Mesures et estimations du DFG pour un usage clinique en 2022

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Service de Néphrologie, Dialyse et Transplantation

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Liège

BELGIQUE

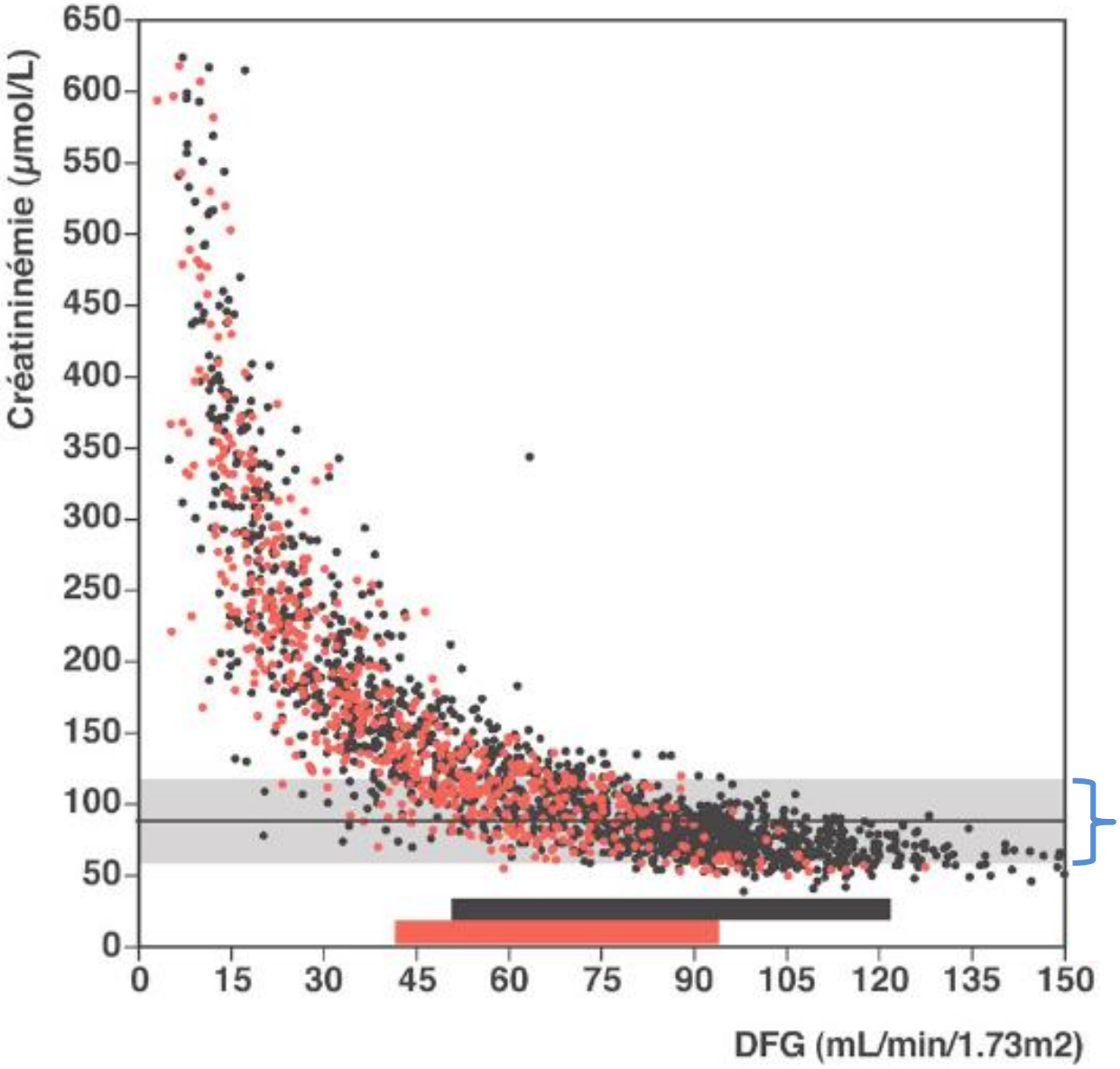
IX^{ème} Symposium Reins & Médicaments
CHR La Citadelle
10 mars 2022

- Estimation du DFG
- Mesure du DFG

Créatinine sérique

- Une des analyses les plus prescrites
- …mais important d'en connaitre les limitations
- Limitations physiologiques
- Limitations analytiques
- Limitations "mathématiques"

Perrone RD, Clin Chem, 1992, 38, 1933
Delanaye P, Ann Biol Clin (Paris), 2010, 68, 531



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

Créatinine: « limitations mathématiques »

- Relation hyperbolique entre créatinine et DFG!!!

  Pour un patient donné,

  si la créatinine augmente de 0.6 à 1.2 mg/dl
  => diminution du DFG de 50%

  si la créatinine augmente de 2.0 à 3.0 mg/dl
  => diminution du DFG de 25%

Mesure de la créatinine sérique
Limitations analytiques

- Méthodes de Jaffe
- Méthodes enzymatiques
- Différentes méthodes mais aussi différents « assays »
- Interférences

Perrone RD, Clin Chem, 1992, 38, 1933
Delanaye P, Ann Biol Clin (Paris), 2010, 68, 531

Beaucoup de progrès ces dernières années…

Clinica Chimica Acta 412 (2011) 2070–2075

Contents lists available at ScienceDirect

Clinica Chimica Acta

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

A multicentric evaluation of IDMS-traceable creatinine enzymatic assays

Laurence Piéroni [a], Pierre Delanaye [b,*], Anne Boutten [c], Anne-Sophie Bargnoux [d], Eric Rozet [e], Vincent Delatour [f], Marie-Christine Carlier [g], Anne-Marie Hanser [h], Etienne Cavalier [i], Marc Froissart [j], and Jean-Paul Cristol [d]
On behalf of the Société Française de Biologie Clinique [1]

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[e] Analytical Chemistry Laboratory, CIRM, University of Liège, Liège, Belgium
[f] Laboratoire National de Métrologie et d'Essais, Paris, France
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[i] Clinical Chemistry, University of Liège, CHU Sart Tilman, Liège, Belgium
[j] Physiologie Rénale, Hôpital Européen Georges Pompidou, APHP, Paris, France

Standardiser

Limitations physiologiques

- Sécrétion tubulaire de créatinine

10 to 40%

Sécrétion augmente alors que DFG diminue

Non prédictible à l'échelon individuel

- Production extra-rénale

Perrone RD, Clin Chem, 1992, 38, 1933
Delanaye P, Ann Biol Clin (Paris), 2010, 68, 531

Limitations physiologiques

- Production (relativement) constante d'origine musculaire => la concentration de créatinine dépend de la masse musculaire, pas seulement du DFG
    - genre
    - âge
    - Ethnicité ?
    - Masse musculaire

Perrone RD, Clin Chem, 1992, 38, 1933
Delanaye P, Ann Biol Clin (Paris), 2010, 68, 531

Créatinine et médicaments

- Inhibiteurs de la sécrétion tubulaire
  cimétidine, triméthoprime, dolutegravir

- Fibrates
- Interactions « à hautes concentrations »
  acétylcystéine, dobutamine, lidocaine, ascorbate

Perrone RD, Clin Chem, 1992, 38, 1933
Delanaye P, Ann Biol Clin (Paris), 2010, 68, 531
Delanaye P, Nephron Clin Pract, 2011, 119, c187

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

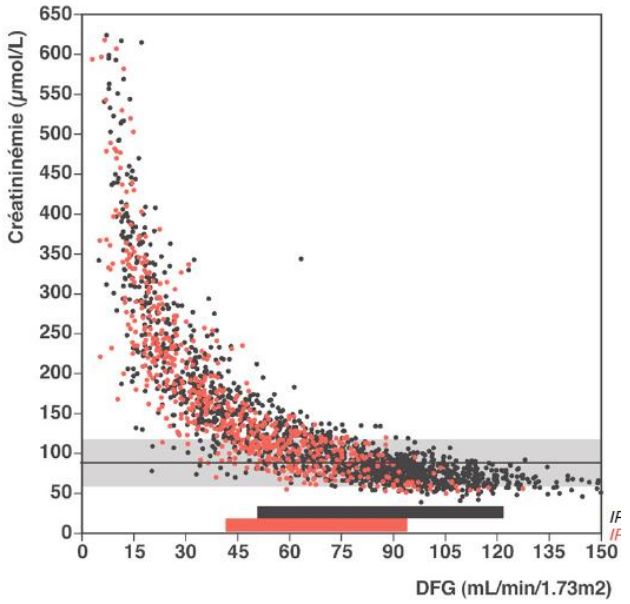
importante variabilité intra-individuelle de l'excrétion urinaire de créatinine

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

Equations basées sur la créatinine

But des équations:

- Conceptualiser la relation hyperbolique
- Adapter la créatinine pour l'âge, le genre, l'ethnicité
- Diminuer l'IC (?)

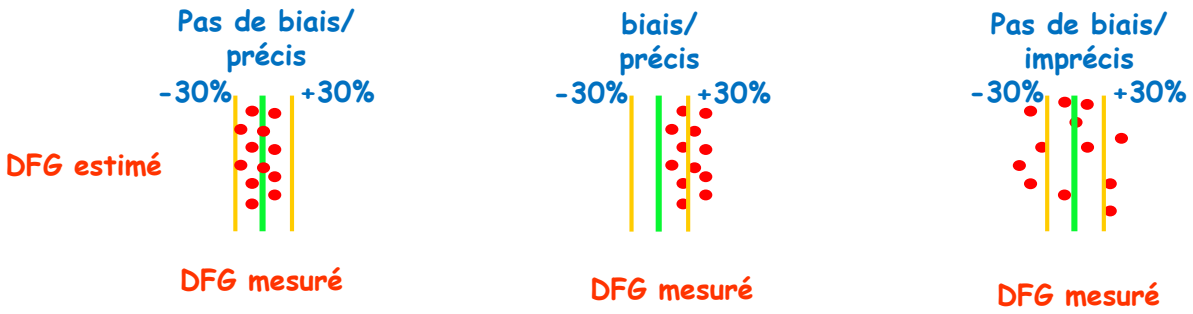


Quelles équations?

- Cockcroft
- MDRD
- CKD-EPI
- EKFC

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

Table 1. MDRD study equations and Cockcroft equation commonly used for GFR estimation

Cockcroft and Gault

$$\text{GFR (ml/min)} = \frac{(140 - \text{age}) \times \text{weight (kg)}}{7.2 \times \text{SCr (mg/dl)}} \times 0.85 \text{ if woman}$$

4-Variable MDRD study equation (IDMS traceable)

$$\text{GFR (ml/min/1.73 m}^2) = 175 \times \text{SCr (mg/dl)}^{-1.154} \times \text{age}^{-0.203} \times 0.742 \text{ (if woman)} \times 1.21 \text{ for Black-American}$$

Cockcroft DW, Nephron, 1976, 16, p31
Levey AS, Ann Intern Med, 1999, 130, p461

Cockcroft Vs MDRD Vs CKD-EPI

	Cockcroft	MDRD	CKD-EPI
Population	Canada 1976	USA 1999	« International » 2009
N	249	1628	5504+2750+3896
DFG moyen	73	40	68
DFG de référence	Clairance de créatinine	Iothalamate	Divers mais référence
Assay	« Jaffe »	Jaffe calibré	Jaffe calibré
% femmes	4	40	43-45%
% noir	0 (?)	12	10-32%
Age moyen	18-92	51	47-50
Poids moyen	72	79.6	79-82
Indexation pour BSA	Non	Oui	Oui
Validation interne	Non	Oui	Oui

Cockcroft DW, Nephron, 1976, 16, p31
Levey AS, Ann Intern Med, 1999, 130, p461
Levey AS, Ann Intern Med, 2009, p604

POIDS !!

Predictive Performance of the Modification of Diet in Renal Disease and Cockcroft-Gault Equations for Estimating Renal Function

Marc Froissart,*†§ Jerome Rossert,†‖ Christian Jacquot,‡§ Michel Paillard,*†§ and Pascal Houillier*†§

*Department of Physiology and Biophysics, Georges Pompidou Hospital (AP-HP); †INSERM U652 and IFR 58; ‡Department of Nephrology, Georges Pompidou Hospital (AP-HP); §René Descartes Medical School, Paris V University; and ‖Paris VI University, Paris, France

Recent recommendations emphasize the need to assess kidney function using creatinine-based predictive equations to optimize the care of patients with chronic kidney disease. The most widely used equations are the Cockcroft-Gault (CG) and the simplified Modification of Diet in Renal Disease (MDRD) formulas. However, they still need to be validated in large samples of subjects, including large non-U.S. cohorts. Renal clearance of ^{51}Cr-EDTA was compared with GFR estimated using either the CG equation or the MDRD formula in a cohort of 2095 adult Europeans (863 female and 1232 male; median age, 53.2 yr; median measured GFR, 59.8 ml/min per 1.73 m^2). When the entire study population was considered, the CG and MDRD equations showed very limited bias. They overestimated measured GFR by 1.94 ml/min per 1.73 m^2 and underestimated it by 0.99 ml/min per 1.73 m^2, respectively. However, analysis of subgroups defined by age, gender, body mass index, and GFR level showed that the biases of the two formulas could be much larger in selected populations. Furthermore, analysis of the SD of the mean difference between estimated and measured GFR showed that both formulas lacked precision; the CG formula was less precise than the MDRD one in most cases. In the whole study population, the SD was 15.1 and 13.5 ml/min per 1.73 m^2 for the CG and MDRD formulas, respectively. Finally, 29.2 and 32.4% of subjects were misclassified when the CG and MDRD formulas were used to categorize subjects according to the Kidney Disease Outcomes Quality Initiative chronic kidney disease classification, respectively.

J Am Soc Nephrol 16: 763–773, 2005. doi: 10.1681/ASN.2004070549

Table 3. Bias, precision, and accuracy of the MDRD and CG formulas[a]

	N	Bland and Altman (ml/min per 1.73 m^2)		Accuracy within (% of Subjects)			CRMSE (ml/min per 1.73 m^2)
		Bias	Precision	15%	30%	50%	
MDRD formula							
high GFR[b]	1044	−3.3	17.2	61.3	92.4	98.8	17.5
low GFR[c]	1051	1.3	8.5	54.8	82.9	93.3	8.6
overall	2095	−1.0	13.7	58.0	87.2	96.0	13.8
CG formula							
high GFR[b]	1044	0.4	19.4	56.1	88.0	97.4	19.4
low GFR[c]	1051	3.5	9.7	41.2	69.0	85.2	10.3
overall	2095	1.9	15.4	48.7	78.5	91.3	15.5

[a]Results obtained with these formulas were compared with GFR values obtained by measuring the renal clearance of ^{51}Cr EDTA. Bias is defined as the mean difference between estimated and measured GFR. Precision is 1 SD of bias. Accuracy was assessed by determining the percentage of subjects who did not deviate >15, 30, and 50% from measured GFR and by calculating the combined root mean square error (CRMSE).

[b]Measured GFR ≥60 ml/min per 1.73 m^2.

[c]Measured GFR <60 ml/min per 1.73 m^2.

- 5
- Cr

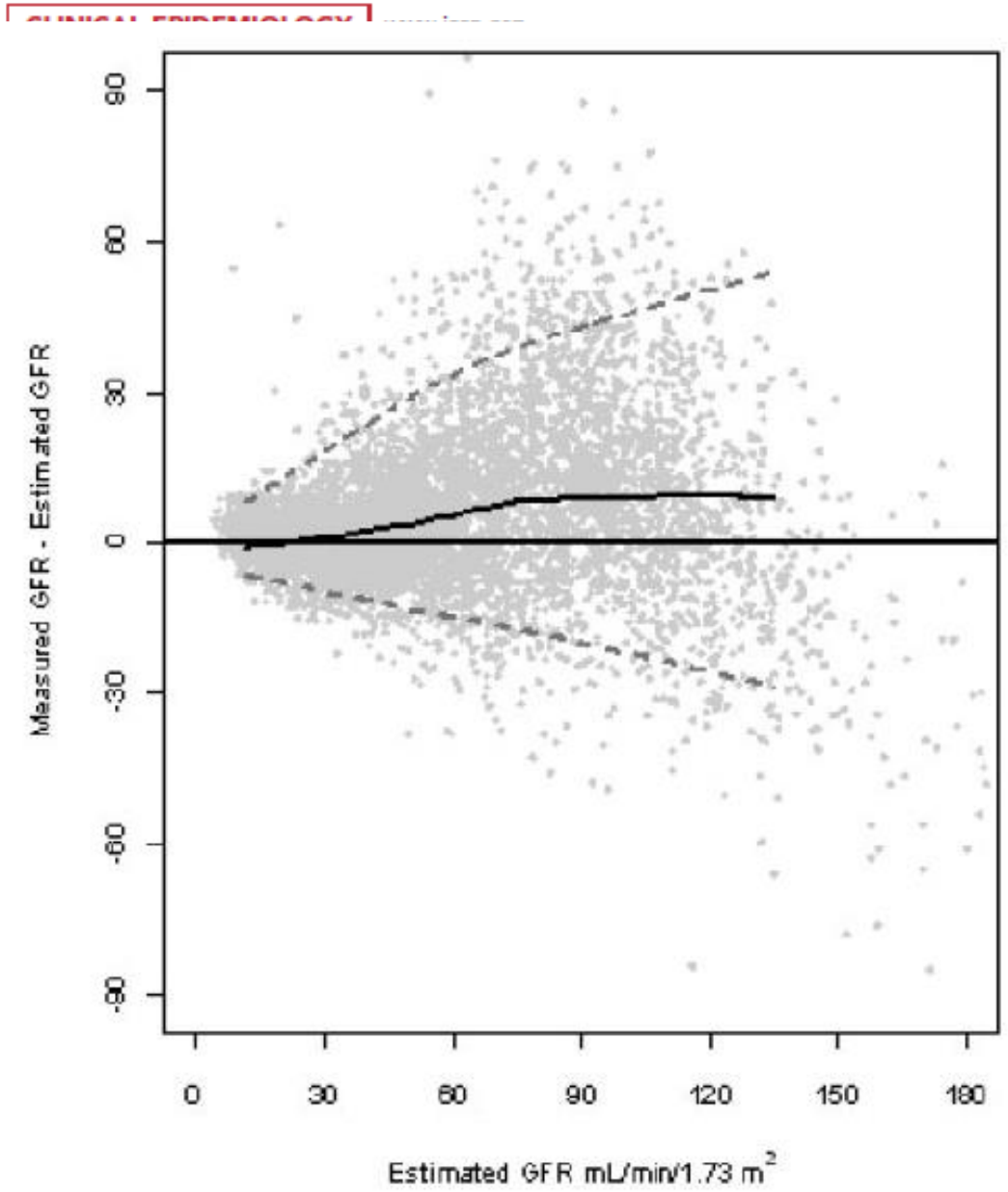


Figure 2. Difference of the MDRD Study equation by level of eGFR. Difference is calculated as (mGFR − eGFR). Solid horizontal

Disease

Lash,
,*

aryland;
ake City, Utah;
**Case

MDRD: les forces

- Bonne performance surtout aux stades 3-4 MRC
- Exactitude attendue: 80-85%
- Mieux que Cockcroft en termes de précision

Equation 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.

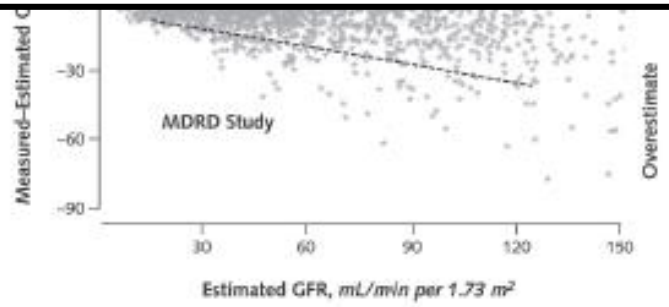


Table 3. Comparison of the CKD-EPI and MDRD Study Equations in Estimating Measured GFR in the Validation Data Set*

Variable and Equation	All Patients	Patients With Estimated GFR <60 mL/min per 1.73 m²	Patients With Estimated GFR ≥60 mL/min per 1.73 m²
Median difference (95% CI), *mL/min per 1.73 m²*†			
CKD-EPI	2.5 (2.1–2.9)	2.1 (1.7–2.4)	3.5 (2.6–4.5)
MDRD Study	5.5 (5.0–5.9)	3.4 (2.9–4.0)	10.6 (9.8–11.3)
Interquartile range for differences (95% CI), *mL/min per 1.73 m²*‡			
CKD-EPI	16.6 (15.9–17.3)	11.3 (10.7–12.1)	24.2 (22.8–25.3)
MDRD Study	18.3 (17.4–19.3)	12.9 (12.0–13.6)	25.7 (24.4–27.1)
P_{30} (95% CI), %§			
CKD-EPI	84.1 (83.0–85.3)	79.9 (78.1–81.7)	88.3 (86.9–89.7)
MDRD Study	80.6 (79.5–82.0)	77.2 (75.5–79.0)	84.7 (83.0–86.3)
Root mean square error (95% CI)			
CKD-EPI	0.250 (0.241–0.259)	0.284 (0.270–0.298)	0.213 (0.203–0.223)
MDRD Study	0.274 (0.265–0.283)	0.294 (0.280–0.308)	0.248 (0.238–0.258)


KIDNEY DISEASE
IMPROVING GLOBAL OUTCOMES
KDIGO

Facteur ethnique CKD/EPI - MDRD

NON

RESEARCH LETTER

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

Flamant M et al Am J Kidney Dis, 2013, 62, p179

Hindawi
International Journal of Nephrology
Volume 2020, Article ID 2141030, 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

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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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

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Check for updates

Yayo ES, Nephrol Ther, 2016 , 12 , 454
Flamant M, Am J Kdiney Dis, 2013, 62, 179
Bukabau JB, Plos One, 2018, 13, e0193384

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

- N=494
- Iohexol
- Créatinine calibrée

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

Equation	Absolute bias (95% CI)	Absolute SD	Accuracy within 30% (95% CI)	Lin's CCC (95% CI)
CKD-EPI	0.0 (−1.6 to 1.6)	18.1	77.7 (74.1 to 81.4)	0.81 (0.76 to 0.84)
CKD-EPI ef	13.3 (11.4 to 15.2)	21.3	64.6 (60.3 to 68.8)	0.71 (0.66 to 0.76)

eGFR

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.

VIEWPOINT

Reconsidering the Consequences of Using Race to Estimate Kidney Function

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
- Black coefficient in MDRD and CKD-EPI equations
- How is race defined?
- Problem of mixed people (Brazil)
- Muscular mass impact is not proven
- A 50 years old woman with creatinine at 2.0 mg/dL

CKD-EPI: 28 mL/min/1.73m² if non-Black vs 33 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)**

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)

AMERICENTRISM IN ESTIMATION OF GFR EQUATIONS

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Word Count- (main Body): 1605

Arguments can be posited in favor of using the previous CKD-EPI creatinine equation in Europe, Africa, Brazil, and elsewhere without any race correction. Should these countries, and others, 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?

THE WORLD ACCORDING TO AMERICANS

MDRD – CKD-EPI: What else?

- Equation Bis
- Equation Lund-Malmö
- Equation EKFC
- Autre biomarqueurs: cystatine C

Schaeffner, Ann intern Med, 2012, 157, 471
Bjork, Scand J Urol Nephrol, 2012, 46, 212
Pottel H, Nephrol Dial Transplant, 2016
Seronie-Vivien, CCLM, 2008

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

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- 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:

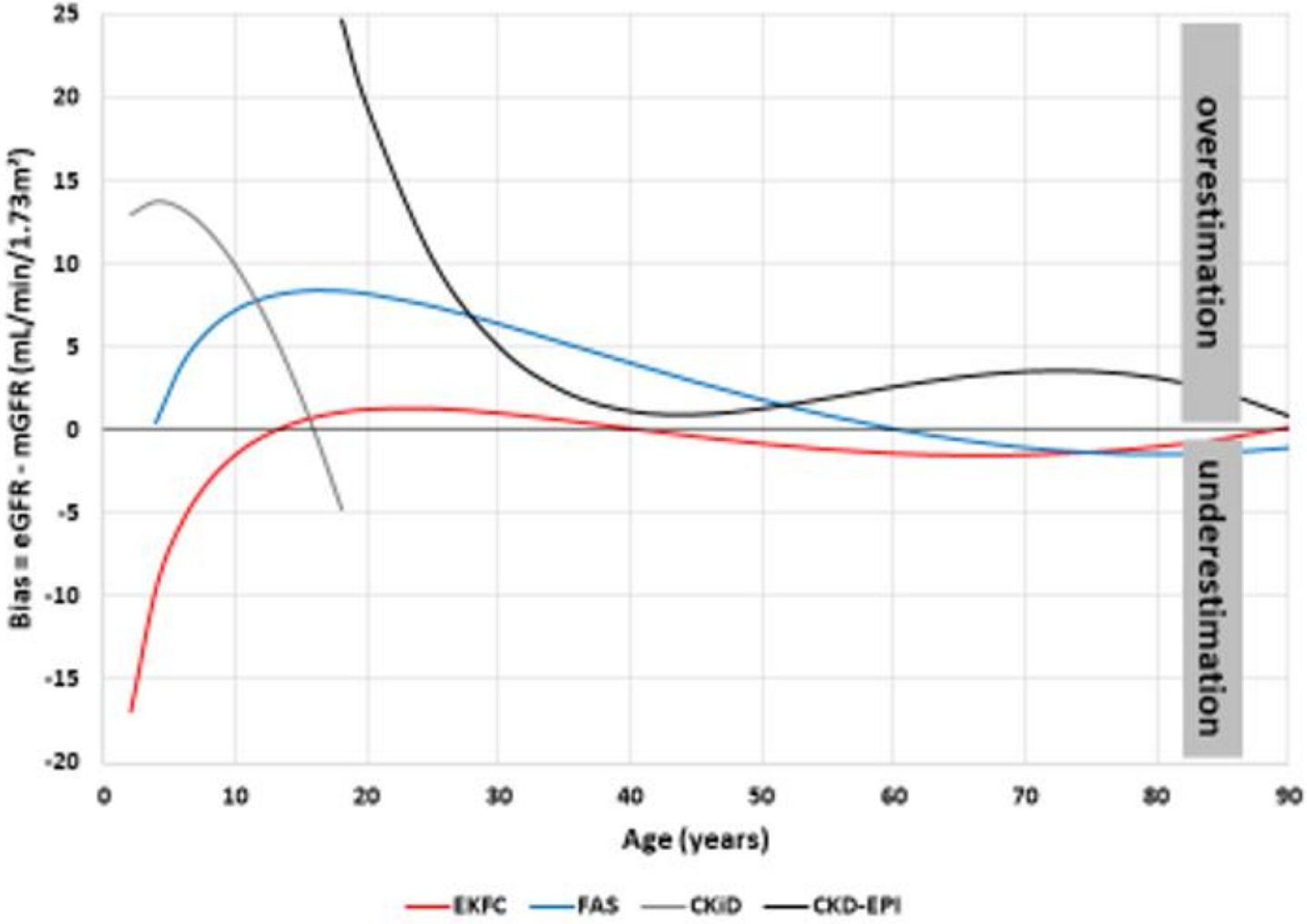
$Q = 80$ µmol/L (0.90 mg/dL)

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.


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

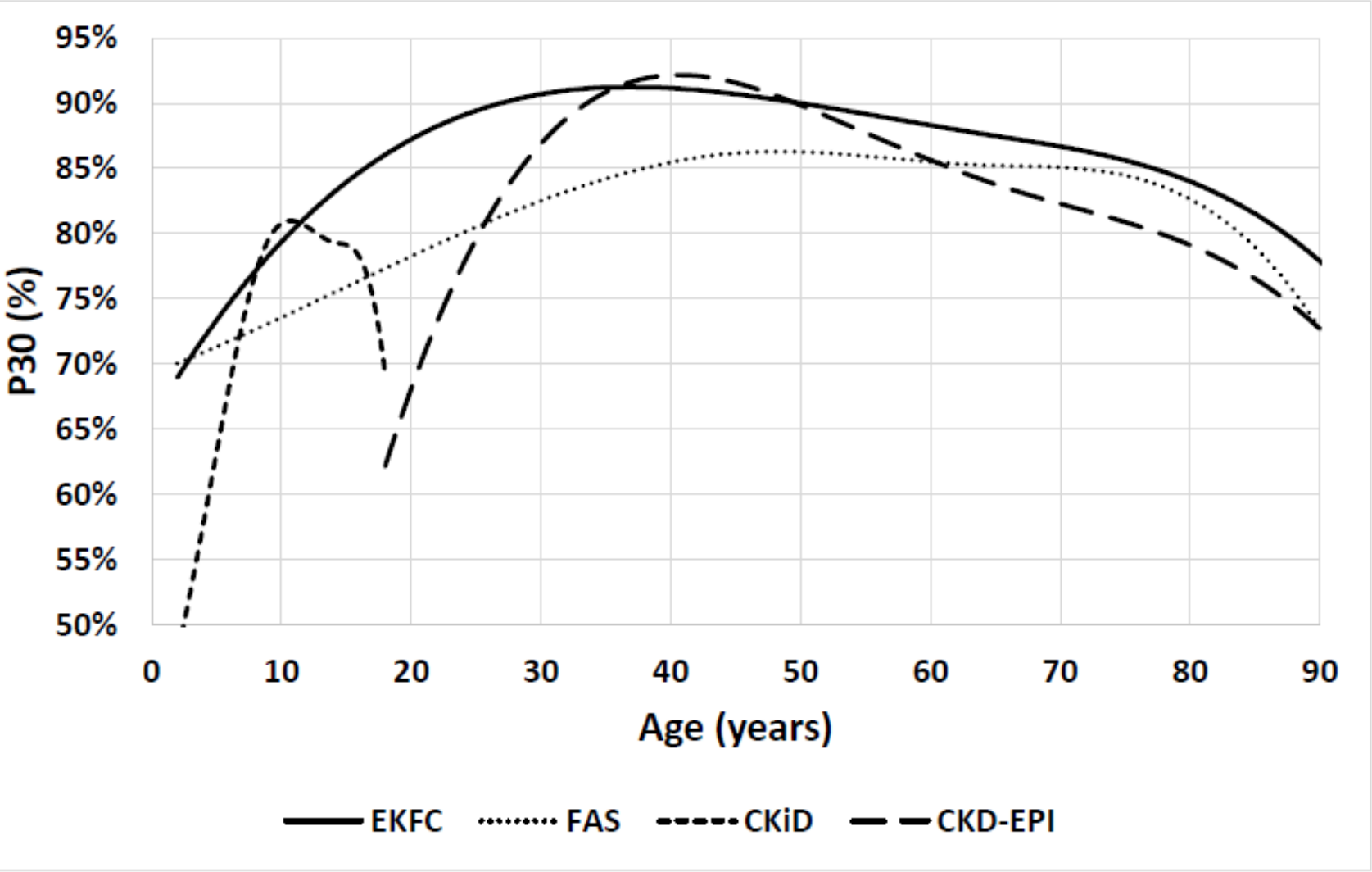


Figure S8. P30-accuracy against age for the EKFC, FAS, CKiD and CKD-EPI equation in the external validation dataset. P30 (%) was graphically presented across the age spectrum using cubic splines with two free knots and using 3rd degree polynomials.

Cystatine 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 1. Characteristics of Study Participants, According to Data Set.*

Characteristic	Development and Internal Validation (N = 5352)	External Validation (N = 1119)	P Value
Age — yr	47±15	50±17	<0.001
Age group — no. (%)			
<40 yr	2008 (38)	357 (32)	<0.001
40–65 yr	2625 (49)	530 (47)	
>65 yr	719 (13)	232 (21)	
Male sex — no. (%)	3107 (58)	663 (59)	0.46
Black race — no. (%)†	2123 (40)	30 (3)	<0.001
Diabetes — no. (%)	1726 (32)	594 (53)	<0.001
Body-mass index‡			
Mean	28±6	25±4	<0.001
<20 — no. (%)	214 (4)	81 (7)	<0.001
20–24 — no. (%)	1585 (30)	503 (45)	
25–30 — no. (%)	1881 (35)	386 (35)	
>30 — no. (%)	1671 (31)	149 (13)	
Mean weight — kg	83±20	74±15	<0.001
Mean height — cm	171±10	170±9	0.017
Mean body-surface area — m^2	1.94±0.24	1.85±0.21	<0.001
Mean serum cystatin C — ml/liter	1.4±0.7	1.5±0.8	0.01
Mean serum creatinine — mg/dl§	1.6±0.9	1.6±1.1	0.15
Mean measured GFR — ml/min/1.73 m^2 of body-surface area	68±39	70±41	0.13
Measured GFR — no. (%)			
<15 ml/min/1.73 m^2	160 (3)	51 (5)	<0.001
15–29 ml/min/1.73 m^2	785 (15)	166 (15)	
30–59 ml/min/1.73 m^2	1765 (33)	316 (28)	
60–89 ml/min/1.73 m^2	1105 (21)	215 (19)	
90–119 ml/min/1.73 m^2	862 (16)	199 (18)	
>120 ml/min/1.73 m^2	675 (13)	172 (15)	

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)

BIS2: $767 \times \text{cystatin C}^{-0.61} \times \text{creatinine}^{-0.40} \times \text{age}^{-0.57} \times 0.87$ (if female)

CKD-EPI:

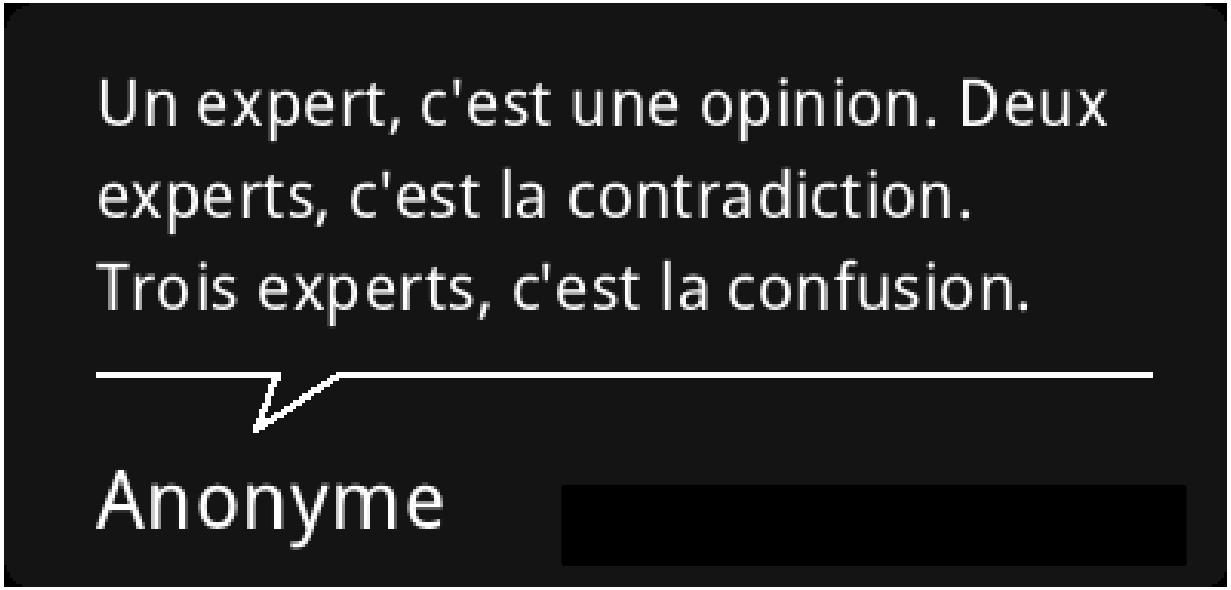
$$\text{eGFR} = 130 \times \text{cystatin C}^{-1.069} \times \text{age}^{-0.117} - 7.$$

$$\text{FAS}_{\text{cysC}} = \frac{107.3}{\frac{\text{ScysC}}{\text{Q}_{\text{cysC}}}} \times \left[0.988^{(\text{Age}-40)} \text{ when age} > 40 \text{ years}\right].$$

$$\text{FAS}_{\text{combi}} = \frac{107.3}{\alpha \times \frac{\text{Scr}}{\text{Q}_{\text{crea}}} + (1-\alpha) \times \frac{\text{ScysC}}{\text{Q}_{\text{cysC}}}} \times \left[0.988^{(\text{Age}-40)} \text{ when age} > 40 \text{ years}\right].$$

Cystatine C

- Combinée
- Pas de facteur(s) ethnique(s), ni de genre
- “Cost-effectiveness?”
- Une certaine imprécision reste au niveau individuel
- Standardisation de la mesure pas complète pour la cystatine C
- Pas remboursé (sauf greffe ou pédiatrie)


Un expert, c'est une opinion. Deux experts, c'est la contradiction.
Trois experts, c'est la confusion.
Anonyme

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)

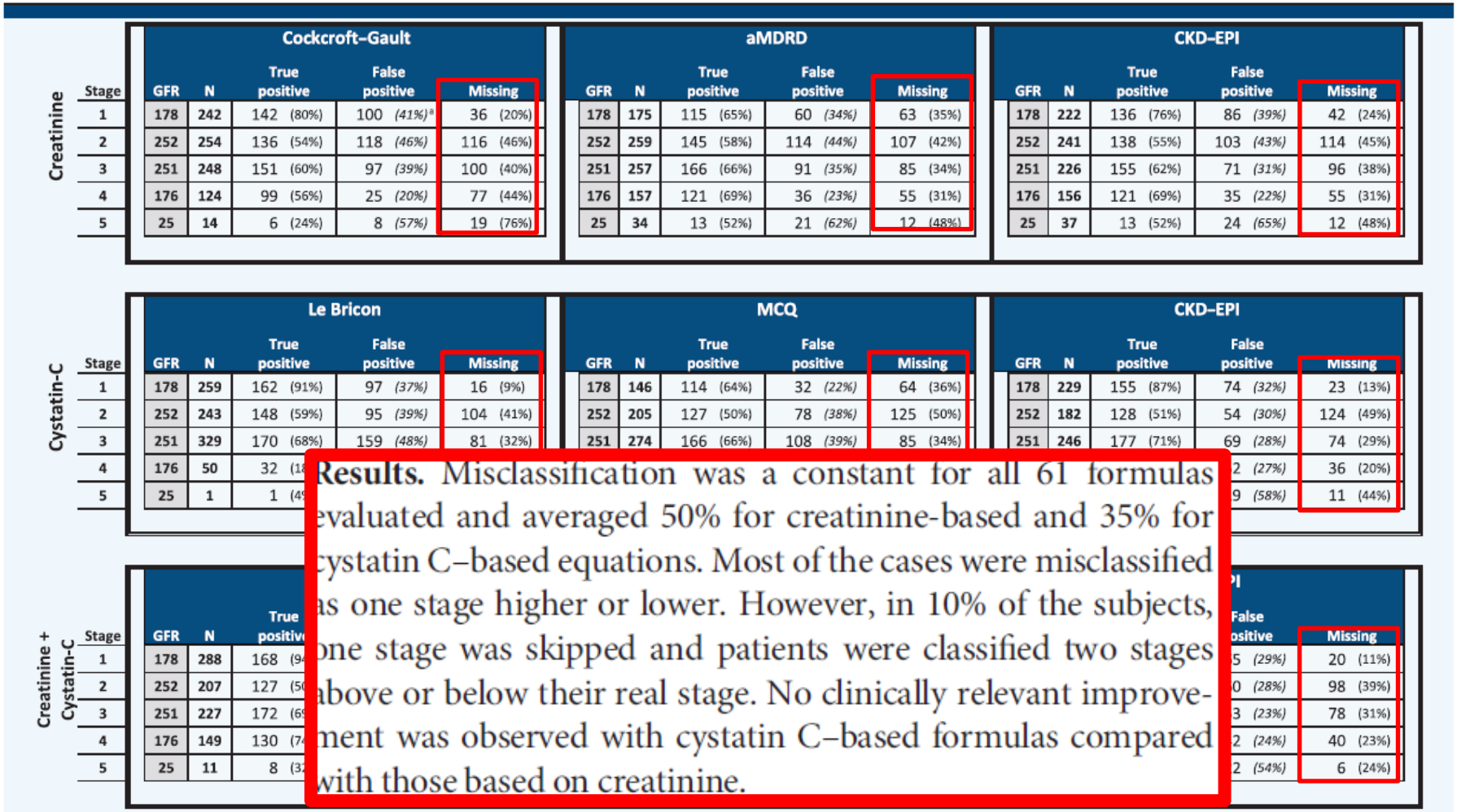
Hospitalisés (Poggio ED, Am J Kidney Dis, 2005, 46, 242)

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

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

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

Table 2. Classification of patients in CKD stages by a representative group of nine creatinine and/or cystatin C–based formulas



Creatinine

Stage	Cockcroft–Gault GFR	N	True positive	False positive	Missing	aMDRD GFR	N	True positive	False positive	Missing	CKD–EPI GFR	N	True positive	False positive	Missing
1	178	242	142 (80%)	100 *(41%)*[a]	36 (20%)	178	175	115 (65%)	60 *(34%)*	63 (35%)	178	222	136 (76%)	86 *(39%)*	42 (24%)
2	252	254	136 (54%)	118 *(46%)*	116 (46%)	252	259	145 (58%)	114 *(44%)*	107 (42%)	252	241	138 (55%)	103 *(43%)*	114 (45%)
3	251	248	151 (60%)	97 *(39%)*	100 (40%)	251	257	166 (66%)	91 *(35%)*	85 (34%)	251	226	155 (62%)	71 *(31%)*	96 (38%)
4	176	124	99 (56%)	25 *(20%)*	77 (44%)	176	157	121 (69%)	36 *(23%)*	55 (31%)	176	156	121 (69%)	35 *(22%)*	55 (31%)
5	25	14	6 (24%)	8 *(57%)*	19 (76%)	25	34	13 (52%)	21 *(62%)*	12 (48%)	25	37	13 (52%)	24 *(65%)*	12 (48%)

Cystatin-C

Stage	Le Bricon GFR	N	True positive	False positive	Missing	MCQ GFR	N	True positive	False positive	Missing	CKD–EPI GFR	N	True positive	False positive	Missing
1	178	259	162 (91%)	97 *(37%)*	16 (9%)	178	146	114 (64%)	32 *(22%)*	64 (36%)	178	229	155 (87%)	74 *(32%)*	23 (13%)
2	252	243	148 (59%)	95 *(39%)*	104 (41%)	252	205	127 (50%)	78 *(38%)*	125 (50%)	252	182	128 (51%)	54 *(30%)*	124 (49%)
3	251	329	170 (68%)	159 *(48%)*	81 (32%)	251	274	166 (66%)	108 *(39%)*	85 (34%)	251	246	177 (71%)	69 *(28%)*	74 (29%)
4	176	50	32 (18											2 *(27%)*	36 (20%)
5	25	1	1 (4											9 *(58%)*	11 (44%)

Creatinine + Cystatin-C

Stage	GFR	N	True positiv	False positive	Missing
1	178	288	168 (9		20 (11%)
2	252	207	127 (5		98 (39%)
3	251	227	172 (6		78 (31%)
4	176	149	130 (7		40 (23%)
5	25	11	8 (3		6 (24%)

Results. Misclassification was a constant for all 61 formulas evaluated and averaged 50% for creatinine-based and 35% for cystatin C–based equations. Most of the cases were misclassified as one stage higher or lower. However, in 10% of the subjects, one stage was skipped and patients were classified two stages above or below their real stage. No clinically relevant improvement was observed with cystatin C–based formulas compared with those based on creatinine.

'True positives cases' represent the subjects that were corretly classified in each CKD stage by eGFR. 'False positives cases' represent the patients who were classified in one CKD stage based on eGFR when actually belonging to a different stage. 'Missing cases' represent the cases that were not classified in the corresponding CKD stage.

[a]The percentage of false positive cases refers to the number of cases defined in each CKD stage by mGFR (grey column). The percentage of true positive and missing cases refers to the number of cases defined in each CKD stage by eGFR.

Ne pas sur-interpreter un résultat…

Toutes les équations restent des estimations

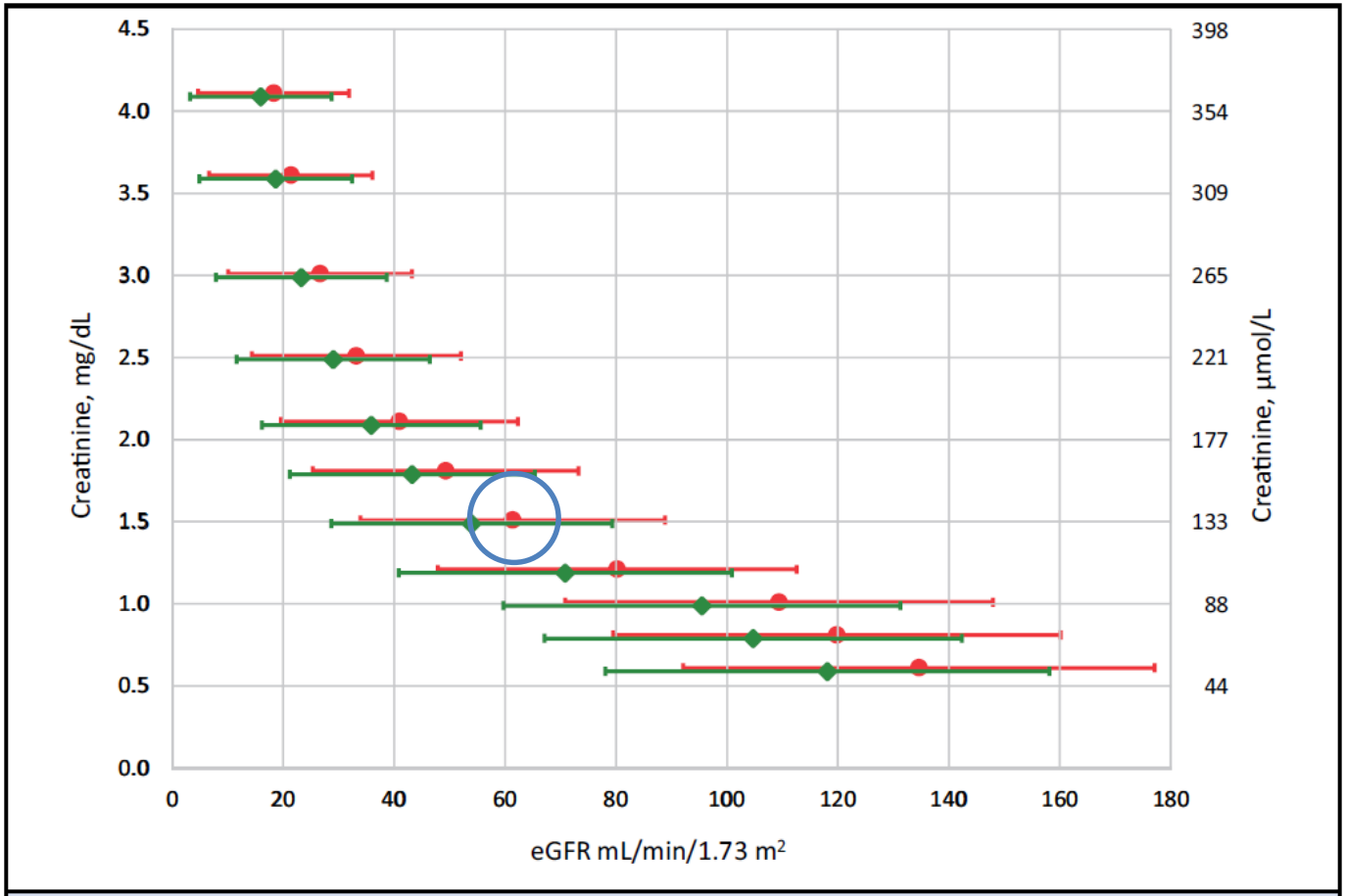


Fig. 1. Uncertainty of eGFR calculated using the CKD-EPI equations for African-Americans and non-African-Americans at various creatinine concentrations for a 50-year-old male. Circles (red, larger values) indicate African-American and diamonds (green, lower values) indicate non-African-American equations. 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

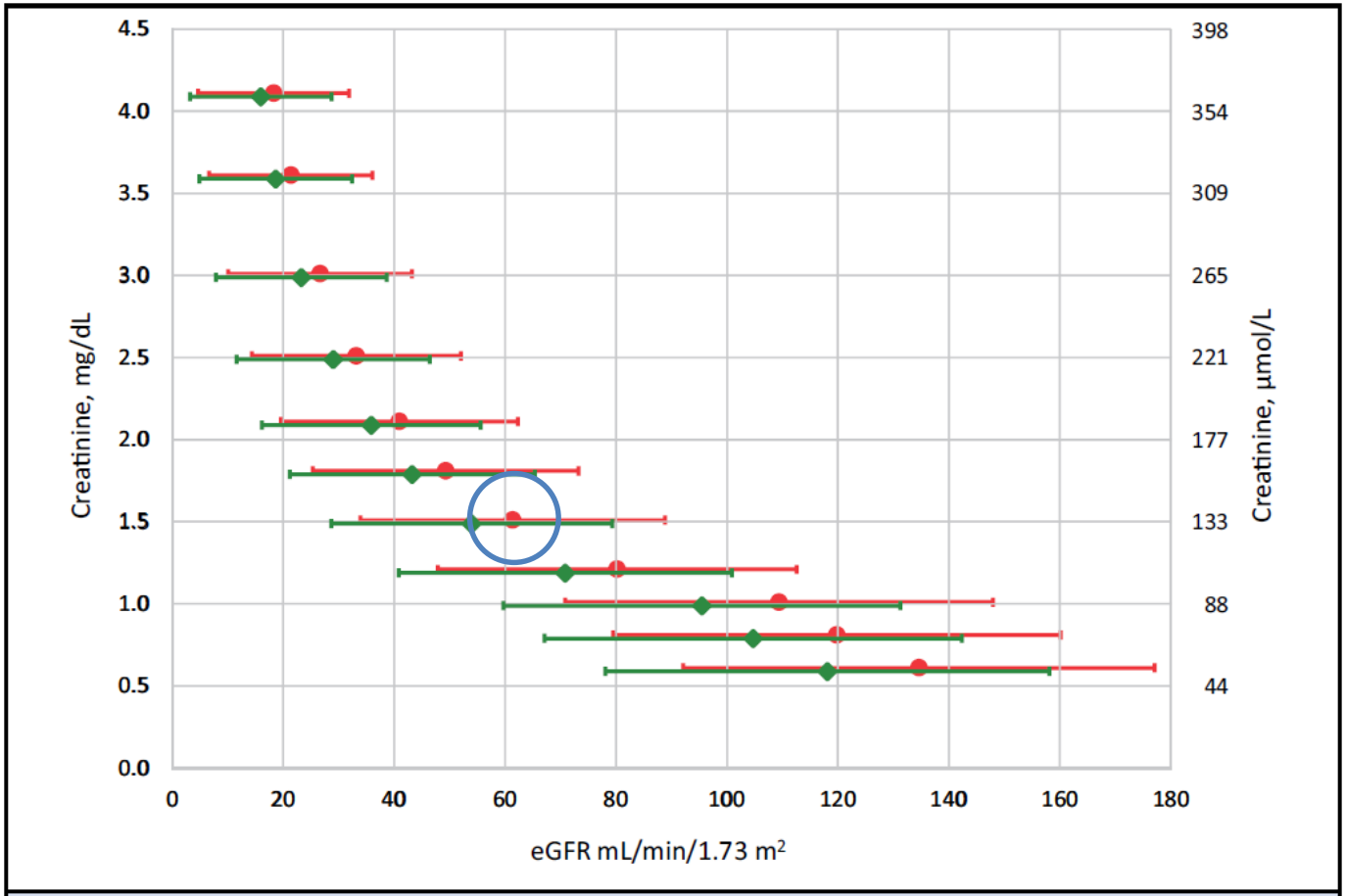


Fig. 1. Uncertainty of eGFR calculated using the CKD-EPI equations for African-Americans and non-African-Americans at various creatinine concentrations for a 50-year-old male. Circles (red, larger values) indicate African-American and diamonds (green, lower values) indicate non-African-American equations.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

eGFR ~~= 60,25 ml/min/1.73m²~~

= 60 ml/min/1.73m² (CI 95%: 33-87)

Miller WG, Clin Chem, 2021, p693 and p820

REVIEWS

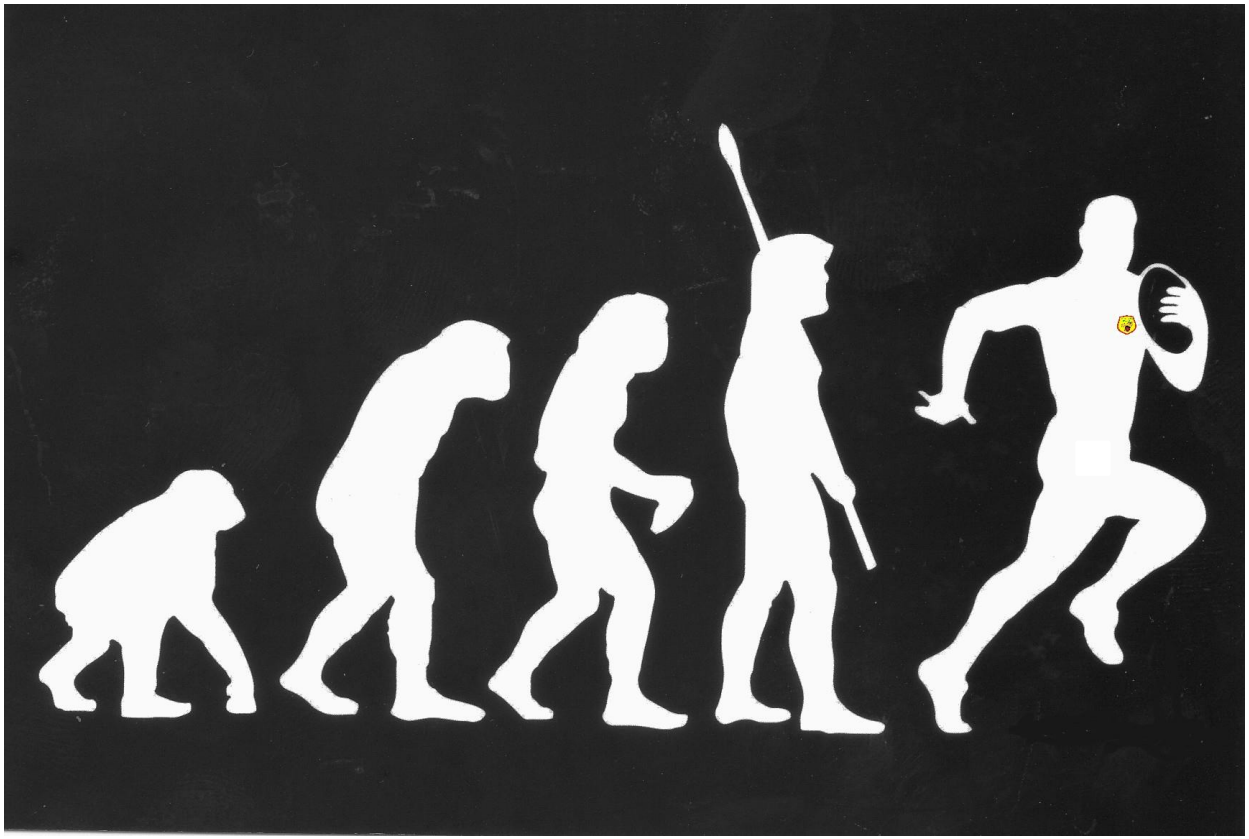
The applicability of eGFR equations to different populations

Pierre Delanaye and Christophe Mariat

Aujourd'hui, la question n'est pas tant de savoir quelle équation est la meilleure mais quand un recours au DFG mesuré est pertinent

Delanaye P, Nature Rev Nephrol, 2013, 9, 513

Comment évoluer?



Et si on mesurait le DFG…

Mesurer le DFG: Pourquoi?
Une question de précision!

- Décision d'initier la dialyse
- Individus sarcopéniques
- Gabarit extrême
- Cirrhose, USI, Hyperfiltration
- Donneur vivant

Agarwal R, Nephrol Dial Transplant, 2019, 34, p2001
Ebert N, Clin Kidney J, 2021, p1861

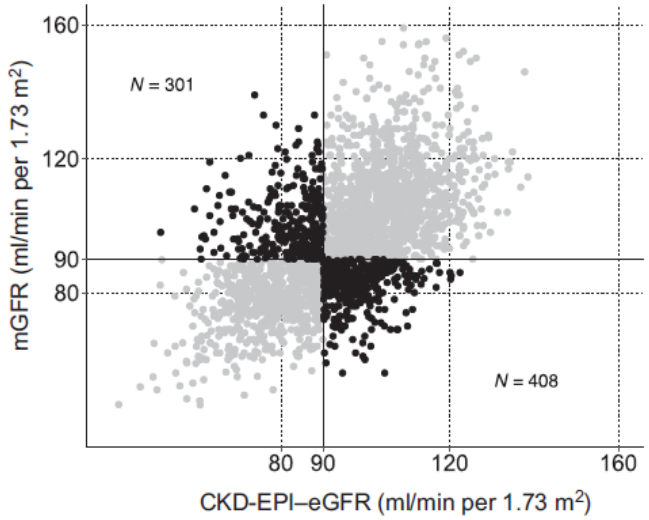
Impact of estimation versus direct measurement of predonation glomerular filtration rate on the eligibility of potential living kidney donors

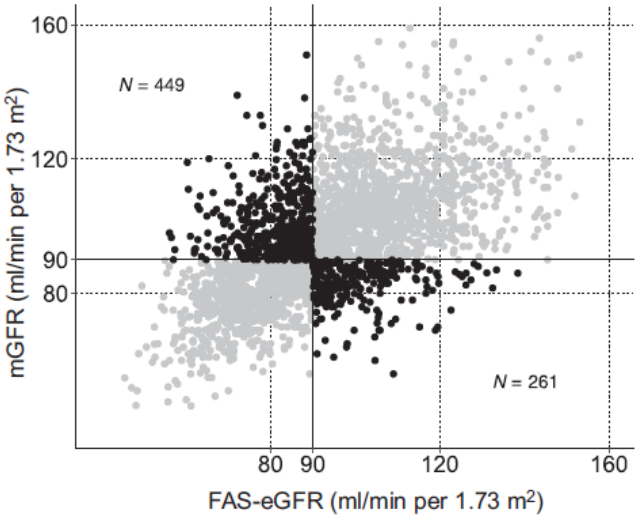
see commentary on page 738

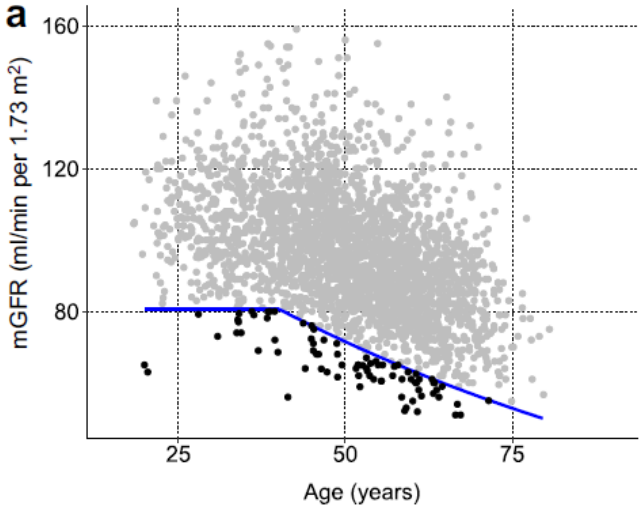
François Gaillard[1,2], Marie Courbebaisse[2,3], Nassim Kamar[4,5,18], Lionel Rostaing[6,18], Lola Jacquemont[7,8], Maryvonne Hourmant[7,8], Arnaud Del Bello[4], Lionel Couzi[9,10], Pierre Merville[9,10], Paolo Malvezzi[6], Benedicte Janbon[6], Bruno Moulin[11], Nicolas Maillard[12], Laurence Dubourg[13,14], Sandrine Lemoine[13], Cyril Garrouste[15], Hans Pottel[16], Christophe Legendre[1,2], Pierre Delanaye[17,19] and Christophe Mariat[12,19]

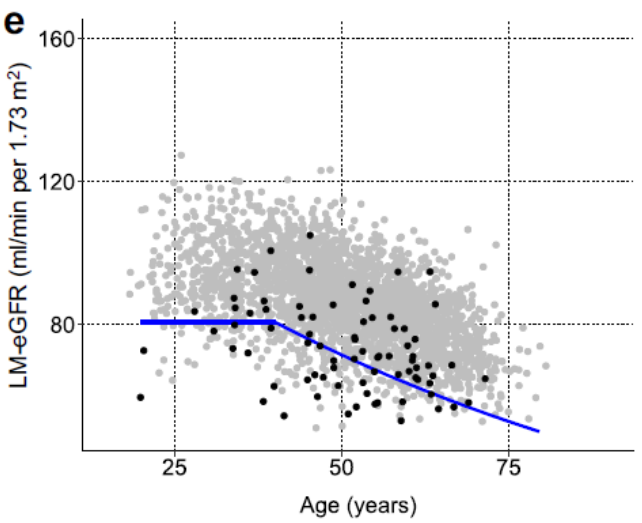
Kidney International (2019) **95,** 896–904;

- N=2,733 donneurs potentiels
- DFG mesuré, créatinine calibrée


160
120
90
80
N = 301
N = 408
mGFR (ml/min per 1.73 m²)
80 90 120 160
CKD-EPI–eGFR (ml/min per 1.73 m²)


160
120
90
80
N = 449
N = 261
mGFR (ml/min per 1.73 m²)
80 90 120 160
FAS-eGFR (ml/min per 1.73 m²)


a
160
120
80
mGFR (ml/min per 1.73 m²)
25 50 75
Age (years)


e
160
120
80
LM-eGFR (ml/min per 1.73 m²)
25 50 75
Age (years)

Mesurer le DFG: Pourquoi? Une question de précision!

- Décision d'initier la dialyse
- Individus sarcopéniques
- Gabarit extrême
- Cirrhose, USI, Hyperfiltration
- Donneur vivant
- Recherche Clinique, EMA
- Dosage d'un médicament potentiellement néphrotoxique (=>2)
- Pas de preuve définitive…

Agarwal R, Nephrol Dial Transplant, 2019, 34, p2001
Ebert N, Clin Kidney J, 2021, p1861

Disponibles sur le marché…

Marqueurs	Forces	Limites
Inuline	"Gold standard" (ou historique)	Coûteux Dosage ni facile ni standardisé Impossible en clairance plasmatique
Iothalamate	Le plus populaire aux USA Isotopique ou "froide"	Sécrétion tubulaire Allergie Iode
Iohexol	Populaire en Europe Froide	Allergie Iode
EDTA	Facile à mesurer	Seulement isotopique Pas disponible aux USA…et plus en Europe!!
DTPA	Facile à mesurer	Seulement isotopique Liaison aux protéines

Stevens LA, J Am Soc Nephrol, 2009, 20, 2305
Cavalier E, Clin Chim Acta, 2008, 396, 80
Delanaye P, Clin Kidney J, 2016, 9, 700

AJKD
Original Investigation

Measuring GFR: A Systematic Review

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Table 1. Bias and Accuracy of Index Methods Compared to Reference Method When Measuring Glomerular Filtration Rate

	No. of Pts/ Studies	Median Bias[a] (95% CI)	Mean Bias (95 % CI)	P_{30} (95% CI)	P_{10} (95% CI)	Sufficient Accuracy	Scientific Evidence	Comments[b]
Criteria for sufficient precision		≤±5%	≤±10%	≥80%	≥50%			
Index method								
DTPA								
Renal clearance	126/5	−2 (−4 to 2)	−1 (−6 to 5)	87 (81 to 93)	53 (45 to 62)	Yes	⊕⊕◯◯	Inconsistency, −1; imprecision, −1
Plasma clearance	89/2	20 (18 to 35)	13 (5 to 22)	56 (47 to 68)	19 (13 to 29)	No	⊕⊕◯◯	Study limitations −1; imprecision −1
^{51}Cr-EDTA								
Renal clearance	198/9	−5 (−7 to −3)	−2 (−8 to 4)	95 (92 to 98)	56 (50 to 64)	Yes	⊕⊕⊕◯	Imprecision, −1
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Iohexol								
Renal clearance	47/2	−7 (−10 to 0)	−7 (−16 to 2)	100[c]	53 (41 to 70)	Yes	⊕⊕◯◯	Imprecision, −2
Plasma clearance	172/5	3 (0 to 6)	2 (−4 to 9)	86 (81 to 91)	50 (43 to 58)	Yes	⊕⊕⊕◯	Imprecision, −1
Iothalamate								
Renal clearance	548/13	−1 (−2 to 0)	6 (1 to 11)	97 (95 to 98)	66 (62 to 70)	Yes	⊕⊕⊕⊕	
Plasma clearance	61/1	9 (0 to 15)	11 (−6 to 29)	82 (73 to 92)	33 (23 to 47)	—	⊕◯◯◯	Study limitations, −1; imprecision, −2
Inulin								
Plasma clearance	39/2	2 (−3 to 6)	1 (−9 to 11)	100[c]	72 (59 to 87)	Yes	⊕⊕◯◯	Imprecision, −1; indirectness, −1

Note: Modified with permission of the Swedish Council on Health Technology Assessment.[3] Accuracy and bias expressed as percentage. Renal inulin clearance served as reference method. Mean bias, P_{10}, and P_{30} were estimated using generalized linear mixed models based on normal distribution (mean bias) or Poisson distribution (P_{10}, P_{30}; log-transformed outcome and robust variance estimation), with a random intercept for each study and a fixed effect for each index method ("unadjusted model results"; see Statistical Methods section). All analyses were weighed with respect to number of participants in each study. Estimates were obtained as marginal means.

Abbreviations and definitions: ⊕⊕⊕⊕, strong evidence; ⊕⊕⊕◯, moderately strong evidence; ⊕⊕◯◯, limited evidence; ⊕◯◯◯, insufficient evidence; ^{51}Cr-EDTA, chromium 51–labeled ethylenediaminetetraacetic acid; DTPA, diethylenetriaminepentaacetic acid; CI, confidence interval; Imprecision, N < 100 in meta-analysis (−1), P_{30} lower 95% CI ≤ 80%, P_{10} lower 95% CI ≤ 50%, or median bias 95% CI ≥ ±5% (−1); Inconsistency, inconsistency in study outcomes that cannot be explained by differences in study design (−1); Indirectness, limited generalizability (−1); P_{10}, percentage of measurements by index method that differed no more than 10% from reference method; P_{30}, percentage of measurements by index method that differed no more than 30% from reference method; pts, patients; Study limitations, risk of bias due to shortcomings in individual studies (−1).

[a]Median bias was calculated directly (using the weights) for each index method together with nonparametric CIs.

[b]Strength of scientific evidence.

[c]The generalized linear mixed model does not yield valid estimates of confidence limits when estimated proportion (eg, P_{30}) is 100%.

Soveri I, Am J Kidney Dis, 2014, 64, 411

Comment mesurer le DFG?

Table 4. Available procedures to perform iohexol clearance

Methodology	Indication in clinical practice	Indication in clinical research	Bibliographic examples where the procedure is described into details
Urinary clearance	Increased extracellular volume (oedema, ascites, intensive care units, etc.)	Basic (physiologic) studies Specific populations (cirrhotic, intensive care, nephrotic syndrome, oedema, etc.)	[36, 77, 125, 170]
Plasma clearance			
Multiple samples (first or fast, second or slow exponential curves and calculation of area under the curve)	High GFR values ('hyperfiltrating') subjects	Development of equations to estimate GFR Studies in hyperfiltrating patients	[52, 93, 171]
Multiple samples only for second and slow component (2 h after injection, 4 samples over 5 or 6 h, 1 sample/h) + BM correction	High precision determination (see text)	Development of equations to estimate GFR Clinical research with GFR as main endpoint	[126, 172]
Idem + late sample (8 h or 24 h)	Pre-dialysis subjects	Research in pre-dialysis subjects	[52, 77]
Simplified two or three sample method (2 samples: first at 2 or 3 h and second at 4 or 5 h) + BM correction	CKD or healthy population	Development of equations to estimate GFR Clinical research with GFR as a secondary endpoint	[69, 116]
Simplified single-sample method + Jacobsson correction [110]	CKD or healthy population	Development of equations to estimate GFR Clinical research with GFR as a secondary endpoint Epidemiological research	[14, 173]

Suggestions (expert opinion-based) according to the clinical or experimental context.
GFR, glomerular filtration rate; CKD, chronic kidney disease; BM, Brochner-Mortensen correction [116].

Delanaye P, Clin Kidney J, 2016, 9, 700

EKFC

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Single- versus multiple-sample method to measure glomerular filtration rate

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KI REPORTS KIReports.org — CLINICAL RESEARCH

Comparison of Plasma Clearance With Early-Compartment Correction Equations and Urinary Clearance in High GFR Ranges

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AJKD
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RESEARCH LETTER

Concordance Iohexol Plasma Clearance

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Original Investigation — AJKD

Comparability of Plasma Iohexol Clearance Across Population-Based Cohorts

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Rationale & Objective: Glomerular filtration rate (GFR) estimation based on creatinine or cystatin C level is currently the standard method for assessing GFR in epidemiologic research and clinical trials despite several important and well-known limitations. Plasma iohexol clearance has been proposed as an inexpensive method for measuring GFR that could replace estimated GFR in many research projects. However, lack of standardization for iohexol assays and the use of different protocols such as single- and multiple-sample methods could potentially hamper comparisons across studies. We compared iohexol assays and GFR measurement protocols in 3 population-based European cohorts.

Study Design: Cross-sectional investigation.

Setting & Participants: Participants in the Age

Results: Frozen samples from the 3 studies were obtained and iohexol concentrations were remeasured in the laboratory at the University Hospital of North Norway. Lin's concordance correlation coefficient ρ was >0.96 and C_b (accuracy) was >0.99 for remeasured versus original serum iohexol concentrations in all 3 cohorts, and Passing-Bablok regression did not find differences between measurements, except for a slope of 1.025 (95% CI, 1.006-1.046) for the log-transformed AGES-Kidney measurements. The multiple-sample iohexol clearance measurements in AGES-Kidney and BIS were compared with single-sample GFRs derived from the same iohexol measurements. Mean bias for multiple-sample relative to single-sample GFRs in AGES-Kidney and BIS were −0.25 and −0.15 mL/min, and 99% and 97% of

Complete author and article information provided before references.

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Comparison of Early-Compartment Correction Equations for GFR Measurements

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Check for updates

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BMC Nephrology

RESEARCH — Open Access

Iohexol plasma clearance for measuring glomerular filtration rate: effect of different ways to calculate the area under the curve

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KI REPORTS KIReports.org — RESEARCH LETTER

Iohexol Plasma Clearance: Impact of Weighing the Syringe

Check for updates

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Choix du marqueur

- Seules les méthodes froides sont facilement implantables partout dans le monde
- Iohexol est disponible partout
- Très stable (labo central et/ou de “référence”)
- EQUAS (Equalis, Sweden) est disponible
- Cr-EDTA, inuline, iothalamate pas ou plus disponibles chez nous…

Iohexol au CHU de Liège

- Iohexol (clairance plasmatique), 5 mL bolus
- 5 heures
- Echantillons à 2, 3, 4 et 5 heures (+long si DFG très bas)
- Bröchner-Mortensen
- 50 à 100 euros

Conclusions

- Mesurer le DFG n’est pas si difficile
- Iohexol est la meilleure balance entre physiologie et faisabilité
- Iohexol est sans danger
- Iohexol est la seule chance pour une mesure du DFG standardisée dans le monde entier
- En Europe, l’iohexol va s’imposer par manque de combattants

Merci de votre attention