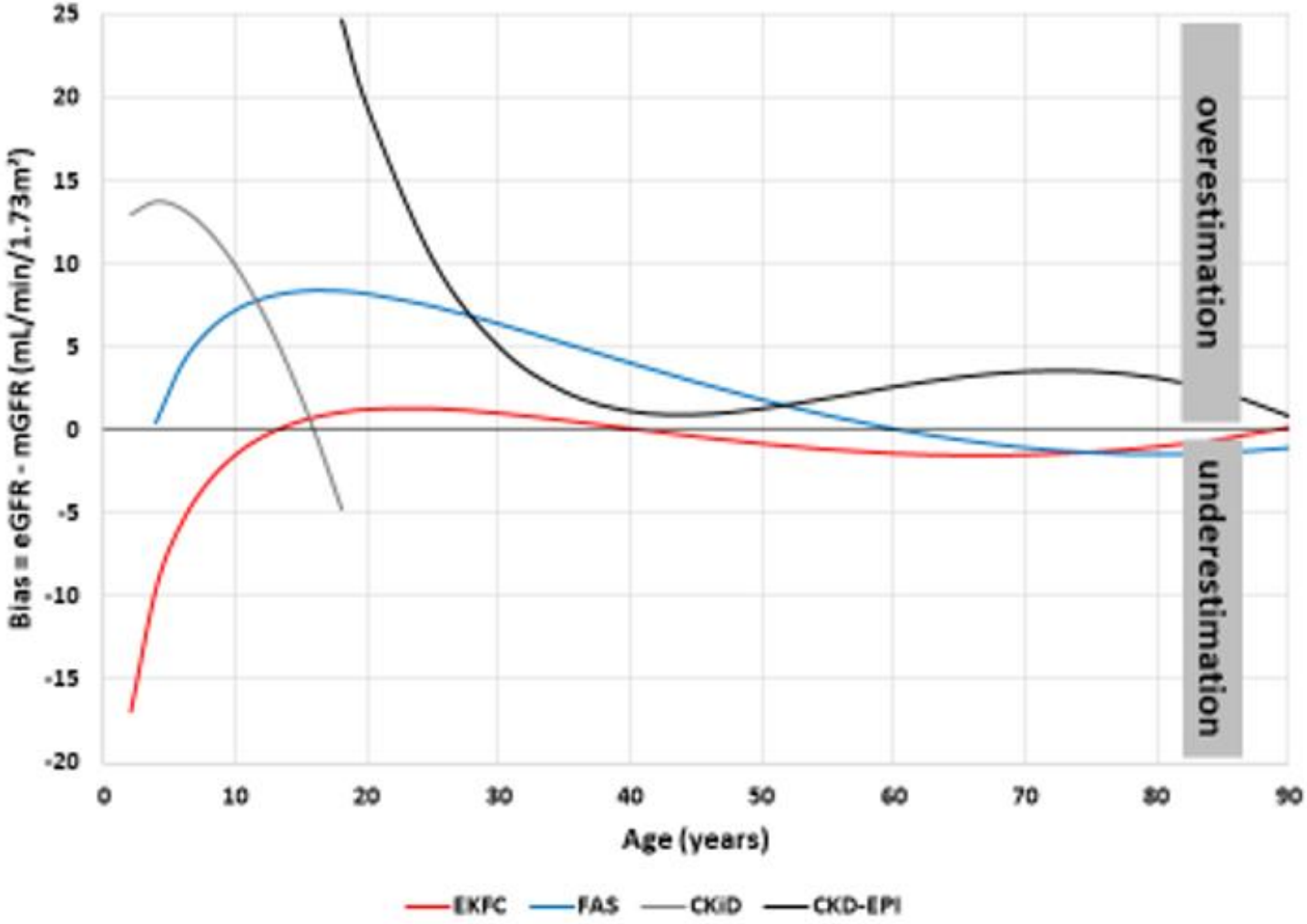

Bias = eGFR - mGFR (mL/min/1.73m²)
25
20
15
10
5
0
-5
-10
-15
-20
0
10
20
30
40
50
60
70
80
90
Age (years)
overestimation
underestimation
EKFC
FAS
CKiD
CKD-EPI

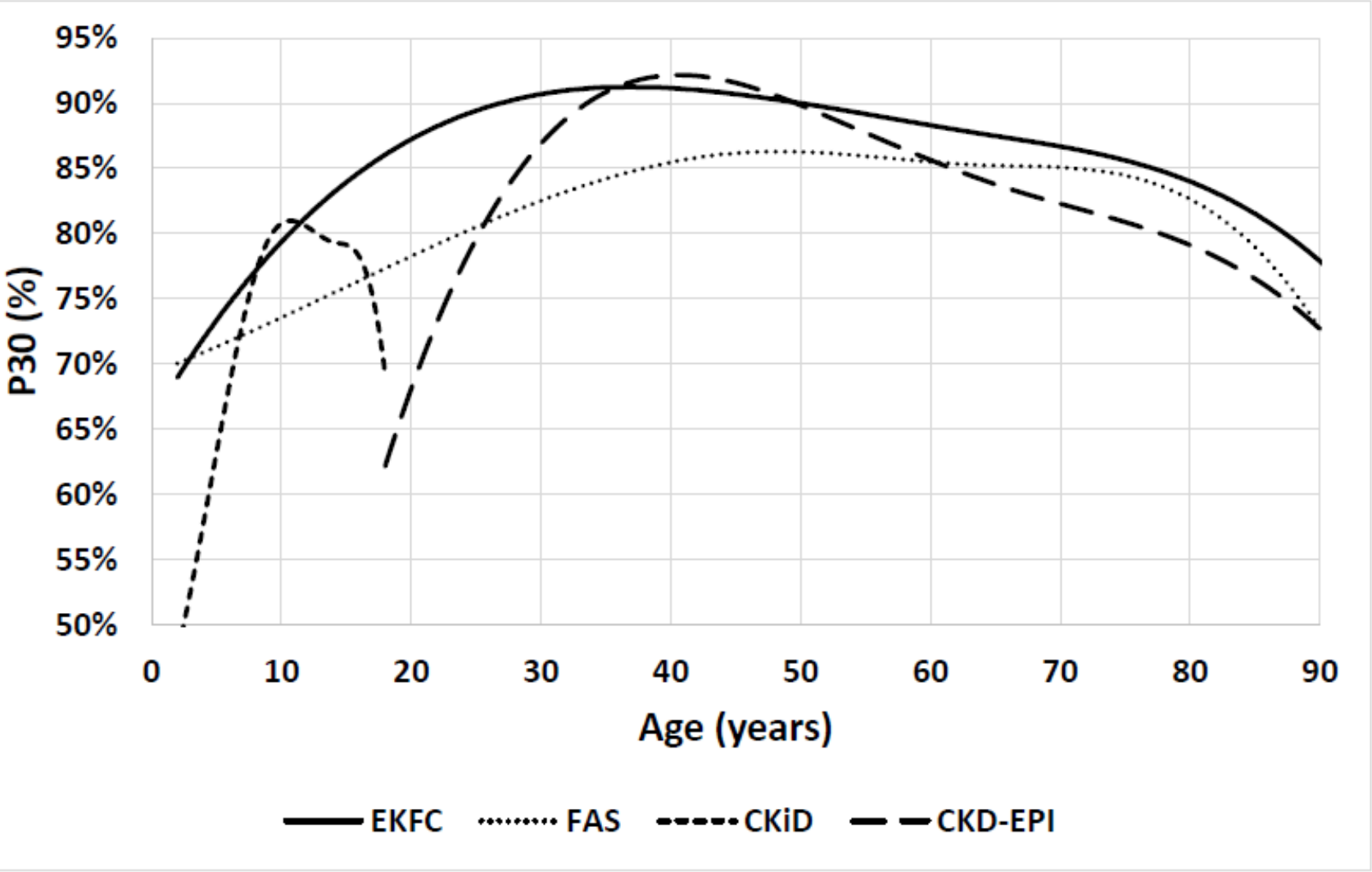


Figure S8. P30-accuracy against age for the EKFC, FAS, CKiD and CKD-EPI equation in the external validation dataset. P30 (%) was graphically presented across the age spectrum using cubic splines with two free knots and using 3rd degree polynomials.

Avantages de EKFC

- Meilleures performances (pas plus cher)
- Plus « physiologique »: correction au niveau de la créatinine (sexe, « race »), âge mieux conceptualisé, « Q » spécifique pour des populations spécifiques
- Valide à tout âge (et pas de « jump » à 18 ans)
- Enfant: pas besoin de la taille
- Même formule (« concept ») pour la cystatine C (et les autres biomarqueurs)

Débat sur la « race » aux USA

Remarque sémantique

La créatinine sérique est différente entre Noir et Blancs aux USA (on ne sait pas pourquoi!)

Le DFGm (normal) n'est pas différent

La correction pour le facteur racial dans CKD-EPI$_{2009}$ a été considéré comme discriminant

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

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)

Nephrology Dialysis Transplantation (2023) 38: 106–118
https://doi.org/10.1093/ndt/gfac241
Advance Access publication date 24 August 2022

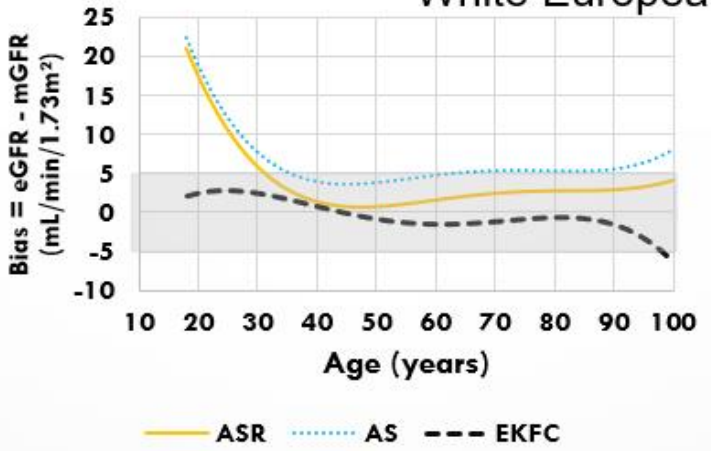
Performance of creatinine-based equations to estimate glomerular filtration rate in White and Black populations in Europe, Brazil and Africa

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], Karin Littmann[11], Christophe Mariat[12], Toralf Melsom[7], Elke Schaeffner[6], Per-Ola Sundin[13], Arend Bökenkamp[14], Ulla B. Berg[15], Kajsa Åsling-Monemi[15], Anna Åkesson[4,5], Anders Larsson[16], Etienne Cavalier[17], R. Neil Dalton[18], Marie Courbebaisse[19], Lionel Couzi[20], Francois Gaillard[21], Cyril Garrouste[22], Lola Jacquemont[23], Nassim Kamar[24], Christophe Legendre[25], Lionel Rostaing[26], Thomas Stehlé[27,28], Jean-Philippe Haymann[29], Luciano da Silva Selistre[30], Jorge P. Strogoff-de-Matos[31], Justine B. Bukabau[32], Ernest K. Sumaili[32], Eric Yayo[33], Dagui Monnet[33], Ulf Nyman[34], Hans Pottel[35,†] and Martin Flamant[36,†]

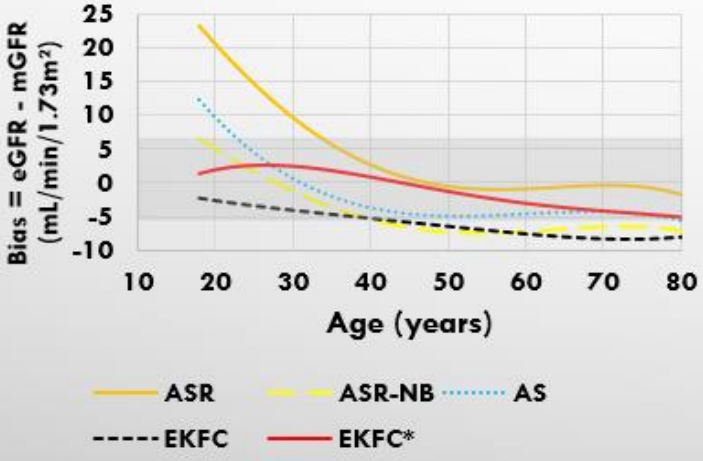
Méthodes

- Sujets de plus de 18 ans, DFG mesuré, créatinine sérique “IDMS traceable”
- EKFC consortium: 11 cohortes d’Europe (n=17,321)
- Données de Paris (n=4,429, parmi lesquels 964 européens noirs)
- Données d’Afrique (RDC et Côte d’Ivoire, n=508)

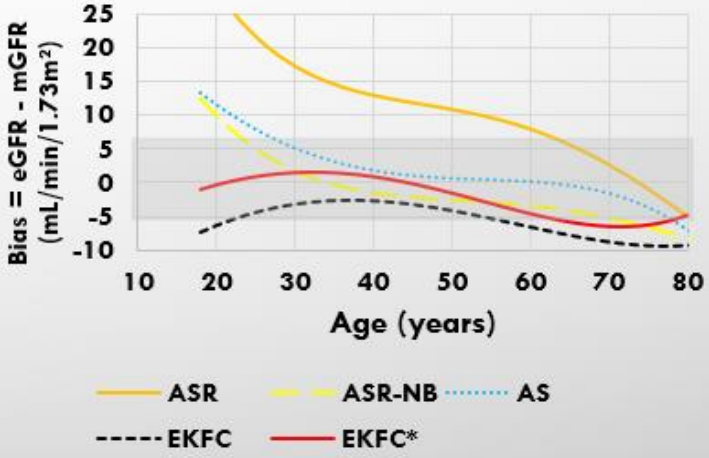
White Europeans (n=17,321)



Black Europeans (n=964)



Black Africans (n=508)



Americentrism in estimation of glomerular filtration rate equations

Check for updates

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

KEYWORDS: glomerular filtration rate; race; serum creatinine

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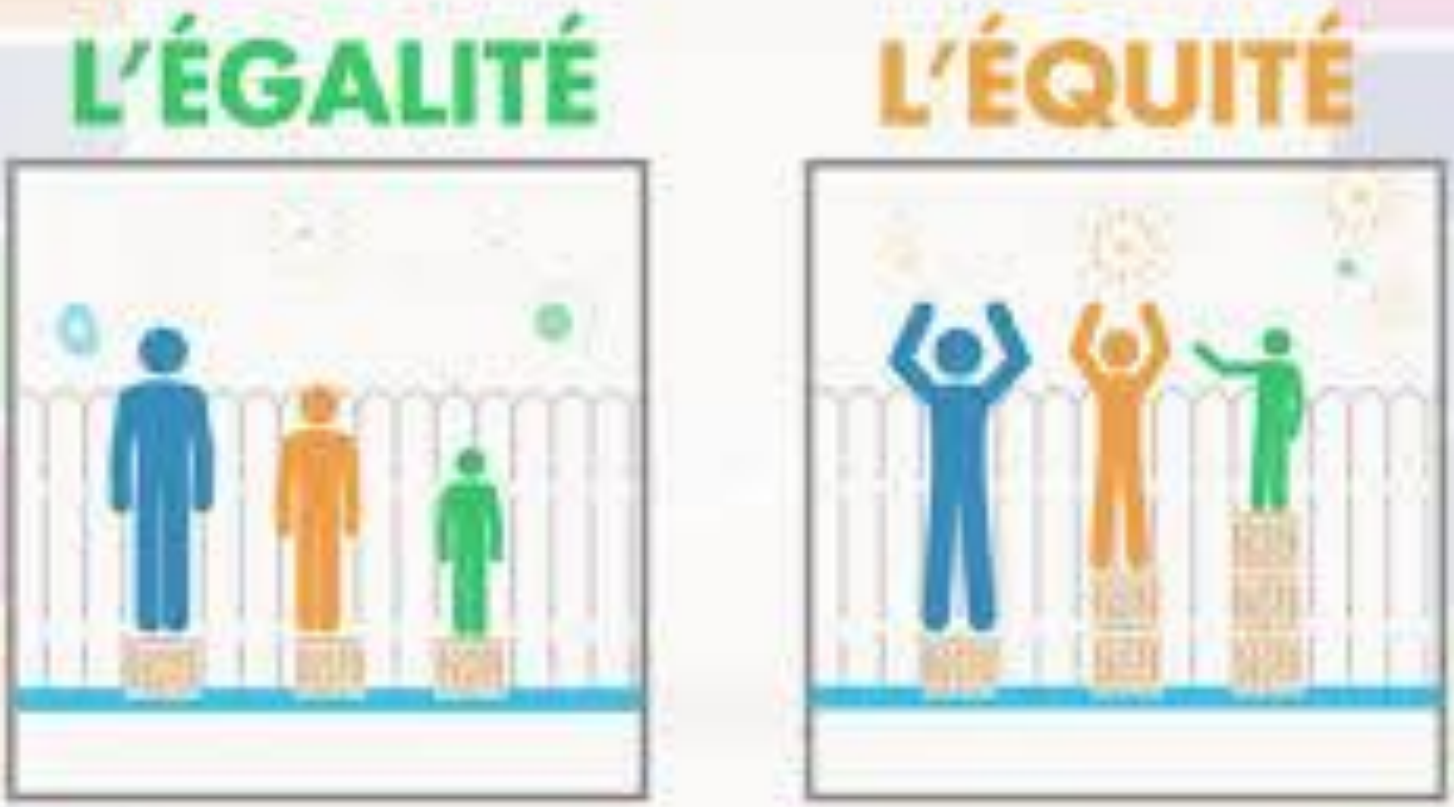

Race-free

Population-specific

EFLM Paper

Pierre Delanaye, Elke Schaeffner, Mario Cozzolino, Michel Langlois, Mario Plebani, Tomris Ozben and Etienne Cavalier*, on behalf of the Board members of the EFLM Task Group Chronic Kidney Diseases

The new, race-free, Chronic Kidney Disease Epidemiology Consortium (CKD-EPI) equation to estimate glomerular filtration rate: is it applicable in Europe? A position statement by the European Federation of Clinical Chemistry and Laboratory Medicine (EFLM)

Nephrol Dial Transplant (2023) 38: 1–6
https://doi.org/10.1093/ndt/gfac254
Advance Access publication date 7 September 2022

What should European nephrology do with the new CKD-EPI equation?

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Le principal avantage de EKFC est sa flexibilité

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]

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

Validation de EKFC aux USA

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

Delanaye P, 2024, Kidney Int, p629

Les valeurs de Q sont adaptées aux populations

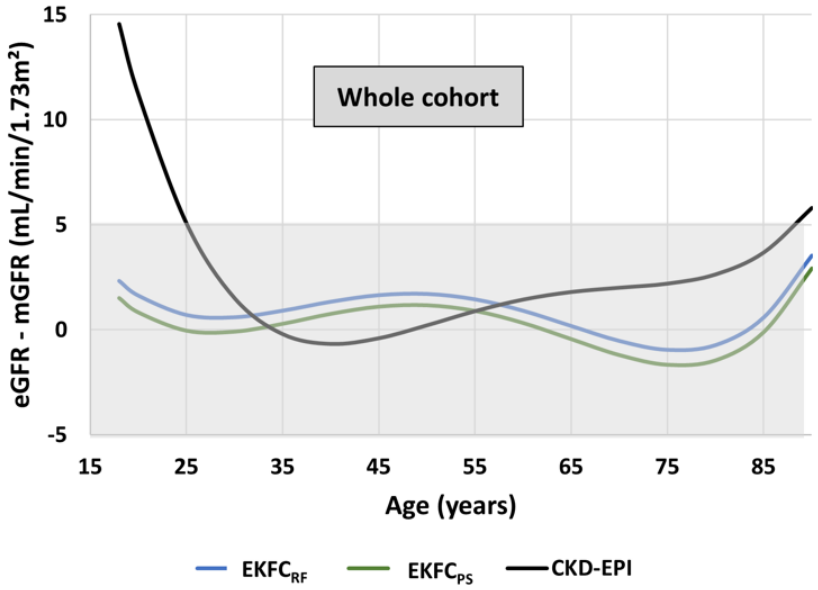
Q-values determined in different populations

	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	27,830 healthy people

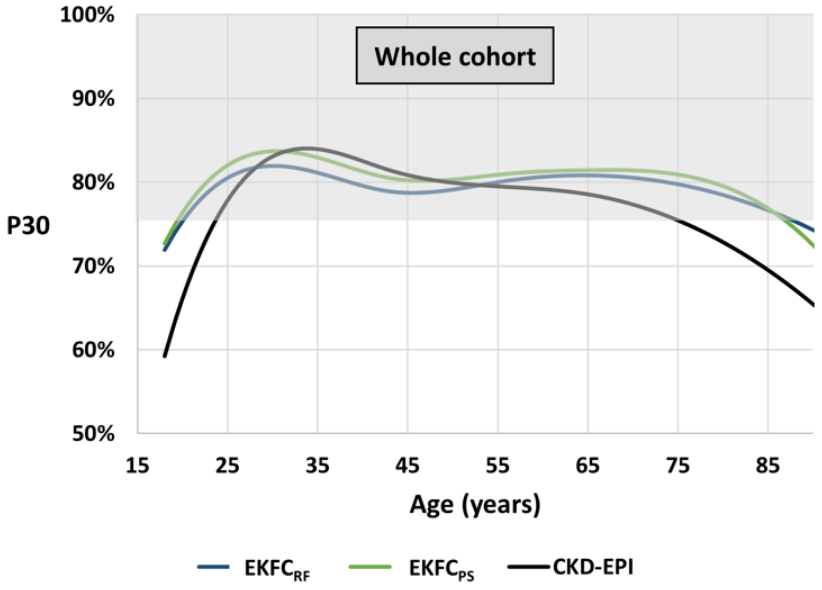
All results are expressed in mg/dL

Shi J, Clin Chim Acta, 2021, 520, p16

A


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

B


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

Les valeurs de Q sont adaptées aux populations

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Nephron

Clinical Practice: Mini-Review

Nephron 2024;148:408–414
DOI: 10.1159/000536243

Received: October 13, 2023
Accepted: December 23, 2023
Published online: January 12, 2024

Glomerular Filtration Rate Estimation in Adults: Myths and Promises

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- Le principal avantage de EKFC est sa flexibilité
- Q peut être adapté à chaque population
- Y compris une population “mixée” ou un concept “race-free”
- Q peut être obtenu à partir de grandes cohortes ou de données spécifiques
- Q peut être obtenu dans chaque hôpital (vrai Q “local”)

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

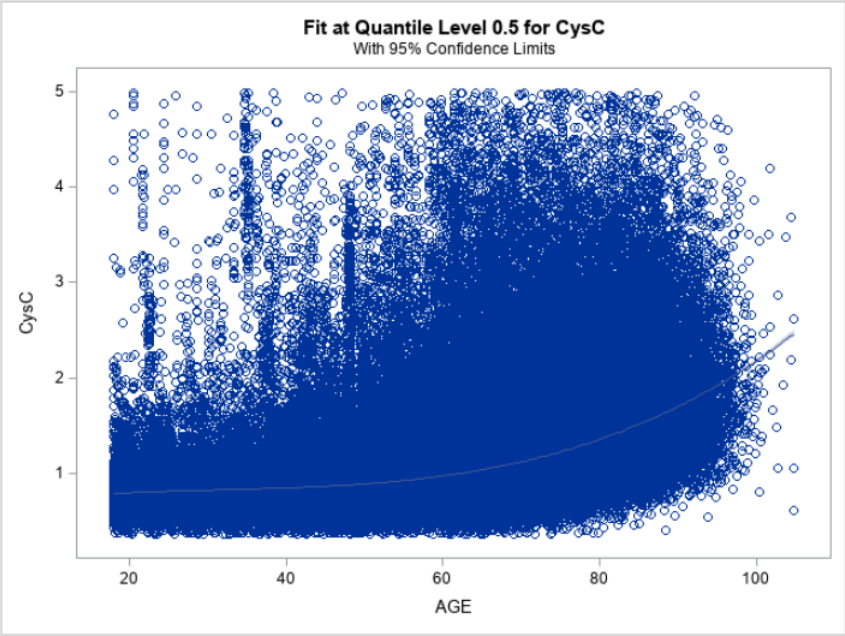
ABSTRACT

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

1er étape: cystatine C et âge

Données de labo de Suède
N=227,643
♀ 95,469
♂ 132,174

Figure S3. Cystatin C versus age and the median quantile line for the 227,643 included subjects.



♀ Q' = 0.79 mg/L jusqu'à 50 ans,
Q' = 0.79 + 0.005 x (Age – 50)
♂ Q' = 0.86 mg/L jusqu'à 50 ans
Q' = 0.86 + 0.005 x (Age – 50)

1er étape: cystatine C et sexe

Données de labo de Suède
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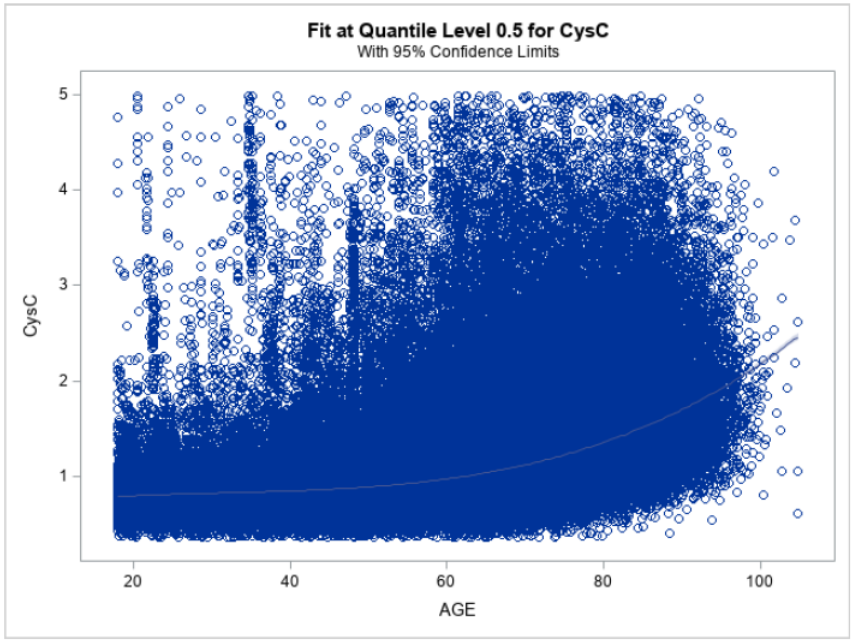

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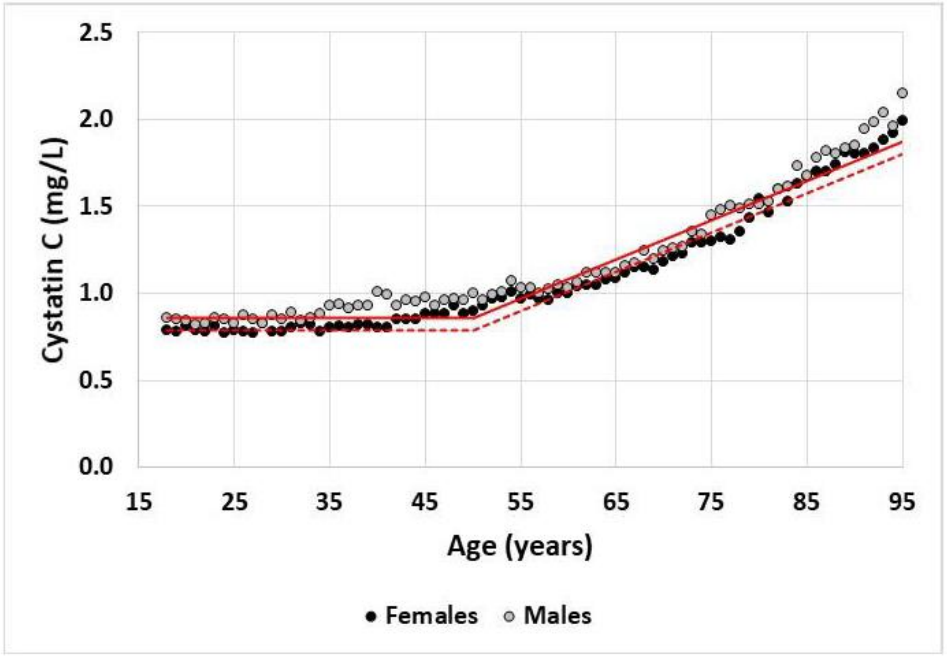
♂ Q' = 0.86 mg/L jusqu'à 50 ans
Q' = 0.86 + 0.005 x (Age – 50)

2ème étape: cystatine C et sexe

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 jusqu'à 50 ans
Q' = 0.83 + 0.005 x (Age – 50)

3ème étape: Cystatine C et “race”

- Données du même centre en France
- Même DFG de référence (Cr-EDTA)
- Même dosage de créatinine et de cystatine C

Table S3. Patient characteristics of the entire cohorts used for the matching analysis (mean ± SD)

Ethnicity/Sex	N	Age (years)	BMI (kg/m²)	mGFR (mL/min/1.73m²)	SCr (mg/dL)	CysC (mg/L)
White Men	1296 (57%)	53.0 ± 14.6	26.2 ± 4.9	61.8 ± 26.0	1.52 ± 0.73	1.52 ± 0.68
Black Men	436 (63%)	50.7 ± 13.1	26.3 ± 4.5	62.0 ± 22.1	1.73 ± 0.81	1.41 ± 0.61
White Women	966 (43%)	52.5 ± 15.2	25.8 ± 6.2	62.8 ± 26.8	1.16 ± 0.61	1.38 ± 0.73
Black Women	261 (37%)	51.9 ± 15.2	27.4 ± 5.8	59.1 ± 25.6	1.40 ± 0.79	1.46 ± 0.76

3ème étape: Cystatin C et “race”

Analyse matchée 1:1

- Pour le sexe
- IMC (±2,5 kg/m²)
- DFG mesuré (±3 mL/min/1.73m²)
- âge (± 3 ans)

Table S4. Demographic and renal characteristics of the matched White and Black subjects (mean ± SD)

Sex	N	Age (years)	BMI (kg/m²)	mGFR (mL/min/1.73m²)	SCr (mg/dL)	CysC (mg/L)
White Men	377	51.1 ± 12.2	25.7 ± 3.4	63.8 ± 21.0	1.43 ± 0.62	1.41 ± 0.56
Black Men	377	50.8 ± 12.3	25.8 ± 3.5	63.6 ± 21.0	1.65 ± 0.64	1.37 ± 0.59
White Women	200	53.4 ± 11.9	26.1 ± 4.6	59.7 ± 23.2	1.16 ± 0.53	1.40 ± 0.69
Black Women	200	53.3 ± 11.9	26.2 ± 4.6	59.8 ± 23.1	1.33 ± 0.61	1.41 ± 0.64

4ème étape:
Validation de la nouvelle équation

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

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

Adultes
DFGm, creatinine et cystatine C calibrées
N=12,832

11 cohortes
Européens blancs: n=7,727
Européens blancs de Paris: n=2,646
US blancs: n=1,093
Européens noirs de Paris: n=858
Africains noirs: n=508

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

Variable	Serum Creatinine–Based Equations			Cystatin C–Based Equations	
	CKD-EPI eGFRcr(ASR)	CKD-EPI eGFRcr(AS)	EKFC eGFRcr	CKD-EPI eGFRcys	EKFC eGFRcys without Sex
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)	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‡	15.5 (–3.0 to 12.5)	16.3 (0.0 to 16.3)	14.5 (–6.5 to 8.0)	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§	14.8 (14.4 to 15.2)	16.3 (15.9 to 16.6)	13.1 (12.8 to 13.4)	15.8 (15.5 to 16.1)	13.5 (12.9 to 14.1)
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)	32.0 (31.0 to 33.0)	41.7 (40.6 to 42.8)
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)	80.8 (79.9 to 81.7)	86.2 (85.4 to 87.0)

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

Variable	Serum Creatinine–Based Equations			Cystatin C–Based Equations	
	CKD-EPI eGFRcr(ASR)	CKD-EPI eGFRcr(AS)	EKFC eGFRcr	CKD-EPI eGFRcys	EKFC eGFRcys without Sex
African cohort, 508 Black patients					
Median bias (95% CI) — ml/min/1.73 m²†	12.2 (10.7 to 15.0)	2.48 (0.72 to 4.15)	−1.45 (−2.82 to 0.62)	2.82 (1.43 to 4.48)	1.74 (0.28 to 3.25)
IQR of estimated GFR − measured GFR — ml/min/1.73 m²‡	30.0 (−3.2 to 26.8)	23.3 (−9.0 to 14.3)	20.4 (−10.6 to 9.9)	23.7 (−7.7 to 16.0)	19.5 (−7.4 to 12.1)
Root-mean-square error (95% CI) — ml/min/1.73 m²§	24.5 (22.7 to 26.1)	18.1 (16.6 to 19.4)	16.4 (15.0 to 17.8)	18.5 (17.1 to 19.8)	16.0 (14.7 to 17.2)
P_{10} — % (95% CI)¶	19.5 (16.0 to 22.9)	34.4 (30.3 to 38.6)	38.0 (33.8 to 42.2)	33.1 (29.0 to 37.2)	40.6 (36.3 to 44.8)
P_{30} — % (95% CI)‖	63.6 (59.4 to 67.8)	74.4 (70.6 to 78.2)	78.9 (75.4 to 82.5)	77.4 (73.7 to 81.0)	83.5 (80.2 to 86.7)

Pas assez de MRC dans la cohorte

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)

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)

Cystatine C

- La cystatine C permet une estimation du DFG sans les variables “âge” ni “sexe”
- L’équation EKFC est mathématiquement la même pour la créatinine et le cystatine C, seul Q change
- Continuum entre enfants et adultes pour $EKFC_{crea}$ et $EKFC_{CC}$
- Les équations EKFC sont un peu meilleures que les équations CKD-EPI correspondantes => alternative valable en Europe et en Afrique
- Les équations basées sur la cystatine C ne sont pas meilleures que les équations basées sur la créatinine
- Les équations combinées sont meilleures (exactitude +5-10%)
- Standardisation
- Plus cher
- Comment gérer les résultats différents entre créatinine et cystatine C?

https://ekfccalculator.pages.dev/

KDIGO 2024 CLINICAL PRACTICE GUIDELINE FOR THE EVALUATION AND MANAGEMENT OF CHRONIC KIDNEY DISEASE

1.2.4 Selection of GFR estimating equations

Recommendation 1.2.4.1: We recommend using a validated GFR estimating equation to derive GFR from serum filtration markers (eGFR) rather than relying on the serum filtration markers alone (*1D*).

Practice Point 1.2.4.1: Use the same equation within geographical regions (as defined locally [e.g., continent, country, and region] and as large as possible). Within such regions, equations may differ for adults and children.

Practice Point 1.2.4.2: Use of race in the computation of eGFR should be avoided.

Special considerations

Pediatric considerations

Practice Point 1.2.4.3: Estimate GFR in children using validated equations that have been developed or validated in comparable populations.

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
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

Calculateurs DFG (dont EKFC)

Limitations des formules = créatinine

Populations spécifiques:
Les équations ne sont pas magiques!!
Gardons notre sens clinique!!

Anorexie nerveuse (Delanaye P, Clin Nephrol, 2009, 71, 482)

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

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

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

Greffés cœur (Delanaye P, Clin Transplant, 2006, 20, 596)

Greffés rein (Masson I, Transplantation, 2013, 95, 1211)

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

Ne pas sur-interpreter un DFG estimé…

Toutes les équations restent des estimations

OK au niveau populationnel

Manque de précision au niveau individuel

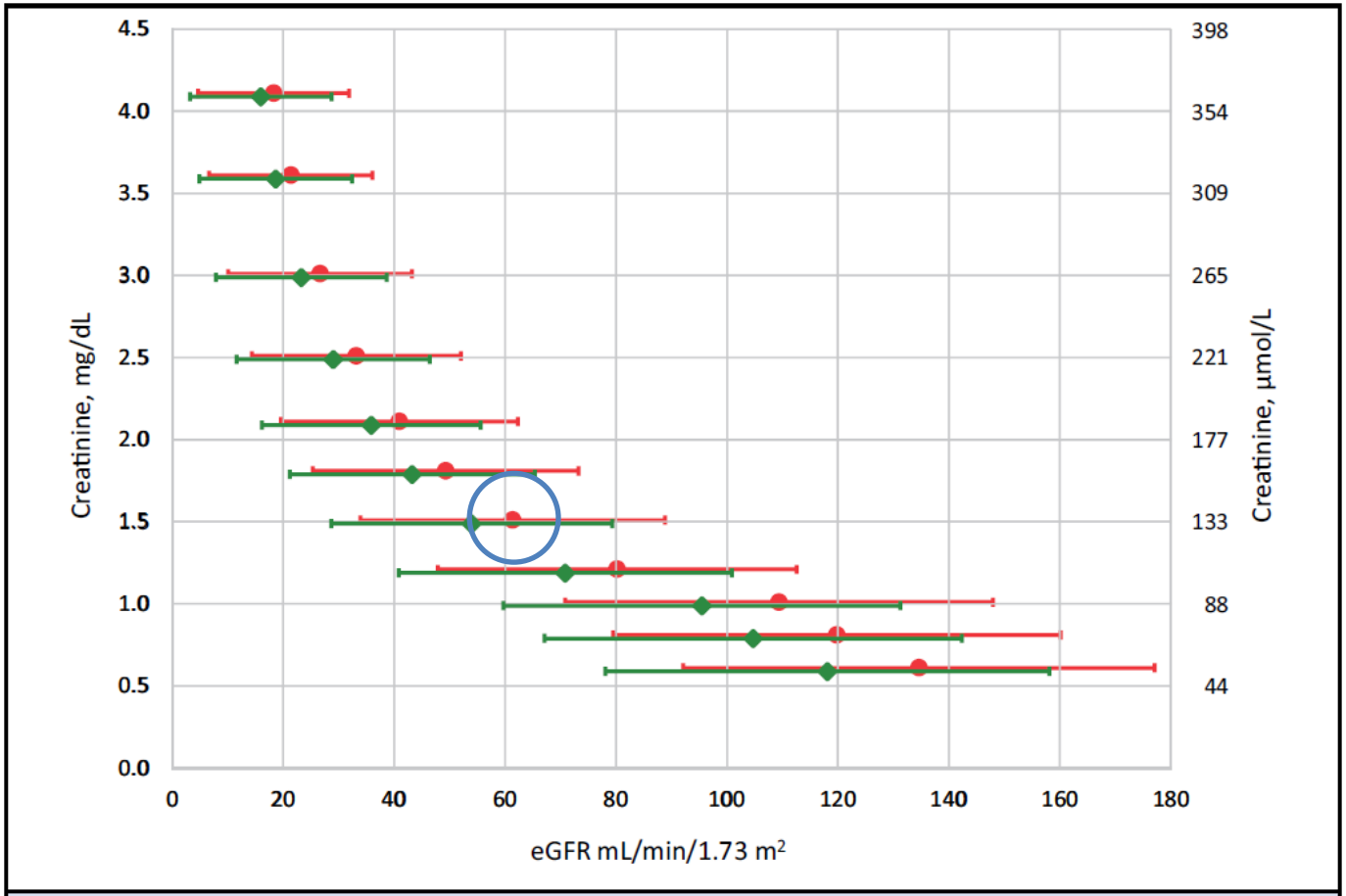

Fig. 1. Uncertainty of eGFR calculated using the CKD-EPI equations for African-Americans and non-African-Americans at various creatinine concentrations for a 50-year-old male. Circles (red, larger values) indicate African-American and diamonds (green, lower values) indicate non-African-American equations.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

DFGe = 60,25 ml/min/1.73m²

Miller WG, Clin Chem, 2021, p693 and p820

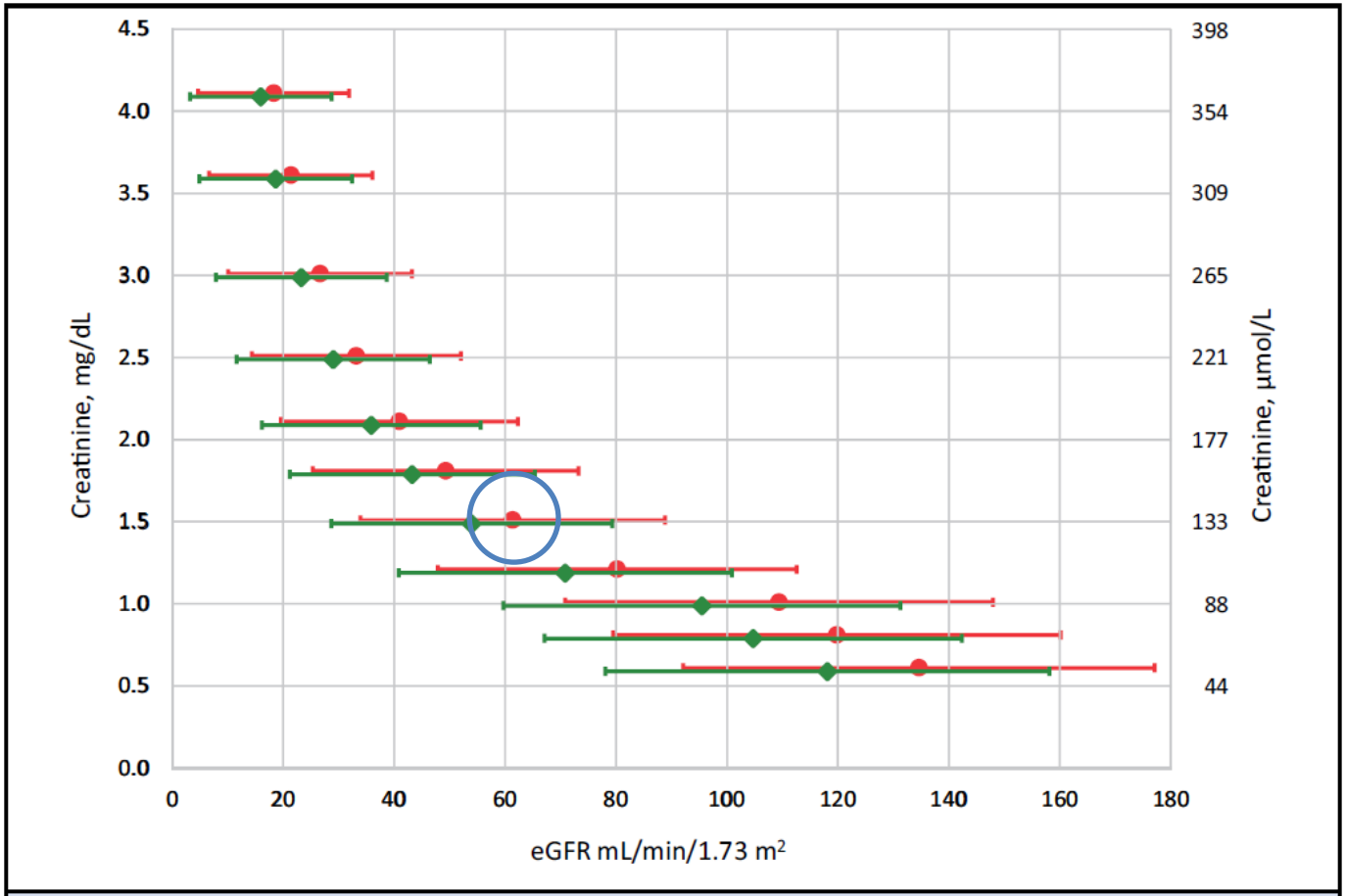

Fig. 1. Uncertainty of eGFR calculated using the CKD-EPI equations for African-Americans and non-African-Americans at various creatinine concentrations for a 50-year-old male. Circles (red, larger values) indicate African-American and diamonds (green, lower values) indicate non-African-American equations.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

DFGe ~~= 60,25 ml/min/1.73m²~~

= 60 ml/min/1.73m² (CI 95%: 33-87)

Miller WG, Clin Chem, 2021, p693 and p820

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

RETOUR à une mesure du DFG

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

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).

Clairance plasmatique d'iohexol

Pas si difficile
Pas si cher

ARTICLE IN PRESS

www.kidney-international.org review

Iohexol plasma clearance measurement protocol standardization for adults: a consensus paper of the European Kidney Function Consortium

OPEN

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Merci