

# Débit de filtration glomérulaire: pour qui? et comment?



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**Category****Disclosure Information**

Employer

Nothing to disclose.

Ownership Interest

Nothing to disclose.

Consultancy

IDS; Nephrolytix; Alentis Therapeutics; ARK Bioscience;

Research Funding

Nothing to disclose.

Honoraria

IDS; Fresenius Kabi; Fresenius Medical Care; Nephrolytix; Alentis Therapeutics; ARK Bioscience;  
AstraZeneca;

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.

- Estimation du DFG
- Mesure du DFG

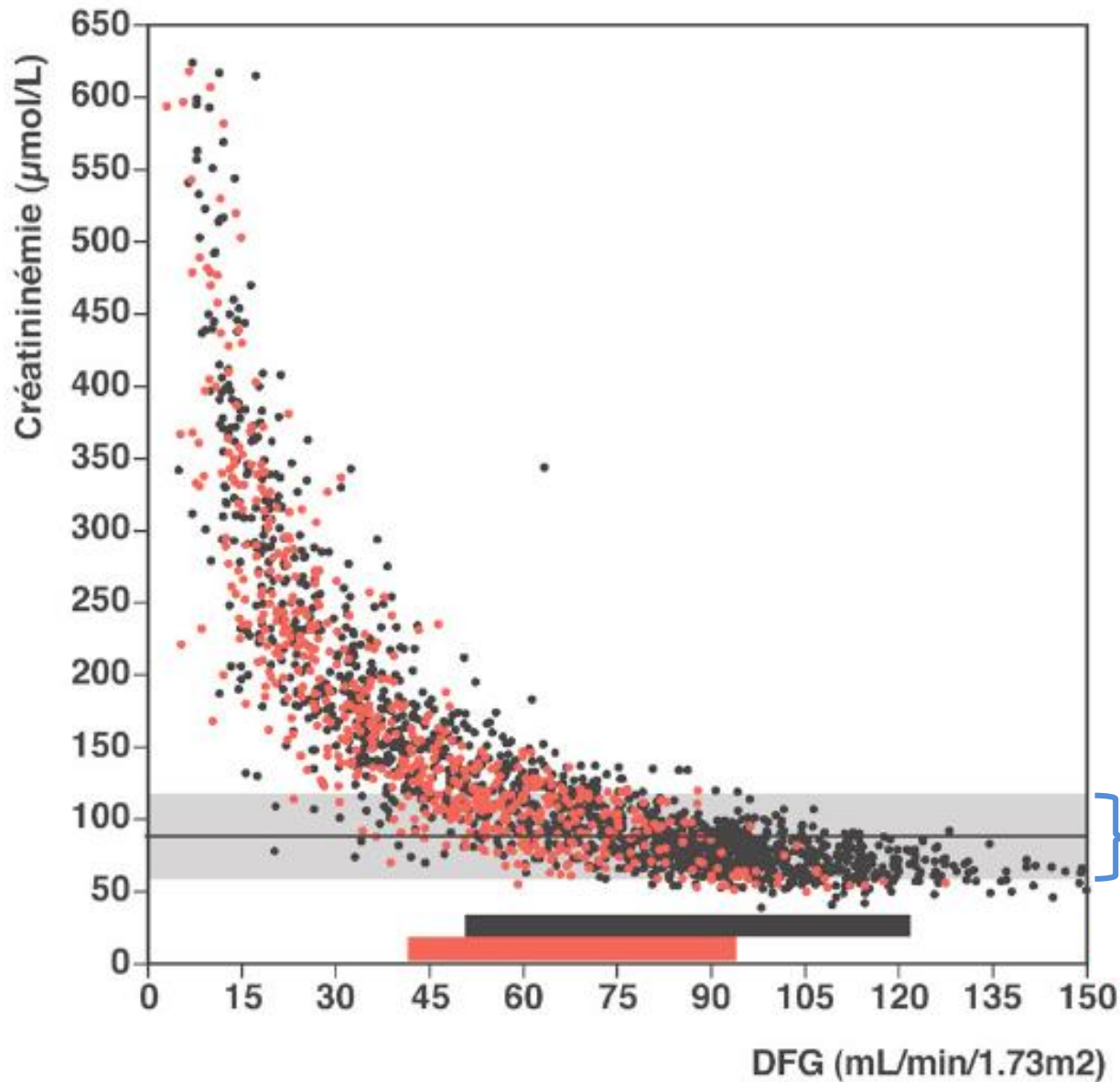
- Estimation du DFG
- Mesure du DFG

# Créatinine sérique

- Une des analyses les plus prescrites
- ...mais important d'en connaître 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  
 $\mu\text{mol/L}$ )** ?

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*

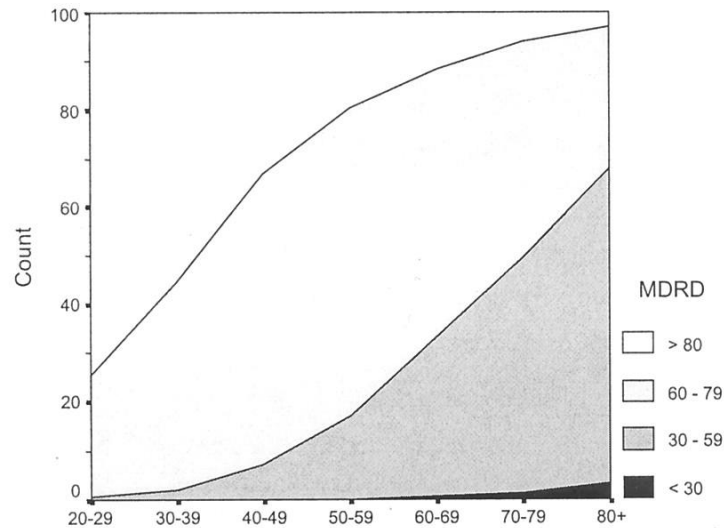
*Delanaye P, Ann Biol Clin (Paris), 2010, 68, 531*



# Mesure de la créatinine sérique

## Limitations analytiques

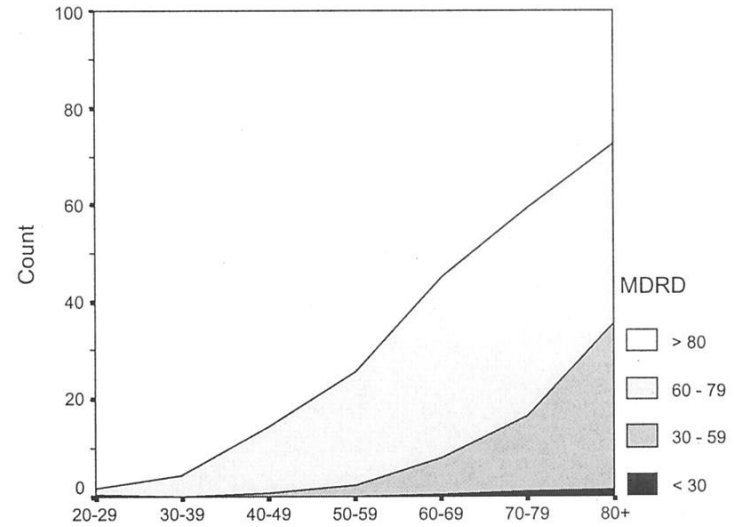
UNCALIBRATED



Age by decade

N	3037	2827	2138	1422	1670	1241	916	Total 13251
≥ 80	74.6%	55.2%	33.0%	19.5%	11.7%	6.1%	2.8%	41.8%
60-79	24.8%	42.7%	59.7%	63.3%	54.9%	44.2%	29.4%	45.4%
30-59	0.6%	2.0%	7.2%	17.2%	32.7%	48.5%	64.6%	12.5%
< 30	<0.1%	<0.1%	<0.1%	<0.1%	0.7%	1.2%	3.2%	0.3%

CALIBRATED



Age by decade

N	3037	2827	2138	1422	1670	1241	916	Total 13251
≥ 80	98.3%	95.7%	85.7%	74.4%	55.1%	40.7%	27.5%	82.1%
60-79	1.5%	4.2%	13.5%	23.3%	36.9%	42.7%	37.0%	14.5%
30-59	0.2%	<0.1%	0.8%	2.4%	7.6%	15.7%	34.3%	3.2%
< 30	<0.1%	<0.1%	<0.1%	<0.1%	0.5%	0.9%	1.2%	0.2%

Coresh, J. et al. *J Am Soc Nephrol* 2002;13:2811-2816

# 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](http://www.elsevier.com/locate/clinchim)



## A multicentric evaluation of IDMS-traceable creatinine enzymatic assays

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

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<sup>b</sup> Nephrology–Dialysis–Transplantation, University of Liège, CHU Sart Tilman, Liège, Belgium

<sup>c</sup> Biochimie, CHU Bichat, APHP, Paris, France

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<sup>e</sup> Analytical Chemistry Laboratory, CIRM, University of Liège, Liège, Belgium

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<sup>g</sup> Biochimie, Hôpitaux de Lyon Sud, Lyon, France

<sup>h</sup> Biochimie, Hospices civils, Colmar, France

<sup>i</sup> Clinical Chemistry, University of Liège, CHU Sart Tilman, Liège, Belgium

<sup>j</sup> Physiologie Rénale, Hôpital Européen Georges Pompidou, APHP, Paris, France

# 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**

# 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 « entraînés »

50 to 70 % pour les autres

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

*KDIGO, Kidney Int, 2012, 3*

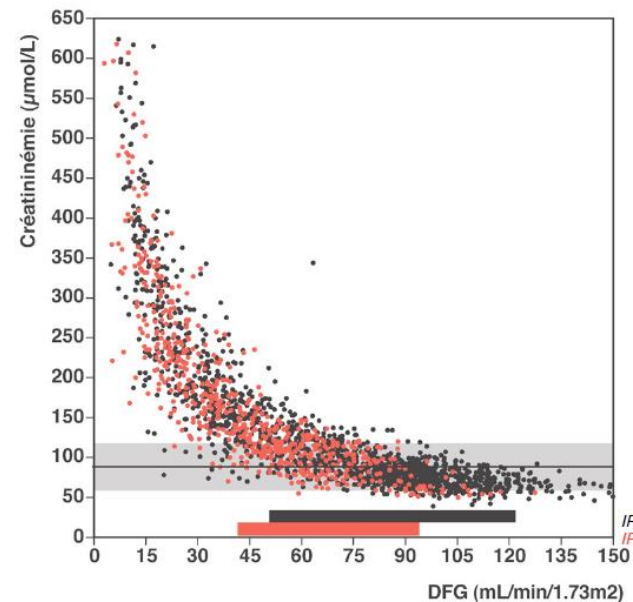
*Perrone RD, Clin Chem, 1992, 38, 1933*

*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 (?)



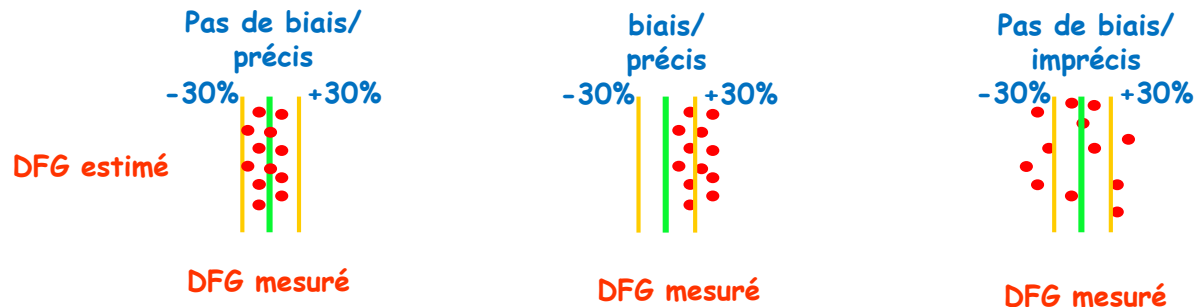


# Quelles équations?

- 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  $\pm 30\%$  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

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Cockcroft and Gault

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

*Cockcroft DW, Nephron, 1976, 16, p31*

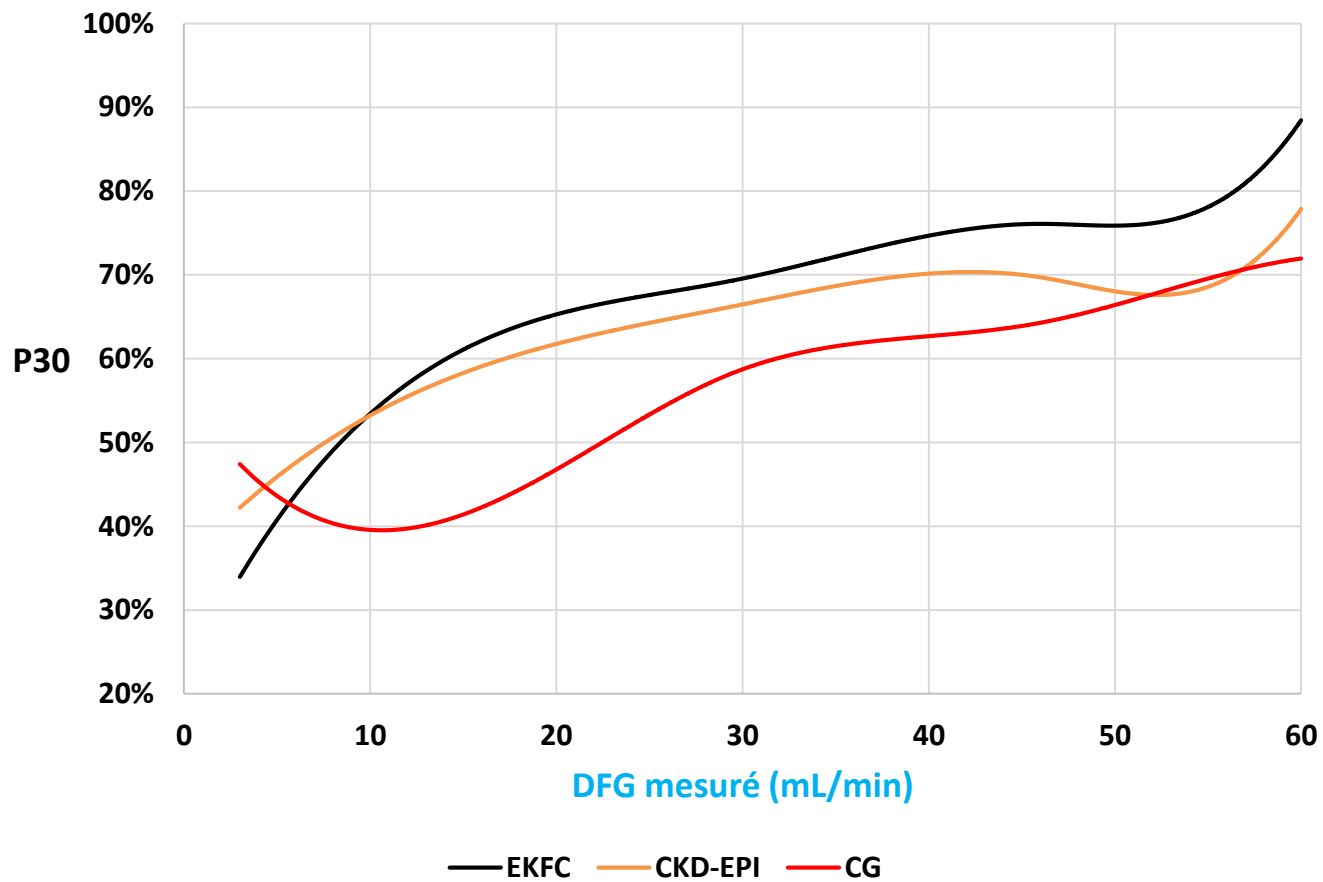
*Levey AS, Ann Intern Med, 1999, 130, p461*

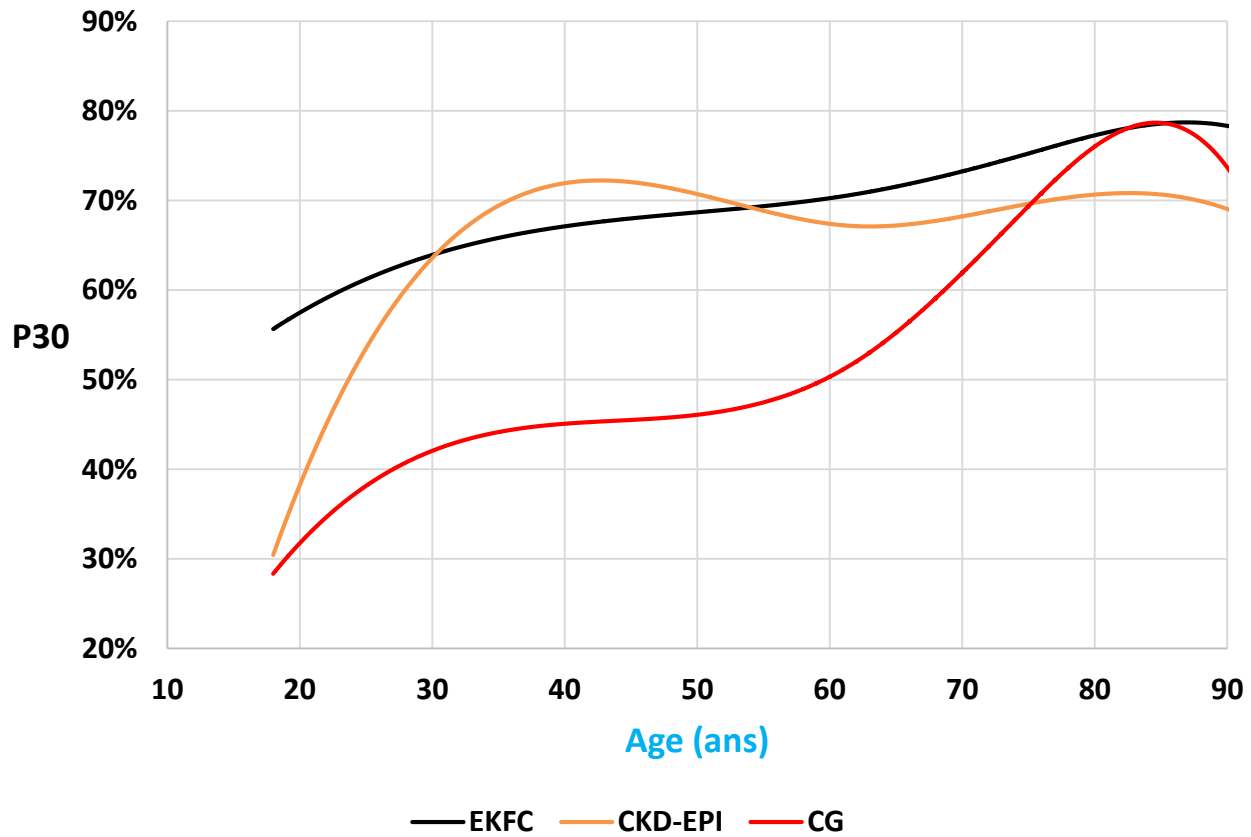
# Performance of creatinine-based equations to estimate glomerular filtration rate with a methodology adapted to the context of drug dosage adjustment

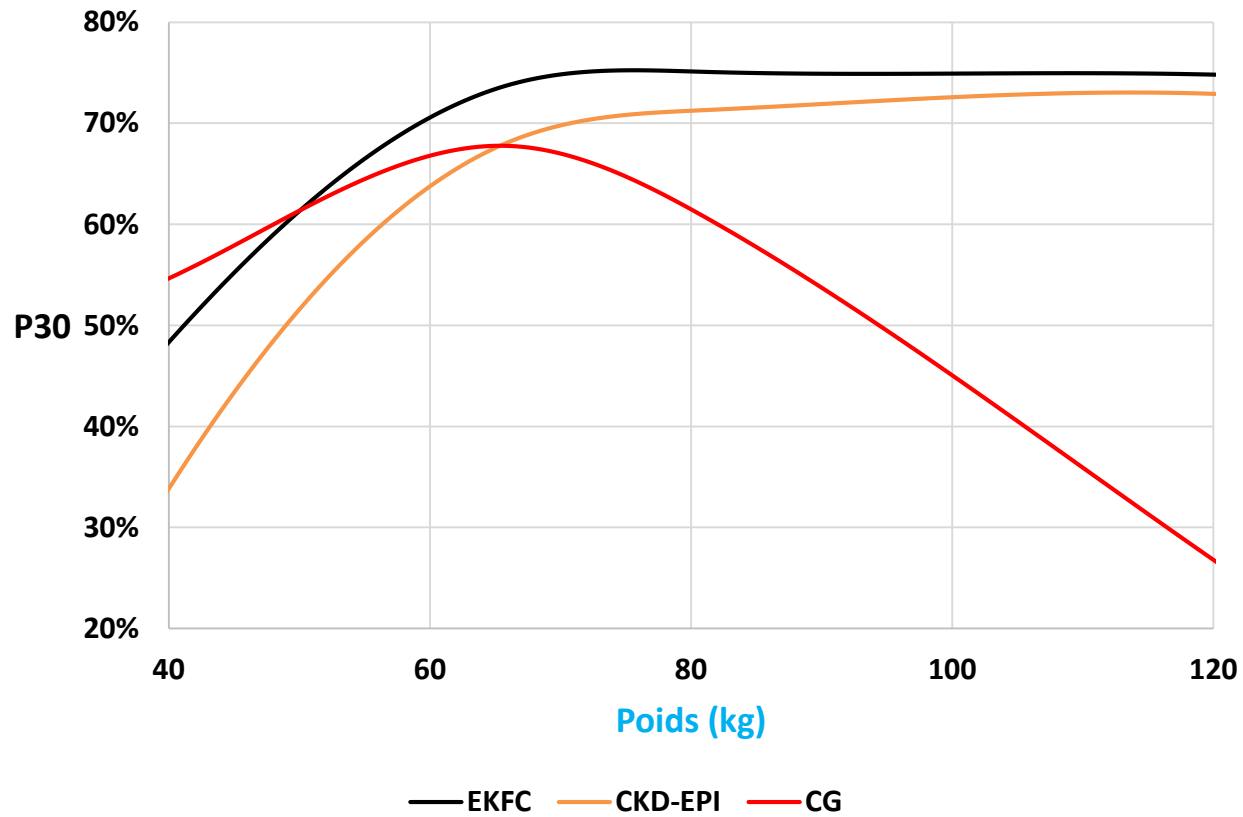
Pierre Delanaye<sup>1,2</sup>  | Jonas Björk<sup>3,4</sup> | Marie Courbebaisse<sup>5</sup> | Lionel Couzi<sup>6</sup> |  
Natalie Ebert<sup>7</sup> | Björn O. Eriksen<sup>8</sup> | R. Neil Dalton<sup>9</sup> | Laurence Dubourg<sup>10</sup> |  
Francois Gaillard<sup>11</sup> | Cyril Garrouste<sup>12</sup> | Anders Grubb<sup>13</sup> | Lola Jacquemont<sup>14</sup> |  
Magnus Hansson<sup>15</sup> | Nassim Kamar<sup>16</sup> | Edmund J. Lamb<sup>17</sup> |  
Christophe Legendre<sup>18</sup> | Karin Littmann<sup>19</sup> | Christophe Mariat<sup>20</sup> |  
Toralf Melsom<sup>8</sup> | Lionel Rostaing<sup>21</sup> | Andrew D. Rule<sup>22</sup> | Elke Schaeffner<sup>7</sup> |  
Per-Ola Sundin<sup>23</sup> | Ulla B. Berg<sup>24</sup> | Kajsa Åsling-Monemi<sup>24</sup> | Luciano Selistre<sup>25</sup> |  
Anna Åkesson<sup>3,4</sup> | Anders Larsson<sup>26</sup> | Arend Bökenkamp<sup>27</sup> | Hans Pottel<sup>28</sup> |  
Ulf Nyman<sup>29</sup>

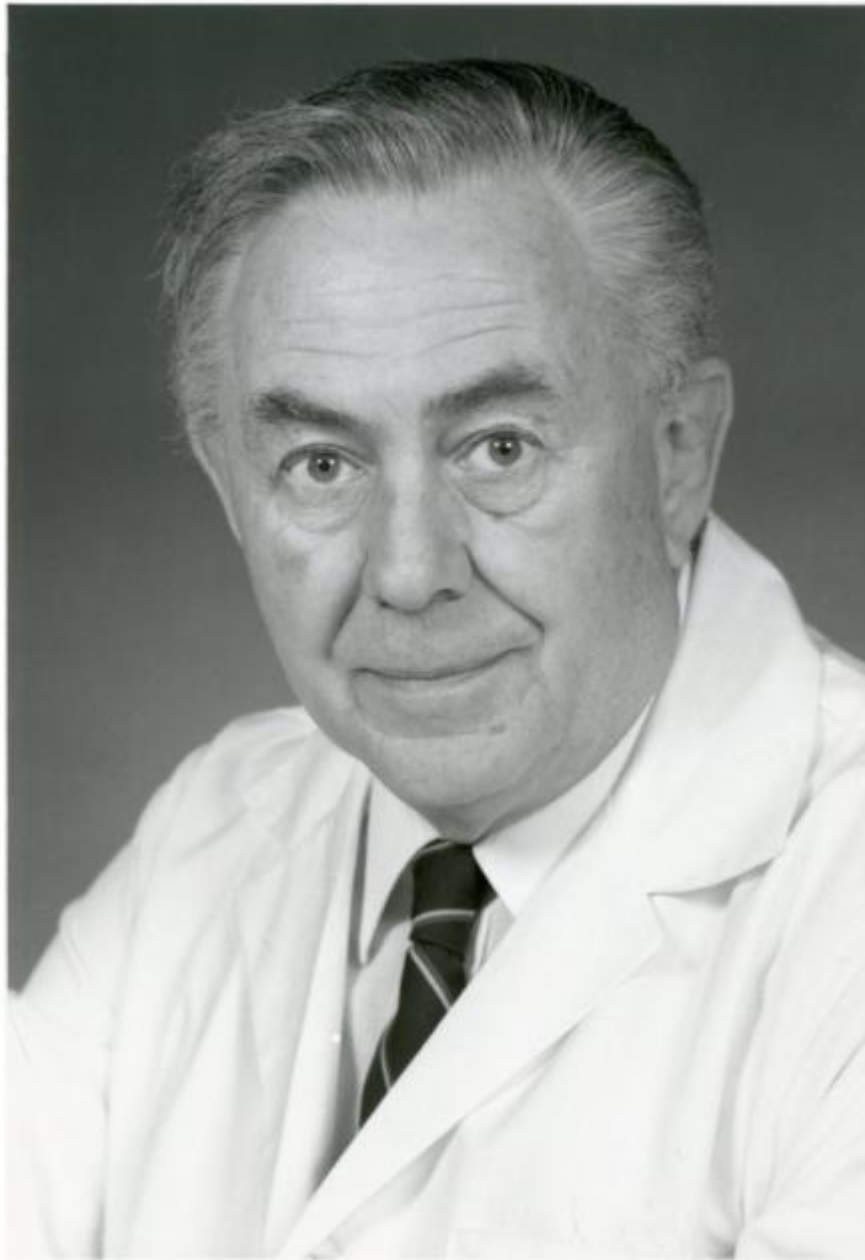
*Br J Clin Pharmacol.* 2022;88:2118–2127.

- 14,804 participants (adultes)
- Cockcroft, CKD-EPI et EKFC
- De-indexé
- Focus sur DFG < 60 mL/min (n=4328)









**Dr. Do**

, MD, FRCPC

Profe

) Medicine



# Equation CKD-EPI

## 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\*

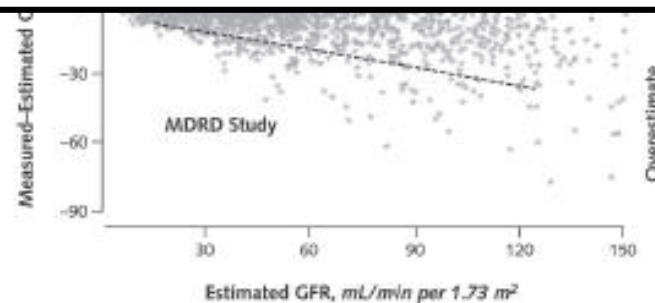
Race and Sex	Serum Creatinine Level, $\mu\text{mol/L}$ (mg/dL)	Equation
<b>Black</b>		
Female	$\leq 62$ ( $\leq 0.7$ )	$\text{GFR} = 166 \times (\text{Scr}/0.7)^{-0.329} \times (0.993)^{\text{Age}}$
	$> 62$ ( $> 0.7$ )	$\text{GFR} = 166 \times (\text{Scr}/0.7)^{-1.209} \times (0.993)^{\text{Age}}$
Male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

- CKD-EPI
- “Development dataset”: n=5504
- “Internal validation”: n=2750
- “External validation”: n=3896
- Créatinine calibrée
- DFG médian = 68 mL/min/1.73 m<sup>2</sup>

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 m <sup>2</sup>	Patients With Estimated GFR ≥60 mL/min per 1.73 m <sup>2</sup>
<b>Median difference (95% CI), mL/min per 1.73 m<sup>2</sup>†</b>			
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)
<b>Interquartile range for differences (95% CI), mL/min per 1.73 m<sup>2</sup>‡</b>			
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)
<b>P<sub>20</sub> (95% CI), %§</b>			
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)
<b>Root mean square error (95% CI)</b>			
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)





# 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*

# Two Novel Equations to Estimate Kidney Function in Persons Aged 70 Years or Older

Elke S. Schaeffner, MD, MS\*; Natalie Ebert, MD, MPH\*; Pierre Delanaye, MD, PhD; Ulrich Frei, MD; Jens Gaedeke, MD; Olga Jakob; Martin K. Kuhlmann, MD; Mirjam Schuchardt, PhD; Markus Tölle, MD; Reinhard Ziebig, PhD; Markus van der Giet, MD; and Peter Martus, PhD

## BIS1:

$$3736 \times \text{creatinine}^{-0.87} \times \text{age}^{-0.95} \times 0.82 \text{ (si femme)}$$

- n=610, iohexol, créatinine enzymatique calibrée
- DFG moyen = 52 mL/min/1,73 m<sup>2</sup>

Ulf Nyman\*, Anders Grubb, Anders Larsson, Lars-Olof Hansson, Mats Flodin, Gunnar Nordin, Veronica Lindström and Jonas Björk

# The revised Lund-Malmö GFR estimating equation outperforms MDRD and CKD-EPI across GFR, age and BMI intervals in a large Swedish population

Clin Chem Lab Med 2014, 52(6), 815-824

*Revised Lund-Malmö Study equation (LM Revised) [34]*

$$e^{X-0.0158 \times \text{Age} + 0.438 \times \ln(\text{Age})}$$

Female pCr < 150  $\mu\text{mol/L}$ :  $X = 2.50 + 0.0121 \times (150 - \text{pCr})$

Female pCr  $\geq$  150  $\mu\text{mol/L}$ :  $X = 2.50 - 0.926 \times \ln(\text{pCr}/150)$

Male pCr < 180  $\mu\text{mol/L}$ :  $X = 2.56 + 0.00968 \times (180 - \text{pCr})$

Male pCr  $\geq$  180  $\mu\text{mol/L}$ :  $X = 2.56 - 0.926 \times \ln(\text{pCr}/180)$

- Lund-Malmö
- n=3495 (chez 2847 sujets), iohexol, créatinine calibrée
- DFG moyen = 60 mL/min/1,73 m<sup>2</sup>

## 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	$107.3 \times (\text{SCr}/\text{Q})^{-0.322}$
	$\geq 1$	$107.3 \times (\text{SCr}/\text{Q})^{-1.132}$
>40 y	<1	$107.3 \times (\text{SCr}/\text{Q})^{-0.322} \times 0.990^{(\text{Age} - 40)}$
	$\geq 1$	$107.3 \times (\text{SCr}/\text{Q})^{-1.132} \times 0.990^{(\text{Age} - 40)}$

#### Q Values

For ages 2–25 y:

Males:

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

Females:

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

For ages >25 y:

Males:

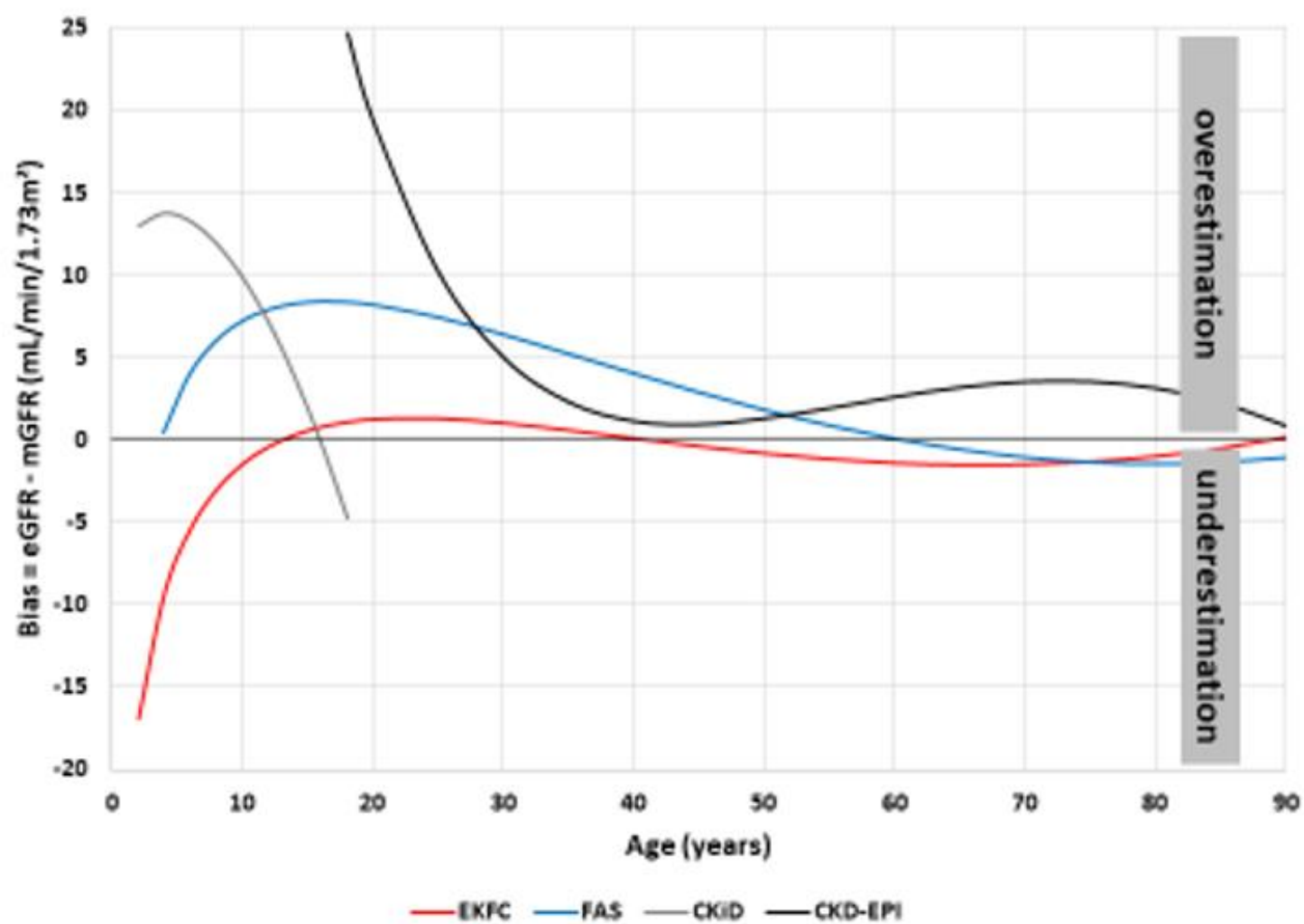
$$\text{Q} = 80 \mu\text{mol/L} (0.90 \text{ mg/dL})$$

Females:

$$\text{Q} = 62 \mu\text{mol/L} (0.70 \text{ mg/dL})$$

SCr and Q in  $\mu\text{mol/L}$  (to convert to mg/dL, divide by 88.4)

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



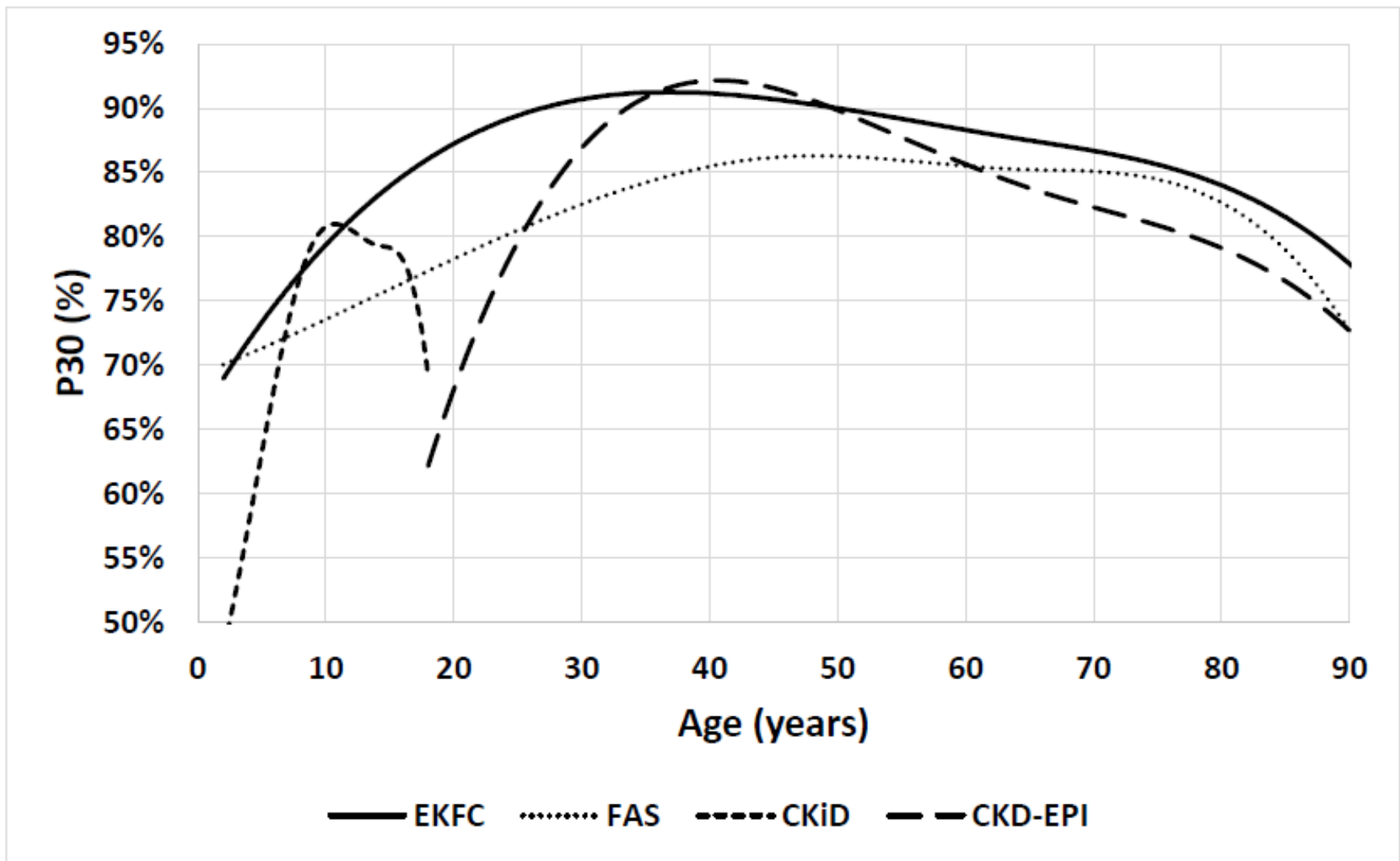


Figure S8. P30-accuracy against age for the EKFC, FAS, CKiD and CKD-EPI equation in the external validation dataset. P30 (%) was graphically presented across the age spectrum using cubic splines with two free knots and using 3<sup>rd</sup> degree polynomials.

# Avantages de EKFC

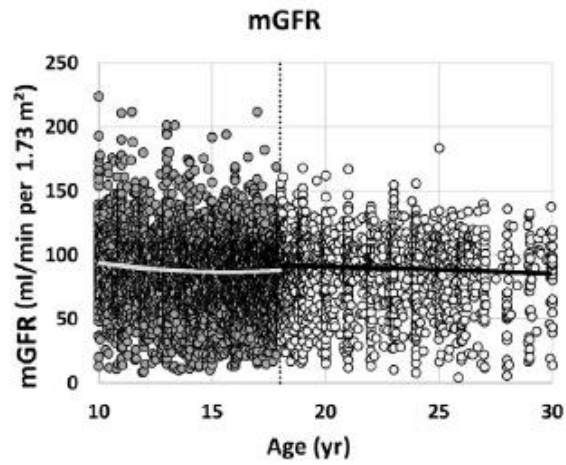
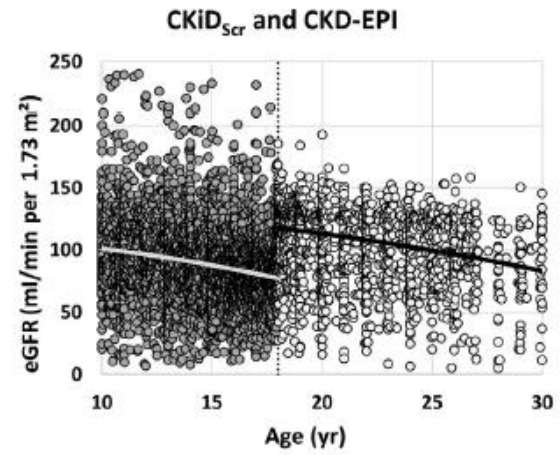
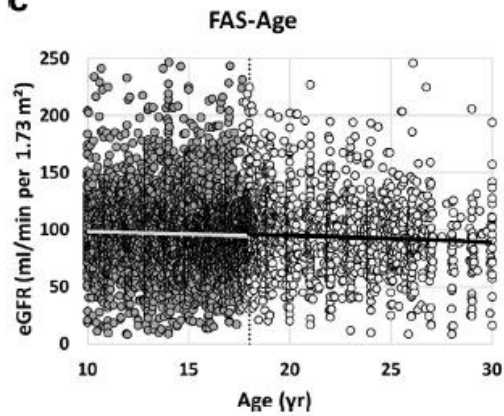
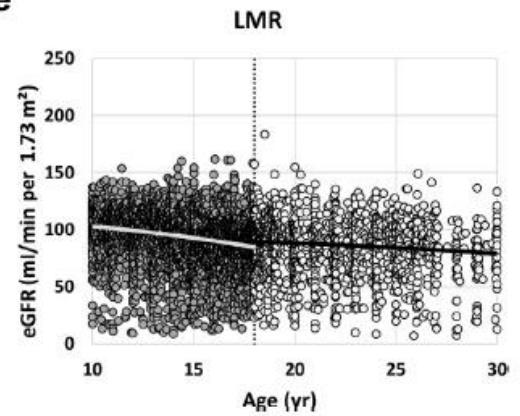
- Meilleures performances (pas plus cher)
- Plus « physiologique »: correction au niveau de la créatinine (sexe, « race »), âge mieux conceptualisé, « Q » spécifique pour des populations spécifiques
- Valide à tout âge (et pas de « jump » à 18 ans)
- Enfant: pas besoin de la taille
- Même formule («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

## Estimating glomerular filtration rate at the transition from pediatric to adult care

Hans Pottel<sup>1,13</sup>, Jonas Björk<sup>2,3,13</sup>, Arend Bökenkamp<sup>4,13</sup>, Ulla Berg<sup>5</sup>, Kajsa Åsling-Monemi<sup>5</sup>, Luciano Selistre<sup>6</sup>, Laurence Dubourg<sup>7,13</sup>, Magnus Hansson<sup>8</sup>, Karin Littmann<sup>8</sup>, Ian Jones<sup>9</sup>, Per Sjöström<sup>9</sup>, Ulf Nyman<sup>10,12,13</sup> and Pierre Delanaye<sup>11,12,13</sup>

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- 5764 enfants, adolescents et jeunes adultes
- Résultats en «médiane»

**a****b****c****e**

# Débat sur le facteur racial aux Etats-Unis



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)‡			
<i>milliliters per minute per 1.73 square meters</i>			
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)

# Facteur ethnique CKD/EPI - MDRD

## 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

# NON

Hindawi  
International Journal of Nephrology  
Volume 2020, Article ID 2141035, 9 pages  
<https://doi.org/10.1155/2020/2141035>



#### Research Article

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

Amanda D. Rocha,<sup>1</sup> Suzane Garcia,<sup>2</sup> Andressa B. Santos,<sup>3</sup> José C. C. Eduardo,<sup>3</sup> Claudio T. Mesquita,<sup>2,4</sup> Jocemir R. Lugon<sup>5,1,3</sup> and Jorge P. Strogoff-de-Matos<sup>6,1,3</sup>

<sup>1</sup>Postgraduation Program in Medical Sciences, Fluminense Federal University (UFF), Niterói, Rio de Janeiro, Brazil  
<sup>2</sup>Postgraduation Program in Cardiovascular Sciences, Fluminense Federal University (UFF), Niterói, Rio de Janeiro, Brazil  
<sup>3</sup>Nephrology Division, Department of Medicine, Fluminense Federal University (UFF), Niterói, Rio de Janeiro, Brazil  
<sup>4</sup>Nuclear Medicine Division, EBESERH/Hospital Antonio Pedro, Fluminense Federal University (UFF), Niterói, Rio de Janeiro, Brazil

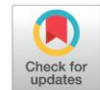
#### RESEARCH ARTICLE

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

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

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

\* [justinebuk@yahoo.fr](mailto:justinebuk@yahoo.fr)



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

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












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

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

- N=494
- Iohexol
- Créatinine calibrée



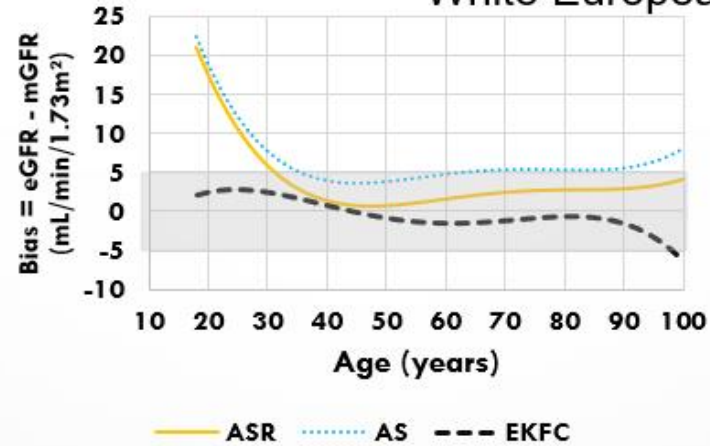
# Performance of creatinine-based equations to estimate glomerular filtration rate in White and Black populations in Europe, Brazil and Africa

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

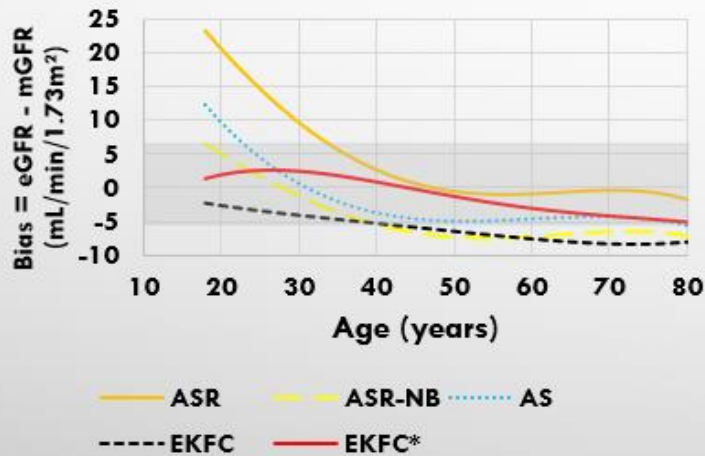
# Méthodes

- 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)

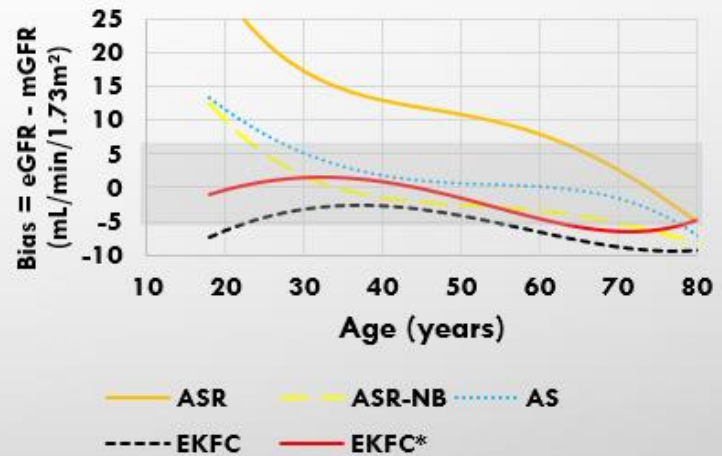
### White Europeans (n=17,321)

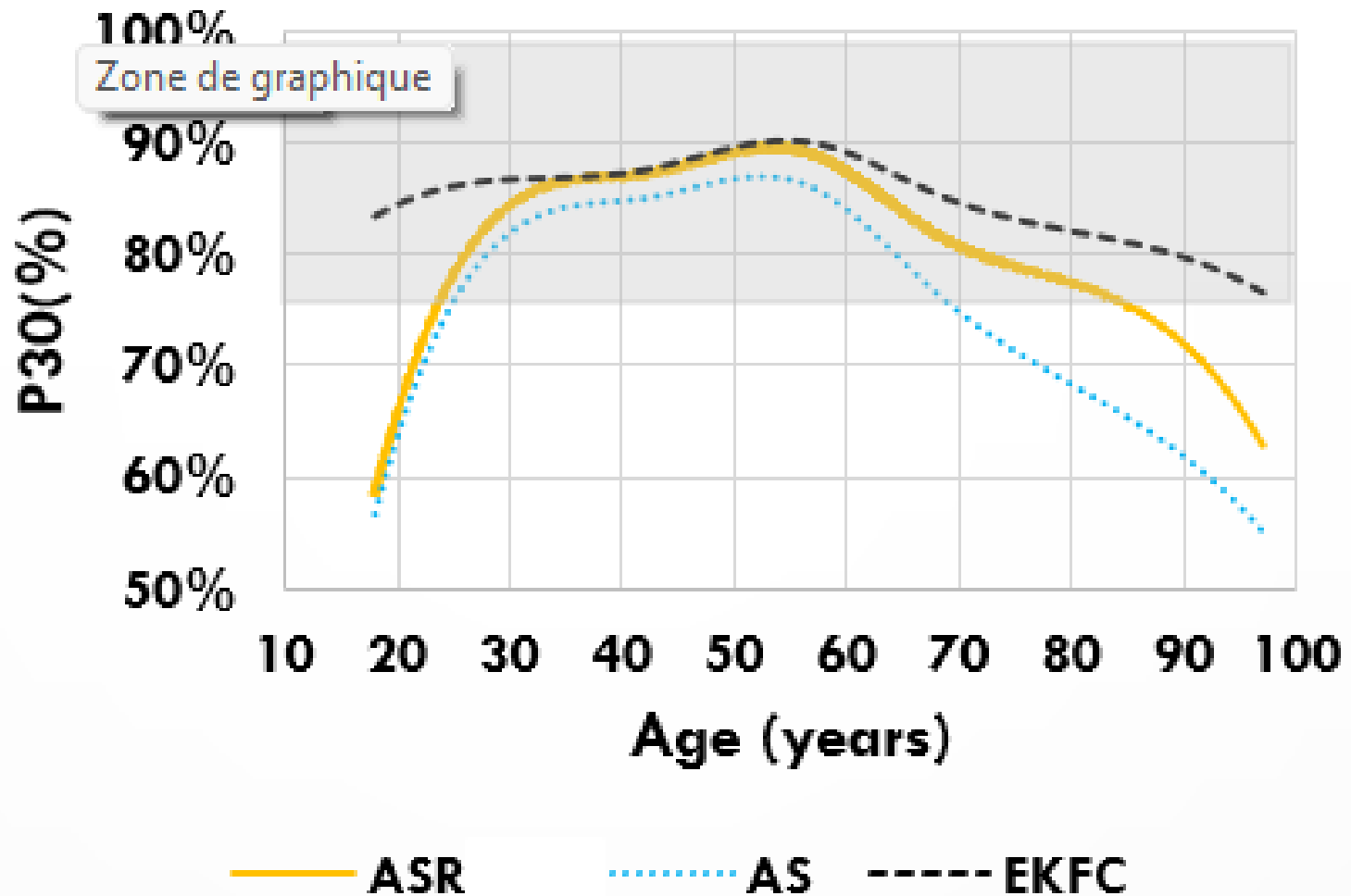


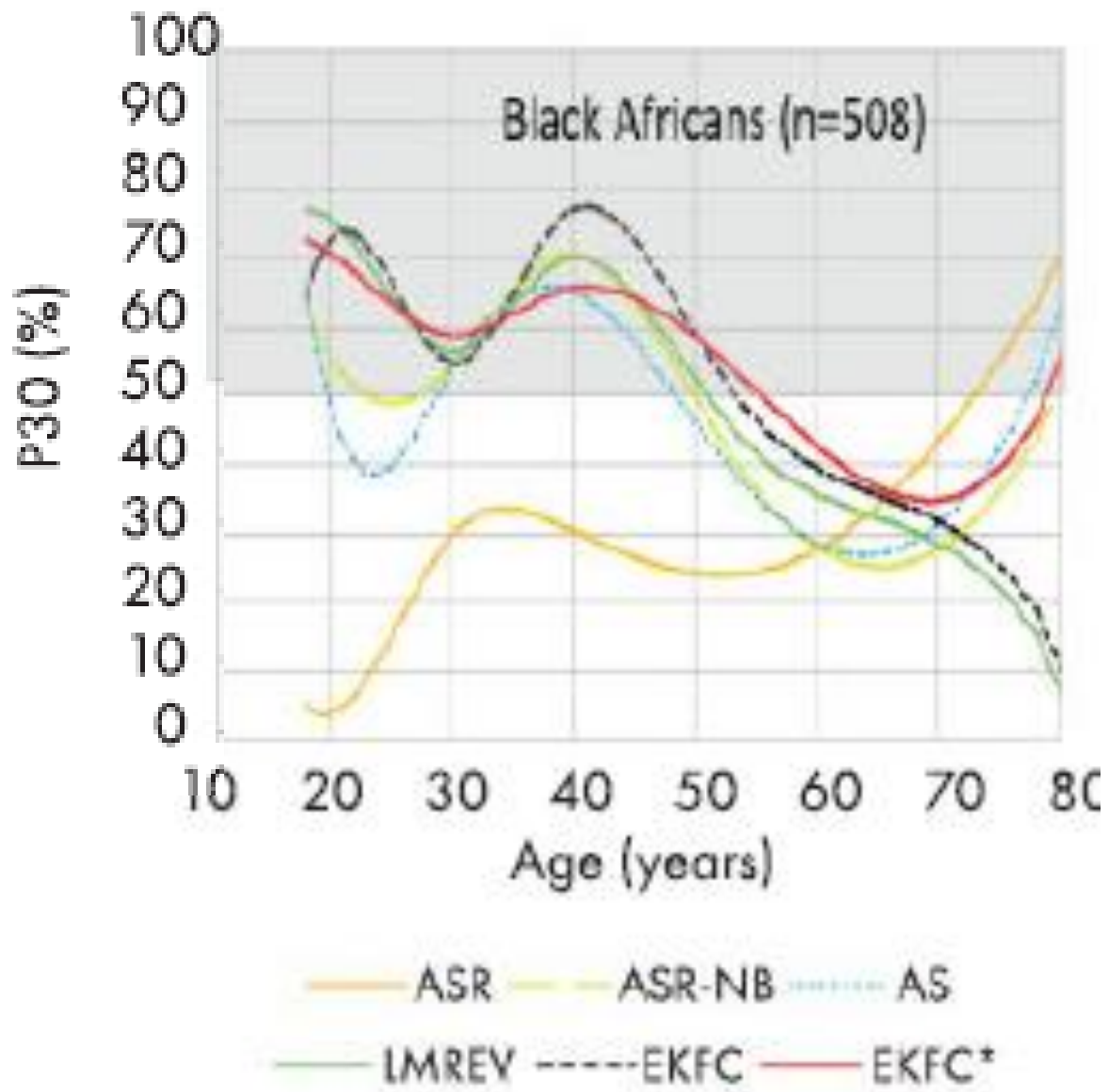
### Black Europeans (n=964)



### Black Africans (n=508)









# Americentrism in estimation of glomerular filtration rate equations



Pierre Delanaye<sup>1,2</sup>,  
Hans Pottel<sup>3</sup> and  
Richard J. Glassock<sup>4</sup>

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*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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## THE WORLD ACCORDING TO AMERICANS



## 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?

Ron T. Gansevoort <sup>1</sup>, Hans-Joachim Anders<sup>2</sup>, Mario Cozzolino<sup>3</sup>, Danilo Fliser<sup>4</sup>, Denis Fouque<sup>5</sup>, Alberto Ortiz<sup>6,7</sup>, Maria José Soler<sup>8</sup> and Christoph Wanner<sup>9</sup>

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# 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\*

**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 <sup>2</sup>	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 <sup>2</sup> of body-surface area	68±39	70±41	0.13
Measured GFR — no. (%)			
<15 ml/min/1.73 m <sup>2</sup>	160 (3)	51 (5)	<0.001
15–29 ml/min/1.73 m <sup>2</sup>	785 (15)	166 (15)	
30–59 ml/min/1.73 m <sup>2</sup>	1765 (33)	316 (28)	
60–89 ml/min/1.73 m <sup>2</sup>	1105 (21)	215 (19)	
90–119 ml/min/1.73 m <sup>2</sup>	862 (16)	199 (18)	
>120 ml/min/1.73 m <sup>2</sup>	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		$144 \times (\text{Scr}/0.7)^{-0.329} \times 0.993^{\text{Age}} [\times 1.159 \text{ if black}]$
Female	>0.7		$144 \times (\text{Scr}/0.7)^{-1.209} \times 0.993^{\text{Age}} [\times 1.159 \text{ if black}]$
Male	≤0.9		$141 \times (\text{Scr}/0.9)^{-0.411} \times 0.993^{\text{Age}} [\times 1.159 \text{ if black}]$
Male	>0.9		$141 \times (\text{Scr}/0.9)^{-1.209} \times 0.993^{\text{Age}} [\times 1.159 \text{ if black}]$
CKD-EPI cystatin C equation§			
Female or male		≤0.8	$133 \times (\text{Scys}/0.8)^{-0.499} \times 0.996^{\text{Age}} [\times 0.932 \text{ if female}]$
Female or male		>0.8	$133 \times (\text{Scys}/0.8)^{-1.328} \times 0.996^{\text{Age}} [\times 0.932 \text{ if female}]$
CKD-EPI creatinine–cystatin C equation¶			
Female	≤0.7	≤0.8	$130 \times (\text{Scr}/0.7)^{-0.248} \times (\text{Scys}/0.8)^{-0.375} \times 0.995^{\text{Age}} [\times 1.08 \text{ if black}]$
		>0.8	$130 \times (\text{Scr}/0.7)^{-0.248} \times (\text{Scys}/0.8)^{-0.711} \times 0.995^{\text{Age}} [\times 1.08 \text{ if black}]$
Female	>0.7	≤0.8	$130 \times (\text{Scr}/0.7)^{-0.601} \times (\text{Scys}/0.8)^{-0.375} \times 0.995^{\text{Age}} [\times 1.08 \text{ if black}]$
		>0.8	$130 \times (\text{Scr}/0.7)^{-0.601} \times (\text{Scys}/0.8)^{-0.711} \times 0.995^{\text{Age}} [\times 1.08 \text{ if black}]$
Male	≤0.9	≤0.8	$135 \times (\text{Scr}/0.9)^{-0.207} \times (\text{Scys}/0.8)^{-0.375} \times 0.995^{\text{Age}} [\times 1.08 \text{ if black}]$
		>0.8	$135 \times (\text{Scr}/0.9)^{-0.207} \times (\text{Scys}/0.8)^{-0.711} \times 0.995^{\text{Age}} [\times 1.08 \text{ if black}]$
Male	>0.9	≤0.8	$135 \times (\text{Scr}/0.9)^{-0.601} \times (\text{Scys}/0.8)^{-0.375} \times 0.995^{\text{Age}} [\times 1.08 \text{ if black}]$
		>0.8	$135 \times (\text{Scr}/0.9)^{-0.601} \times (\text{Scys}/0.8)^{-0.711} \times 0.995^{\text{Age}} [\times 1.08 \text{ if black}]$

**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
	<i>ml/min/1.73 m<sup>2</sup> of body-surface area</i>			
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 <sub>30</sub>				
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 <sub>20</sub>				
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)

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.**

# 1<sup>er</sup> étape: cystatine C et âge

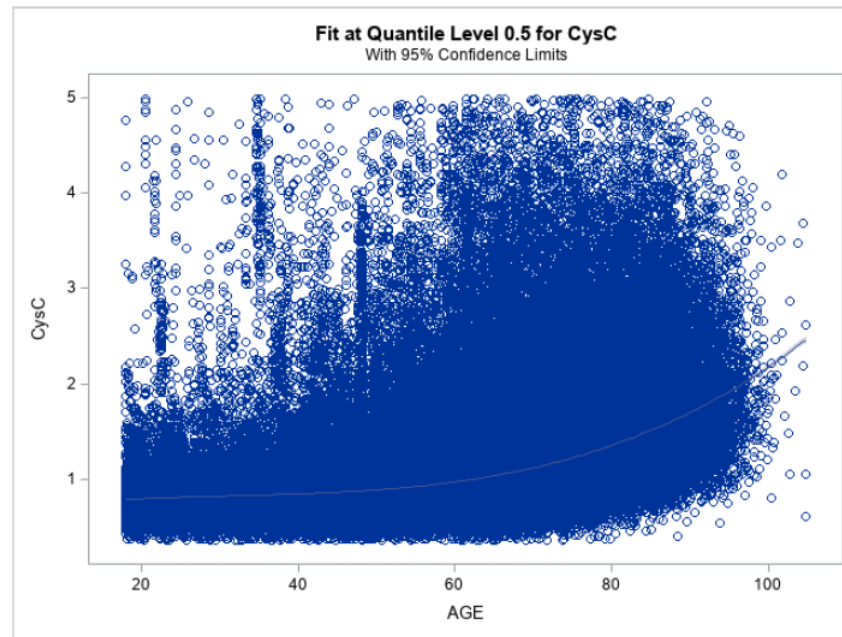
Figure S3. Cystatin C versus age and the median quantile line for the 227,643 included subjects.

Données de labo de Suède

N=227,643

♀ 95,469

♂ 132,174



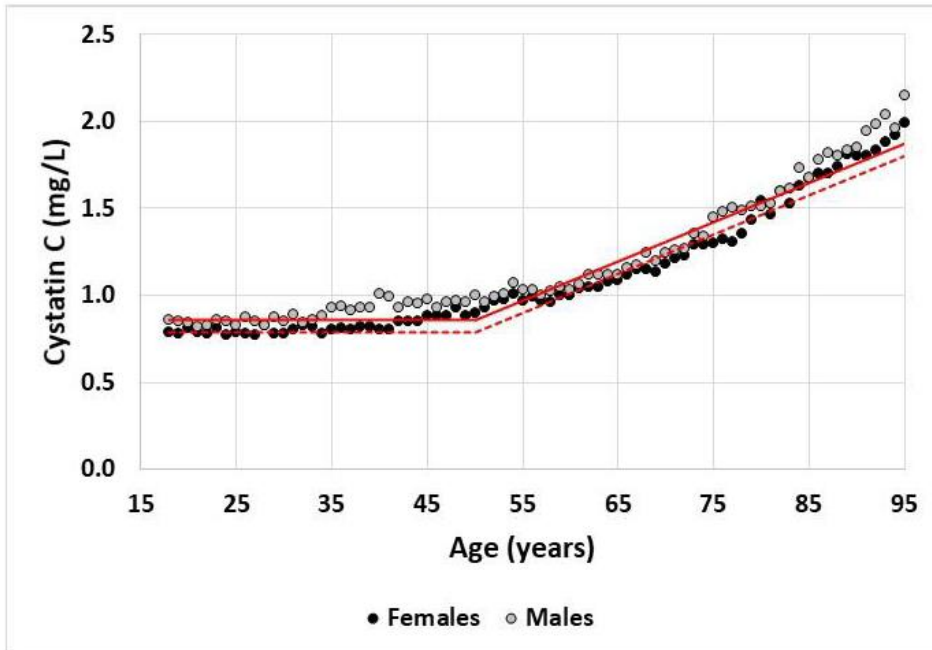
♀  $Q' = 0.79 \text{ mg/L}$  jusqu'à 50 ans,  
 $Q' = 0.79 + 0.005 \times (\text{Age} - 50)$

♂  $Q' = 0.86 \text{ mg/L}$  jusqu'à 50 ans,  
 $Q' = 0.86 + 0.005 \times (\text{Age} - 50)$



# 2<sup>ème</sup> 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.



$$Q' = 0.83 \text{ mg/L jusqu'à 50 ans}$$
$$Q' = 0.83 + 0.005 \times (\text{Age} - 50)$$

# 3<sup>ème</sup> 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  $\pm$  SD)

Ethnicity/Sex	N	Age (years)	BMI (kg/m <sup>2</sup> )	mGFR (mL/min/1.73m <sup>2</sup> )	SCr (mg/dL)	CysC (mg/L)
White Men	1296 (57%)	53.0 $\pm$ 14.6	26.2 $\pm$ 4.9	61.8 $\pm$ 26.0	1.52 $\pm$ 0.73	1.52 $\pm$ 0.68
Black Men	436 (63%)	50.7 $\pm$ 13.1	26.3 $\pm$ 4.5	62.0 $\pm$ 22.1	1.73 $\pm$ 0.81	1.41 $\pm$ 0.61
White Women	966 (43%)	52.5 $\pm$ 15.2	25.8 $\pm$ 6.2	62.8 $\pm$ 26.8	1.16 $\pm$ 0.61	1.38 $\pm$ 0.73
Black Women	261 (37%)	51.9 $\pm$ 15.2	27.4 $\pm$ 5.8	59.1 $\pm$ 25.6	1.40 $\pm$ 0.79	1.46 $\pm$ 0.76

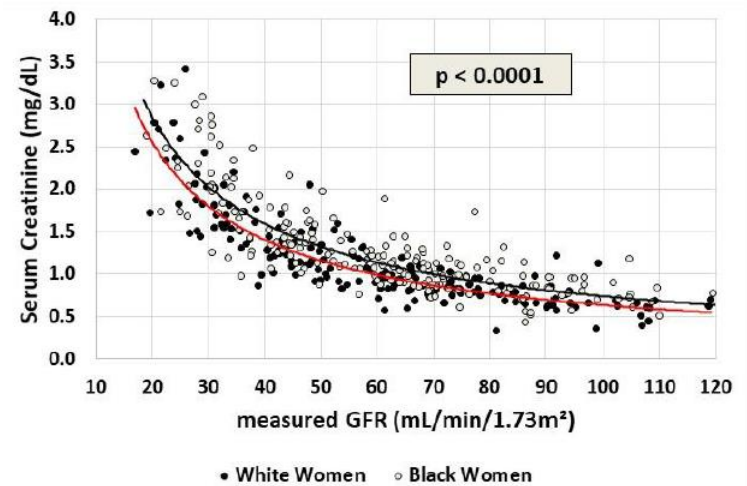
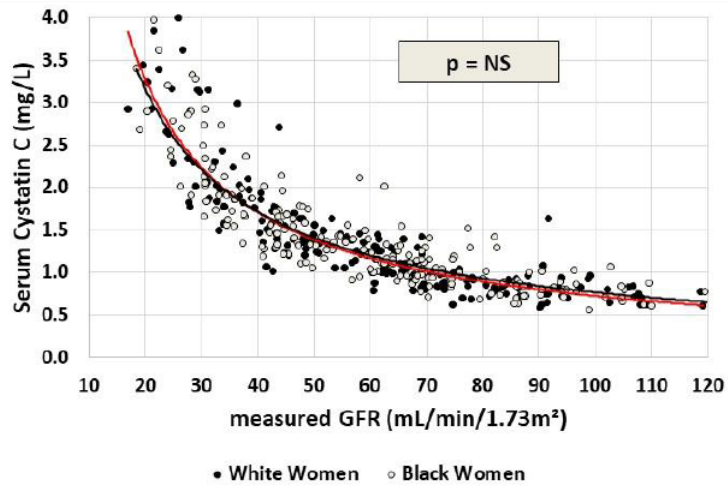
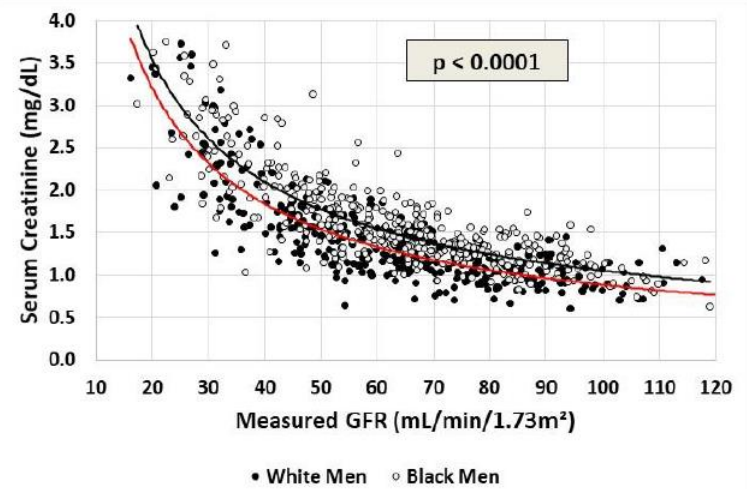
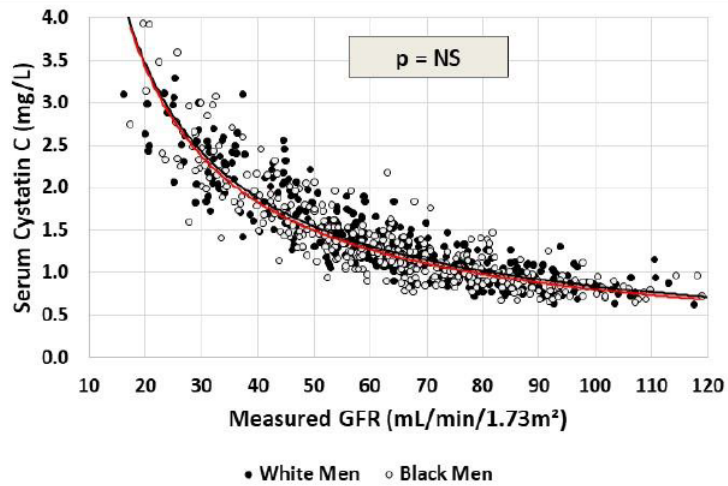
# 3<sup>ème</sup> étape: Cystatin C et “race”

Analyse matchée 1:1

- Pour le sexe
- IMC ( $\pm 2,5$  kg/m<sup>2</sup>)
- DFG mesuré ( $\pm 3$  mL/min/1.73m<sup>2</sup>)
- âge ( $\pm 3$  ans)

**Table S4.** Demographic and renal characteristics of the matched White and Black subjects (mean  $\pm$  SD)

Sex	N	Age (years)	BMI (kg/m <sup>2</sup> )	mGFR (mL/min/1.73m <sup>2</sup> )	SCr (mg/dL)	CysC (mg/L)
White Men	377	51.1 $\pm$ 12.2	25.7 $\pm$ 3.4	63.8 $\pm$ 21.0	1.43 $\pm$ 0.62	1.41 $\pm$ 0.56
Black Men	377	50.8 $\pm$ 12.3	25.8 $\pm$ 3.5	63.6 $\pm$ 21.0	1.65 $\pm$ 0.64	1.37 $\pm$ 0.59
White Women	200	53.4 $\pm$ 11.9	26.1 $\pm$ 4.6	59.7 $\pm$ 23.2	1.16 $\pm$ 0.53	1.40 $\pm$ 0.69
Black Women	200	53.3 $\pm$ 11.9	26.2 $\pm$ 4.6	59.8 $\pm$ 23.1	1.33 $\pm$ 0.61	1.41 $\pm$ 0.64



# 4<sup>ème</sup> étape:

## Validation de la nouvelle équation

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

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

**Table S1:** Patient and method characteristics of the different validation cohorts

Name	Country	Cohort	n	Method mGFR	Age median [IQR]	mGFR median [IQR]	Crea/Q median [IQR]	CysC/Q' median [IQR]	% men
<b>EKFC (White)</b>			<b>7,727</b>		<b>62.0</b> [53.0 – 73.9]	<b>70.8</b> [43.4 – 90.6]	<b>1.13</b> [0.94 – 1.65]	<b>1.28</b> [0.97 – 2.02]	<b>53.4</b>
Berlin	Germany	BIS-study [1]	657	PC / iohexol	77.0 [73.6 – 82.5]	57.9 [43.4 – 70.0]	1.18 [1.00 – 1.52]	1.33 [1.12 – 1.72]	58.3
Kent#	UK	GFR in old adults study [2]	394	PC / <sup>51</sup> Cr-EDTA	80.0 [77.0 – 83.0]	53.4 [35.3 – 67.8]	1.34 [1.08 – 2.02]	1.44 [1.19 – 2.26]	48.0
Lund#	Sweden	CAPA-study [3]	2,847	PC / iohexol	63.0 [50.0 – 72.0]	56.4 [31.2 – 81.6]	1.34 [1.01 – 2.15]	1.75 [1.27 – 2.72]	51.5
Lyon	France	Referrals*	914	PC/RC inulin/iohexol	51.6 [37.9 – 62.5]	79.6 [55.6 – 99.0]	1.10 [0.92 – 1.45]	1.13 [0.94 – 1.59]	54.9
Saint-Etienne	France	HIV-study [4]	203	RC / inulin	48.0 [42.0 – 56.0]	95.9 [80.3 – 107.7]	0.97 [0.87 – 1.09]	1.04 [0.92 – 1.16]	81.8
Stockholm	Sweden	Referrals*	577	PC / iohexol	75.0 [72.0 – 79.0]	42.2 [24.7 – 62.9]	1.65 [1.18 – 2.44]	1.99 [1.43 – 3.00]	52.5
Tromsö	Norway	RENIS-T6 study [5]	1,627	PC / iohexol	58.7 [54.7 – 61.4]	91.5 [82.9 – 101.2]	0.94 [0.85 – 1.04]	0.87 [0.79 – 0.97]	49.2
Örebro	Sweden	Referrals*	508	PC / iohexol	58.1 [43.2 – 68.4]	71.5 [41.5 – 93.0]	1.31 [1.02 – 1.74]	1.29 [0.98 – 2.04]	61.8
<b>USA (White)#</b>	Rochester, Minnesota	GENOA / ECAC study [6]	<b>1,093</b>	<b>RC / iothalamate</b>	<b>66.1</b> [59.1 – 71.2]	<b>80.0</b> [66.0 – 93.0]	<b>1.04</b> [0.92 – 1.17]	<b>0.96</b> [0.84 – 1.09]	<b>43.4</b>
<b>Africa (Black)#</b>			<b>508</b>		<b>39.0</b> [30.0 – 53.0]	<b>86.8</b> [71.7 – 99.2]	<b>1.16</b> [1.02 – 1.41]	<b>1.07</b> [0.95 – 1.28]	<b>53.3</b>
	Côte d'Ivoire	eGFR-study [7]	285	PC / iohexol	34.0 [27.0 – 43.0]	89.1 [73.9 – 100.8]	1.18 [1.04 – 1.48]	1.05 [0.93 – 1.32]	57.9
	Congo	eGFR-study [8]	223	PC / iohexol	49.0 [37.5 – 60.0]	84.4 [65.2 – 97.3]	1.13 [1.01 – 1.35]	1.13 [0.99 – 1.22]	47.5
<b>Paris (White and Black)#</b>			<b>3,504</b>		<b>53.4</b> [42.0 – 63.0]	<b>63.2</b> [44.3 – 84.5]	<b>1.42</b> [1.12 – 1.90]	<b>1.48</b> [1.11 – 2.07]	<b>57.4</b>
	Paris White	Referrals*	2,646	PC / <sup>51</sup> Cr EDTA	54.2 [42.3 – 64.0]	62.7 [43.8 – 85.3]	1.42 [1.09 – 1.90]	1.49 [1.11 – 2.11]	56.1
	Paris Black	Referrals*	858	PC / <sup>51</sup> Cr EDTA	51.2 [41.0 – 60.4]	64.3 [45.9 – 81.7]	1.46 [1.19 – 1.94]	1.45 [1.12 – 1.96]	61.3

mGFR= measured glomerular filtration rate, IQR= interquartile range, PC= plasma clearance (only blood samples are required), RC= renal clearance (both blood and urine samples are required). Crea/Q = scaled creatinine, CysC/Q' = scaled cystatin C (both scaled markers equal '1' for the average healthy subject); Referrals\*: subjects referred for measured GFR; # = Cohorts are true "external" validation cohorts

# Comparateur = équations CKD-EPI

- = 2009 and **2021**  
= CKD-EPI équation cystatine C 2012  
= CKD-EPI equation combinée

Q creatinine

EKFC	Q female/male
European cohort White	0.70/0.90
European cohort Black	0.74/1.02
African cohort	0.72/0.96

**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 eGFR <sub>cr</sub> (ASR)	CKD-EPI eGFR <sub>cr</sub> (AS)	EKFC eGFR <sub>cr</sub>
<b>EKFC cohort, 7727 White patients</b>			
Median bias (95% CI) — ml/min/1.73 m <sup>2</sup> †	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 m <sup>2</sup> ‡	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 m <sup>2</sup> §	14.8 (14.4 to 15.2)	16.3 (15.9 to 16.6)	13.1 (12.8 to 13.4)
P <sub>30</sub> — % (95% CI)¶	40.3 (39.2 to 41.4)	34.7 (33.6 to 35.8)	43.3 (42.2 to 44.4)
P <sub>30</sub> — % (95% CI)¶	81.6 (80.8 to 82.5)	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 eGFR <sub>cys</sub>	EKFC eGFR <sub>cys</sub> without Sex
<b>EKFC cohort, 7727 White patients</b>		
Median bias (95% CI) — ml/min/1.73 m <sup>2</sup> †	0.28 (–0.02 to 0.64)	0.00 (–0.37 to 0.27)
IQR of estimated GFR– measured GFR— ml/min/1.73 m <sup>2</sup> ‡	19.1 (–7.9 to 11.2)	14.4 (–7.9 to 6.5)
Root-mean-square error (95% CI) — ml/min/1.73 m <sup>2</sup> §	15.8 (15.5 to 16.1)	13.5 (12.9 to 14.1)
P <sub>30</sub> — % (95% CI)¶	32.0 (31.0 to 33.0)	41.7 (40.6 to 42.8)
P <sub>30</sub> — % (95% CI)‖	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 eGFR <sub>cr</sub> (ASR)	CKD-EPI eGFR <sub>cr</sub> (AS)	EKFC eGFR <sub>cr</sub>	CKD-EPI eGFR <sub>cys</sub>	EKFC eGFR <sub>cys</sub> without Sex
<b>EKFC cohort, 7727 White patients</b>					
Median bias (95% CI) — ml/min/1.73 m <sup>2</sup> †	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 m <sup>2</sup> ‡	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 m <sup>2</sup> §	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 <sub>30</sub> — % (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 <sub>30</sub> — % (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		
	CKD-EPI eGFR <sub>cr</sub> (ASR)	CKD-EPI eGFR <sub>cr</sub> (AS)	EKFC eGFR <sub>cr</sub>
<b>Paris cohort, 2646 White patients</b>			
Median bias (95% CI) — ml/min/1.73 m <sup>2</sup> †	0.30 (-0.21 to 0.78)	3.22 (2.69 to 3.86)	-1.24 (-1.75 to -0.74)
IQR of estimated GFR - measured GFR — ml/min/1.73 m <sup>2</sup> ‡	15.2 (-6.8 to 8.4)	15.9 (-4.1 to 11.7)	14.6 (-8.3 to 6.3)
Root-mean-square error (95% CI) — ml/min/1.73 m <sup>2</sup> §	14.2 (13.6 to 14.8)	14.8 (14.2 to 15.4)	13.6 (13.0 to 14.1)
P <sub>10</sub> — % (95% CI)¶	39.5 (37.7 to 41.4)	38.2 (36.4 to 40.1)	40.9 (39.0 to 42.7)
P <sub>90</sub> — % (95% CI)‖	84.5 (83.1 to 85.8)	82.5 (81.1 to 84.0)	86.5 (85.2 to 87.7)

**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 eGFR <sub>cys</sub>	EKFC eGFR <sub>cys</sub> without Sex
<b>Paris cohort, 2646 White patients</b>		
Median bias (95% CI) — ml/min/1.73 m <sup>2</sup> †	-2.85 (-3.35 to -2.21)	-0.79 (-1.26 to -0.31)
IQR of estimated GFR - measured GFR — ml/min/1.73 m <sup>2</sup> ‡	16.4 (-10.3 to 6.1)	15.3 (-8.5 to 6.7)
Root-mean-square error (95% CI) — ml/min/1.73 m <sup>2</sup> §	14.5 (13.9 to 15.1)	13.5 (12.9 to 14.1)
P <sub>10</sub> — % (95% CI)¶	34.2 (32.4 to 36.0)	38.2 (36.4 to 40.1)
P <sub>90</sub> — % (95% CI)‖	82.7 (81.3 to 84.2)	87.6 (86.3 to 88.9)

**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 eGFR <sub>cr</sub> (ASR)	CKD-EPI eGFR <sub>cr</sub> (AS)	EKFC eGFR <sub>cr</sub>	CKD-EPI eGFR <sub>cys</sub>	EKFC eGFR <sub>cys</sub> without Sex
<b>Paris cohort, 2646 White patients</b>					
Median bias (95% CI) — ml/min/1.73 m <sup>2</sup> †	0.30 (–0.21 to 0.78)	3.22 (2.69 to 3.86)	–1.24 (–1.75 to –0.74)	–2.85 (–3.35 to –2.21)	–0.79 (–1.26 to –0.31)
IQR of estimated GFR – measured GFR — ml/min/1.73 m <sup>2</sup> ‡	15.2 (–6.8 to 8.4)	15.9 (–4.1 to 11.7)	14.6 (–8.3 to 6.3)	16.4 (–10.3 to 6.1)	15.3 (–8.5 to 6.7)
Root-mean-square error (95% CI) — ml/min/1.73 m <sup>2</sup> §	14.2 (13.6 to 14.8)	14.8 (14.2 to 15.4)	13.6 (13.0 to 14.1)	14.5 (13.9 to 15.1)	13.5 (12.9 to 14.1)
P <sub>10</sub> — % (95% CI)¶	39.5 (37.7 to 41.4)	38.2 (36.4 to 40.1)	40.9 (39.0 to 42.7)	34.2 (32.4 to 36.0)	38.2 (36.4 to 40.1)
P <sub>90</sub> — % (95% CI)‖	84.5 (83.1 to 85.8)	82.5 (81.1 to 84.0)	86.5 (85.2 to 87.7)	82.7 (81.3 to 84.2)	87.6 (86.3 to 88.9)

**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
<b>U.S. cohort, 1093 White patients</b>			
Median bias (95% CI) — ml/min/1.73 m <sup>2</sup> †	2.83 (1.65 to 3.64)	7.11 (6.15 to 7.97)	-2.69 (-3.68 to -1.79)
IQR of estimated GFR—measured GFR— ml/min/1.73 m <sup>2</sup> ‡	18.8 (-6.6 to 12.2)	18.7 (-2.2 to 16.5)	18.5 (-11.9 to 6.6)
Root-mean-square error (95% CI) — ml/min/1.73 m <sup>2</sup> §	16.2 (15.0 to 17.4)	17.5 (16.4 to 18.6)	16.2 (14.9 to 17.4)
P <sub>30</sub> — % (95% CI)¶	41.9 (39.0 to 44.8)	39.4 (36.5 to 42.3)	41.4 (38.5 to 44.4)
P <sub>30</sub> — % (95% CI)¶	86.0 (83.9 to 88.1)	81.0 (78.6 to 83.3)	89.3 (87.5 to 91.1)

**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 eGFR <sub>cys</sub>	EKFC eGFR <sub>cys</sub> without Sex
<b>U.S. cohort, 1093 White patients</b>		
Median bias (95% CI) — ml/min/1.73 m <sup>2</sup> †	12.1 (11.1 to 13.3)	4.26 (3.33 to 5.08)
IQR of estimated GFR—measured GFR— ml/min/1.73 m <sup>2</sup> ‡	21.5 (1.5 to 23.0)	18.3 (-5.3 to 13.0)
Root-mean-square error (95% CI) — ml/min/1.73 m <sup>2</sup> §	21.3 (20.3 to 22.2)	16.8 (15.7 to 17.9)
P <sub>30</sub> — % (95% CI)¶	29.4 (26.7 to 32.1)	41.5 (38.6 to 44.5)
P <sub>30</sub> — % (95% CI)‖	72.9 (70.3 to 75.6)	83.9 (81.7 to 86.1)

**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 eGFR <sub>cr</sub> (ASR)	CKD-EPI eGFR <sub>cr</sub> (AS)	EKFC eGFR <sub>cr</sub>	CKD-EPI eGFR <sub>cys</sub>	EKFC eGFR <sub>cys</sub> without Sex
<b>U.S. cohort, 1093 White patients</b>					
Median bias (95% CI) — ml/min/1.73 m <sup>2</sup> †	2.83 (1.65 to 3.64)	7.11 (6.15 to 7.97)	-2.69 (-3.68 to -1.79)	12.1 (11.1 to 13.3)	4.26 (3.33 to 5.08)
IQR of estimated GFR—measured GFR— ml/min/1.73 m <sup>2</sup> ‡	18.8 (-6.6 to 12.2)	18.7 (-2.2 to 16.5)	18.5 (-11.9 to 6.6)	21.5 (1.5 to 23.0)	18.3 (-5.3 to 13.0)
Root-mean-square error (95% CI) — ml/min/1.73 m <sup>2</sup> §	16.2 (15.0 to 17.4)	17.5 (16.4 to 18.6)	16.2 (14.9 to 17.4)	21.3 (20.3 to 22.2)	16.8 (15.7 to 17.9)
P <sub>30</sub> — % (95% CI)¶	41.9 (39.0 to 44.8)	39.4 (36.5 to 42.3)	41.4 (38.5 to 44.4)	29.4 (26.7 to 32.1)	41.5 (38.6 to 44.5)
P <sub>30</sub> — % (95% CI)¶	86.0 (83.9 to 88.1)	81.0 (78.6 to 83.3)	89.3 (87.5 to 91.1)	72.9 (70.3 to 75.6)	83.9 (81.7 to 86.1)



**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 eGFR <sub>cr</sub> (ASR)	CKD-EPI eGFR <sub>cr</sub> (AS)	EKFC eGFR <sub>cr</sub>
<b>Paris cohort, 858 Black patients</b>			
Median bias (95% CI) — ml/min/1.73 m <sup>2</sup> †	0.24 (-0.64 to 0.81)	-5.09 (-5.68 to -4.14)	-2.58 (-3.49 to -1.71)
IQR of estimated GFR—measured GFR— ml/min/1.73 m <sup>2</sup> ‡	19.3 (-12.7 to 4.1)	16.8 (-12.7 to 4.1)	14.9 (-9.9 to 5.1)
Root-mean-square error (95% CI) — ml/min/1.73 m <sup>2</sup> §	16.0 (14.7 to 17.2)	14.9 (13.5 to 16.1)	13.9 (12.4 to 15.2)
P <sub>30</sub> — % (95% CI)¶	35.4 (32.2 to 38.6)	33.0 (29.8 to 36.1)	37.5 (34.3 to 40.8)
P <sub>30</sub> — % (95% CI)¶	79.8 (77.1 to 82.5)	82.3 (79.7 to 84.8)	85.5 (83.2 to 87.9)

**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 eGFR <sub>cys</sub>	EKFC eGFR <sub>cys</sub> without Sex
<b>Paris cohort, 858 Black patients</b>		
Median bias (95% CI) — ml/min/1.73 m <sup>2</sup> †	-0.62 (-1.71 to 0.28)	1.40 (0.38 to 2.23)
IQR of estimated GFR- measured GFR— ml/min/1.73 m <sup>2</sup> ‡	17.9 (-8.1 to 9.8)	14.3 (-5.6 to 8.8)
Root-mean-square error (95% CI) — ml/min/1.73 m <sup>2</sup> §	15.4 (14.0 to 16.6)	13.5 (12.1 to 14.7)
P <sub>30</sub> — % (95% CI)¶	36.2 (33.0 to 39.5)	41.0 (37.7 to 44.3)
P <sub>30</sub> — % (95% CI)¶	81.5 (78.9 to 84.1)	87.4 (85.2 to 89.6)

**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 eGFR <sub>cr</sub> (ASR)	CKD-EPI eGFR <sub>cr</sub> (AS)	EKFC eGFR <sub>cr</sub>	CKD-EPI eGFR <sub>cys</sub>	EKFC eGFR <sub>cys</sub> without Sex
<b>Paris cohort, 858 Black patients</b>					
Median bias (95% CI) — ml/min/1.73 m <sup>2</sup> †	0.24 (-0.64 to 0.81)	-5.09 (-5.68 to -4.14)	-2.58 (-3.49 to -1.71)	-0.62 (-1.71 to 0.28)	1.40 (0.38 to 2.23)
IQR of estimated GFR—measured GFR— ml/min/1.73 m <sup>2</sup> ‡	19.3 (-12.7 to 4.1)	16.8 (-12.7 to 4.1)	14.9 (-9.9 to 5.1)	17.9 (-8.1 to 9.8)	14.3 (-5.6 to 8.8)
Root-mean-square error (95% CI) — ml/min/1.73 m <sup>2</sup> §	16.0 (14.7 to 17.2)	14.9 (13.5 to 16.1)	13.9 (12.4 to 15.2)	15.4 (14.0 to 16.6)	13.5 (12.1 to 14.7)
P <sub>30</sub> — % (95% CI)¶	35.4 (32.2 to 38.6)	33.0 (29.8 to 36.1)	37.5 (34.3 to 40.8)	36.2 (33.0 to 39.5)	41.0 (37.7 to 44.3)
P <sub>30</sub> — % (95% CI)¶	79.8 (77.1 to 82.5)	82.3 (79.7 to 84.8)	85.5 (83.2 to 87.9)	81.5 (78.9 to 84.1)	87.4 (85.2 to 89.6)

**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 eGFR <sub>cr</sub> (ASR)	CKD-EPI eGFR <sub>cr</sub> (AS)	EKFC eGFR <sub>cr</sub>
<b>African cohort, 508 Black patients</b>			
Median bias (95% CI) — ml/min/1.73 m <sup>2</sup> †	12.2 (10.7 to 15.0)	2.48 (0.72 to 4.15)	-1.45 (-2.82 to 0.62)
IQR of estimated GFR — measured GFR — ml/min/1.73 m <sup>2</sup> ‡	30.0 (-3.2 to 26.8)	23.3 (-9.0 to 14.3)	20.4 (-10.6 to 9.9)
Root-mean-square error (95% CI) — ml/min/1.73 m <sup>2</sup> §	24.5 (22.7 to 26.1)	18.1 (16.6 to 19.4)	16.4 (15.0 to 17.8)
P <sub>e</sub> — % (95% CI)¶	19.5 (16.0 to 22.9)	34.4 (30.3 to 38.6)	38.0 (33.8 to 42.2)
P <sub>x</sub> — % (95% CI)‖	63.6 (59.4 to 67.8)	74.4 (70.6 to 78.2)	78.9 (75.4 to 82.5)

**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 eGFR <sub>cys</sub>	EKFC eGFR <sub>cys</sub> without Sex
<b>African cohort, 508 Black patients</b>		
Median bias (95% CI) — ml/min/1.73 m <sup>2</sup> †	2.82 (1.43 to 4.48)	1.74 (0.28 to 3.25)
IQR of estimated GFR — measured GFR — ml/min/1.73 m <sup>2</sup> ‡	23.7 (-7.7 to 16.0)	19.5 (-7.4 to 12.1)
Root-mean-square error (95% CI) — ml/min/1.73 m <sup>2</sup> §	18.5 (17.1 to 19.8)	16.0 (14.7 to 17.2)
P <sub>e</sub> — % (95% CI)¶	33.1 (29.0 to 37.2)	40.6 (36.3 to 44.8)
P <sub>x</sub> — % (95% CI)‖	77.4 (73.7 to 81.0)	83.5 (80.2 to 86.7)

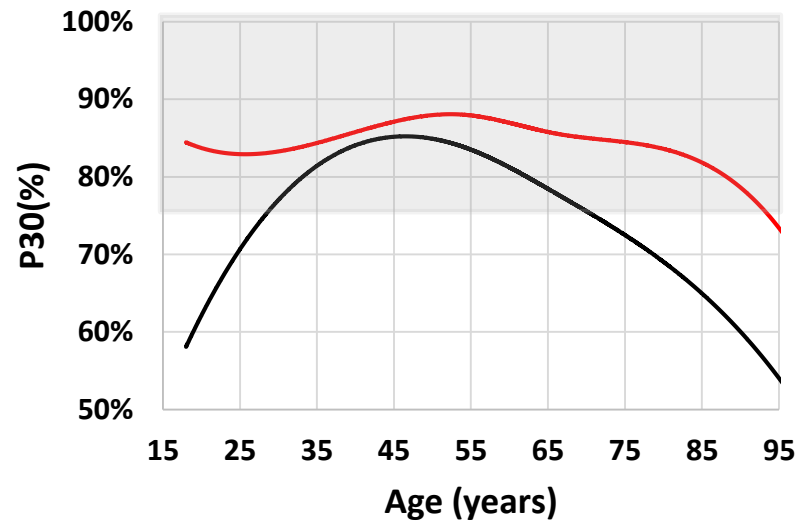
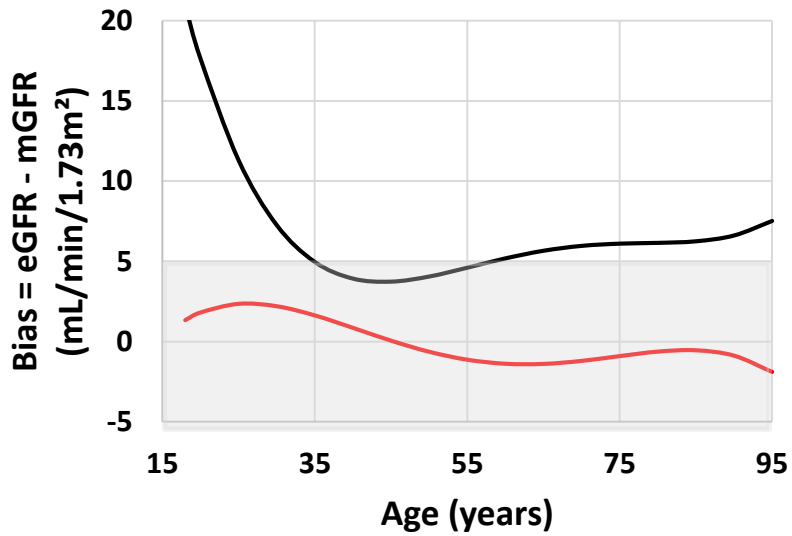
**Table 1. Performance of Single Biomarker (Serum Creatinine or Cystatin C)-Based Equations to Estimate the Glomerular Filtration Rate.\***

Variable	Serum Creatinine-Based Equations			Cystatin C-Based Equations	
	CKD-EPI eGFR <sub>cr</sub> (ASR)	CKD-EPI eGFR <sub>cr</sub> (AS)	EKFC eGFR <sub>cr</sub>	CKD-EPI eGFR <sub>cys</sub>	EKFC eGFR <sub>cys</sub> without Sex
<b>African cohort, 508 Black patients</b>					
Median bias (95% CI) — ml/min/1.73 m <sup>2</sup> †	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 m <sup>2</sup> ‡	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 m <sup>2</sup> §	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 <sub>e</sub> — % (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 <sub>x</sub> — % (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)

**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
<b>EKFC cohort, 7727 White patients</b>			
Median bias (95% CI) — ml/min/1.73 m <sup>2</sup> ‡	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 m <sup>2</sup> ‡	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 m <sup>2</sup> §	13.1 (12.8 to 13.4)	14.7 (14.4 to 15.0)	11.3 (11.0 to 11.6)
P <sub>10</sub> — % (95% CI) ¶	41.5 (40.4 to 42.6)	37.2 (36.2 to 38.3)	48.9 (47.8 to 50.0)
P <sub>30</sub> — % (95% CI) ¶	88.3 (87.6 to 89.0)	84.2 (83.4 to 85.0)	90.4 (89.8 to 91.1)
<b>Paris cohort, 2646 White patients</b>			
Median bias (95% CI) — ml/min/1.73 m <sup>2</sup> ‡	–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 m <sup>2</sup> ‡	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 m <sup>2</sup> §	12.1 (11.6 to 12.7)	12.6 (12.0 to 13.1)	11.8 (11.2 to 12.4)
P <sub>10</sub> — % (95% CI) ¶	43.9 (42.0 to 45.8)	42.3 (40.4 to 44.1)	45.8 (43.9 to 47.7)
P <sub>30</sub> — % (95% CI) ¶	89.7 (88.5 to 90.8)	89.2 (88.0 to 90.4)	92.1 (91.1 to 93.1)
<b>U.S. cohort, 1093 White patients</b>			
Median bias (95% CI) — ml/min/1.73 m <sup>2</sup> ‡	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 m <sup>2</sup> ‡	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 m <sup>2</sup> §	18.1 (17.1 to 19.1)	21.0 (20.1 to 22.0)	15.5 (14.3 to 16.7)
P <sub>10</sub> — % (95% CI) ¶	37.1 (34.3 to 40.0)	28.1 (25.4 to 30.8)	45.7 (42.7 to 48.6)
P <sub>30</sub> — % (95% CI) ¶	79.5 (77.1 to 81.9)	72.1 (69.4 to 74.8)	88.7 (86.9 to 90.6)
<b>Paris cohort, 858 Black patients</b>			
Median bias (95% CI) — ml/min/1.73 m <sup>2</sup> ‡	–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 m <sup>2</sup> ‡	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 m <sup>2</sup> §	13.3 (11.9 to 14.6)	12.6 (11.2 to 13.9)	11.6 (10.0 to 13.0)
P <sub>10</sub> — % (95% CI) ¶	38.7 (35.4 to 42.0)	38.9 (35.7 to 42.2)	48.3 (44.9 to 51.6)
P <sub>30</sub> — % (95% CI) ¶	87.9 (85.7 to 90.1)	89.0 (87.0 to 91.1)	92.0 (90.1 to 93.8)
<b>African cohort, 508 Black patients</b>			
Median bias (95% CI) — ml/min/1.73 m <sup>2</sup> ‡	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 m <sup>2</sup> ‡	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 m <sup>2</sup> §	19.7 (18.2 to 21.1)	17.2 (15.8 to 18.5)	14.7 (13.3 to 16.0)
P <sub>10</sub> — % (95% CI) ¶	28.7 (24.8 to 32.7)	34.3 (30.1 to 38.4)	43.5 (39.2 to 47.8)
P <sub>30</sub> — % (95% CI) ¶	75.0 (71.2 to 78.8)	77.6 (73.9 to 81.2)	84.3 (81.1 to 87.4)

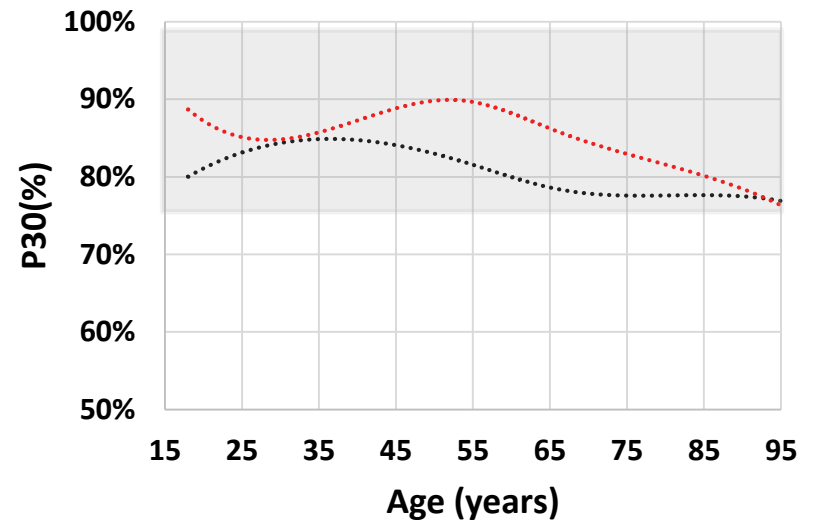
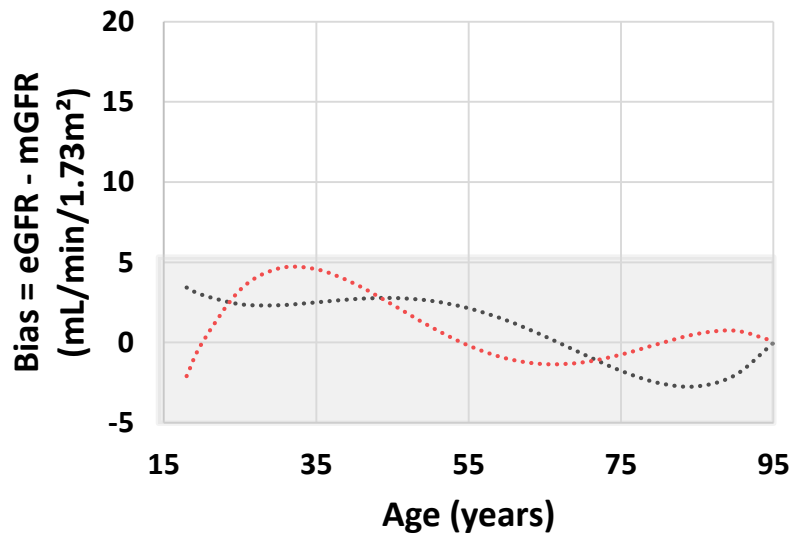
SCr-based eGFR: CKD-EPI<sub>Crea</sub> (AS) (black) versus EKFC<sub>Crea</sub> (red)



N=12,832

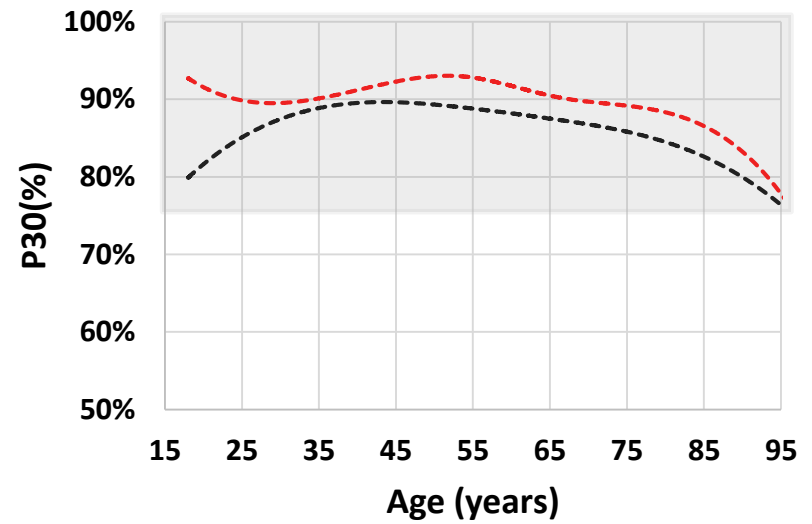
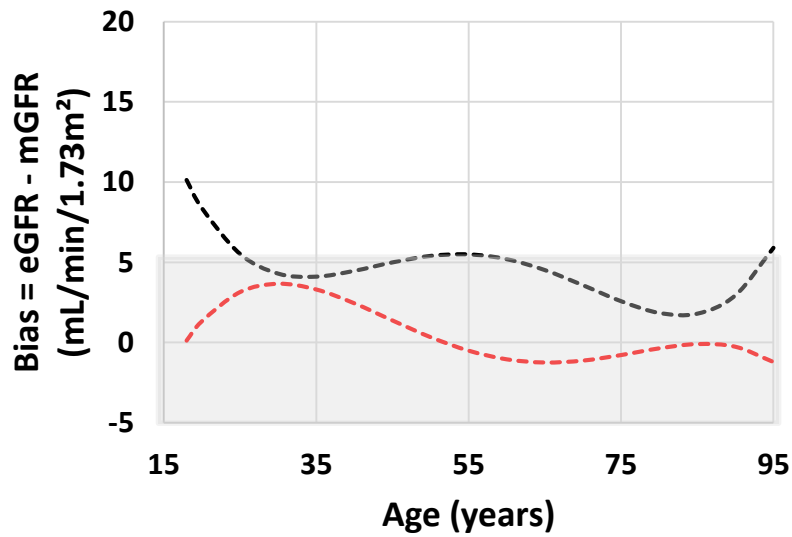


CysC-based eGFR: CKD-EPI<sub>CysC</sub> (black) versus EKFC<sub>CysC</sub> (red)

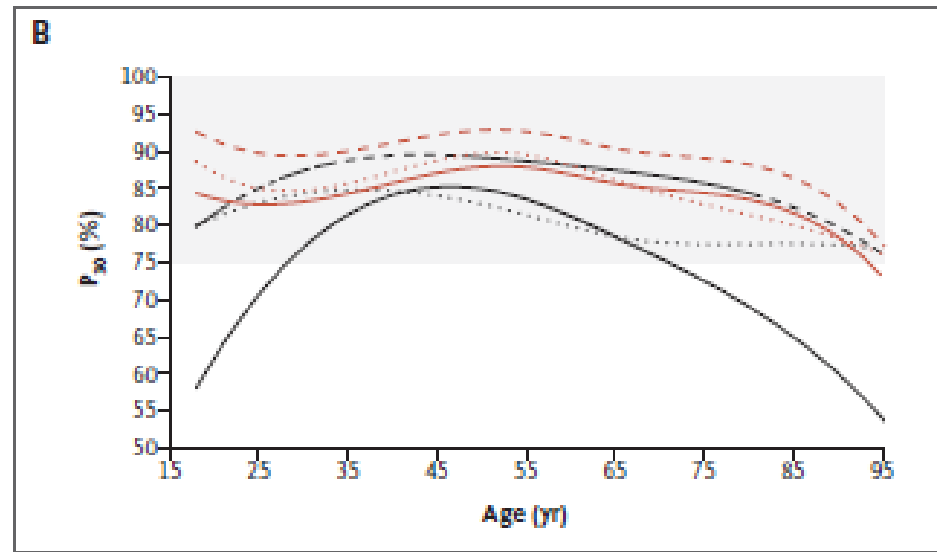
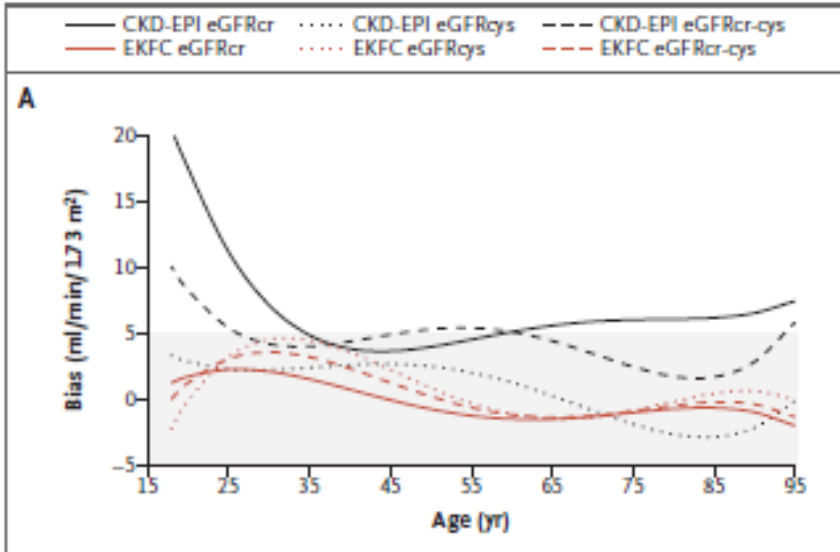


N=12,832

Scr/CysC-based eGFR: CKD-EPI<sub>Crea+CysC</sub> (AS) (black) versus EKFC<sub>Crea+CysC</sub> (red)



N=12,832



N=12,832

**Table S9.4a.** P30-accuracy (% of subjects with eGFR within 30% of mGFR) for **mGFR < 60 mL/min/1.73m<sup>2</sup>**

P30 [95%CI]	Men			Women		
	age 18-40	age 40-65	age ≥ 65	age 18-40	age 40-65	age ≥ 65
<b>N</b>	223	1008	1556	184	741	1197
EKFC-eGFR <sub>Cr</sub>	69.5 [63.4; 75.6]	70.6 [67.8; 73.5]	77.2 [75.1; 79.3]	65.2 [58.3; 72.2]	72.2 [69.0; 75.4]	76.4 [74.0; 78.8]
CKD-EPI-eGFR <sub>Cr</sub> (AS)	62.8 [56.4; 69.2]	66.4 [63.4; 69.3]	63.2 [60.8; 65.6]	56.5 [49.3; 63.8]	66.7 [63.3; 70.1]	62.4 [59.7; 65.2]
EKFC-eGFR <sub>Cys</sub> (S)	77.1 [71.6; 82.7]	80.3 [77.8; 82.7]	78.9 [76.8; 80.9]	69.0 [62.3; 75.8]	76.1 [73.0; 79.2]	76.7 [74.3; 79.1]
EKFC-eGFR <sub>Cys</sub>	80.7 [75.5; 85.9]	81.9 [79.6; 84.3]	80.5 [78.5; 82.4]	65.2 [58.3; 72.2]	74.9 [71.8; 78.0]	75.5 [73.1; 78.0]
CKD-EPI-eGFR <sub>Cys</sub>	80.7 [75.5; 85.9]	78.8 [76.2; 81.3]	77.3 [75.2; 79.4]	72.8 [66.3; 79.3]	74.0 [70.8; 77.1]	71.6 [69.0; 74.2]
EKFC-eGFR <sub>Cr+Cys</sub> (S)	78.0 [72.6; 83.5]	81.2 [78.7; 83.6]	84.4 [82.6; 86.2]	74.5 [68.1; 80.8]	80.2 [77.3; 83.0]	82.7 [80.6; 84.9]
EKFC-eGFR <sub>Cr+Cys</sub>	79.8 [74.5; 85.1]	82.5 [80.2; 84.9]	85.3 [83.5; 87.0]	70.1 [63.4; 76.8]	79.6 [76.7; 82.5]	81.5 [79.2; 83.7]
CKD-EPI-eGFR <sub>Cr+Cys</sub> (AS)	85.2 [80.5; 89.9]	83.3 [81.0; 85.6]	81.0 [79.1; 83.0]	75.0 [68.7; 71.3]	79.9 [77.0; 82.8]	78.1 [75.8; 80.5]

**Table S9.4b.** P30-accuracy (% of subjects with eGFR within 30% of mGFR) for **mGFR ≥ 60 mL/min/1.73m<sup>2</sup>**

P30 [95%CI]	Men			Women		
	age 18-40	age 40-65	age ≥ 65	age 18-40	age 40-65	age ≥ 65
<b>N</b>	782	2452	858	640	2243	948
EKFC-eGFR <sub>Cr</sub>	89.5 [87.4; 91.7]	93.3 [92.3; 94.3]	94.1 [92.5; 95.6]	89.2 [86.8; 91.6]	94.6 [93.7; 95.5]	95.0 [93.7; 96.4]
CKD-EPI-eGFR <sub>Cr</sub> (AS)	80.6 [77.8; 83.3]	89.4 [88.1; 90.6]	86.8 [84.6; 89.1]	79.8 [76.7; 83.0]	88.5 [87.2; 89.8]	84.8 [82.5; 87.1]
EKFC-eGFR <sub>Cys</sub> (S)	89.0 [86.8; 91.2]	92.4 [91.3; 93.4]	91.3 [89.4; 93.2]	90.6 [88.4; 92.9]	92.5 [91.4; 93.6]	90.5 [88.6; 92.4]
EKFC-eGFR <sub>Cys</sub>	91.0 [89.0; 93.1]	91.7 [90.6; 92.8]	90.2 [88.2; 92.2]	88.0 [85.4; 90.5]	91.9 [90.8; 93.1]	92.0 [90.3; 93.7]
CKD-EPI-eGFR <sub>Cys</sub>	84.9 [82.4; 87.4]	83.5 [92.1; 85.0]	83.8 [81.3; 86.3]	85.2 [82.4; 87.9]	82.7 [81.1; 84.2]	81.9 [79.4; 84.3]
EKFC-eGFR <sub>Cr+Cys</sub> (S)	94.5 [92.9; 96.1]	95.4 [94.6; 96.2]	95.8 [94.5; 97.1]	94.4 [92.6; 96.2]	97.0 [96.3; 97.7]	96.6 [95.5; 97.8]
EKFC-eGFR <sub>Cr+Cys</sub>	94.8 [93.2; 96.3]	95.7 [94.9; 96.5]	95.5 [94.1; 96.9]	93.1 [91.2; 95.1]	96.3 [95.5; 97.1]	96.9 [85.8; 98.0]
CKD-EPI-eGFR <sub>Cr+Cys</sub> (AS)	89.6 [87.5; 91.8]	88.9 [87.7; 90.2]	87.1 [84.8; 89.3]	87.0 [84.4; 89.6]	83.3 [81.8; 84.9]	84.7 [82.4; 87.0]

# Cystatine C

- La cystatin 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  $EKFC_{crea}$  (analyse en cours pour  $EKFC_{cc}$ )
- Les équations basées sur la cystatine C ne sont pas meilleures que les équations basées sur la créatinine
- Les équations EKFC sont un peu meilleures que les équations CKD-EPI correspondantes => **alternative valable en Europe et en Afrique**
- Les équations combinées sont meilleures (exactitude +5-10%)
- Standardisation
- Plus cher

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

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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)*

# Chronic kidney disease staging with cystatin C or creatinine-based formulas: flipping the coin

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

Creatinine	Cockcroft-Gault						aMDRD						CKD-EPI					
	Stage	GFR	N	True positive		Missing	GFR	N	True positive		Missing	GFR	N	True positive		Missing		
				True positive	False positive				True positive	False positive				True positive	False positive			
1	178	242	142 (80%)	100 (41%) <sup>a</sup>	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	Le Bricon						MCQ						CKD-EPI					
	Stage	GFR	N	True positive		Missing	GFR	N	True positive		Missing	GFR	N	True positive		Missing		
				True positive	False positive				True positive	False positive				True positive	False positive			
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%)	14 (7%)	18 (10%)	176	146	114 (64%)	32 (22%)	64 (36%)	176	146	114 (64%)	32 (22%)	64 (36%)			
5	25	1	1 (4%)	0 (0%)	0 (0%)	25	1	1 (4%)	0 (0%)	0 (0%)	25	1	1 (4%)	0 (0%)	0 (0%)			

Creatinine + Cystatin-C	Le Bricon						MCQ						CKD-EPI					
	Stage	GFR	N	True positive		Missing	GFR	N	True positive		Missing	GFR	N	True positive		Missing		
				True positive	False positive				True positive	False positive				True positive	False positive			
1	178	288	168 (94%)	100 (35%)	16 (6%)	178	146	114 (64%)	32 (22%)	64 (36%)	178	229	155 (87%)	74 (32%)	23 (13%)			
2	252	207	127 (50%)	95 (39%)	104 (41%)	252	205	127 (50%)	78 (38%)	125 (50%)	252	182	128 (51%)	54 (30%)	124 (49%)			
3	251	227	172 (69%)	159 (48%)	81 (32%)	251	274	166 (66%)	108 (39%)	85 (34%)	251	246	177 (71%)	69 (28%)	74 (29%)			
4	176	149	130 (74%)	14 (7%)	18 (10%)	176	146	114 (64%)	32 (22%)	64 (36%)	176	146	114 (64%)	32 (22%)	64 (36%)			
5	25	11	8 (32%)	0 (0%)	0 (0%)	25	11	8 (32%)	0 (0%)	0 (0%)	25	11	8 (32%)	0 (0%)	0 (0%)			

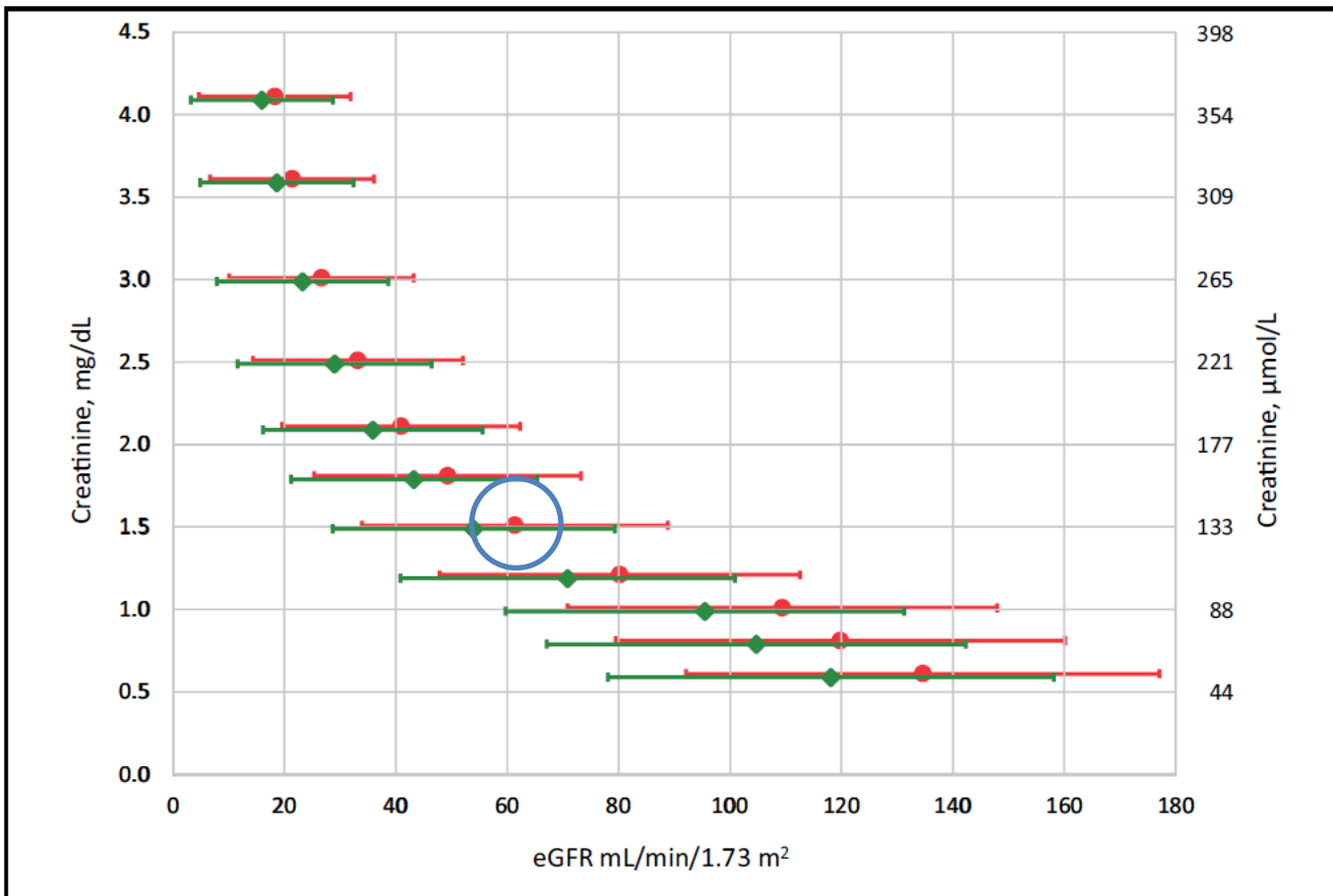
**Results.** Misclassification was a constant for all 61 formulas evaluated and averaged 50% for creatinine-based and 35% for cystatin C-based equations. Most of the cases were misclassified as one stage higher or lower. However, in 10% of the subjects, one stage was skipped and patients were classified 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 correctly 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.

<sup>a</sup>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.

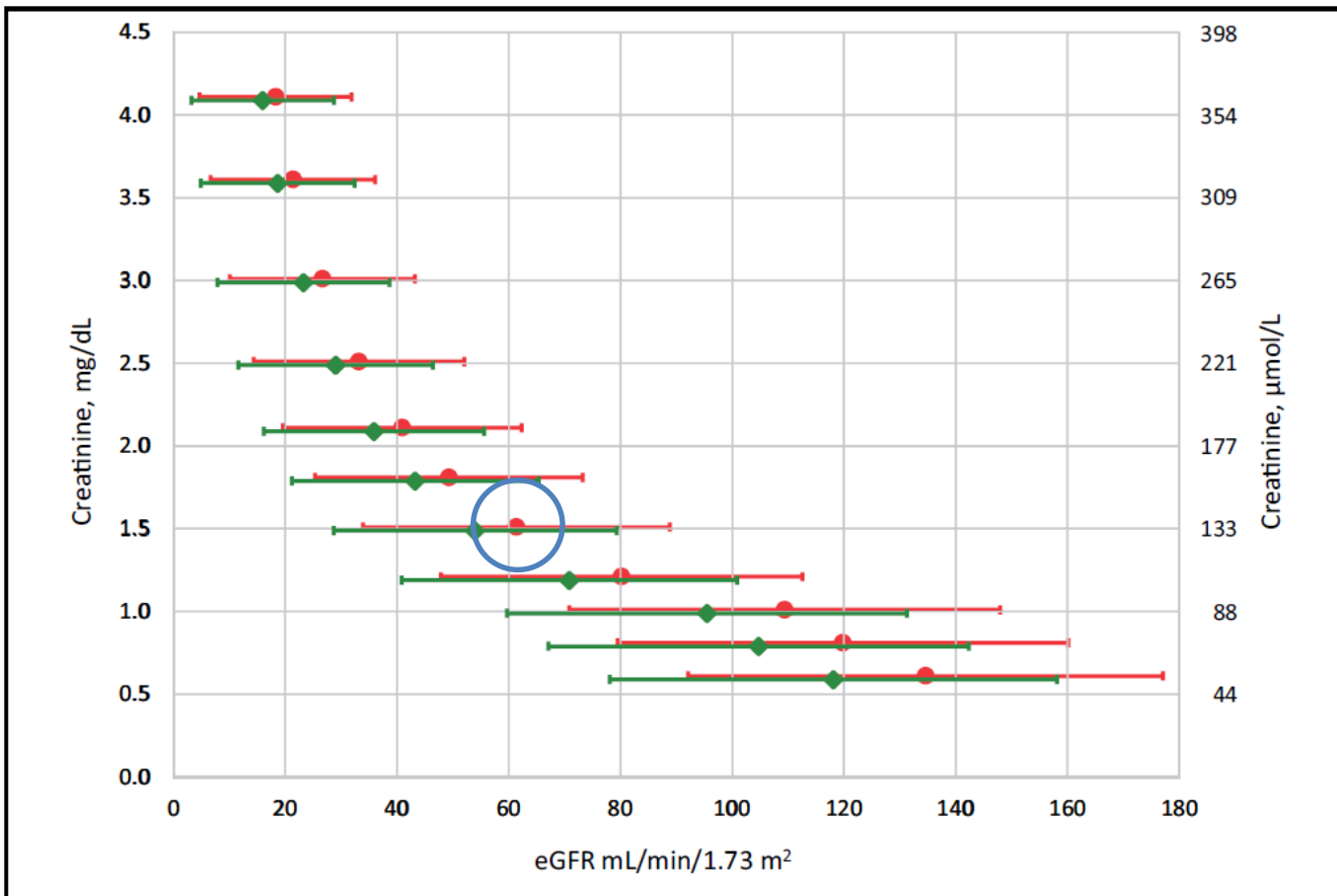
# Ne pas sur-interpreter un résultat...

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.

$$eGFR = 60,25 \text{ ml/min/1.73m}^2$$



**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.

$$\begin{aligned}
 \text{eGFR} &= \cancel{60.25} \text{ ml/min/1.73m}^2 \\
 &= 60 \text{ ml/min/1.73m}^2 \quad (\text{CI } 95\%: 33-87)
 \end{aligned}$$

## The applicability of eGFR equations to different populations

*Pierre Delanaye and Christophe Mariat*

---

Et si on mesurait le DFG...

- Estimation du DFG
- Mesure du DFG

# Mesurer le DFG: Pourquoi?

## Une question de précision!

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



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

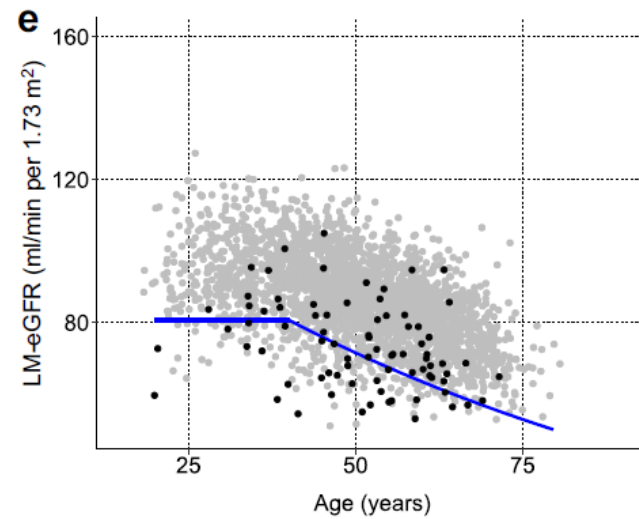
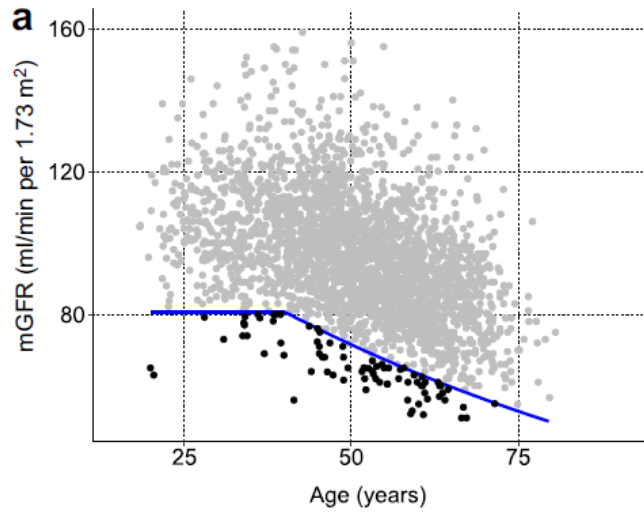
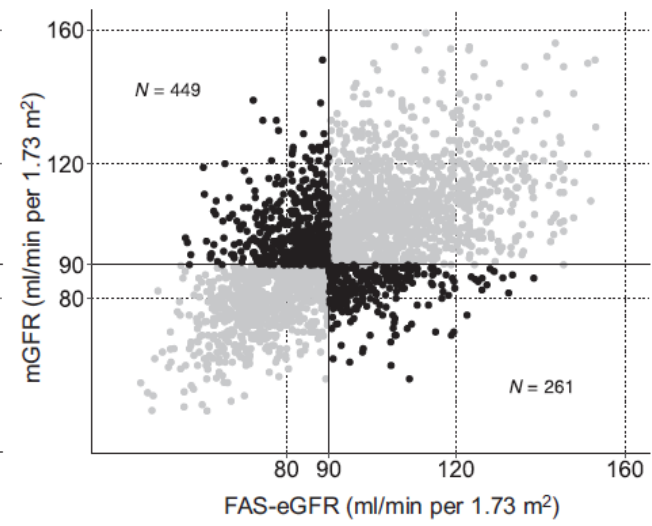
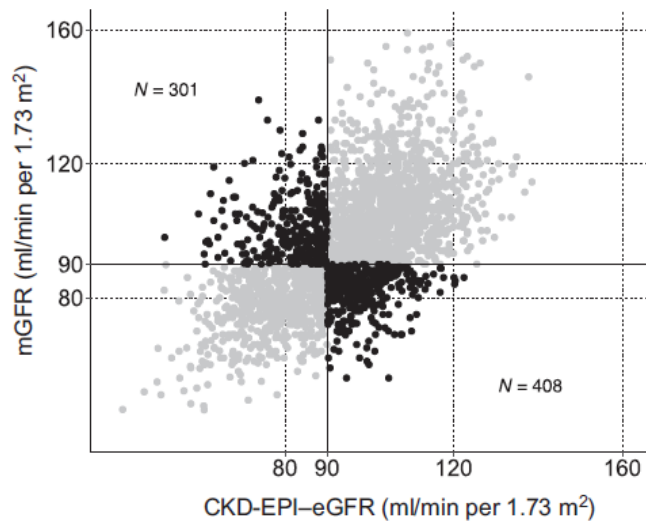


see commentary on page 738

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

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

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



# Mesurer le DFG: Pourquoi?

## Une question de précision!

- Décision d'initier la dialyse
- Individus sarcopéniques
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- Cirrhose, USI, Hyperfiltration
- Donneur vivant
- Recherche Clinique, EMA

# Mesurer le DFG: Pourquoi?

## Une question de précision!

- Décision d'initier la dialyse
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- Recherche Clinique, EMA
- Dosage d'un médicament potentiellement néphrotoxique (=>2)

# 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...

# Disponibles sur le marché...

Marqueurs	Forces	Limites
<i>Inuline</i>	“Gold standard” (ou historique)	Coûteux Dosage ni facile ni standardisé Impossible en clairance plasmatique
<i>Iothalamate</i>	Le plus populaire aux USA Isotopique ou “froide”	Sécrétion tubulaire Allergie Iode
<i>Iohexol</i>	Populaire en Europe Froide	Allergie Iode
<i>EDTA</i>	Facile à mesurer	Seulement isotopique Pas disponible aux USA...et plus en Europe!!
<i>DTPA</i>	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*

### Measuring GFR: A Systematic Review

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 Carl-Gustaf Elinder, MD, PhD,<sup>4</sup> Anders Grubb, MD, PhD,<sup>5</sup> Ingegerd Mejare, PhD,<sup>6</sup>  
 Gunnar Sterner, MD, PhD,<sup>7</sup> and Sten-Erik Bäck, MSc, PhD,<sup>5</sup> on behalf of the SBU  
 GFR Review Group\*

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

	No. of Pts/ Studies	Median Bias* (95% CI)	Mean Bias (95% CI)	P <sub>30</sub> (95% CI)	P <sub>10</sub> (95% CI)	Sufficient Accuracy	Scientific Evidence	Comments <sup>b</sup>
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
<sup>51</sup> 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
Plasma clearance	198/5	2 (-1 to 8)	2 (1 to 15)	86 (80 to 92)	50 (43 to 59)	Yes	⊕⊕⊕○	Imprecision, -1
Iohexol								
Renal clearance	47/2	-7 (-10 to 0)	-7 (-16 to 2)	100 <sup>c</sup>	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
Iodinated contrast								
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 <sup>c</sup>	72 (59 to 87)	Yes	⊕⊕○○	Imprecision, -1; indirectness, -1

Note: Modified with permission of the Swedish Council on Health Technology Assessment.<sup>3</sup> Accuracy and bias expressed as percentage. Renal inulin clearance served as reference method. Mean bias, P<sub>10</sub>, and P<sub>30</sub> were estimated using generalized linear mixed models based on normal distribution (mean bias) or Poisson distribution (P<sub>10</sub>, P<sub>30</sub>; 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; ⊕○○○, insufficient evidence; <sup>51</sup>Cr-EDTA, chromium 51-labeled ethylenediaminetetraacetic acid; DTPA, diethylenetriaminepentaacetic acid; CI, confidence interval; Imprecision, N < 100 in meta-analysis (-1), P<sub>30</sub> lower 95% CI ≤ 80%, P<sub>10</sub> 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<sub>10</sub>, percentage of measurements by index method that differed no more than 10% from reference method; P<sub>30</sub>, 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).

\*Median bias was calculated directly (using the weights) for each index method together with nonparametric CIs.

<sup>b</sup>Strength of scientific evidence.

<sup>c</sup>The generalized linear mixed model does not yield valid estimates of confidence limits when estimated proportion (eg, P<sub>30</sub>) is 100%.

# 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
<i>Urinary clearance</i>	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]
<i>Plasma clearance</i>			
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].



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

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\*\*These authors equally contributed as last senior author.



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

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# AJKD

## Correspondence

### RESEARCH LETTER

#### Concordance Iohexol Plasma Clearance

To the Editor:

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Caroline Le Goff, EuSpLM, Etienne Cavalier, EuSpLM, PhD  
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Pottel et al. *BMC Nephrology* (2021) 22:166  
https://doi.org/10.1186/s12882-021-02376-0

### RESEARCH

### Open Access

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

Hans Pottel<sup>1</sup>, Elke Schaeffner<sup>2</sup>, Natalie Ebert<sup>2</sup>, Markus van der Giet<sup>3</sup> and Pierre Delanaye<sup>4,5</sup>

### Original Investigation

# AJKD

## Comparability of Plasma Iohexol Clearance Across Population-Based Cohorts

Bjørn O. Eriksen, Elke Schaeffner, Toralf Melsom, Natalie Ebert, Markus van der Giet, Vilmundur Gudnason, Olafur S. Indridasson, Amy B. Karger, Andrew S. Levey, Mirjam Schuchardt, Liv K. Sørensen, and Runolfur Palsson

**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  $\rho$  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 90% and 90% of

Complete author and article information provided below references.

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## Comparison of Early-Compartment Correction Equations for GFR Measurements

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RESEARCH LETTER

BMC Nephrology

### Iohexol Plasma Clearance: Impact of Weighing the Syringe

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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...

# 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 DFG mesuré

- 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

# Conclusions

- Limitations de la créatinine
- Plusieurs formules
- Avantages de la formule EKFC
- Cystatine C
- Mesure du DFG est possible (iohexol)

Merci de votre attention



3 - 6 OCTOBRE 2023

8<sup>ÈME</sup> CONGRÈS  
DE LA SOCIÉTÉ  
FRANCOPHONE  
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