

Comment j'explore la fonction rénale?

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BELGIQUE



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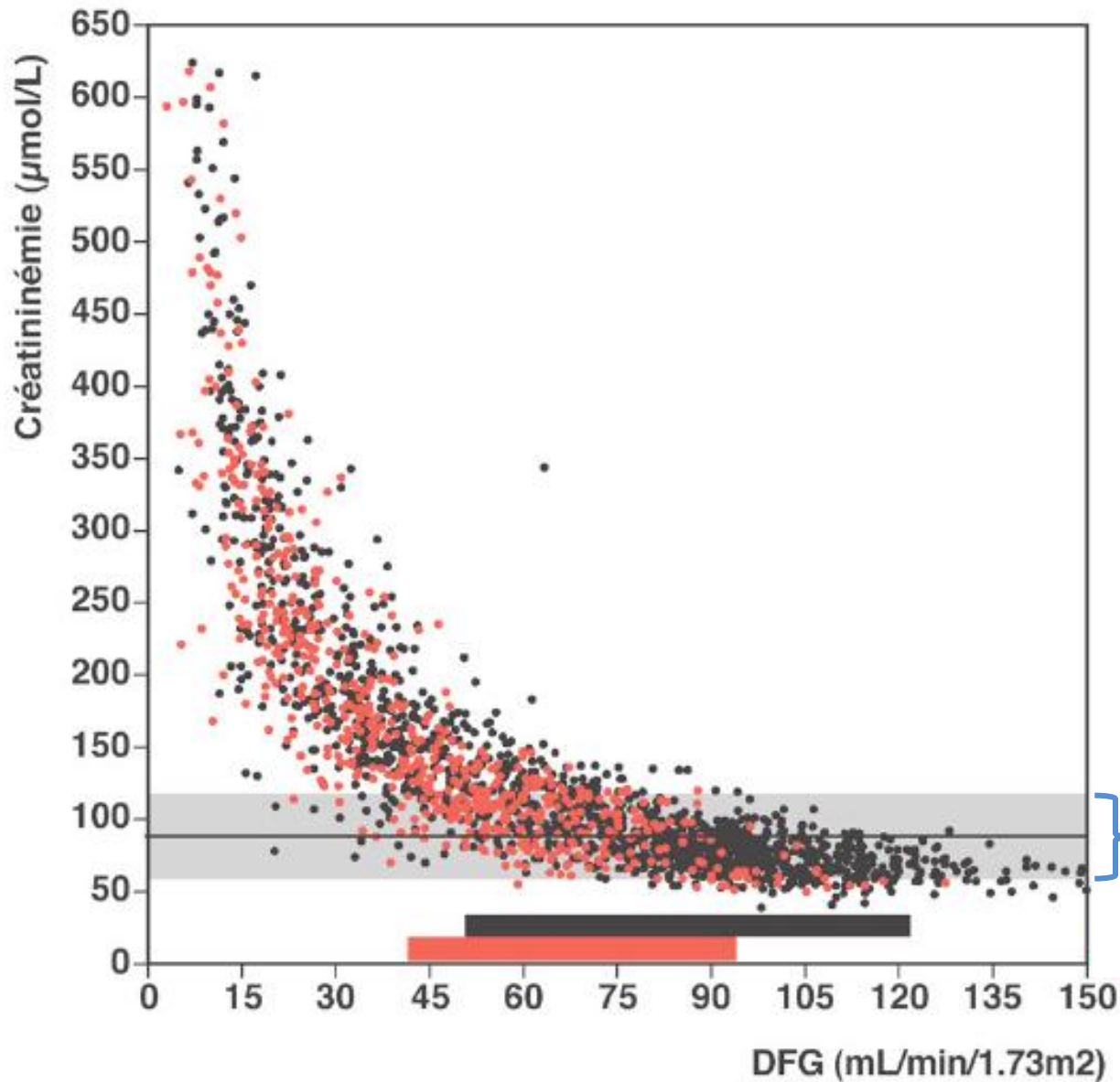
Measuring and estimating the GFR in children: state of the art in 2025

Hans Pottel¹ · George J. Schwartz² 

Received: 11 October 2024 / Revised: 9 February 2025 / Accepted: 10 February 2025 / Published online: 11 March 2025
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Le DFG est le paramètre le plus utilisé pour estimer la fonction globale du rein

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



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

Autres Limites

Analytiques

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

Physiologiques: Sécrétion tubulaire

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

Physiologiques: Masse musculaire

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

Perrone RD, Clin Chem, 1992, 38, p1933

Delanaye P, Nephron, 2017, 136, p302

Créatinine: à la poubelle?

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

Créatinine: à la poubelle?

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

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

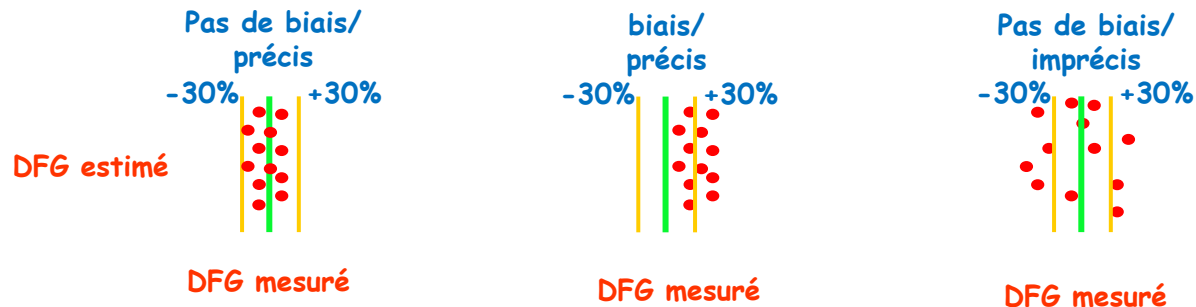
KDIGO, Kidney Int, 2012, 3

Perrone RD, Clin Chem, 1992, 38, 1933

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

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

Quelles équations?

- ~~• Cockcroft~~
- Schwartz – Schwartz updated - CKiDU25
- EKFC



Establishing age/sex related serum creatinine reference intervals from hospital laboratory data based on different statistical methods

Hans Pottel ^{a,*}, Nicolas Vrydags ^b, Boris Mahieu ^b, Emmanuel Vandewynckele ^b, Kathleen Croes ^b, Frank Martens ^b

^a Interdisciplinary Research Center, Katholieke Universiteit Leuven Campus Kortrijk, Kortrijk, Belgium

^b Department of Clinical Chemistry, AZ Groeninge Hospital, Kortrijk, Belgium

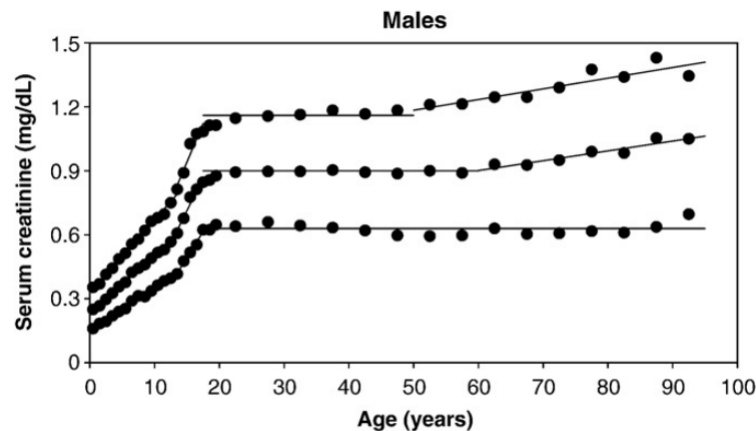


Fig. 3. Age dependency of Scr (mg/dL) for males for lower limit, mean and upper limit.

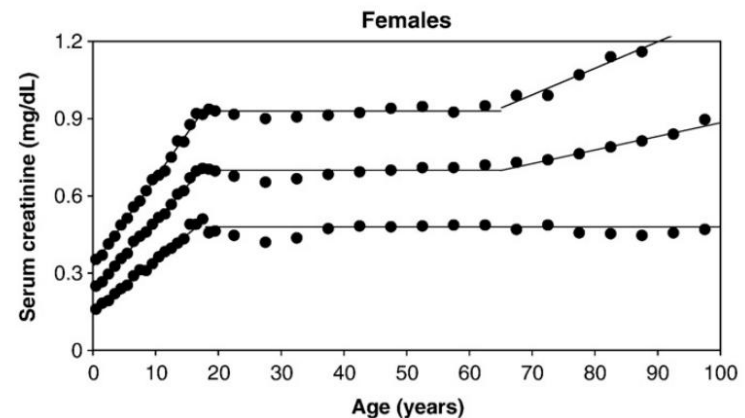


Fig. 4. Age dependency of Scr (mg/dL) for females for lower limit, mean and upper limit.

Fig. 2. GFR values (MAG3 series), corrected for body surface area. The 10th, 25th, 50th, 75th and 90th percentiles

2 years of age. **b** Values up to 15 years. After 2 years of age, the GFR remains constant

Original article

Revisiting normal ^{51}Cr -ethylenediaminetetraacetic acid clearance values in children

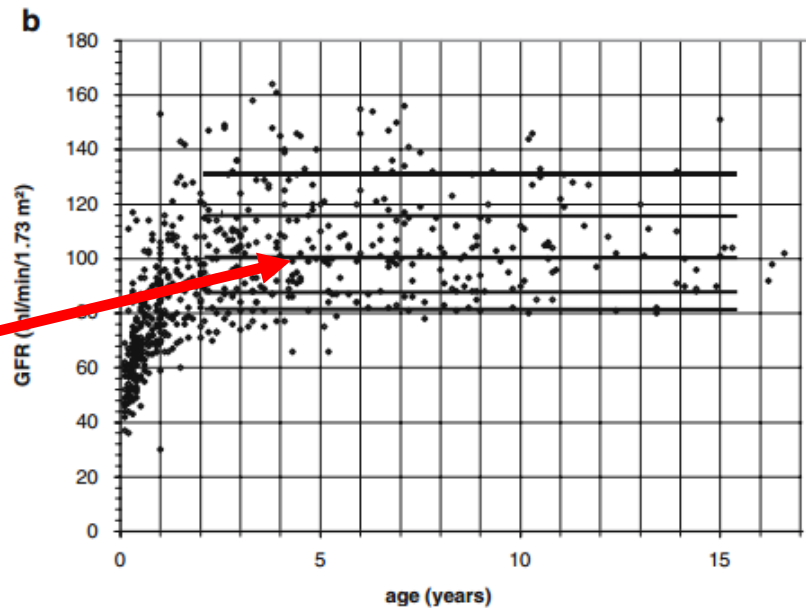
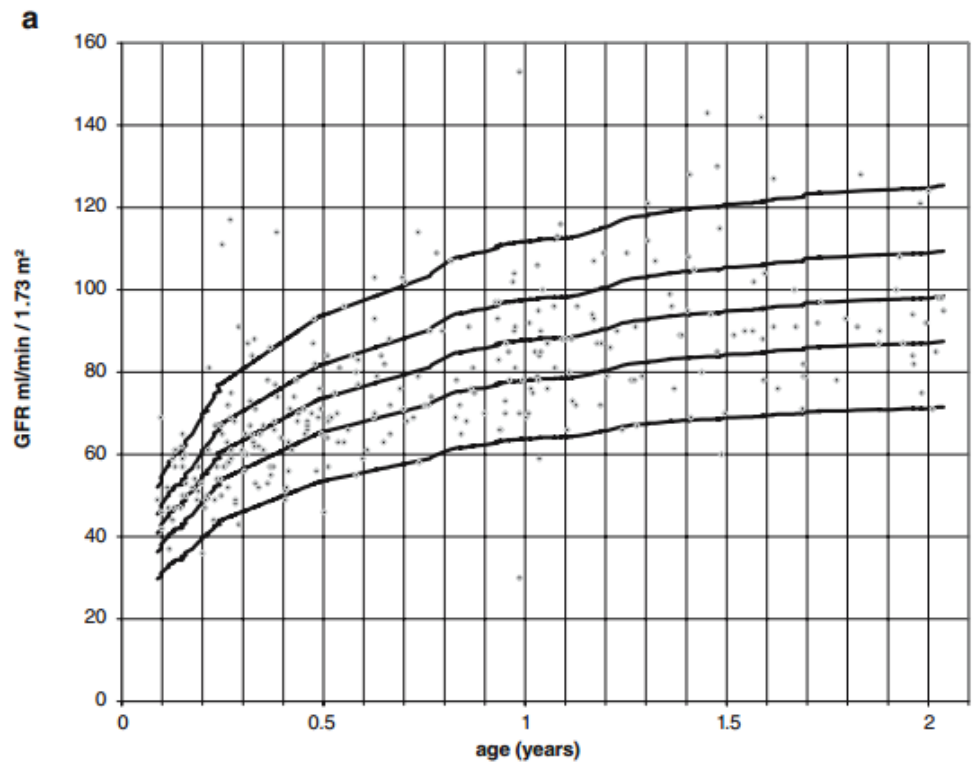
A. Piepsz¹, M. Tondeur¹, H. Ham²

¹ CHU St Pierre, Department of Radiolotopes, 322, Rue Haute, 1000 Brussels, Belgium

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© Springer-Verlag 2006

Eur J Nucl Med Mol Imaging (2006) 33:1477–1482
DOI 10.1007/s00259-006-0179-2



104
mL/min/1.73m²

A Simple Estimate of Glomerular Filtration Rate in Children Derived From Body Length and Plasma Creatinine

G. J. Schwartz, M.D., G. B. Haycock, M.B., C. M. Edelmann, Jr., M.D., and Adrian Spitzer, M.D.

From the Division of Nephrology, Department of Pediatrics, Albert Einstein College of Medicine and Rose F. Kennedy Center, New York, New York

Pediatrics 1976;58;259

- Développée chez 186 enfants (6 mois à 20 ans) (régression, $r=0,893$)
- GFR \sim clairance de créatinine
- Créatinine mesurée par « Technicon autoanalyzer »
- Validée chez 146 enfants avec clairance de créatinine ($r=0,935$)
- Validée chez 77 enfants avec clairance d'inuline

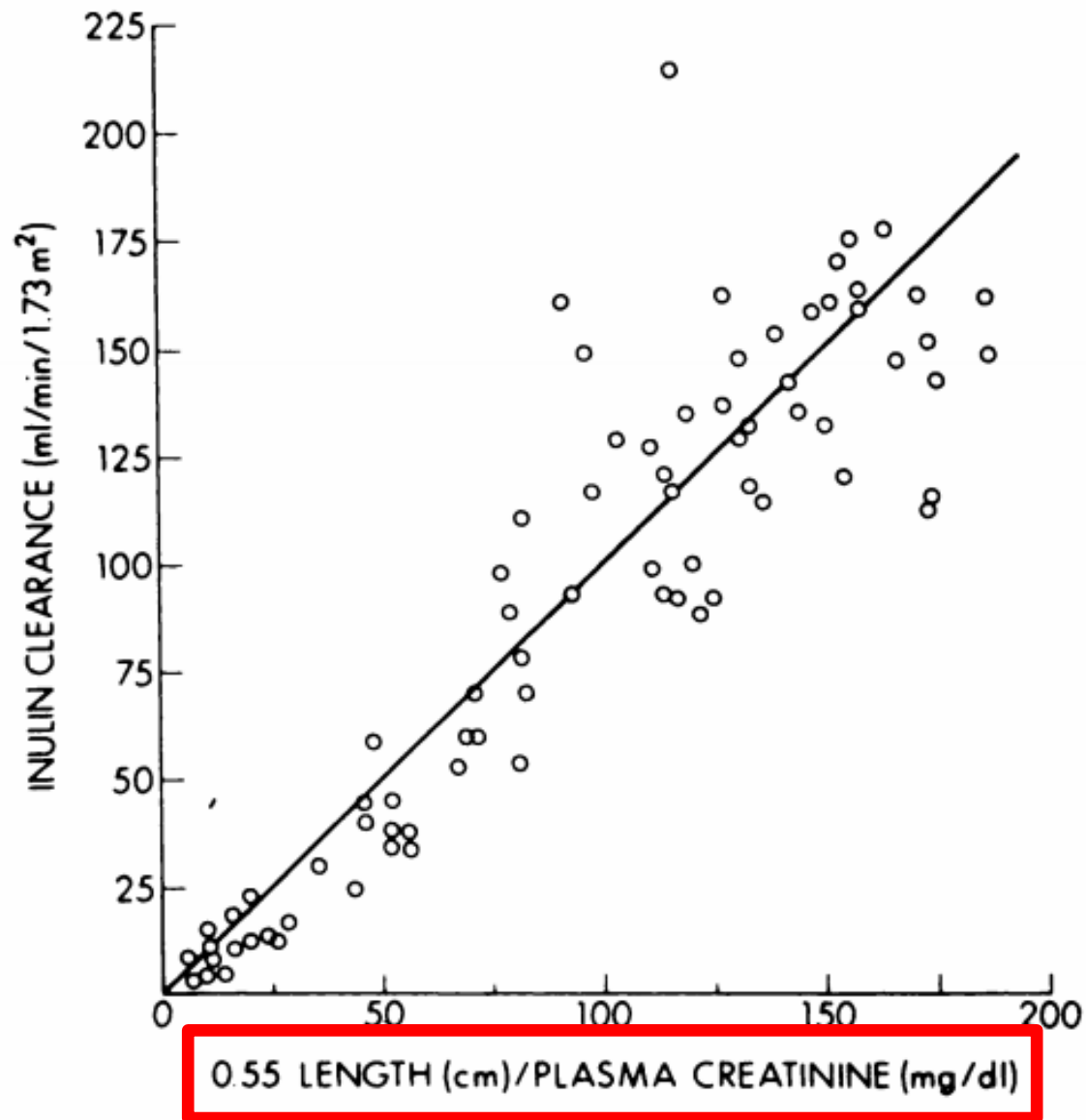


FIG. 4. Relationship between C_{in} and GFR as predicted by the formula $0.55 L/P_{cr}$ (No. = 77; $r = .905$). The line of identity is superimposed.

> [J Pediatr. 1984 Jun;104\(6\):849-54. doi: 10.1016/s0022-3476\(84\)80479-5.](#)

A simple estimate of glomerular filtration rate in full-term infants during the first year of life

K=0,45

> [J Pediatr. 1985 Mar;106\(3\):522-6. doi: 10.1016/s0022-3476\(85\)80697-1.](#)

A simple estimate of glomerular filtration rate in adolescent boys

[G J Schwartz, B Gauthier](#)

K=0,70 à partir de 13 ans chez garçon

K reste à 0,55 chez fille

CRÉATININE MESURÉE PAR JAFFE (SPECIAL) (ET NON STANDARDISÉE)

New Equations to Estimate GFR in Children with CKD

George J. Schwartz,* Alvaro Muñoz,[†] Michael F. Schneider,[†] Robert H. Mak,[‡]
Frederick Kaskel,[§] Bradley A. Warady,^{||} and Susan L. Furth^{†¶}

*Department of Pediatrics, University of Rochester School of Medicine, Rochester, and [§]Department of Pediatrics, Albert Einstein College of Medicine, Bronx, New York; [†]Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health and [¶]Department of Pediatrics, Johns Hopkins School of Medicine, Baltimore, Maryland; [‡]Department of Pediatrics, Children's Hospital of San Diego, San Diego, California; ^{||}Department of Pediatrics, Children's Mercy Hospital, Kansas City, Missouri

J Am Soc Nephrol 20: 629–637, 2009

- Chronic Kidney Disease in Children (CKiD)
- N=349, 61% garçons
- DFG=clairance plasmatique iohexol
- Créatinine enzymatique (Siemens, Advia)
- 1 à 16 ans (médiane: 10,8 ans)
- DFG médian: 41 ml/min/1.73m² (15-75 mL/min/1.73m²)

$$eGFR = 41.3[height/Scr],$$

Table 3. Precision, goodness of fit, and agreement of eGFR derived from coefficients of indicated regression model; n = 349 children of the CKD study^a

Model	eGFR = a [height/Scr] ^b [1.8/Cystatin C] ^c [30/BUN] ^d [e ^{1.20b}] [height/1.4] ^f						RMSE	R ² (%)	% of eGFR within 30% of iGFR	% of eGFR within 10% of iGFR
	a	b	c	d	e	f				
None	41.0 ± 0.8	0	0	0	1	0	0.351	0.0	52.2	20.3
Updated Schwartz	41.3 ± 0.5	1	0	0	1	0	0.223	59.6	79.4	37.0

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**% of eGFR
within 30%
of iGFR**

52.2

79.4

$$eGFR = 41.3[height/Scr],$$

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Model	eGFR = a [height/Scr] ^b [1.8/Cystatin C] ^c [30/BUN] ^d [e ^{1.04b}] [height/1.4] ^f						RMSE	R ² (%)	% of eGFR within 30% of iGFR	% of eGFR within 10% of iGFR
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Updated Schwartz	41.3 ± 0.5	1	0	0	1	0	0.223	59.6	79.4	37.0
IA	41.6 ± 0.4	0.599 ± 0.038	0.317 ± 0.044	0	1	0	0.194	69.4	84.0	38.4
IB	40.7 ± 0.4	0.640 ± 0.035	0	0.202 ± 0.030	1	0	0.196	69.1	83.7	38.4
IC	40.9 ± 0.5	0	0.569 ± 0.045	0.313 ± 0.032	1	0	0.226	58.6	78.2	35.0
II	41.1 ± 0.4	0.510 ± 0.039	0.272 ± 0.043	0.171 ± 0.029	1	0	0.185	72.3	86.3	38.7
III	39.1 ± 0.6	0.516 ± 0.037	0.294 ± 0.041	0.169 ± 0.027	1.099 ± 0.021	0.188 ± 0.048	0.176	75.2	87.7	45.6

^aeGFR and iGFR, mL/min per 1.73m²; height, m; Scr, mg/dL; cystatin C, mg/L; BUN, mg/dL. Entries for a through f are regression coefficient ± SE. RMSE, root mean square error.

Taille chez MRC = ?

K unique donc pas valable chez ado plus vieux et jeune enfant

Updated “bedside” equation

Age- and sex-dependent clinical equations to estimate glomerular filtration rates in children and young adults with chronic kidney disease



see commentary on page 808

Christopher B. Pierce¹, Alvaro Muñoz¹, Derek K. Ng¹, Bradley A. Warady², Susan L. Furth³ and George J. Schwartz⁴

¹Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland, USA; ²Division of Pediatric Nephrology, Children's Mercy Kansas City, Kansas City, Missouri, USA; ³Department of Pediatrics, Perelman School of Medicine at the University of Pennsylvania, and Division of Nephrology, Children's Hospital of Philadelphia, Philadelphia, Pennsylvania, USA; and ⁴Department of Pediatrics, Pediatric Nephrology, University of Rochester Medical Center, Rochester, New York, USA

Kidney International (2021) **99**, 948–956;

- Chronic Kidney Disease in Children (CKiD)
- N=928 (2655 résultats) (37% filles)
- DFG=clairance plasmatique iohexol
- Créatinine et cystatine C standardisées
- 1 à 25 ans (médiane: 13 ans)
- DFG médian: 41 à 49 ml/min/1.73m²

Table 2 | Sex-specific values of *K* in constant and age-dependent models for *height/sCr* and *1/cysC* glomerular filtration rate estimating equations

Age, yr	K for height / sCr			
	Male (N = 387; 1093 pv) ^a		Female (N = 231; 671 pv) ^a	
	Constant	Age dependent	Constant	Age dependent
1–12		$39.0 \times 1.008^{(\text{age}-12)}$		$36.1 \times 1.008^{(\text{age}-12)}$
12–15	41.8	$39.0 \times 1.045^{(\text{age}-12)}$	37.6	$36.1 \times 1.023^{(\text{age}-12)}$
15–18				
18–25		50.8		41.4

CysC, cystatin-C; pv, person-visits; sCr, serum creatinine.

^aThe number of participants and pv in the model training data set. CysC was missing for 81 pv in the training data.

Height is measured in meters; sCr, mg/dl; and cysC, mg/L.

eGFR equation	Arithmetic bias, eGFR – mGFR (95% CI) ^a		p10: eGFR within 10% of mGFR		p30: eGFR within 30% of mGFR	
	Aged <18 yr	Aged ≥18 yr	Aged <18 yr	Aged ≥18 yr	Aged <18 yr	Aged ≥18 yr
	Plasma/sCr-based equations					
CKiD U25 age and sex dependent	0.0 (–0.9 to 1.0)	0.7 (–1.6 to 3.0)	36.4	44.9	86.2	90.7
CKiD “bedside”	2.3 (1.1 to 3.5)	–5.4 (–7.7 to –3.1)	34.6	33.6	77.2	86.0

CKiD U25 equation

eGFR equation	Arithmetic bias, eGFR – mGFR (95% CI) ^a		p10: eGFR within 10% of mGFR		p30: eGFR within 30% of mGFR		Test RMSE ^b	
	Aged <18 yr	Aged ≥18 yr	Aged <18 yr	Aged ≥18 yr	Aged <18 yr	Aged ≥18 yr	Aged <18 yr	Aged ≥18 yr
	Plasma/sCr-based equations							
CKiD U25 age and sex dependent	0.0 (–0.9 to 1.0)	0.7 (–1.6 to 3.0)	36.4	44.9	86.2	90.7	9.9	9.6
Full age spectrum (FAS)								
Q(age)	3.8 (2.7 to 4.9)	5.9 (3.4 to 8.3)	36.9	36.4	77.8	77.6	12.1	11.6
Q(height)	2.2 (1.1 to 3.2)	0.5 (–2.1 to 3.2)	38.0	43.0	82.1	87.9	10.6	11.0

CKiD U25 equation

What else?

L'équation 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
Black		
Female	≤ 62 (≤ 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	≤ 80 (≤ 0.9)	$\text{GFR} = 163 \times (\text{Scr}/0.9)^{-0.411} \times (0.993)^{\text{Age}}$
	> 80 (> 0.9)	$\text{GFR} = 163 \times (\text{Scr}/0.9)^{-1.209} \times (0.993)^{\text{Age}}$
White or other		
Female	≤ 62 (≤ 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	≤ 80 (≤ 0.9)	$\text{GFR} = 141 \times (\text{Scr}/0.9)^{-0.411} \times (0.993)^{\text{Age}}$
	> 80 (> 0.9)	$\text{GFR} = 141 \times (\text{Scr}/0.9)^{-1.209} \times (0.993)^{\text{Age}}$

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

VOLUME 3 | ISSUE 1 | JANUARY 2013

<http://www.kidney-international.org>



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”
- 7 + 6 cohortes
- « Caucasiens »

1-18 ans

- Développement: n=2056
- Validation interne: n=695
- Validation externe: n=1254

TOTAL: 4,005

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:

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

Females:

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

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.

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

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

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

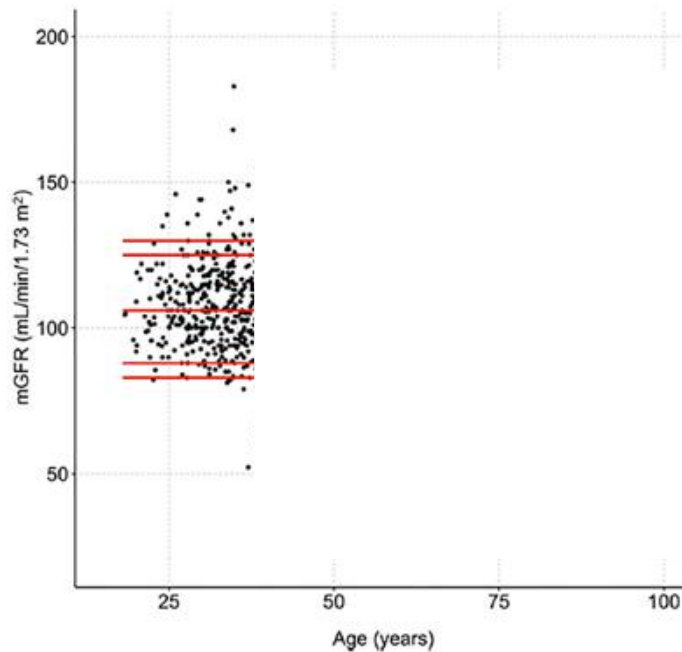


Figure 3: mGFR according to age in the development (dark dots) and external validation cohort (n=329) (gray dots). Red lines are percentiles 5, 10, 50, 90 and 95, calculated from kidney donors younger than 65 years and extrapolated for ages >65 years.

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

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

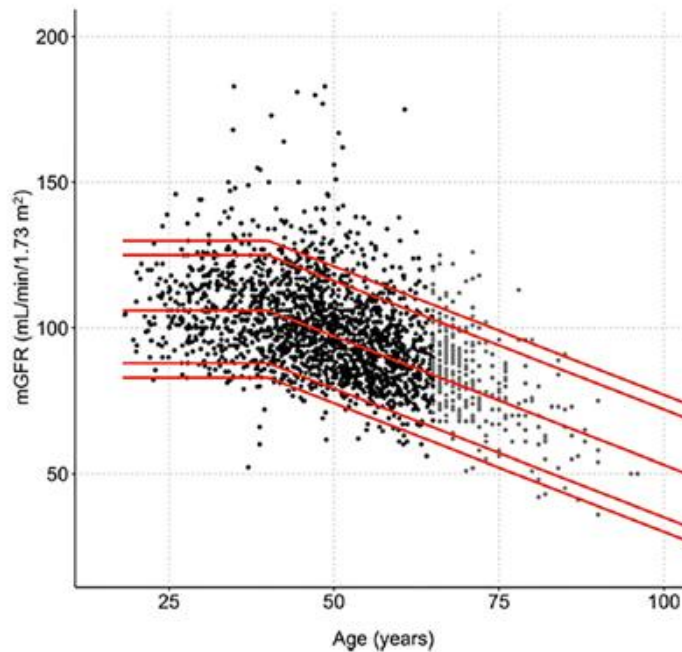
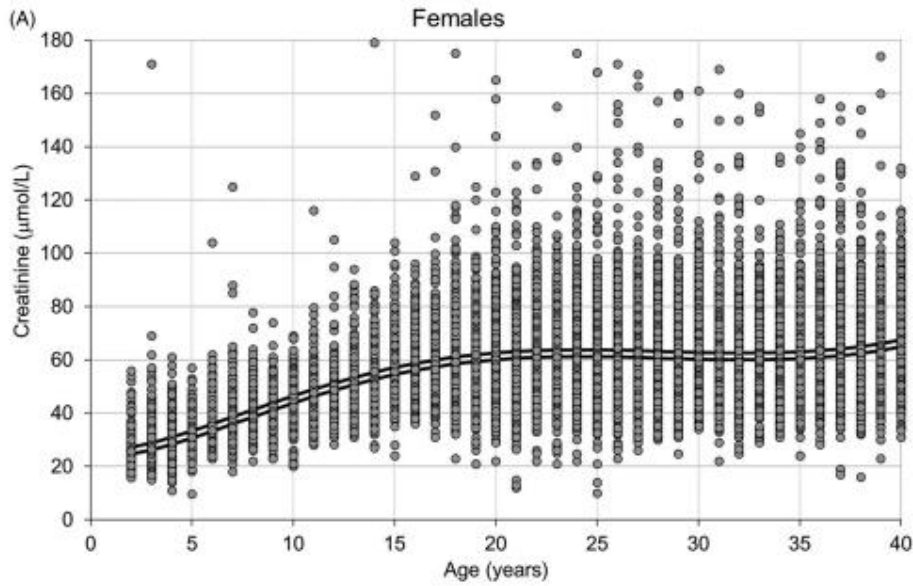
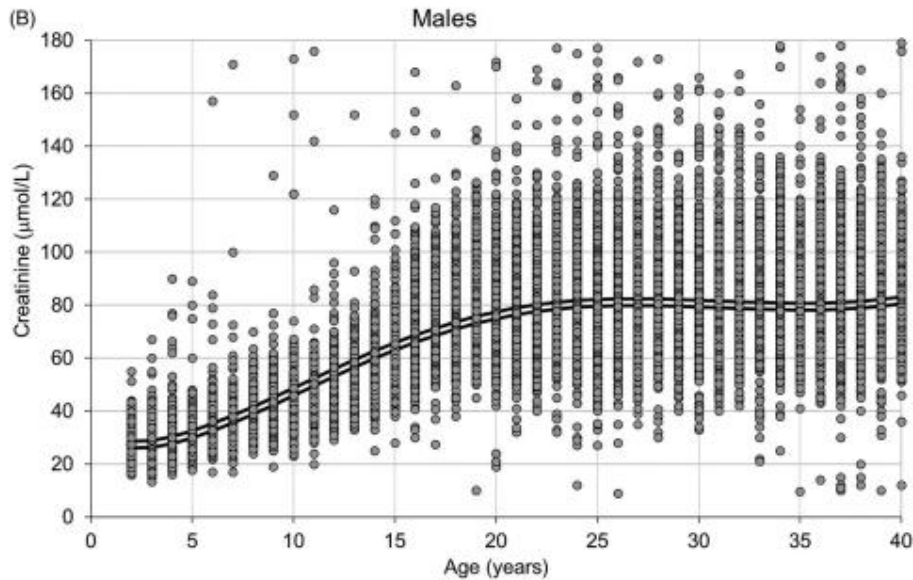


Figure 3: mGFR according to age in the development (dark dots) and external validation cohort (n=329) (gray dots). Red lines are percentiles 5, 10, 50, 90 and 95, calculated from kidney donors younger than 65 years and extrapolated for ages >65 years.



N=83,257 de 3 labos (Suède, Belgique)

62 $\mu\text{mol/L}$ = 0,70 mg/dL



80 $\mu\text{mol/L}$ = 0,90 mg/dL

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:

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

Females:

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

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 1. The new EKFC equation.

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

Q Values

For ages 2–25 y:

Males:

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

Females:

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

For ages >25 y:

Males:

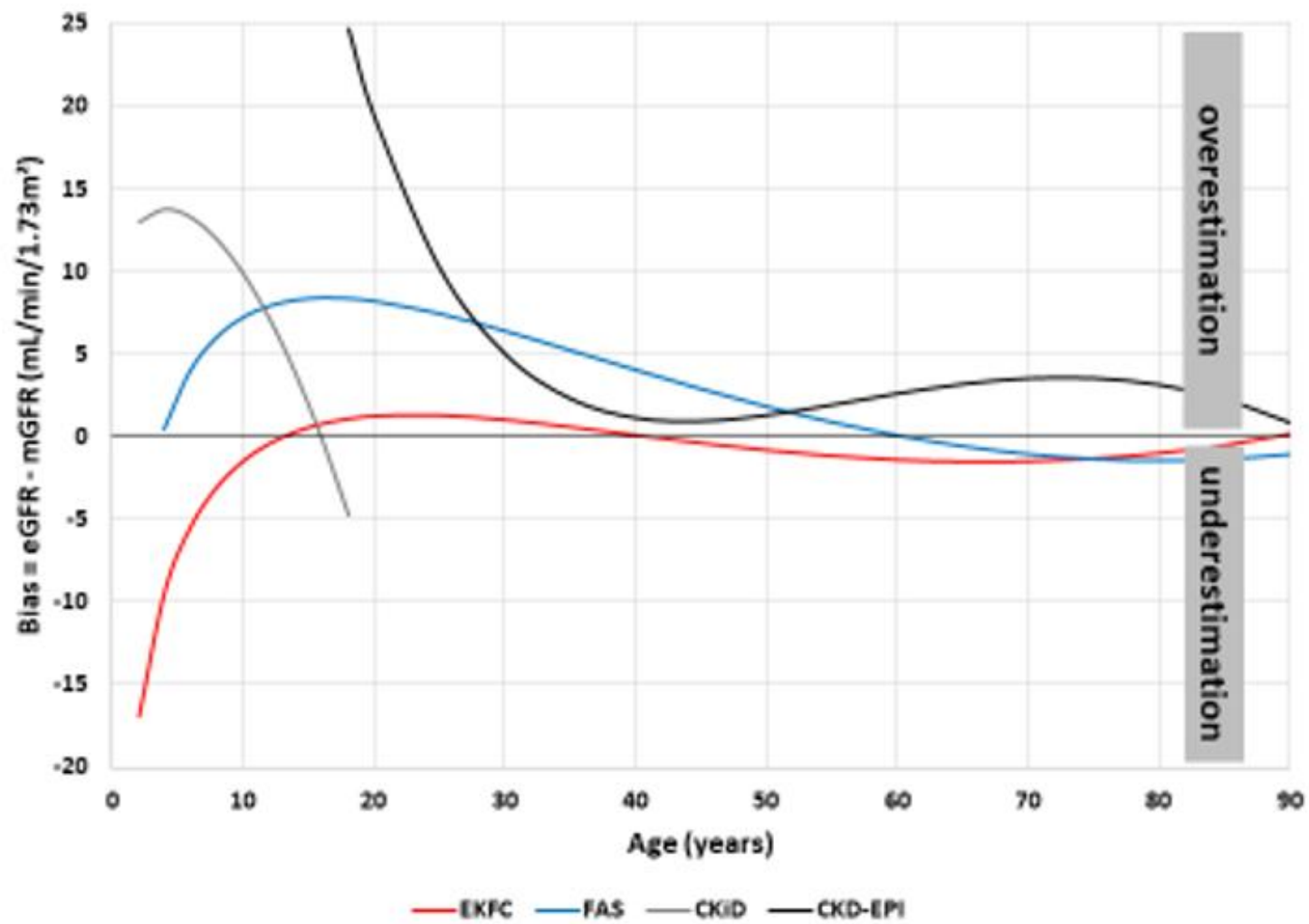
$$Q = 80 \mu\text{mol/L} (0.90 \text{ mg/dL})$$

Females:

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

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.



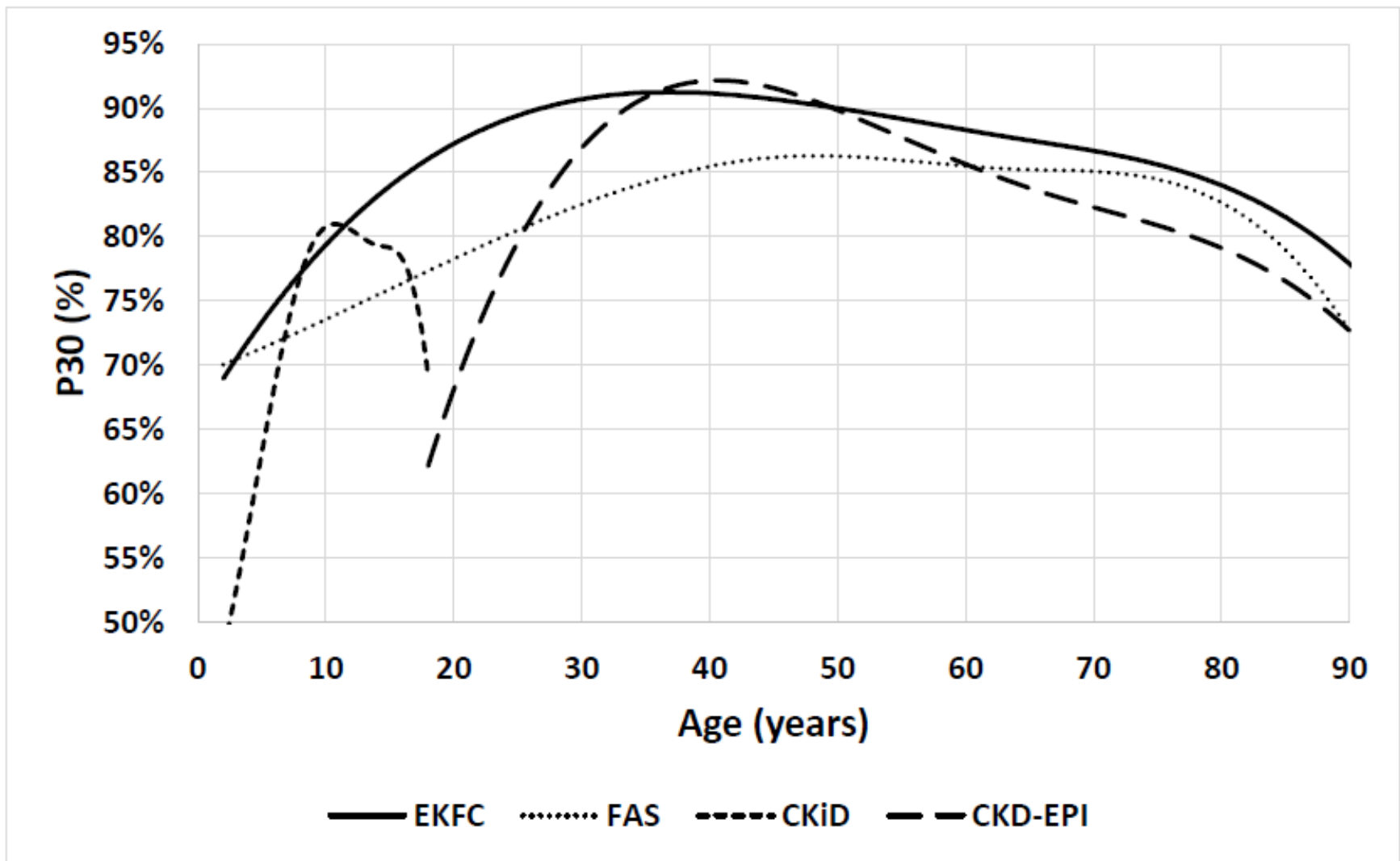


Figure S8. P30-accuracy against age for the EKFC, FAS, CKiD and CKD-EPI equation in the external validation dataset. P30 (%) was graphically presented across the age spectrum using cubic splines with two free knots and using 3rd degree polynomials.

Table 1. Performance Statistics for the EKFC, FAS, CKiD, and CKD-EPI Equations in the External Validation Data Set*

Age Group	Equation		
	EKFC	FAS	CKiD
Children (2 to <18 y)			
Median bias (95% CI), mL/min/1.73 m ²			
All (n = 1254)	-1.2 (-2.7 to 0.0)	6.7 (4.8 to 8.1)	6.2 (4.6 to 7.7)
eGFR <75 mL/min/1.73 m ² (n = 324)	-5.7 (-7.0 to -3.9)	-0.8 (-2.6 to 0.8)	-1.8 (-2.9 to -0.1)
eGFR ≥75 mL/min/1.73 m ² (n = 930)	1.1 (-0.4 to 3.0)	10.8 (9.0 to 13.1)	11.2 (9.2 to 13.4)
Imprecision, SD (P25-P75)			
All (n = 1254)	27.8 (-14.9 to 11.0)	70.6 (-7.4 to 22.8)	56.6 (-7.7 to 23.6)
eGFR <75 mL/min/1.73 m ² (n = 324)	20.3 (-18.1 to 2.3)	20.0 (-12.2 to 7.6)	18.2 (-10.2 to 7.2)
eGFR ≥75 mL/min/1.73 m ² (n = 930)	29.6 (-14.4 to 14.3)	80.1 (-5.3 to 29.1)	63.7 (-6.5 to 30.9)
Accuracy P30 (95% CI), %			
All (n = 1254)	79.7 (77.4 to 81.9)	74.2 (71.7 to 76.6)	73.2 (70.8 to 75.7)
eGFR <75 mL/min/1.73 m ² (n = 324)	73.8 (68.9 to 78.6)	77.8 (73.2 to 82.3)	80.2 (75.9 to 84.6)
eGFR ≥75 mL/min/1.73 m ² (n = 930)	81.7 (79.2 to 84.2)	72.9 (70.0 to 75.8)	70.8 (67.8 to 73.7)

EKFC-Height

$107.3 \times (\text{Scr}/Q)^{-0.322} [\times 0.990^{(\text{Age}-40)} \text{ if age } > 40 \text{ years}] \text{ for } \text{Scr}/Q < 1$
 $107.3 \times (\text{Scr}/Q)^{-1.132} [\times 0.990^{(\text{Age}-40)} \text{ if age } > 40 \text{ years}] \text{ for } \text{Scr}/Q \geq 1 \text{ (Scr in mg/dL or } \mu\text{mol/L)}$
 $Q = 3.94 - 13.4 \times \text{Ht} + 17.6 \times \text{Ht}^2 - 9.84 \times \text{Ht}^3 + 2.04 \times \text{Ht}^4 \text{ (Ht in m, Q in mg/dL } \gg \text{ or multiply Q by 88.4}$
 to convert to $\mu\text{mol/L}$)
 $Q = 0.90 \text{ mg/dL (80 } \mu\text{mol/L) when Ht } > 1.81 \text{ m}$

Table S6a. Median bias (eGFR – mGFR) (in mL/min/1.73m²) in age subgroups of the external validation dataset. Results have grey background when |bias| ≥ 10 mL/min/1.73m².

Age	N	EKFC	EKFC-Ht	KDIGO
[02-04]	134	-10.9	-7.4	13.2
[04-06]	122	-7.1	-1.9	16.0
[06-08]	133	-6.9	-3.8	10.9
[08-10]	75	-4.4	-2.0	11.5
[10-12]	121	-2.6	-5.8	8.8
[12-14]	196	1.5	-1.5	5.6
[14-16]	215	1.8	1.1	3.3
[16-18]	258	2.0	2.8	-2.1

Table S7a. P30-values (%) in age subgroups. P30-values < 75% are shaded in grey.

Age range	N	EKFC	EKFC-Ht	KDIGO
[02-04]	134	63.4%	69.4%	52.2%
[04-06]	122	72.1%	77.9%	60.7%
[06-08]	133	81.2%	82.7%	70.7%
[08-10]	75	90.7%	90.7%	84.0%
[10-12]	121	84.3%	85.1%	78.5%
[12-14]	196	87.8%	87.8%	81.1%
[14-16]	215	80.0%	85.1%	78.1%
[16-18]	258	79.1%	79.8%	75.6%

The Modified CKiD Study Estimated GFR Equations for Children and Young Adults Under 25 Years of Age: Performance in a European Multicenter Cohort



Ulf Nyman, MD, PhD, Jonas Björk, PhD, Ulla Berg, MD, PhD, Arend Bökenkamp, MD, PhD, Laurence Dubourg, MD, PhD, Karolien Goffin, MD, PhD, Anders Grubb, MD, PhD, Magnus Hansson, MD, PhD, Anders Larsson, MD, PhD, Karin Littmann, MD, PhD, Kajsa Åsling-Monemi, MD, PhD, Hans Pottel, PhD, and Pierre Delanaye, MD, PhD

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Table 1. Patient Characteristics of the Cohorts

	Children With Creatinine and Cystatin C Measured (N = 2,293)	Young Adults (N = 1,816)	
		With Creatinine Measured (n = 1,816)	With Cystatin C Measured (n = 348)
Age, y	11.9 (2.3-17.8)	20.0 (18.0-24.6)	18.9 (18.0-24.1)
Female sex	949 (41%)	846 (47%)	144 (41%)
Body mass index, kg/m ²	18 (14-29)	21 (16-31)	22 (15-35)
Body surface area, m ²	1.29 (0.54-2.05)	1.68 (1.29-2.14)	1.73 (1.33-2.36)
Plasma/serum creatinine, μmol/L	52 (19-155)	75 (41-191)	78 (38-196)
Plasma/serum cystatin, mg/L	0.96 (0.61-2.72)	–	0.96 (0.62-2.39)
mGFR, mL/min/1.73 m ²	97 (28-169)	92 (31-141)	91 (30-134)
mGFR <75 mL/min/1.73 m ²	503 (22%)	543 (30%)	95 (27%)

Children defined as aged 2.0-17.9 years; young adults as 18.0-24.9 years. Continuous variables given as median (2.5 and 97.5 percentiles).

Table 2. Bias, Precision, and Accuracy of eGFR Equations in Children and Young Adults

	Creatinine Equations			
	CKiDU25	CKD-EPI40	EKFC	LMR18
Children (n = 2,293 for creatinine equations)				
Bias, median	1.3 (0.6; 2.2)	-5.3 (-6.1; -4.5)	-1.6 (-2.4; -0.4)	-4.5 (-5.3; -3.7)
Precision, IQR	23.6	23.9	23.4	23.0
Accuracy, P ₃₀	83.8 (82.3; 85.3)	83.9 (82.4; 85.4)	85.2 (83.8; 86.7)	86.3 (84.9; 87.8)
P ₃₀ difference	Reference	0.1 (-1.4; 1.6)	1.4 (0.1; 2.7)	2.5 (1.1; 3.8)
Young adults (n = 1,816 for creatinine equations)				
Bias, median	2.1 (1.3; 2.9)	-1.7 (-2.8; -1.1)	2.5 (1.8; 3.1)	-2.6 (-3.5; -1.5)
Precision, IQR	22.3	21.8	21.3	21.5
Accuracy, P ₃₀	82.8 (81.0; 84.5)	85.4 (83.7; 87.0)	84.0 (82.3; 85.7)	86.1 (84.5; 87.7)
P ₃₀ difference	Reference	2.6 (1.2; 4.0)	1.3 (-0.2; 2.7)	3.4 (1.9; 4.8)

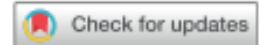
TAILLE !!!!

Stratified for eGFR of creatinine-based equation

eGFR intervals	Stratified for eGFR (CKiDU25)		Stratified for eGFR (EKFC)	
	CKiDU25cr	EKFC	EKFC	CKiDU25cr
<75 mL/min/1.73 m²	n=1012		n=953	
Bias, median	0.9 (0.1; 1.7)	1.6 (0.5; 2.3)	0.4 (-0.4; 1.6)	0.9 (0.0; 1.6)
Precision, IQR	15.9	16.4	15.8	15.5
Accuracy, P ₃₀	82.1 (79.8; 84.5)	77.7 (75.1; 80.2)	78.5 (75.9; 81.1)	81.7 (79.3; 84.2)
-difference	Reference	-4.5 (-6.4; -2.5)	Reference	3.2 (1.5; 5.0)
≥75 mL/min/1.73 m²	n=3097		n=3156	
Bias, median	2.1 (1.3; 2.9)	0.0 (-0.8; 0.9)	0.6 (-0.2; 1.3)	2.1 (1.3; 2.9)
Precision, IQR	26.5	25.4	25.2	26.5
Accuracy, P ₃₀	83.8 (82.5; 85.1)	87.0 (85.8; 88.2)	86.6 (85.4; 87.8)	83.8 (82.6; 85.1)
-difference	Reference	3.2 (2.1; 4.4)	Reference	-2.7 (-3.9; -1.6)

Bias (median error eGFR-mGFR) and precision (interquartile range eGFR-mGFR, IQR), and accuracy expressed in percentage of GFR estimates within ±30 % of mGFR (P₃₀). Differences in P₃₀ were hence evaluated statistically using 95% confidence intervals for paired proportions. CKiDU25 = Chronic Kidney Disease in Children equation for individuals under 25 years [6] and EKFC = European Kidney Function Consortium equation [1].

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

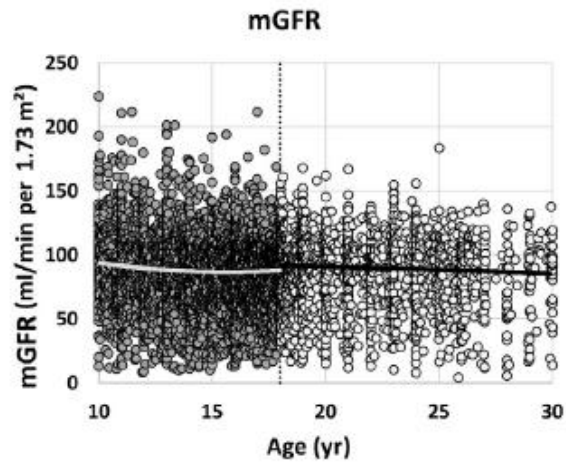
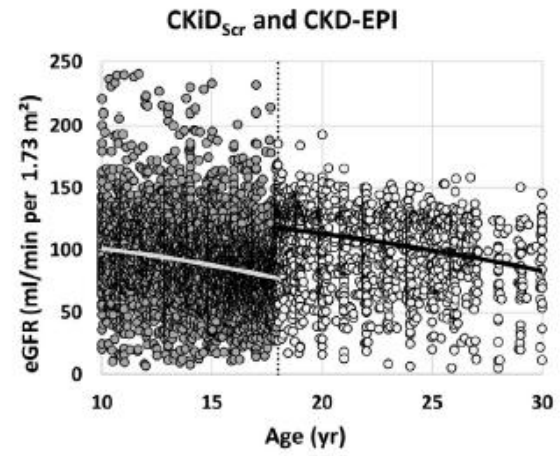
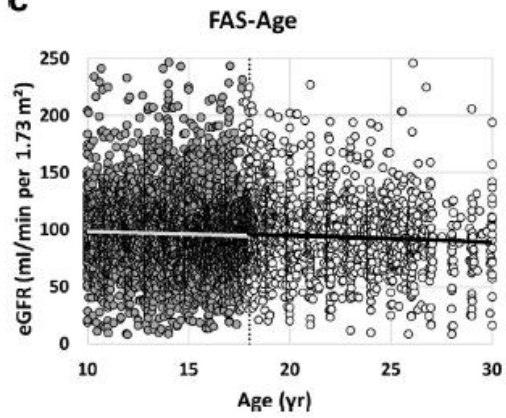


Hans Pottel^{1,13}, Jonas Björk^{2,3,13}, Arend Bökenkamp^{4,13}, Ulla Berg⁵, Kajsa Åsling-Monemi⁵, Luciano Selistre⁶, Laurence Dubourg^{7,13}, Magnus Hansson⁸, Karin Littmann⁸, Ian Jones⁹, Per Sjöström⁹, Ulf Nyman^{10,12,13} and Pierre Delanaye^{11,12,13}

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Kidney International (2019) **95**, 1234–1243;

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

a**b****c**

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
- Meilleur que Schwartz/Ckid dans les valeurs normales de DFG, moins bonne dans les valeurs basses
- Attention chez jeune enfant

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

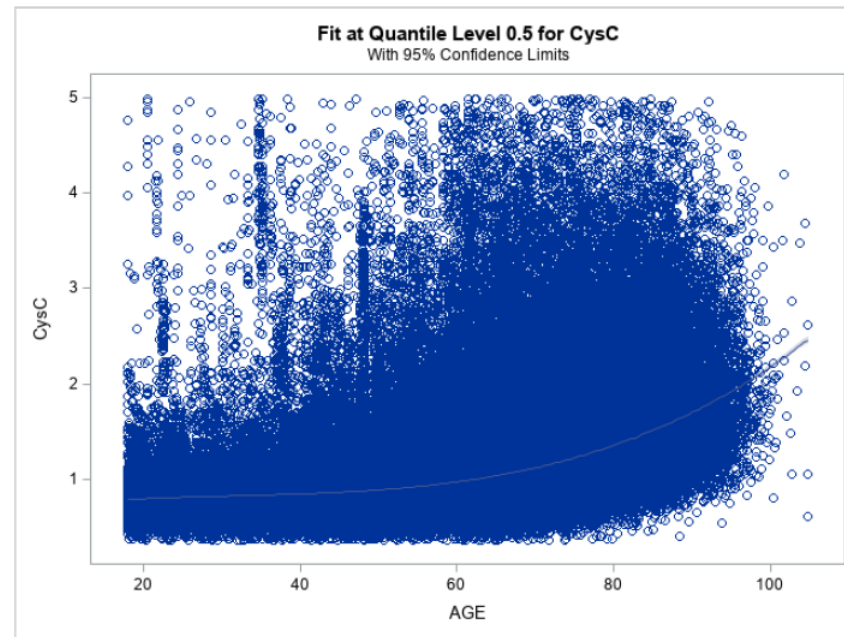
ABSTRACT

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

1^{er} étape: cystatine C et âge

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

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

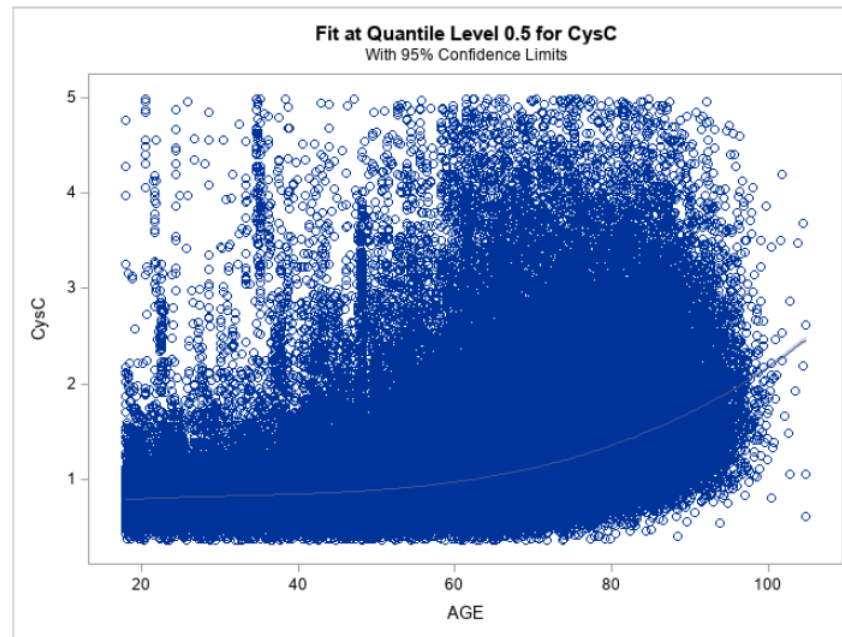


$$\begin{aligned} \text{♀ } Q' &= 0.79 \text{ mg/L jusqu'à 50 ans,} \\ & Q' = 0.79 + 0.005 \times (\text{Age} - 50) \\ \text{♂ } Q' &= 0.86 \text{ mg/L jusqu'à 50 ans} \\ & Q' = 0.86 + 0.005 \times (\text{Age} - 50) \end{aligned}$$

1^{er} étape: cystatine C et **sexe**

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

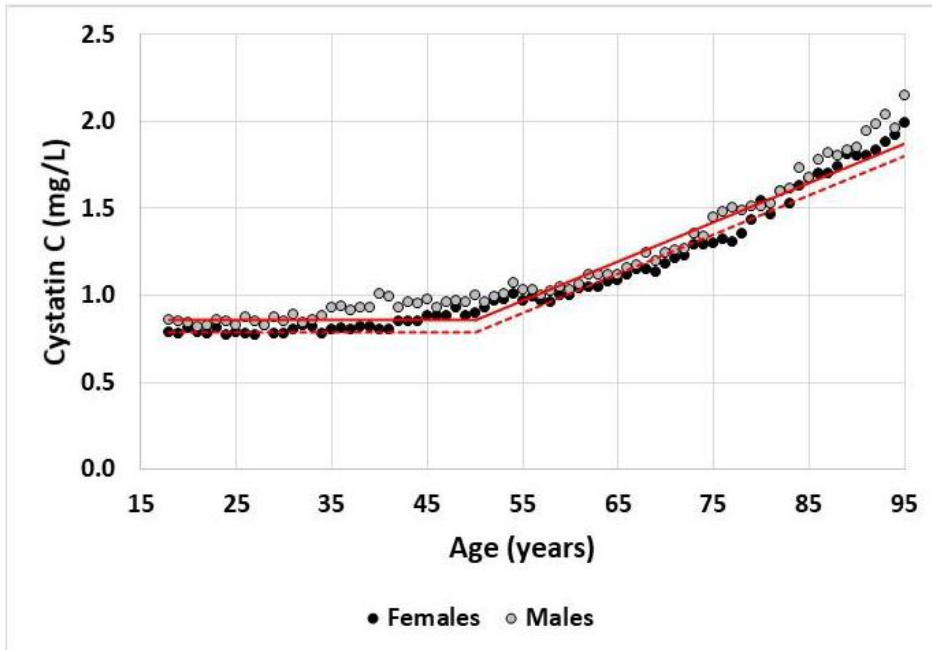
Figure S3. Cystatin C versus age and the median quantile line for the 227,643 included subjects.



♀ $Q' = 0.79 \text{ mg/L}$ 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^{ème} 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^{ème} 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 ²)	mGFR (mL/min/1.73m ²)	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^{ème} étape: Cystatin C et “race”

Analyse matchée 1:1

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

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

Sex	N	Age (years)	BMI (kg/m ²)	mGFR (mL/min/1.73m ²)	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^{ème} 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.

Adultes

DFGm, créatinine et cystatine C calibrées

N=12,832

11 cohortes

Européens blancs: n=7,727

Européens blancs de Paris: n=2,646

US blancs: n=1,093

Européens noirs de Paris: n=858

Africains noirs: n=508

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

Variable	Serum Creatinine–Based Equations		
	CKD-EPI eGFR _{cr} (ASR)	CKD-EPI eGFR _{cr} (AS)	EKFC eGFR _{cr}
EKFC cohort, 7727 White patients			
Median bias (95% CI) — ml/min/1.73 m ² †	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 ² ‡	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 ² §	14.8 (14.4 to 15.2)	16.3 (15.9 to 16.6)	13.1 (12.8 to 13.4)
P ₃₀ — % (95% CI)¶	40.3 (39.2 to 41.4)	34.7 (33.6 to 35.8)	43.3 (42.2 to 44.4)
P ₉₀ — % (95% CI)‖	81.6 (80.8 to 82.5)	75.7 (74.8 to 76.7)	85.8 (85.0 to 86.5)

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

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

Variable	Cystatin C–Based Equations	
	CKD-EPI eGFR _{cys}	EKFC eGFR _{cys} without Sex
EKFC cohort, 7727 White patients		
Median bias (95% CI) — ml/min/1.73 m ² †	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 ² ‡	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 ² §	15.8 (15.5 to 16.1)	13.5 (12.9 to 14.1)
P ₃₀ — % (95% CI)¶	32.0 (31.0 to 33.0)	41.7 (40.6 to 42.8)
P ₃₀ — % (95% CI)‖	80.8 (79.9 to 81.7)	86.2 (85.4 to 87.0)

Cystatin C–Based Equations

CKD-EPI eGFR _{cys}	EKFC eGFR _{cys} without Sex
0.28 (–0.02 to 0.64)	0.00 (–0.37 to 0.27)
19.1 (–7.9 to 11.2)	14.4 (–7.9 to 6.5)
15.8 (15.5 to 16.1)	13.5 (12.9 to 14.1)
32.0 (31.0 to 33.0)	41.7 (40.6 to 42.8)
80.8 (79.9 to 81.7)	86.2 (85.4 to 87.0)

Table 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 _{cr} (ASR)	CKD-EPI eGFR _{cr} (AS)	EKFC eGFR _{cr}	CKD-EPI eGFR _{cys}	EKFC eGFR _{cys} without Sex
EKFC cohort, 7727 White patients					
Median bias (95% CI) — ml/min/1.73 m ² †	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 ² ‡	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 ² §	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 ₃₀ — % (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 ₉₀ — % (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 2. Performance of Combined Serum Creatinine– and Cystatin C–Based Equations to Estimate GFR.*

Variable	CKD-EPI eGFR _{cr-cys} (ASR)	CKD-EPI eGFR _{cr-cys} (AS)	EKFC eGFR _{cr-cys} without Sex
EKFC cohort, 7727 White patients			
Median bias (95% CI) — ml/min/1.73 m ² †	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 ² ‡	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 ² §	13.1 (12.8 to 13.4)	14.7 (14.4 to 15.0)	11.3 (11.0 to 11.6)
P ₁₀ — % (95% CI) ¶	41.5 (40.4 to 42.6)	37.2 (36.2 to 38.3)	48.9 (47.8 to 50.0)
P ₃₀ — % (95% CI)	88.3 (87.6 to 89.0)	84.2 (83.4 to 85.0)	90.4 (89.8 to 91.1)
Paris cohort, 2646 White patients			
Median bias (95% CI) — ml/min/1.73 m ² †	–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 ² ‡	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 ² §	12.1 (11.6 to 12.7)	12.6 (12.0 to 13.1)	11.8 (11.2 to 12.4)
P ₁₀ — % (95% CI) ¶	43.9 (42.0 to 45.8)	42.3 (40.4 to 44.1)	45.8 (43.9 to 47.7)
P ₃₀ — % (95% CI)	89.7 (88.5 to 90.8)	89.2 (88.0 to 90.4)	92.1 (91.1 to 93.1)
U.S. cohort, 1093 White patients			
Median bias (95% CI) — ml/min/1.73 m ² †	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 ² ‡	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 ² §	18.1 (17.1 to 19.1)	21.0 (20.1 to 22.0)	15.5 (14.3 to 16.7)
P ₁₀ — % (95% CI) ¶	37.1 (34.3 to 40.0)	28.1 (25.4 to 30.8)	45.7 (42.7 to 48.6)
P ₃₀ — % (95% CI)	79.5 (77.1 to 81.9)	72.1 (69.4 to 74.8)	88.7 (86.9 to 90.6)
Paris cohort, 858 Black patients			
Median bias (95% CI) — ml/min/1.73 m ² †	–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 ² ‡	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 ² §	13.3 (11.9 to 14.6)	12.6 (11.2 to 13.9)	11.6 (10.0 to 13.0)
P ₁₀ — % (95% CI) ¶	38.7 (35.4 to 42.0)	38.9 (35.7 to 42.2)	48.3 (44.9 to 51.6)
P ₃₀ — % (95% CI)	87.9 (85.7 to 90.1)	89.0 (87.0 to 91.1)	92.0 (90.1 to 93.8)
African cohort, 508 Black patients			
Median bias (95% CI) — ml/min/1.73 m ² †	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 ² ‡	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 ² §	19.7 (18.2 to 21.1)	17.2 (15.8 to 18.5)	14.7 (13.3 to 16.0)
P ₁₀ — % (95% CI) ¶	28.7 (24.8 to 32.7)	34.3 (30.1 to 38.4)	43.5 (39.2 to 47.8)
P ₃₀ — % (95% CI)	75.0 (71.2 to 78.8)	77.6 (73.9 to 81.2)	84.3 (81.1 to 87.4)



Extending the cystatin C based EKFC-equation to children – validation results from Europe

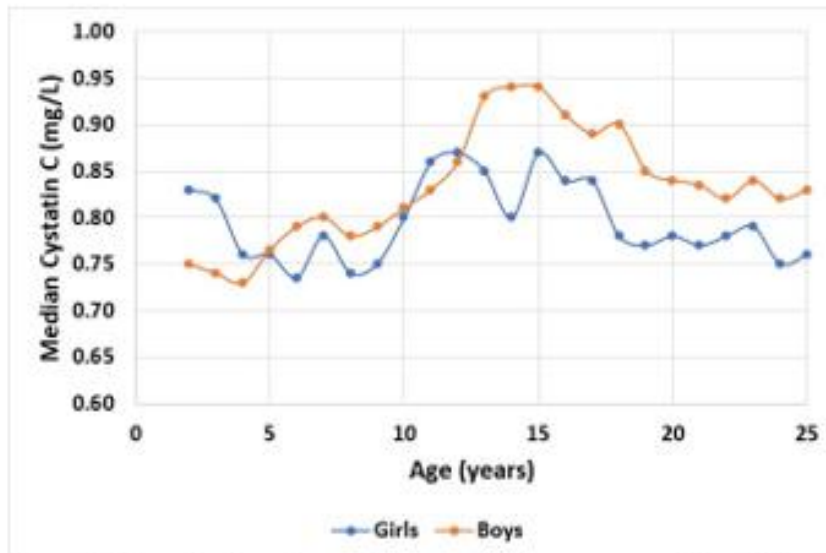
Hans Pottel¹ · Ulf Nyman² · Jonas Björk^{3,4} · Ulla Berg⁵ · Arend Bökenkamp⁶ · Laurence Derain Dubourg⁷ · Sandrine Lemoine⁷ · Karolien Goffin⁸ · Anders Grubb⁹ · Magnus Hansson¹⁰ · Anders Larsson¹¹ · Karin Littmann¹² · Kajsa Åsling-Monemi⁵ · Khosrow Adeli¹³ · Etienne Cavalier¹⁴ · Pierre Delanaye^{15,16}

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Table 1 Patient characteristics of the validation dataset $n=2,293$

Age (years)	11.9 (2.3–17.8)
Females, number (%)	949 (41)
Body mass index	18 (14–29)
Body surface area (m ²)	1.29 (0.54–2.05)
Plasma/serum creatinine (μmol/L; mg/dL)	52 (19–155); 0.59 (0.21– 1.75)
Plasma/serum cystatin C (mg/L)	0.96 (0.61–2.72)
Measured GFR (mL/min/1.73 m ²)	97 (28–169)
Number below 75 mL/min/1.73 m ² (%)	503 (22)

Continuous variables are presented as median (2.5th–97.5th Percentiles)



Garçons: 0,83 mg/L
 Filles: 0,81 mg/L

Figure 53. Zooming in on the median cystatin C versus age relationship in children, adolescents and young adults

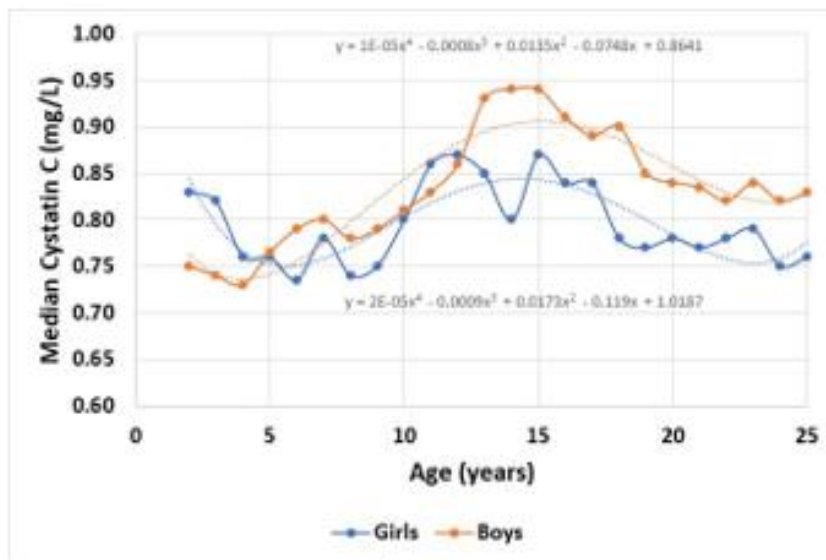


Figure 54. Q-values modelled as 4th degree polynomials

Table 3 Performance characteristics (bias = median of eGFR–mGFR; IQR = interquartile range; P10 and P30 = % of patients with eGFR within 10% or 30% of mGFR) of EKFC-equations (CKiD_{crea} is used as a benchmark) in = 2,293 children (2 – 18 years)

Statistic	CKiD _{Crea}	EKFC _{Crea}	EKFC _{CysC}	EKFC _{CysC-u}	EKFC _{Mean}	EKFC _{Mean-u}
Bias (mL/min/1.73 m ²)	+6.21 [5.1; 7.5]	-1.6 [-2.4; -0.4]	-7.6 [-8.4; -6.5]	-7.6 [-8.6; -6.8]	-4.0 [-4.5; -3.1]	-4.0 [-4.6; -3.2]
IQR [Q1–Q3] (mL/min/1.73 m ²)	27.5 [-6.5; 21.1]	23.4 [-13.9; 9.5]	23.5 [-19.8; +3.6]	24.1 [-21.2; +2.9]	20.4 [-15.5; +5.0]	20.8 [-15.0; +6.3]
P10 (%)	32.9 [31.0; 34.9]	39.9 [37.9; 41.9]	36.9 [34.9; 38.9]	35.6 [33.6; 37.6]	44.4 [42.4; 46.4]	44.3 [42.3; 46.3]
P30 (%)	78.0 [76.3; 79.7]	85.2 [83.8; 86.7]	85.8 [84.4; 87.3]	85.0 [83.6; 86.5]	90.4 [89.2; 91.6]	89.9 [88.7; 91.1]

u = Q-values modelled as 4th degree polynomials based on the Uppsala data

Cystatin C equations

Table S4 Performance characteristics (bias = mean of eGFR – mGFR; IQR = interquartile range; P10/P30 = % of patients with eGFR within 10/30% of mGFR) of cystatin C based equations in = 2,293 children (2 – 18 years)

	CKiDU25	CAPA	CKD-EPI	FAS	EKFC	EKFC-u
Bias	-12.8 [-13.8; -11.8]	-0.6 [-1.7; +0.3]	-2.5 [-3.3; -1.3]	-4.2 [-4.8; -3.4]	-7.6 [-8.4; -6.5]	-7.6 [-8.6; -6.8]
IQR [Q1-Q3]	24.2 [-25.9; -1.7]	26.9 [-13.1; +13.8]	24.5 [-14.0; +10.5]	23.9 [-17.2; +6.8]	23.5 [-19.8; +3.6]	24.1 [-21.2; +2.9]
P10	29.7 [27.9; 31.6]	34.6 [32.6; 36.5]	37.4 [35.4; 39.4]	37.9 [35.9; 39.9]	36.9 [34.9; 38.9]	35.6 [33.6; 37.6]
P30	82.6 [81.0; 84.1]	82.0 [80.4; 83.6]	84.3 [82.9; 85.8]	85.9 [84.5; 87.3]	85.8 [84.4; 87.3]	85.0 [83.6; 86.5]

EKFC-u = EKFC-equation with Q_{cysC} obtained from the 4th degree polynomials fitted on the data from Uppsala

Table S5. Performance characteristics (bias = mean of eGFR – mGFR; IQR = interquartile range; P10/P30 = % of patients with eGFR within 10/30% of mGFR) of the arithmetic mean of the EKFC equations in = 2,293 children (2 – 18 years)

EKFC_{Mean}

	EKFC	EKFC-u
Bias	-4.0 [-4.5; -3.1]	-4.0 [-4.6; -3.2]
IQR [Q1-Q3]	20.4 [-15.5; +5.0]	20.8 [-15.0; +6.3]
P10	44.4 [42.4; 46.4]	44.3 [42.3; 46.3]
P30	90.4 [89.2; 91.6]	89.9 [88.7; 91.1]

Age- and sex-dependent clinical equations to estimate glomerular filtration rates in children and young adults with chronic kidney disease



see commentary on page 808

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Kidney International (2021) **99**, 948–956;

- Chronic Kidney Disease in Children (CKiD)
- N=928 (2655 résultats) (37% filles)
- DFG=clairance plasmatique iohexol
- Créatinine et cystatine C standardisées
- 1 à 25 ans (médiane: 13 ans)
- DFG médian: 41 à 49 ml/min/1.73m²

Table 2 | Sex-specific values of K in constant and age-dependent models for height/sCr and 1/cysC glomerular filtration rate estimating equations

Age, yr	K for height / sCr				K for 1 / cysC						
	Male (N = 387; 1093 pv) ^a		Female (N = 231; 671 pv) ^a		Male (N = 387; 1039 pv) ^a		Female (N = 231; 644 pv) ^a				
	Constant	Age dependent	Constant	Age dependent	Constant	Age dependent	Constant	Age dependent			
1-12		39.0 × 1.008 ^(age-12)		36.1 × 1.008 ^(age-12)		87.2 × 1.011 ^(age-15)		79.9 × 1.004 ^(age-12)			
12-15	41.8	39.0 × 1.045 ^(age-12)	37.6	36.1 × 1.023 ^(age-12)	81.9	87.2 × 0.960 ^(age-15)	74.9	79.9 × 0.974 ^(age-12)			
15-18											
18-25		50.8		41.4				77.1	68.3		

CysC, cystatin-C; pv, person-visits; sCr, serum creatinine.

eGFR equation	Arithmetic bias, eGFR – mGFR (95% CI) ^a		p10: eGFR within 10% of mGFR		p30: eGFR within 30% of mGFR		Test RMSE ^b	
	Aged <18 yr	Aged ≥18 yr	Aged <18 yr	Aged ≥18 yr	Aged <18 yr	Aged ≥18 yr	Aged <18 yr	Aged ≥18 yr
	Plasma/sCr-based equations							
CKiD U25 age and sex dependent	0.0 (-0.9 to 1.0)	0.7 (-1.6 to 3.0)	36.4	44.9	86.2	90.7	9.9	9.6
CKiD "bedside"	2.3 (1.1 to 3.5)	-5.4 (-7.7 to -3.1)	34.6	33.6	77.2	86.0	12.0	11.7
Full age spectrum (FAS)								
Q(age)	3.8 (2.7 to 4.9)	5.9 (3.4 to 8.3)	36.9	36.4	77.8	77.6	12.1	11.6
Q(height)	2.2 (1.1 to 3.2)	0.5 (-2.1 to 3.2)	38.0	43.0	82.1	87.9	10.6	11.0
Lund-Malmö revised for sCr, including those aged <18 yr (LMR18)	-2.3 (-3.5 to -1.2)	-3.8 (-5.9 to -1.6)	29.8	36.4	81.3	88.8	11.6	10.1
Schwartz-Lyon	-2.0 (-3.0 to -0.9)	-7.4 (-9.8 to -5.1)	36.6	30.8	85.6	83.2	10.4	12.7
Flanders metadata (FM)	0.3 (-0.8 to 1.4)	-4.2 (-6.5 to -1.8)	40.2	35.5	83.7	89.7	10.8	11.0
Gao quadratic (GQ)	2.9 (1.7 to 4.1)	-2.1 (-4.3 to 0.1)	28.7	40.2	69.6	89.7	12.4	9.8
IFCC cysC-based equations								
CKiD U25, age and sex dependent	-0.8 (-1.7 to 0.1)	-0.9 (-3.1 to 1.3)	39.3	45.7	86.6	85.7	10.5	10.8
Full age spectrum (FAS)	4.1 (3.2 to 5.1)	8.7 (6.6 to 10.8)	36.9	22.9	79.8	71.4	11.8	13.9
Caucasian, Asian, pediatric and adult (CAPA)	2.2 (1.0 to 3.3)	3.0 (0.6 to 5.3)	30.9	32.4	76.4	81.0	13.5	12.1
Berg	1.4 (0.4 to 2.4)	7.1 (4.5 to 9.8)	35.4	27.6	82.2	76.2	12.5	15.0
Non-IFCC cysC-based equations								
CKiD 2012 ^c	1.9 (1.0 to 2.9)	5.8 (3.7 to 7.8)	38.3	27.6	82.0	75.2	10.9	11.9

Cystatine C

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

<https://ekfccalculator.pages.dev/>



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

1.2.4 Selection of GFR estimating equations

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

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

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

Special considerations

Pediatric considerations

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

Table 14 | Validated GFR estimating equations

Marker	Equation name and year	Age	Variables	Development populations
Creatinine	CKD-EPI 2009 ²³⁸	≥18; modification CKD-EPI 40 for pediatric available	Developed using A, S, R but reported not using the Black race coefficient, A, S, R (NB)	8254 Black and NB individuals from 10 studies in the United States and Europe ^a
	CKiD U25 2021 ²³⁹	1–25	A, S, height	928 children with CKD in the United States and Canada
	CKD-EPI 2021 ¹⁴⁷	≥18	A, S	8254 Black and NB individuals from 10 studies in the United States and Europe ^a
	EKFC 2021 ²⁴⁰	2–100	A, S, European Black and NB specific Q-value; separate Q-values for Africa vs. Europe	mGFR vs. SCr (11,251 participants in 7 studies in Europe and 1 study from the United States) Normal GFR from 5482 participants in 12 studies of kidney donor candidates (100% Caucasian) European NB Q from 83,157 laboratory samples (age 2–40 years) in 3 European hospital clinical laboratories; European Black Q-value (N = 90 living kidney donors from Paris); African Black Q-value (N = 470 healthy individuals from République Démocratique de Congo); All Q-values developed in cohorts independent for EKFC development and validation
Cystatin C	CKD-EPI 2012 ¹⁴⁸	≥18	A, S	5352 Black and NB individuals from 13 studies in the United States and Europe
	EKFC 2023 ⁹¹	18–100	A	mGFR vs. SCys (assumed to be the same as mGFR vs. SCr) Normal GFR (same as for the SCr equation) Q from laboratory samples from 227,643 (42% female) laboratory samples from Uppsala University Hospital, Sweden

Calculateurs DFG (dont EKFC)



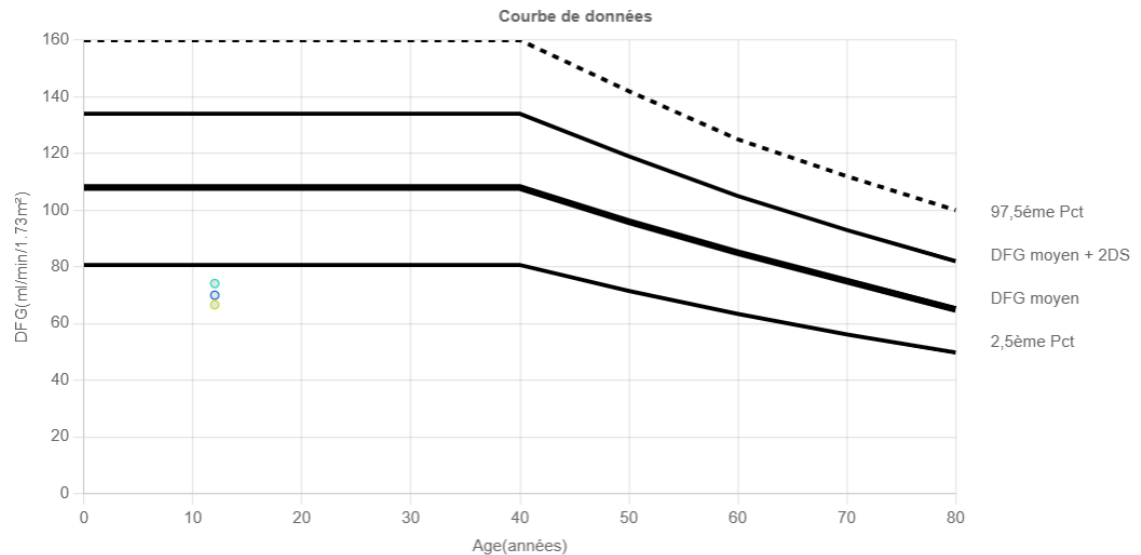
Résultats

EKFC créatinine **82** ml/min/1.73m²

EKFC créatinine taille **67** ml/min/1.73m²

CKiD **74** ml/min/1.73m²

CKiDU25 **70** ml/min/1.73m²



Limitations des formules = créatinine

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

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

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

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

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

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

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

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

Ne pas sur-interpreter un DFG estimé...

Toutes les équations restent des estimations

OK au niveau populationnel

Manque de précision au niveau individuel

Variable	CKD-EPI eGFRcr-cys(ASR)	CKD-EPI eGFRcr-cys(AS)	EKFC eGFRcr-cys without Sex
EKFC cohort, 7727 White patients			
Median bias (95% CI) — ml/min/1.73 m ² †	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 ² ‡	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 ² §	13.1 (12.8 to 13.4)	14.7 (14.4 to 15.0)	11.3 (11.0 to 11.6)
P ₃₀ — % (95% CI)¶	41.5 (40.4 to 42.6)	37.2 (36.2 to 38.3)	48.9 (47.8 to 50.0)
P ₃₀ — % (95% CI)	88.3 (87.6 to 89.0)	84.2 (83.4 to 85.0)	90.4 (89.8 to 91.1)

The applicability of eGFR equations to different populations

Pierre Delanaye and Christophe Mariat



RETOUR à une mesure du DFG

Delanaye P, Nature Rev Nephrol, 2013, 9, p513

Ebert N, Clin Kidney J, 2021, 14, p1861

Agarwal R, Nephrol Dial Transplant, 2019, 34, p2001

Shafi T, Ann Intern Med, 2022, 175, p1073

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

Clairance plasmatique d'iohexol

Pas si difficile

Pas si cher

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

OPEN

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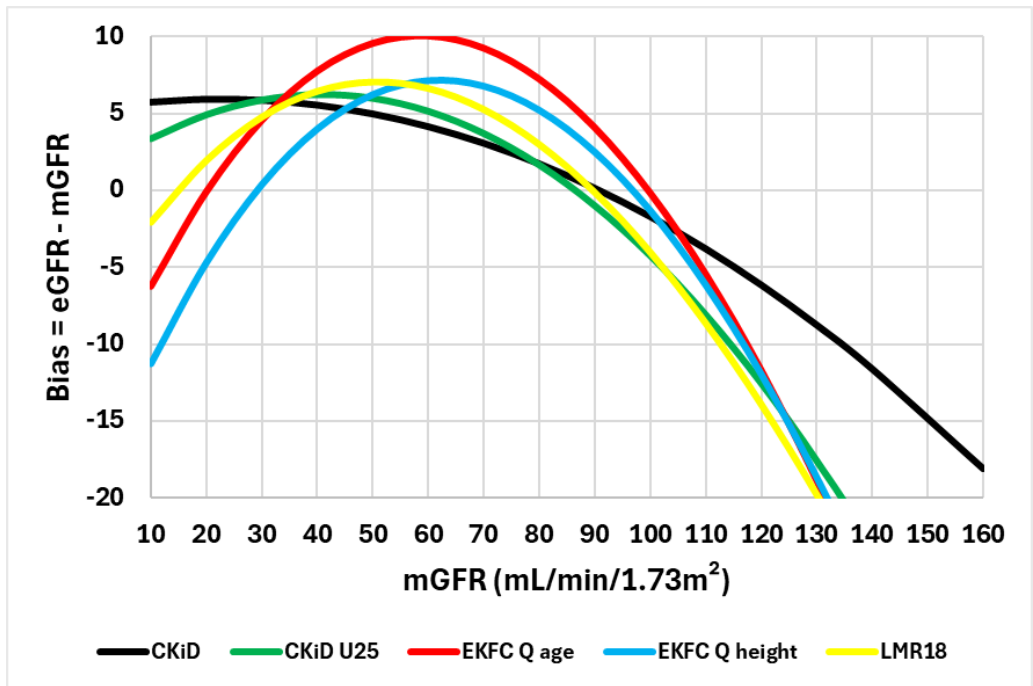
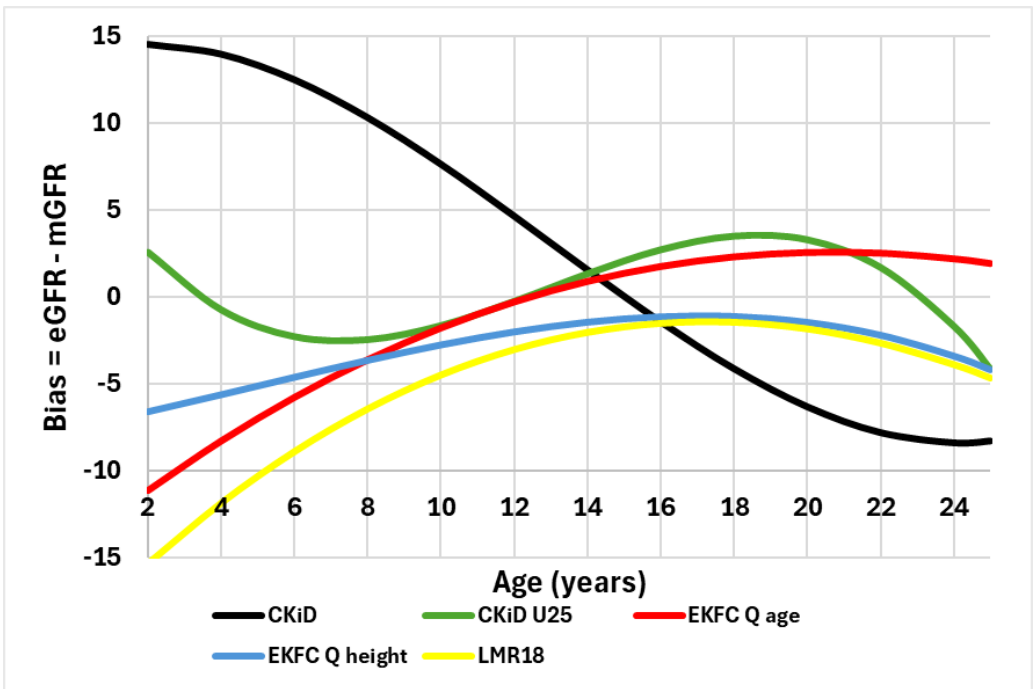


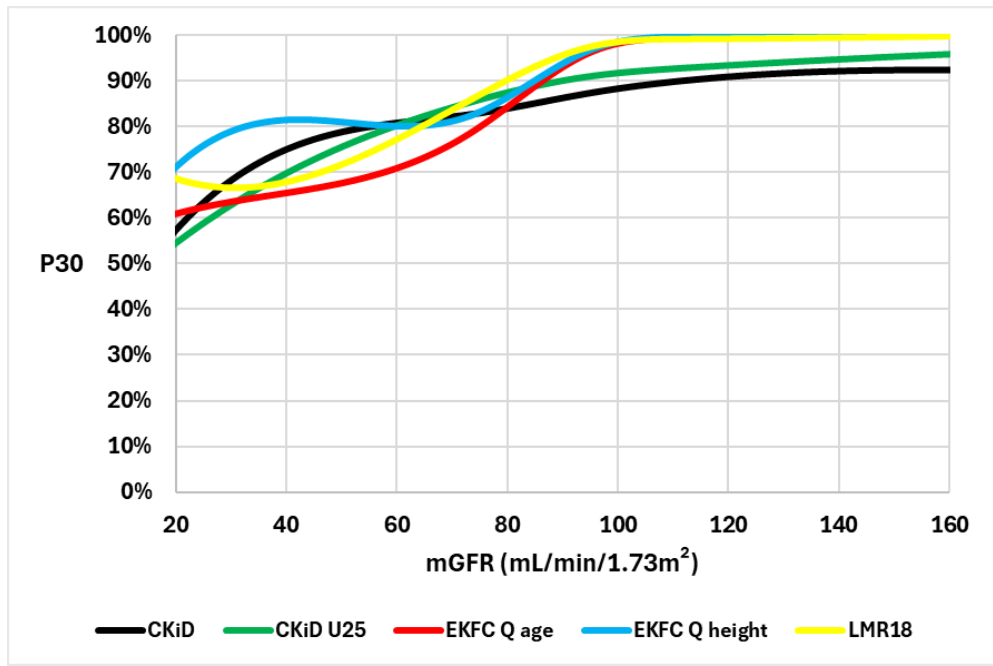
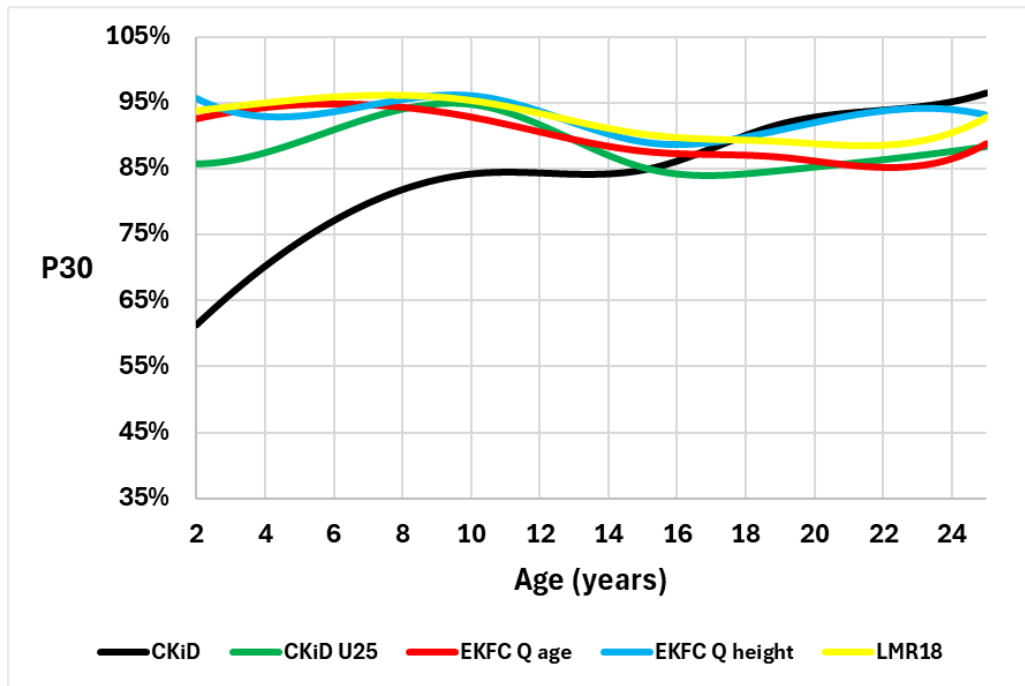
Andrew Rule, Rochester



Merci







3359 garçons (1-25 ans)

	CKiD	CKiD U25	EKFC Q age	EKFC Q height
Bias	-2,45 [-3,08; -1,73]	2,79 [2,15; 3,33]	-0,13 [-0,72; 0,46]	-3,29 [-3,90; -2,73]
IQR	27,3 [-15,8; 11,5]	22,5 [-8,0; 14,5]	22,6 [-12,2; 10,3]	22,5 [-14,8; 7,7]
P20	62,3 [60,6; 63,9]	67,9 [66,3; 69,5]	69,6 [68,1; 71,2]	68,2 [66,6; 69,8]
P30	80,8 [79,5; 82,2]	83,1 [81,8; 84,3]	84,6 [83,4; 85,8]	85,4 [84,2; 86,6]

2599 filles (1-25 ans)

	CKiD	CKiD U25	EKFC Q age	EKFC Q height
Bias	4,91 [4,14; 5,78]	-1,71 [-2,38; -0,64]	0,29 [-0,41; 1,08]	-1,43 [-2,17; -0,79]
IQR	25,3 [-6,7; 18,6]	23,1 [-12,9; 10,2]	23,0 [-11,0; 11,9]	22,9 [-12,7; 10,2]
P20	63,8 [61,9; 65,6]	69,1 [67,4; 70,9]	70,1 [68,4; 71,9]	69,0 [67,2; 70,8]
P30	80,7 [79,2; 82,2]	86,0 [84,7; 87,3]	85,5 [84,1; 86,8]	87,0 [85,7; 88,3]