Glomerular Filtration Rate

eGFR and mGFR

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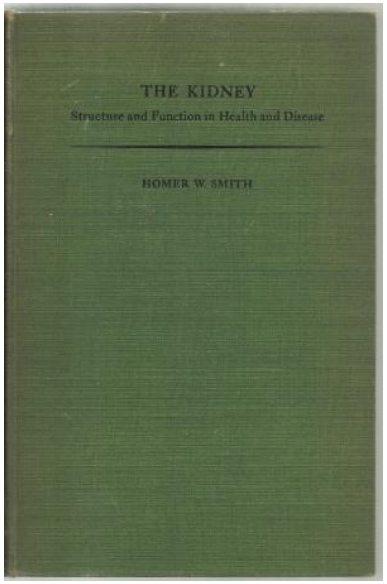
The Glomerular Filtration Rate is usually the best parameter to assess the global kidney function.

So, how to measure (or estimate GFR)?



Renal function: concept of clearance

- Clearance of a solute (ml/min):

  volume of plasma cleared (« purified ») of this substance per time

  $$Cl = [U] \times [V] / [P]$$

- Ideal marker for GFR:
  - Constant production
  - No effect on GFR, non toxic
  - Not bound to protein, freely filtrated through glomerulus
  - No secretion, no absorption in the tubules
  - No extra renal clearance
  - Easy to measure

Serum creatinine

- One of the most prescribed analyte in clinical chemistry
- …but the most important is to know its limitations
- Physiological limitations
- Analytical limitations

Measurements of serum creatinine

- Jaffe method: colorimetric
- Enzymatic methods
- Jaffe and enzymatic methods gives slightly different results

Analytical limitations

- Jaffe: Pseudochromogen: glucose, fructose, ascorbate, proteins, urate, acetoacetate, acetone, pyruvate => false « high »
- Bilirubins: false « low »
- Few (fewer) interferences with enzymatic methods

Analytical limitations

- Different Jaffe-Enzymatic methods, different calibration by different manufacturers

Physiological limitations

- Production (relatively) constant but muscular production => serum creatinine is dependent of muscualr mass, not only GFR
    - gender
    - age
    - ethnicity
    - Muscular mass(creatine)
- Extra-renal production (bacterial)

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

Physiological limitations

Tubular secretion of creatinine

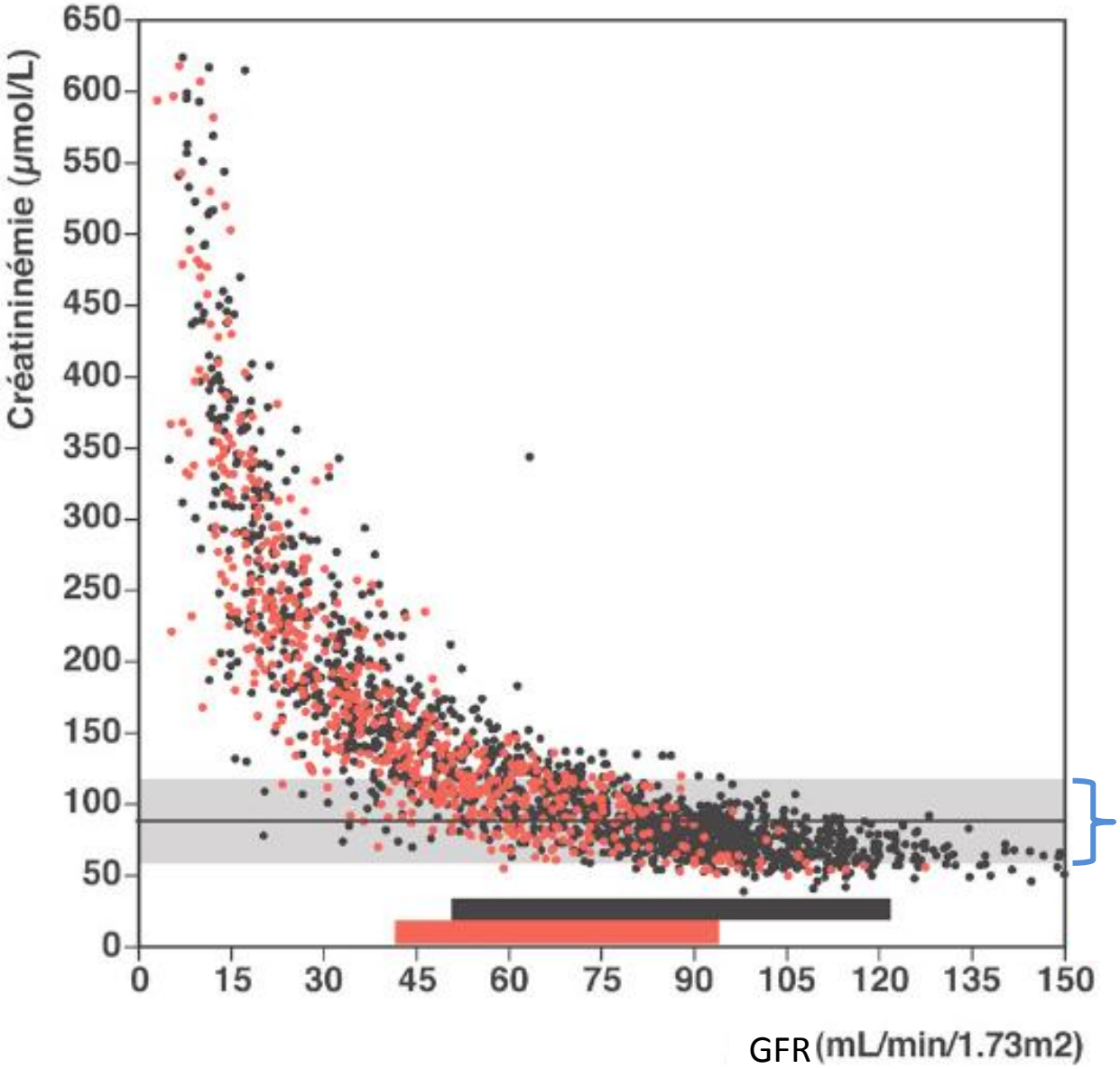
- 10 to 40%
- Increase with decreased GFR
- Unpredictable at the individual level !

Drugs interaction with creatinine

- tubular secretion inhibitor
  cimetidin, trimethoprim
- fibrates
- « high concentrations » interactions
  acetylcystein, dobutamin, lidocain, ascorbate

Creatinine: to the trash?

- Very cheap (0.04€ /Jaffe)
- Good specificty
- Good analytical CV
- Favor for enzymatic methods



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

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

S. Creatinine lab normality range

With the kind permission of Marc Froissart

Serum Creatinine

- Exponential relationship between serum creatinine and GFR!!!

  In a given patient,

  if serum creatinine increased from 0.6 to 1.2 mg/dl
  => decrease in GFR of 50%

  if serum creatinine increased from 2.0 to 3.0 mg/dl
  => decrease in GFR of 25%

Creatinine clearance

- Not recommended by guidelines
- Creatinine tubular secretion
- Lack of precision:

errors in urine collection

22 to 27% for « trained » patients

50 to 70 % for others

large intra-individual variability for creatinine excretion

Creatinine clearance

- The Cockcroft original study
- Final sample n=236
- But the starting sample was 534 with 2 available creatinine clearance in medical wards
- Exclusion of 56% (!) because :

1. Variability of serum creatinine > 20%: n=29
2. Creatinine excretion/24 h < 10 mg/d: n=31
3. Inadequate (?) data: n=65
4. Variability of creatinine excretion > 20%: n=173 (32%)

Creatinine-based equations

Goals of the equations:

- Conceptualize the exponential relationship
- Adapt creatinine for age, gender, ethnicity
- Decrease the IC

Creatinine-based equations

- MDRD, Cockcroft
- Strengths
- Limitations
- CKD-EPI
- Others (FAS)

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

Cockcroft and Gault

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

4-Variable MDRD study equation (IDMS traceable)

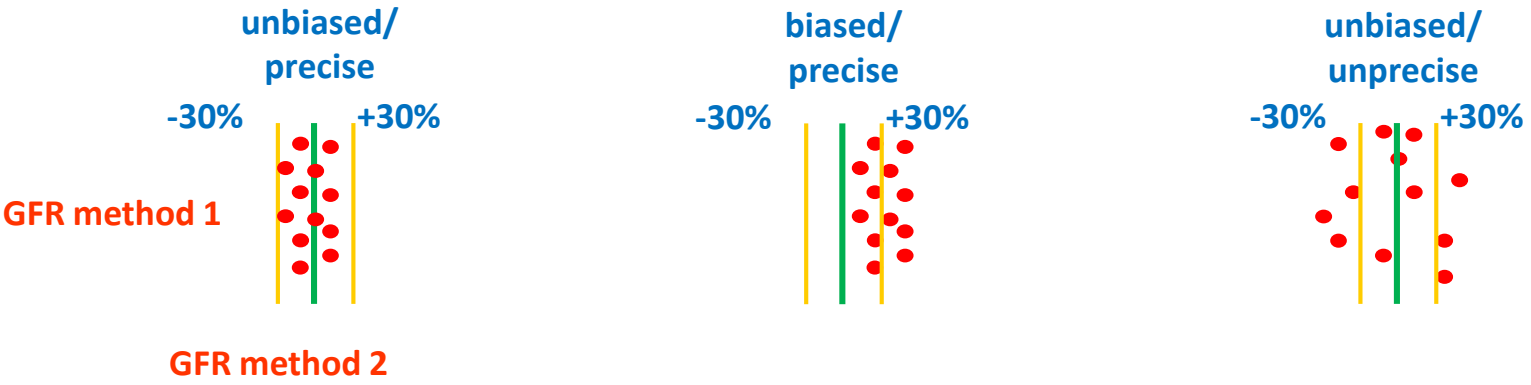
$$\text{GFR (ml/min/1.73 m}^2) = 175 \times \text{SCr (mg/dl)}^{-1.154} \times \text{age}^{-0.203} \times 0.742 \text{ (if woman)} \times 1.21 \text{ for Black-American}$$

Cockcroft versus MDRD

	Cockcroft	MDRD
Population	Canada 1976	USA 1999
N	249	1628
Mean GFR	73	40
Measured GFR	Creatinine Clearance	Iothalamate
Assay	Jaffe	Jaffe
% women	4	40
% black	0 (?)	12
Mean age	18-92	51
Mean weight	72	79.6
Indexation for BSA	No	yes
Internal validation	no	yes

Statistics

- Good correlation: a *"sine qua non"* condition but insufficient
- Bias: mean difference between two values = the systematic error
- Precision: SD around the bias = the random error
- Accuracy 30% = % of eGFR between ± 30% of measured GFR



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

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

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

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

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

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

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

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

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

CLINICAL EPIDEMIOLOGY www.jasn.org

Evaluation of the Modification of Diet in Renal Disease Study Equation in a Large Diverse Population

Lesley A. Stevens,* Josef Coresh,† Harold I. Feldman,‡ Tom Greene,§ James P. Lash,‖ Robert G. Nelson,¶ Mahboob Rahman,** Amy E. Deysher,* Yaping (Lucy) Zhang,* Christopher H. Schmid,* and Andrew S. Levey*

*Tufts-New England Medical Center, Boston, Massachusetts; †Johns Hopkins University, Baltimore, Maryland; ‡University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania; §University of Utah, Salt Lake City, Utah; ‖University of Illinois at Chicago, Chicago, Illinois; ¶National Institutes of Health, Phoenix, Arizona; and **Case Western Reserve University, Cleveland, Ohio

J Am Soc Nephrol 18: 2749–2757, 2007.

- CKD-EPI
- Urinary clearance of iothalamate in at least 250 subjects
- 5504 subjects (2874 with GFR<60)
- Creatinine calibrated (different ways)

Table 2. Comparison of performance of MDRD Study equation by level of eGFR[a]

eGFR	*N*	Difference		% Difference		P_{30} (CI)
		Median (CI)	IQR	Median (CI)	IQR	
Overall	5504	2.7 (2.4 to 3.1)	16.4	5.8 (5.1 to 6.4)	27.6	83 (83 to 84)
>120	325	−9.0 (−12.3 to −5.9)	31.2	−7.1 (−10.1 to −4.6)	26.6	82 (80 to 84)
90 to 119	941	11.1 (9.7 to 12.6)	25.6	9.9 (8.6 to 11)	20.8	89 (88 to 90)
60 to 89	1364	9.5 (8.3 to 10.7)	25.4	11.7 (10.2 to 12.7)	28.0	82 (81 to 83)
30 to 59	1782	1.7 (1.1 to 2.3)	13.0	3.5 (2.4 to 4.9)	27.4	84 (83 to 85)
16 to 29	793	0.0 (−0.4 to 0.5)	6.7	0.0 (−1.8 to 2.4)	31.4	81 (80 to 82)
<15	299	0.8 (0.3 to 1.4)	5.0	6.3 (2.5 to 11.1)	34.5	72 (69 to 75)

[a]Units of GFR are in ml/min per 1.73 m^2. Difference is calculated as mGFR − eGFR. Percentage difference is calculated as (mGFR − eGFR)/mGFR. Median values measure bias, and IQR measure precision. mGFR ranges in the rows correspond to GFR cutoffs for CKD stages: Stage 1, GFR >90; stage 2, GFR 60 to 89; stage 3, GFR 30 to 59; stage 4, GFR 15 to 29; stage 5, GFR <15. CI, confidence interval.

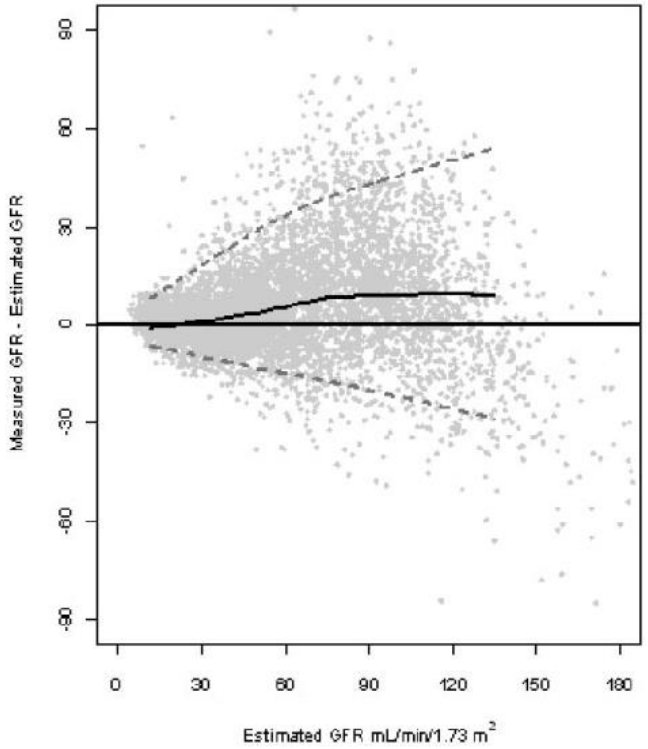


Figure 2. Difference of the MDRD Study equation by level of eGFR. Difference is calculated as (mGFR − eGFR). Solid horizontal

MDRD: the strengths

- Excellent accuracy, bias, precision in stage 3-4 CKD
- Best accuracy observed: 80-85%
- Better than Cockcroft especially in precision, in stage 3-4, in obese

MDRD: the limitations

- MDRD more bias (absolute) and less precision in high GFR
- Non negligible proportion of subjects with stage 2 classified as stage 3 CKD
- Trend to underestimate GFR especially in young women

MDRD: limitations = creatinine (exp -1.154)
1) analytical limitation

- MDRD study equation: Cleveland Laboratory

  Modified Kinetic Jaffe (Beckman Astra CX3)

- NHANES study :

  Modified Kinetic Jaffe (Hitachi 737)

difference of 0.23 mg/dl between two methods

(higher results with Hitachi)

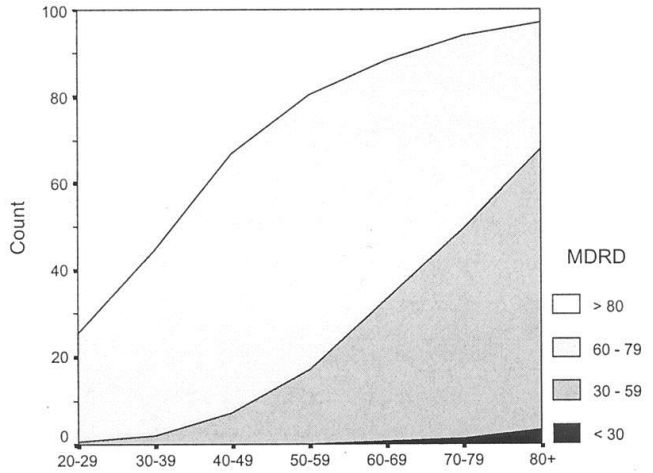
If creatinine is 1 mg/dL: difference in eGFR will be 21 ml/min/1.73m² with MDRD

If creatinine is 2 mg/dL: difference in eGFR will be 6 ml/min/1.73m² with MDRD

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

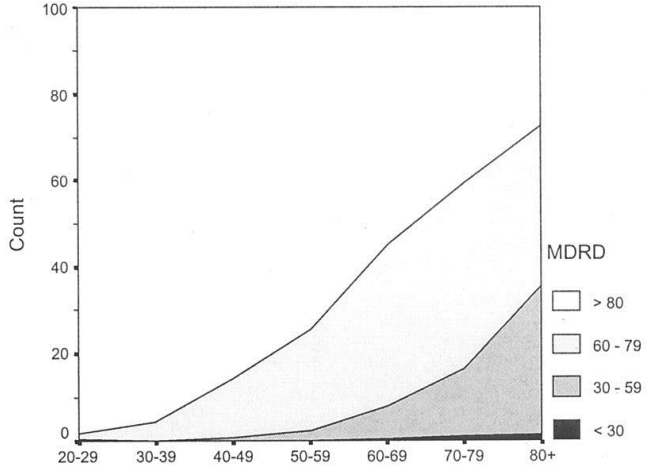
MDRD: limitations = creatinine
1) analytical limitation

UNCALIBRATED



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



3037	2827	2138	1422	1670	1241	916	Total 13251
98.3%	95.7%	85.7%	74.4%	55.1%	40.7%	27.5%	82.1%
1.5%	4.2%	13.5%	23.3%	36.9%	42.7%	37.0%	14.5%
0.2%	<0.1%	0.8%	2.4%	7.6%	15.7%	34.3%	3.2%
<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

IDMS traceability

A multicentric evaluation of IDMS-traceable creatinine enzymatic assays

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

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[e] Analytical Chemistry Laboratory, CIRM, University of Liège, Liège, Belgium
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[i] Clinical Chemistry, University of Liège, CHU Sart Tilman, Liège, Belgium
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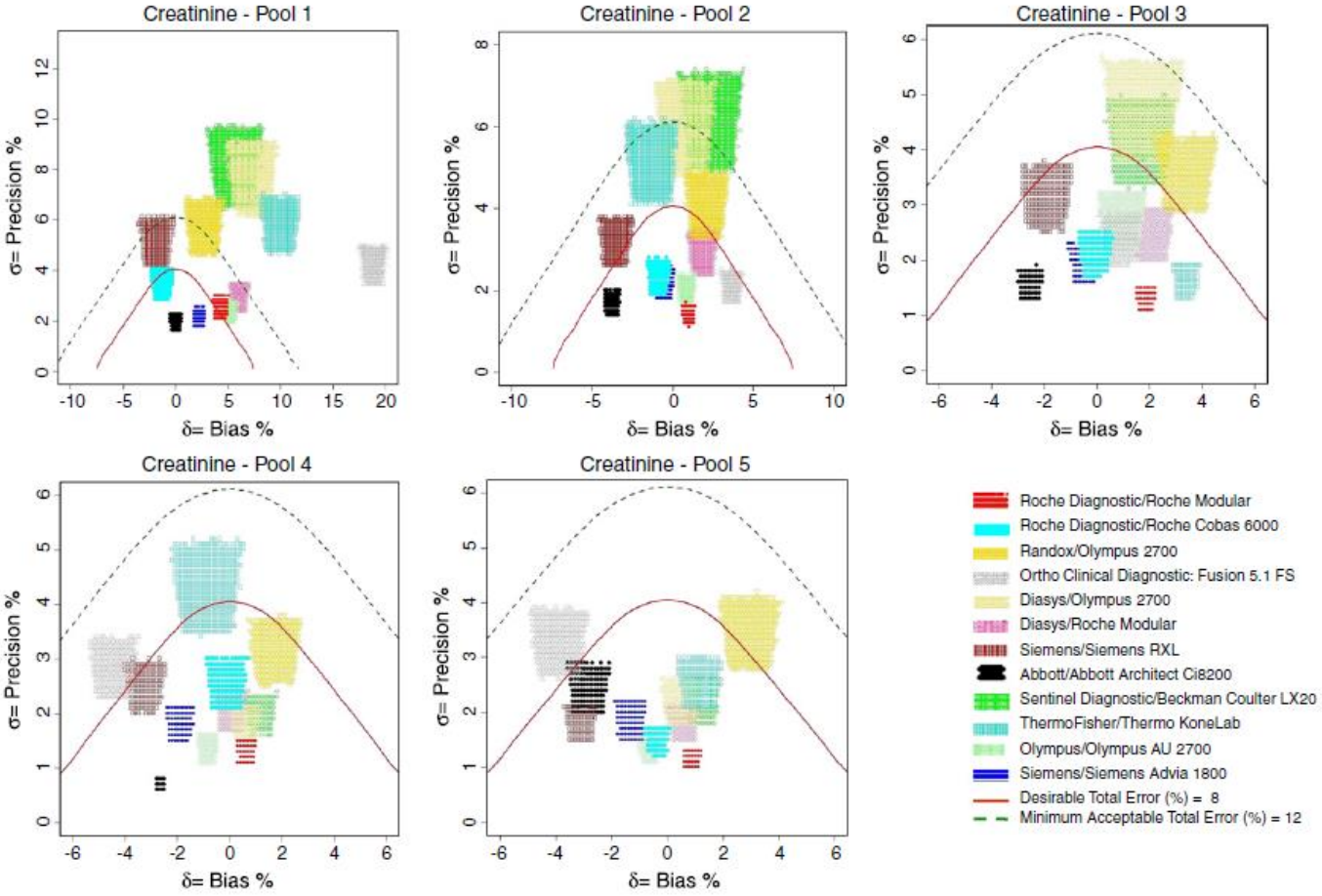
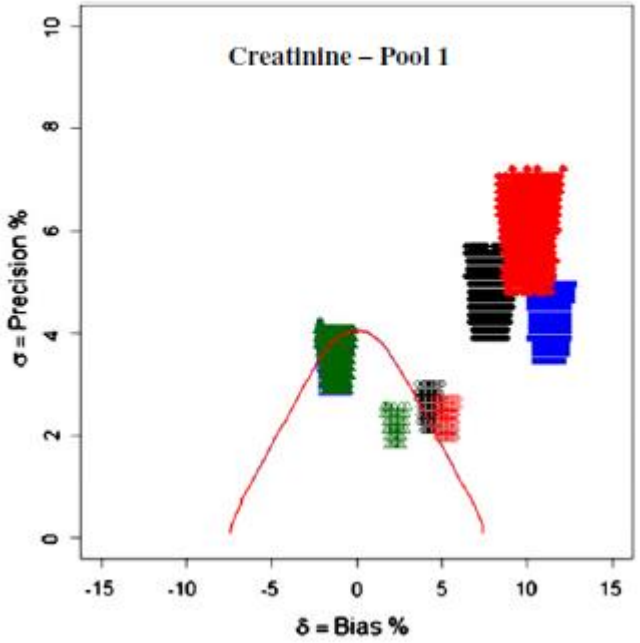
Clinica Chimica Acta 412 (2011) 2070–2075

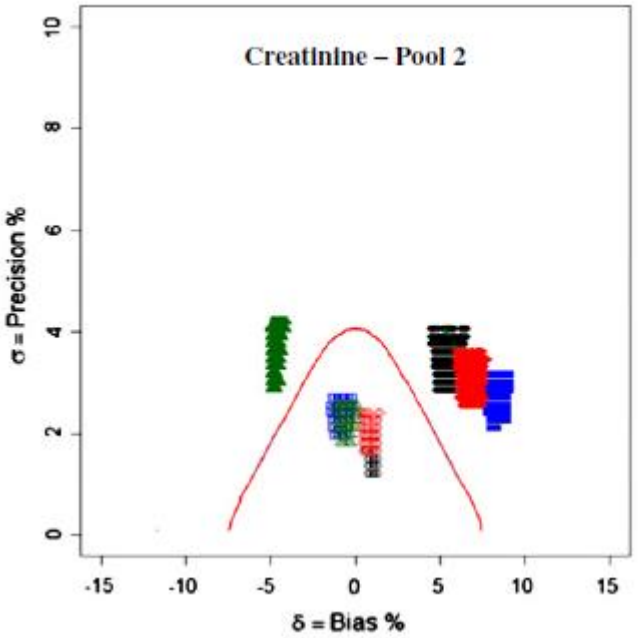
MDRD: 186 => 175

Results of GC-IDMS from LNE

Pool 5: 174.5 +/-3.1 µmol/L
Pool 4: 149.7 +/-2.9 µmol/L
Pool 3: 97.9 +/-1.7 µmol/L
Pool 2: 74.4 +/-1.4 µmol/L
Pool 1 : 35.9 +/-0.9 µmol/L




Creatinine – Pool 1
σ = Precision %
δ = Bias %
0
2
4
6
8
10
-15
-10
-5
0
5
10
15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-15
-10
-5
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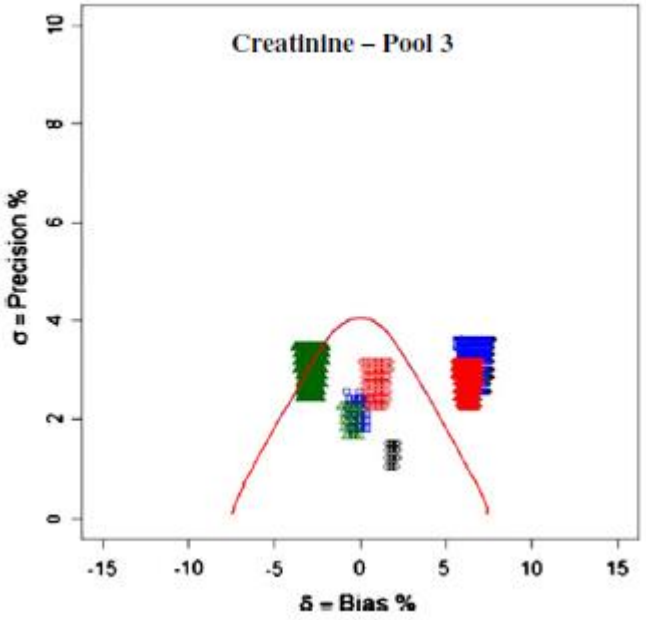
15


Creatinine – Pool 3
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δ = Bias %
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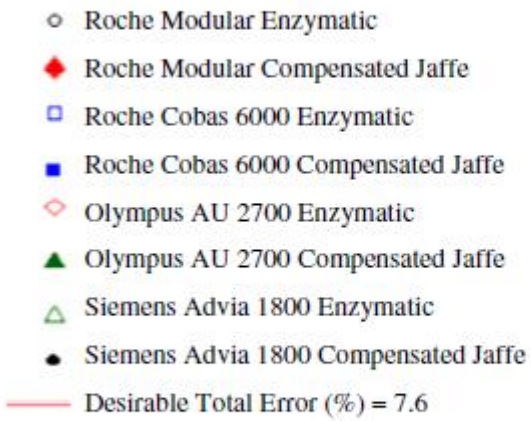

Roche Modular Enzymatic
Roche Modular Compensated Jaffe
Roche Cobas 6000 Enzymatic
Roche Cobas 6000 Compensated Jaffe
Olympus AU 2700 Enzymatic
Olympus AU 2700 Compensated Jaffe
Siemens Advia 1800 Enzymatic
Siemens Advia 1800 Compensated Jaffe
Desirable Total Error (%) = 7.6

MDRD: limitations = creatinine
1) analytical limitations

CRITICAL DIFFERENCE = f(CVa, CVi)

= 19% (Jaffe)

Male, Caucasian, 60 y:

If MDRD higher than 60 ml/min/1,73m² => just use >60 mL/min/1.73 m²

Creat = 1.00 mg/dL

≈ GFR_{MDRD}=76 ml/min/1.73m²

Creatinine= 0.81 mg/dL

GFR_{MDRD}= 97 ml/min/1,73m²

Creatinine= 1.19 mg/dL

GFR_{MDRD}= 62 ml/min/1,73m²

Kuster N, Clinica Chimica Acta, 2014, 428C, 89
Delanaye P, J Nephrol, 2014, 27, 467

MDRD: limitations = creatinine
2) clinical limitations

Specific population: MDRD is not magic!!
Keep our clinical feeling!!

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

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

Intensive Care (Delanaye P, BMC Nephrology, 2014, 15, 9)

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

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

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

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

Elderly (Schaeffner E, Ann Intern Med, 2012, 157, 471)

MDRD: limitations
3) the ethnicity factors

- Asian factor: Chinese: 1.233 Japan: 0.808

  How explain this discrepancy?

(Delanaye P, Rule AD, Kidney Int, 2011 80, 439*)*

- African-American factor: 1.21

  Factor too high in AA “healthy” population

(Delanaye P, Clin J Am Soc, 2011, 6, 906)

Epidemiological paradox

(Peralta CA, NDT, 2010, 25, 3934)

The new CKD-EPI equation

ARTICLE | Annals of Internal Medicine

A New Equation to Estimate Glomerular Filtration Rate

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

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

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

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

- CKD-EPI
- Development dataset: n=5504
- Internal validation: n=2750
- External validation: n=3896
- Creatinine calibrated
- Median GFR in the development = 68 mL/min/1.73 m^2

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

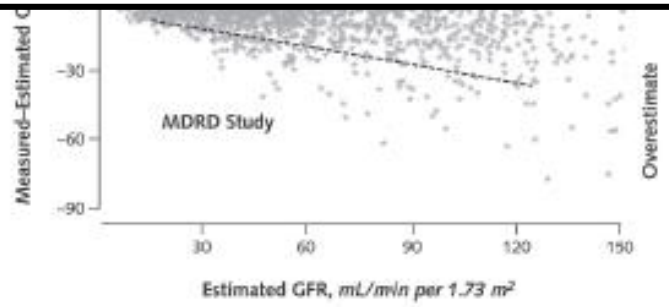


Table 3. Comparison of the CKD-EPI and MDRD Study Equations in Estimating Measured GFR in the Validation Data Set*

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

CKD-EPI: discussion

- PubMed database (last accessed June 18, 2012)
- Research for GFR, MDRD, and CKD-EPI in adults with a minimum of 50 mGFRs

Provided data for ±30% accuracy

recovered 26 publications

Delanaye P, Nephrol Dial Transplant, 2013, 28, 1396

Study	GFR method	SCr calibration	Population	N mGFRs	Mean mGFR±SD (range)	Accuracy				Bias				Precision	
						30%		15%		Mean		Median		SD of Mean Bias	
						MDRD	CKD-EPI	MDRD	CKD-EPI	MDRD	CKD-EPI	MDRD	CKD-EPI	MDRD	CKD-EPI
Murata et al.[21]	Iothalamate	Yes IDMS	Mixed	5238	56±30	77.6	78.4			*-4.1*	*-0.7*				
Levey et al.[7]	^{125}I-iothalamate, Iohexol, ^{99m}Tc-DTPA	Yes IDMS	Mixed	3896	68±36	80.6	84.1					5.5	2.5		
Eriksen et al.[39]	Iohexol plasma	Yes IDMS	General (no CKD)	1621	92±14	93	95					1.3	2.9		
Bjork et al.[32]	Iohexol plasma	Yes IDMS	Mixed	1397	44 (12-116)	79.5	79.1			*-2.0*	*2.0*	-0.8	0.8		
Buron et al.[58]	Inulin	Yes LCMS	KT recipients	1249	54±18 (15-90)	85	81			-0.5	3.9			12.2	12.6
Nyman et al.[47]	Iohexol plasma	Yes IDMS	Mixed	850	55 (9-121)	79.9	79.5			*1.0*	*4.0*	1.2	2.3		
Iliadis et al. [57]	^{51}Cr-EDTA plasma	Yes IDMS	DM Type 2	448	73±23	78.8	80.7			7.5	7.1			13.4	12.0
Lane et al.[60]	^{125}I-iothalamate	Yes ClClin	Pre and Post Nephrectomy	425	50 (median) (4-142)	75	80					-1.0	-1.7		
Cirillo et al.[56]	Inulin	Yes IDMS	Mixed	356	72±36	87.4	88.2			-5.2	-0.9			14.9	13.2
Michels et al. [@26]	^{125}I-iothalamate	Yes IDMS	Mixed	271	73±30	81.2	84.5			0.8	4.5			24.7	16.7
Tent et al.[50]	^{125}I-iothalamate	Yes ClClin	Pre nephrectomy	253	103±15	73	89			*-22.0*	*-14.0*	-22.0	-14.0		
			Post nephrectomy	253	66±11	71	89			*-15.0*	*-10.0*	-15.0	-11.0		
Teo et al.[54]	^{99m}Tc-DTPA plasma	Yes IDMS	CKD	232	52±28	79.7	82.8	50	50	*-1.0*	*1.1*	-3.0	-1.2		
White et al.[46]	^{99m}Tc-DTPA plasma	Yes IDMS	KT recipients	207	58±22	79	84			-8.0	-4.5	-7.4	-5.2	12.1	12.6
Redal-Baigorri et al. [@48]	^{51}Cr-EDTA plasma	Yes IDMS	Oncology	185	85±20	88.6	89.7			0.8	1.2			16.5	13.4
Poge et al.[55]	^{99m}Tc-DTPA plasma	Yes IDMS	KT recipients	170	40 12-83	71.8	64.1			4.5	8.1	4.1	7.4	10.0	10.9
Jones et al.[63]	^{99m}Tc-DTPA plasma	Yes IDMS	Evaluation of GFR	169	71 (5-150)	81	86								
Kukla et al.[51]	^{125}I-iothalamate	Yes IDMS	KT recipients	107	56±17	71.7	58.5			8.2	13.3			16.0	16.3
			KT recipients 1 year post KT	81	57±18	75.0	66.7			2.4	6.9			15.7	15.9
Silveiro et al.[59]	^{51}Cr-EDTA plasma	Yes IDMS	DM Type 2	105	103±23	64	67			-25.0	-20.0			22.0	21.0
Orskov et al. [@52]	^{51}Cr-EDTA plasma	Yes IDMS	Polycystic kidney disease	101	64 (7-118)	83	90	37	50	-10.8	-5.0			10.5	10.2
Praditprnsilpa et al.[62]	^{99m}Tc-DTPA plasma	Yes IDMS	CKD	100	51±28	62.7	68.0	27.3	30.7	*-9.2*	*-7.9*				
Soares et al.[53]	^{51}Cr-EDTA plasma	Yes IDMS	Healthy	96	112±24	69	85	40	55	-18.0	-10.0			26.0	24.0
Bargnoux et al.[64]	^{99m}Tc-DTPA	Yes IDMS	KT recipients	85	53±21	72.9	72.9			-4.3	-0.2			14.1	14.7
Tent et al.[61]	^{125}I-iothalamate	Yes ClClin	CKD	65	78±27	66	82			*-15.0*	*-8.0*	-15.0	-8.0		
			CKD	65	58±29	77	82			*-11.0*	*-7.0*	-8.0	-6.0		
Gerhardt et al.[44]	^{99m}Tc-DTPA plasma	Yes IDMS	Liver transplant	59	52 (48-57)	69.5	64.4			-4.3	-9.7				
Camargo et al.[49]	^{51}Cr-EDTA plasma	Yes IDMS	DM Type 2	56	106±27	64	66	27	41	-26.0	-24.0			26.0	24.0
			Healthy	55	98±20	80	90	47	60	-19.0	-9.0			20.0	18.0
Van Deventer et al.[45]	^{51}Cr-EDTA plasma	Yes IDMS	CKD	50	N/A	74	72	52	46			-1.5	4.9		

CKD-EPI: really better?

	Accuracy		Bias		Precision	
	30%		Mean		SD	
	MDRD	CKD-EPI	MDRD	CKD-EPI	MDRD	CKD-EPI
Calculated average weighted values from available data in **all studies**	**80.2**	**82.0**	**-3.5**	**0.0**	**14.9**	**13.8**
Calculated average weighted values from available data in all studies with analysis for strata of **mGFR>60 ml/min/1.73m^2**	**87.1**	**89.4**	**-2.0**	**2.2**	**13.4**	**13.0**

Delanaye P, Nephrol Dial Transplant, 2013, 28, 1396

Discussion:
MDRD or CKD-EPI ?

- Lower CKD prevalence in epidemiological studies
- Better prediction of CVD => better at the population level
- Better bias in GFR >60 (90?) ml/min/1.73m² but not better precision => not better at the individual level

- Ethnicity factor: probably not better
- Impact of the analytical error is less in high GFR

The price to pay…

Annals of Internal Medicine | REVIEW

Estimating Equations for Glomerular Filtration Rate in the Era of Creatinine Standardization

A Systematic Review

Amy Earley, BS; Dana Miskulin, MD, MS; Edmund J. Lamb, PhD; Andrew S. Levey, MD; and Katrin Uhlig, MD, MS

Background: Clinical laboratories are increasingly reporting estimated glomerular filtration rate (GFR) by using serum creatinine assays traceable to a standard reference material.

Purpose: To review the performance of GFR estimating equations to inform the selection of a single equation by laboratories and the interpretation of estimated GFR by clinicians.

Data Sources: A systematic search of MEDLINE, without language restriction, between 1999 and 21 October 2011.

Study Selection: Cross-sectional studies in adults that compared the performance of 2 or more creatinine-based GFR estimating equations with a reference GFR measurement. Eligible equations were derived or reexpressed and validated by using creatinine measurements traceable to the standard reference material.

Data Extraction: Reviewers extracted data on study population characteristics, measured GFR, creatinine assay, and equation performance.

Data Synthesis: Eligible studies compared the MDRD (Modification of Diet in Renal Disease) Study and CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration) equations or modifications thereof. In 12 studies in North America, Europe, and Australia, the CKD-EPI equation performed better at higher GFRs (approximately >60 mL/min per 1.73 m^2) and the MDRD Study equation performed better at lower GFRs. In 5 of 8 studies in Asia and Africa, the equations were modified to improve their performance by adding a coefficient derived in the local population or removing a coefficient.

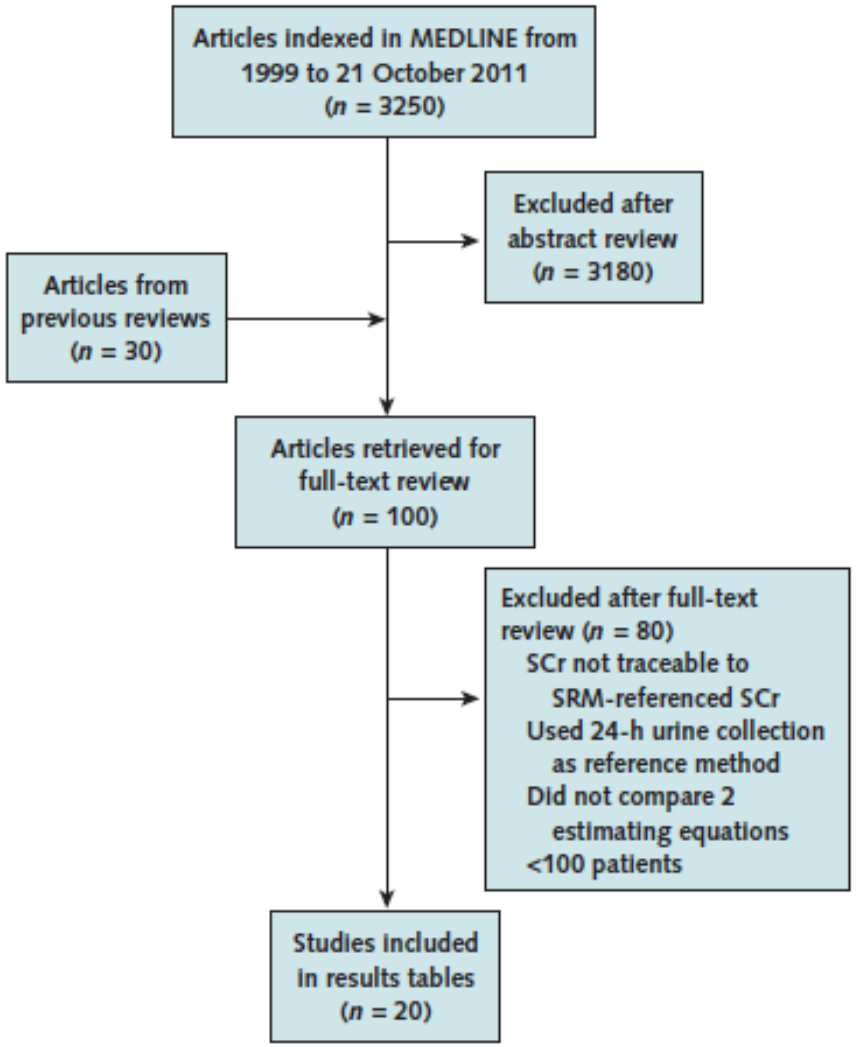
Limitation: Methods of GFR measurement and study populations were heterogeneous.

Conclusion: Neither the CKD-EPI nor the MDRD Study equation is optimal for all populations and GFR ranges. Using a single equation for reporting requires a tradeoff to optimize performance at either higher or lower GFR ranges. A general practice and public health perspective favors the CKD-EPI equation.

Primary Funding Source: Kidney Disease: Improving Global Outcomes.

Ann Intern Med. 2012;156:785-795. www.annals.org
For author affiliations, see end of text.
This article was published at www.annals.org on 7 February 2012.

Figure 1. **Summary of evidence search and selection.**



SCr = serum creatinine; SRM = standard reference material.

The CKD-EPI equation seems to be more accurate and less biased in studies with higher mean measured GFRs (approximately >60 mL/min per 1.73 m^2), whereas the MDRD Study equation has greater accuracy and less bias at lower GFRs.

Because the differences between the equations are greater at higher GFRs, the implications of introducing the CKD-EPI equation would be larger for public health and general clinical practice than for nephrology practices.

In summary, neither the CKD-EPI nor the MDRD Study equation is optimal across all populations and GFR ranges.

The price to pay…

Relative Performance of the MDRD and CKD-EPI Equations for Estimating Glomerular Filtration Rate among Patients with Varied Clinical Presentations

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Summary

Background The Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation was developed using both CKD and non-CKD patients to potentially replace the Modification of Diet in Renal Disease (MDRD) equation that was derived with only CKD patients. The objective of our study was to compare the accuracy of the MDRD and CKD-EPI equations for estimating GFR in a large group of patients having GFR measurements for diverse clinical indications.

Design, setting, participants, and measurements A cross-sectional study was conducted of patients who underwent renal function assessment for clinical purposes by simultaneous measurements of serum creatinine and estimation of GFR using the MDRD and CKD-EPI equations and renal clearance of iothalamate (n = 5238).

Results Bias compared with measured GFR (mGFR) varied for each equation depending on clinical presentation. The CKD-EPI equation demonstrated less bias than the MDRD equation in potential kidney donors (−8% *versus* −18%) and postnephrectomy donors (−7% *versus* −15%). However, the CKD-EPI equation was slightly more biased than the MDRD equation in native CKD patients (6% *versus* 3%), kidney recipients (8% *versus* 1%), and other organ recipients (9% *versus* 3%). Among potential kidney donors, the CKD-EPI equation had higher specificity than the MDRD equation for detecting an mGFR <60 ml/min per 1.73 m^2 (98% *versus* 94%) but lower sensitivity (50% *versus* 70%).

Conclusions Clinical presentation influences the estimation of GFR from serum creatinine, and neither the CKD-EPI nor MDRD equation account for this. Use of the CKD-EPI equation misclassifies fewer low-risk patients as having reduced mGFR, although it is also less sensitive for detecting mGFR below specific threshold values used to define CKD stages.

Clin J Am Soc Nephrol 6: 1963–1972, 2011. doi: 10.2215/CJN.02300311

The price to pay…

- What would be your choice?

Better estimate the GFR of a *subject* with measured GFR between 90 and 120 mL/min/1.73 m^2?

Better estimate the GFR of a *patient* with measured GFR between 30 and 60 mL/min/1.73 m^2?

MDRD – CKD-EPI: nothing else?

- The Bis Equation
- The Lund-Malmö equation
- The FAS equation
- Other biomarkers: cystatin 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

The elderly


SI ON AVAIT SON ANNIVERSAIRE DEUX FOIS PAR AN
ON VIVRAIT DEUX FOIS PLUS VIEUX
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Annals of Internal Medicine | ORIGINAL RESEARCH

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

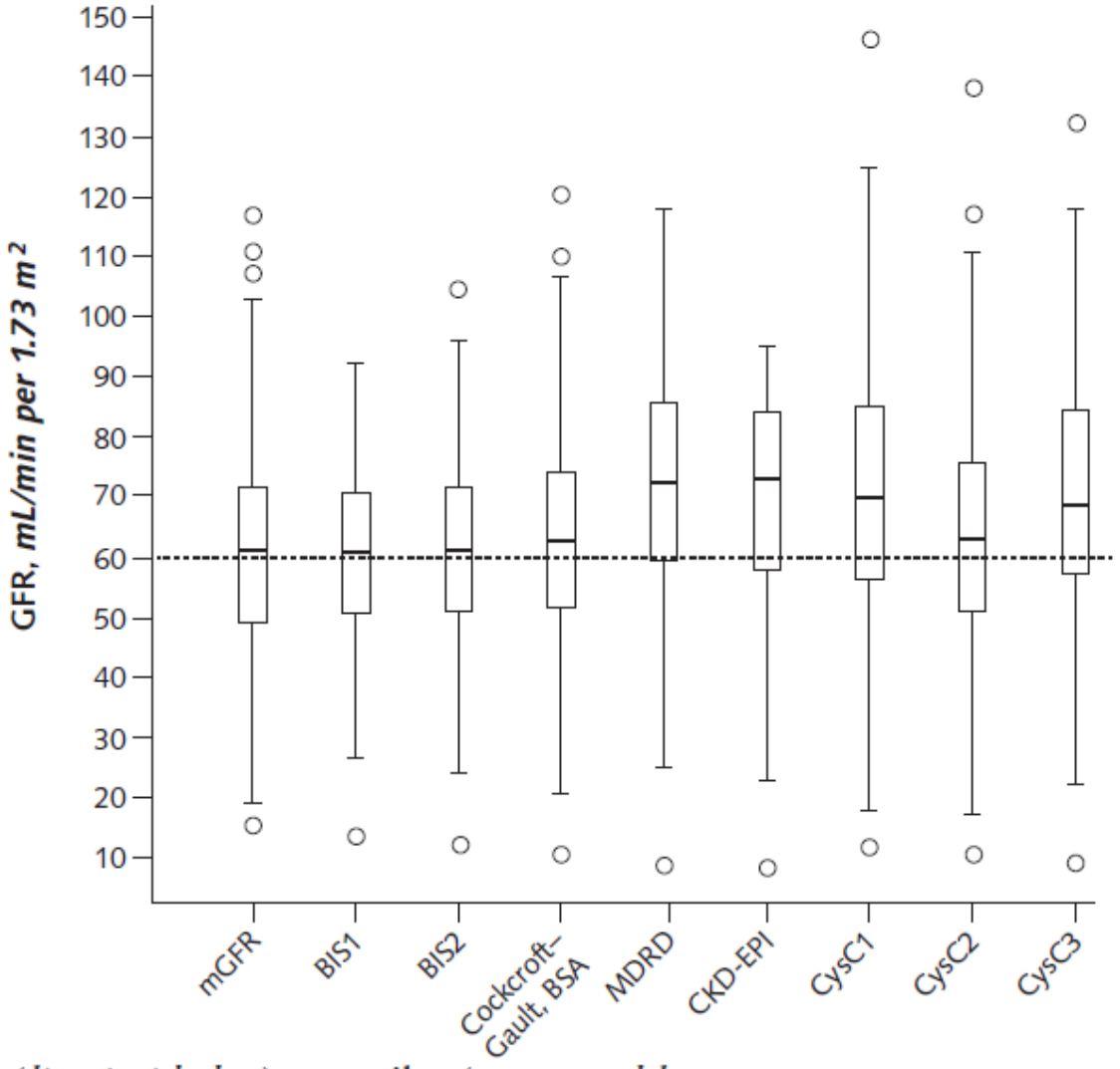
Elke S. Schaeffner, MD, MS*; Natalie Ebert, MD, MPH*; Pierre Delanaye, MD, PhD; Ulrich Frei, MD; Jens Gaedeke, MD; Olga Jakob; Martin K. Kuhlmann, MD; Mirjam Schuchardt, PhD; Markus Tölle, MD; Reinhard Ziebig, PhD; Markus van der Giet, MD; and Peter Martus, PhD

BIS1:

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

Ann Intern Med. 2012;157:471-481

Figure 1. **Comparison of mGFR with eGFR equations in the validation sample.**



Boxes indicate medians (*line inside box*), quartiles (*upper and lower margins of box*). Antennae are defined by the rule upper–lower box margin ± 1.5 × interquartile range. Circles indicate outliers.

CKD-EPI Equation *vs* BIS Equation

n=5504

- Mean Age: 47
- Mean GFR: 68 ml/min/1.73m^2
- Reference: Iothalamate
- Creatinine Assay: Multiple – recalibration

n=570

- Mean Age: 78.5
- Mean GFR: 60 ml/min/1.73m^2
- Reference: Iohexol
- Creatinine Assay:
- IDMS - Enzymatic

COMPARATIVE ACCURACY-30%
- CKD-EPI vs BIS -

- *Koppe L et al. J Nephrol, 2013*
  - **n=224, Mean Age=75** 72% vs 76%
- *Lopes M et al. BMC Nephrology, 2013*
  - **n=95, Mean Age=85** 75% vs 80%
- *Alshoer I et al. AJKD, 2014*
  - **n=394, Median Age=80** 83% vs 88%
- *Vidal-Petiot E et al. AJKD, 2014*
  - **N=609, Mean Age=76** 82% vs 84%

Comparing GFR Estimating Equations Using Cystatin C and Creatinine in Elderly Individuals

Li Fan,*† Andrew S. Levey,* Vilmundur Gudnason,‡§ Gudny Eiriksdottir,‡ Margret B. Andresdottir,‖ Hrefna Gudmundsdottir,§‖ Olafur S. Indridason,‖ Runolfur Palsson,§‖ Gary Mitchell,¶ and Lesley A. Inker*

J Am Soc Nephrol 26: 1982–1989, 2015.

Equation	Bias Median Difference	Precision IQR	Accuracy P_{30}
eGFRcr			
CKD-EPI	−2.7 (−3.3 to −2.1)	12.1 (11.2 to 13.4)	91.7 (89.9 to 93.4)
Japanese	10.5 (9.8 to 11.2)[c]	10.9 (9.7 to 12.1)[a]	86.3 (83.9 to 88.6)[c]
BIS	5.7 (5.1 to 6.4)[c]	11.9 (10.6 to 12.7)[a]	95.8 (94.4 to 97.1)[b]

- The BIS Equation is more accurate than the CKD-EPI Equation to predict the true GFR of the elderly.

- This better ACCURACY is likely to be explained by a better PRECISION.

Do We Want a System Using 2 Separate Equations Depending on Patient Age?

- The Elderly : A growing population
- The Elderly: A vulnerable population
- Haven't we already endorsed such a system ?

…the SCHWARTZ equation

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]

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

Female	pCr<150 µmol/L:	$X=2.50+0.0121\times(150-pCr)$
Female	pCr≥150 µmol/L:	$X=2.50-0.926\times\ln(pCr/150)$
Male	pCr<180 µmol/L:	$X=2.56+0.00968\times(180-pCr)$
Male	pCr≥180 µmol/L:	$X=2.56-0.926\times\ln(pCr/180)$

- Lund-Malmo study
- n=3495 (chez 2847 sujets), iohexol, standardized creatinine
- Mean GFR = 52 mL/min/1,73 m²

Nephrol Dial Transplant (2016) 31: 798–806
doi: 10.1093/ndt/gfv454
Advance Access publication 29 February 2016

An estimated glomerular filtration rate equation for the full age spectrum

Hans Pottel[1], Liesbeth Hoste[1], Laurence Dubourg[2], Natalie Ebert[3], Elke Schaeffner[3], Bjørn Odvar Eriksen[4], Toralf Melsom[4], Edmund J. Lamb[5], Andrew D. Rule[6], Stephen T. Turner[6], Richard J. Glassock[7], Vandréa De Souza[8], Luciano Selistre[9], Christophe Mariat[10], Frank Martens[11] and Pierre Delanaye[12]

$$\text{FAS} - \text{eGFR} = \frac{107.3}{(\text{SCr}/Q)} \quad \text{for } 2 \leq \text{age} \leq 40 \text{ years}$$

$$\text{FAS} - \text{eGFR} = \frac{107.3}{(\text{SCr}/Q)} \times 0.988^{(\text{Age}-40)} \quad \text{for age} > 40 \text{ years}$$

A concept more than a regression…

Table 1. *Q*-values [=median serum creatinine in µmol/L (mg/dL)] for the FAS equation, according to age or height (from refs [4, 5, 10])

Age, years	Height[a], cm	*Q*[b], µmol/L (mg/dL)
Boys and girls		
1	75.0	23 (0.26)
2	87.0	26 (0.29)
3	95.5	27 (0.31)
4	102.5	30 (0.34)
5	110.0	34 (0.38)
6	116.7	36 (0.41)
7	123.5	39 (0.44)
8	129.5	41 (0.46)
9	135.0	43 (0.49)
10	140.0	45 (0.51)
11	146.0	47 (0.53)
12	152.5	50 (0.57)
13	159.0	52 (0.59)
14	165.0	54 (0.61)
Male adolescents		
15	172.0	64 (0.72)
16	176.0	69 (0.78)
17	178.0	72 (0.82)
18	179.0	75 (0.85)
19	180.0	78 (0.88)
Male adults		
≥20	≥181.5	80 (0.90)
Female adolescents		
15	164.5	57 (0.64)
16	166.0	59 (0.67)
17	166.5	61 (0.69)
18	167.0	61 (0.69)
19	167.5	62 (0.70)
Female adults		
≥20	≥168.0	62 (0.70)

[a]Height is the median height of a child or adolescent at the specified age (Belgian growth curves).

Table 3. Prediction performance results of different eGFR equations on the pooled databases according to age group and measured GFR categories (mGFR below or above 60 mL/min/1.73 m^2)

Pooled data	eGFR equivalent	RMSE (95% CI)	Constant bias (95% CI)	Proportional bias (95% CI)	P10, % (95% CI)	P30, % (95% CI)
Children and adolescents <18 years						
All (n = 735)	FAS	20.1 (18.5, 21.6)	−1.7 (−3.1, −0.2)*,†	1.01 (0.99, 1.03)*,†	40.1 (36.6, 43.7)	87.5 (85.1, 89.9)*
mGFR = 94.5	FAS-height	19.8 (18.1, 21.4)	−2.7 (−4.1, −1.3)*,‡	1.00 (0.98, 1.01)*,‡	41.9 (38.3, 45.5)	88.8 (86.6, 91.1)†
	Schwartz	21.7 (19.5, 23.7)	6.0 (4.5, 7.5)†,‡	1.09 (1.07, 1.11)†,‡	40.1 (36.6, 43.7)	83.8 (81.1, 86.5)*,†
mGFR < 60 (n = 99)	FAS	14.6 (8.5, 18.9)	6.2 (3.6, 8.9)*,†	1.15 (1.09, 1.21)*,†	34.3 (24.8, 43.9)	75.8 (67.2, 84.3)
mGFR = 45.1	FAS-height	13.5 (4.2, 18.6)	4.7 (2.2, 7.2)*,‡	1.12 (1.06, 1.17)*,‡	39.4 (25.6, 49.2)	77.8 (69.4, 86.1)*
	Schwartz	16.7 (8.2, 22.1)	9.4 (6.7, 12.2)†,‡	1.22 (1.16, 1.28)†,‡	31.3 (22.0, 40.6)	70.7 (61.6, 79.8)*
mGFR ≥ 60 (n = 636)	FAS	20.8 (19.1, 22.4)	−2.9 (−4.5, −1.3)*,†	0.99 (0.97, 1.00)*,†	41.0 (37.2, 44.9)	89.3 (86.9, 91.7)*
mGFR = 102.2	FAS-height	20.6 (18.9, 22.3)	−3.8 (−5.4, −2.3)*,‡	0.98 (0.96, 0.99)*,‡	42.3 (38.4, 46.1)	90.6 (88.3, 92.8)†
	Schwartz	22.4 (20.0, 24.5)	5.4 (3.7, 7.1)†,‡	1.07 (1.05, 1.09)†,‡	41.5 (37.7, 45.3)	85.8 (83.1, 88.6)*,†
Adults 18–70 years						
All (n = 4371)	FAS	17.2 (16.6, 17.8)	5.0 (4.5, 5.5)*	1.12 (1.11, 1.12)*	40.4 (38.9, 41.9)*	81.6 (80.4, 82.7)
mGFR = 78.6	CKD-EPI	16.4 (15.8, 16.9)	6.3 (5.9, 6.8)*	1.13 (1.12, 1.14)*	42.5 (41.1, 44.0)*	81.9 (80.7, 83.0)
mGFR < 60 (n = 1089)	FAS	19.0 (17.7, 20.2)	13.4 (12.6, 14.2)*	1.35 (1.33, 1.37)*	19.1 (16.8, 21.4)*	52.2 (49.3, 55.2)*
mGFR = 42.3	CKD-EPI	19.2 (18.1, 20.3)	12.7 (11.8, 13.5)*	1.31 (1.29, 1.34)*	21.9 (19.4, 24.3)*	55.2 (52.2, 58.1)*
mGFR ≥ 60 (n = 3282)	FAS	16.6 (15.9, 17.2)*	2.2 (1.6, 2.7)*	1.04 (1.03, 1.04)*	47.5 (45.8, 49.2)*	91.3 (90.3, 92.3)
mGFR = 90.6	CKD-EPI	15.3 (14.7, 15.8)*	4.2 (3.7, 4.7)*	1.07 (1.06, 1.07)*	49.4 (47.7, 51.1)*	90.7 (89.7, 91.7)
Older adults ≥70 years						
All (n = 1764)	FAS	11.2 (10.7, 11.7)*	−1.1 (−1.6, −0.6)*	1.02 (1.01, 1.03)*	39.7 (37.5, 42.0)*	86.1 (84.4, 87.7)*
mGFR = 55.6	CKD-EPI	12.9 (12.4, 13.4)*	5.6 (5.1, 6.2)*	1.13 (1.12, 1.15)*	35.0 (32.8, 37.3)*	77.6 (75.7, 79.6)*
	BIS1[a]	12.0 (11.4, 12.6)	−1.2 (−1.9, −0.6)	1.05 (1.03, 1.07)	34.7 (32.0, 37.4)	81.8 (79.7, 84.0)
mGFR < 60 (n = 986)	FAS	9.5 (8.8, 10.1)*	2.2 (1.6, 2.7)*	1.09 (1.07, 1.11)*	36.6 (33.6, 39.6)*	81.0 (78.6, 83.5)*
mGFR = 40.7	CKD-EPI	13.1 (12.3, 13.8)*	6.9 (6.2, 7.6)*	1.19 (1.17, 1.21)*	29.5 (26.7, 32.4)*	67.7 (64.8, 70.7)*
	BIS1[a]	9.7 (9.0, 10.3)	3.7 (3.0, 4.4)	1.16 (1.13, 1.18)	35.3 (31.8, 38.8)	75.4 (72.2, 78.5)
mGFR ≥ 60 (n = 778)	FAS	13.1 (12.3, 13.8)	−5.2 (−6.1, −4.4)*	0.94 (0.93, 0.95)*	43.7 (40.2, 47.2)	92.4 (90.6, 94.3)
mGFR = 74.4	CKD-EPI	12.7 (12.1, 13.3)	4.1 (3.2, 4.9)*	1.07 (1.06, 1.08)*	42.0 (38.6, 45.5)	90.1 (88.0, 92.2)
	BIS1[a]	14.8 (13.7, 15.7)	−8.6 (−9.7, −7.5)	0.90 (0.88, 0.91)	33.9 (29.6, 38.1)	91.5 (89.0, 94.0)

The same symbols (*,†,‡) within each subgroup and column indicate significant differences (paired t-test for constant and proportional bias, McNemar's test for P10 and P30 = % of subjects with an eGFR value within 10% and 30% of measured GFR).

[a]For the BIS1 performance results, the data (n= 570) from the BIS1 study were not included (therefore, no comparisons with FAS and CKD-EPI were made).

MDRD – CKD-EPI: nothing else?

- The Bis Equation
- The Lund-Malmö equation
- The FAS equation
- Other biomarkers: cystatin 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

Cystatin C

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Estimating Glomerular Filtration Rate from Serum Creatinine and Cystatin C

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

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

Table 2. Creatinine Equation (CKD-EPI 2009), Cystatin C Equation (CKD-EPI 2012), and Creatinine–Cystatin C Equation (CKD-EPI 2012) for Estimating GFR, Expressed for Specified Sex, Serum Creatinine Level, and Serum Cystatin C Level.*

Basis of Equation and Sex	Serum Creatinine†	Serum Cystatin C	Equation for Estimating GFR
	mg/dl	*mg/liter*	
CKD-EPI creatinine equation‡			
Female	≤0.7		$144 \times (\text{Scr}/0.7)^{-0.329} \times 0.993^{\text{Age}}$ [× 1.159 if black]
Female	>0.7		$144 \times (\text{Scr}/0.7)^{-1.209} \times 0.993^{\text{Age}}$ [× 1.159 if black]
Male	≤0.9		$141 \times (\text{Scr}/0.9)^{-0.411} \times 0.993^{\text{Age}}$ [× 1.159 if black]
Male	>0.9		$141 \times (\text{Scr}/0.9)^{-1.209} \times 0.993^{\text{Age}}$ [× 1.159 if black]
CKD-EPI cystatin C equation§			
Female or male		≤0.8	$133 \times (\text{Scys}/0.8)^{-0.499} \times 0.996^{\text{Age}}$ [× 0.932 if female]
Female or male		>0.8	$133 \times (\text{Scys}/0.8)^{-1.328} \times 0.996^{\text{Age}}$ [× 0.932 if female]
CKD-EPI creatinine–cystatin C equation¶			
Female	≤0.7	≤0.8	$130 \times (\text{Scr}/0.7)^{-0.248} \times (\text{Scys}/0.8)^{-0.375} \times 0.995^{\text{Age}}$ [× 1.08 if black]
		>0.8	$130 \times (\text{Scr}/0.7)^{-0.248} \times (\text{Scys}/0.8)^{-0.711} \times 0.995^{\text{Age}}$ [× 1.08 if black]
Female	>0.7	≤0.8	$130 \times (\text{Scr}/0.7)^{-0.601} \times (\text{Scys}/0.8)^{-0.375} \times 0.995^{\text{Age}}$ [× 1.08 if black]
		>0.8	$130 \times (\text{Scr}/0.7)^{-0.601} \times (\text{Scys}/0.8)^{-0.711} \times 0.995^{\text{Age}}$ [× 1.08 if black]
Male	≤0.9	≤0.8	$135 \times (\text{Scr}/0.9)^{-0.207} \times (\text{Scys}/0.8)^{-0.375} \times 0.995^{\text{Age}}$ [× 1.08 if black]
		>0.8	$135 \times (\text{Scr}/0.9)^{-0.207} \times (\text{Scys}/0.8)^{-0.711} \times 0.995^{\text{Age}}$ [× 1.08 if black]
Male	>0.9	≤0.8	$135 \times (\text{Scr}/0.9)^{-0.601} \times (\text{Scys}/0.8)^{-0.375} \times 0.995^{\text{Age}}$ [× 1.08 if black]
		>0.8	$135 \times (\text{Scr}/0.9)^{-0.601} \times (\text{Scys}/0.8)^{-0.711} \times 0.995^{\text{Age}}$ [× 1.08 if black]

Table 3. Use of the CKD-EPI Creatinine Equation (2009), CKD-EPI Cystatin C Equation (2012), and CKD-EPI Creatinine–Cystatin C Equations (2012) in the External-Validation Data Set Comprising 1119 Participants.*

Variable	Estimated GFR			
	Overall	<60	60–89	≥90
		ml/min/1.73 m² of body-surface area		
Bias — median difference (95% CI)				
Creatinine equation	3.7 (2.8 to 4.6)	1.8 (1.1 to 2.5)	6.6 (3.5 to 9.2)	11.1 (8.0 to 12.5)
Cystatin C equation	3.4 (2.3 to 4.4)	0.4 (–0.5 to 1.4)	6.0 (4.6 to 8.5)	8.5 (6.5 to 11.2)
Creatinine–cystatin C equation	3.9 (3.2 to 4.5)	1.3 (0.5 to 1.8)	6.9 (5.0 to 8.9)	10.6 (9.5 to 12.7)
Average of creatinine and cystatin C†	3.5 (2.8 to 4.1)	0.4 (–0.3 to 0.8)	6.5 (4.6 to 8.4)	11.9 (9.9 to 13.9)
Precision — IQR of the difference (95% CI)				
Creatinine equation	15.4 (14.3 to 16.5)	10.0 (8.9 to 11.0)	19.6 (17.3 to 23.2)	25.0 (21.6 to 28.1)
Cystatin C equation	16.4 (14.8 to 17.8)	11.0 (10.0 to 12.4)	19.6 (16.1 to 23.1)	22.6 (18.8 to 26.3)
Creatinine–cystatin C equation	13.4 (12.3 to 14.5)	8.1 (7.3 to 9.1)	15.9 (13.9 to 18.1)	18.8 (16.8 to 22.5)
Average of creatinine and cystatin C equations†	13.9 (12.9 to 14.7)	7.9 (7.1 to 9.0)	15.8 (13.9 to 17.7)	18.6 (16.1 to 22.2)
Accuracy — % (95% CI)‡				
$1-P_{30}$				
Creatinine equation	12.8 (10.9 to 14.7)	16.6 (13.6 to 19.7)	10.2 (6.4 to 14.2)	7.8 (5.1 to 11.0)
Cystatin C equation	14.1 (12.2 to 16.2)	21.4 (18.2 to 24.9)	12.7 (8.5 to 17.4)	2.2 (0.6 to 3.9)
Creatinine–cystatin C equation	8.5 (7.0 to 10.2)	13.3 (10.7 to 16.1)	5.3 (2.7 to 8.2)	2.3 (0.9 to 4.2)
Average of creatinine and cystatin C equations†	8.2 (6.7 to 9.9)	12.1 (9.5 to 14.8)	6.4 (3.6 to 9.7)	2.9 (1.3 to 4.9)
$1-P_{20}$				
Creatinine equation	32.9 (30.1 to 35.7)	37.2 (33.1 to 41.2)	31.1 (25.1 to 37.4)	26.5 (21.7 to 31.4)
Cystatin C equation	33.0 (30.3 to 35.7)	42.1 (38.2 to 46.1)	29.3 (23.6 to 35.4)	19.4 (15.4 to 23.7)
Creatinine–cystatin C equation	22.8 (20.4 to 25.2)	28.6 (25.1 to 32.4)	17.8 (13.3 to 22.9)	16.2 (12.4 to 20.5)
Average of creatinine and cystatin C equations†	23.7 (21.3 to 26.1)	29.1 (25.7 to 32.8)	17.6 (13.2 to 22.4)	18.8 (14.6 to 23.2)

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Original Article

Estimating glomerular filtration rate for the full age spectrum from serum creatinine and cystatin C

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

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

Table 5. Patient characteristics in the different age groups (mean ± SD)

Group	*n*	No. of males	No. of females	mGFR	Scr	ScysC
Children ≤18 years	368	193	175	89.2 ± 30.4	0.65 ± 0.31	1.15 ± 0.42
Adults 18–70 years	4295	2301	1994	80.2 ± 25.6	1.00 ± 0.50	0.99 ± 0.51
Older adults ≥70 years	1469	771	698	58.5 ± 20.0	1.13 ± 0.52	1.24 ± 0.51
Total	6132	3265	2867			

n, number of patients; mGFR, measured glomerular filtration rate (mL/min/1.73 m^2); Scr, serum creatinine (mg/dL); ScysC, serum cystatin C (mg/L).

Performances vis-à-vis des autres équations

Results. In children and adolescents, the new FAS_{cysC} equation showed significantly better performance [percentage of patients within 30% of mGFR (P30) = 86.1%] than the Caucasian Asian Paediatric Adult Cohort equation (P30 = 76.6%; $P < 0.0001$), or the ScysC-based Schwartz equation (P30 = 68.8%; $P < 0.0001$) and the FAS_{combi} equation outperformed all equations with P30 = 92.1% ($P < 0.0001$). In adults, the FAS_{cysC} equation (P30 = 82.6%) performed equally as well as the Chronic Kidney Disease Epidemiology Collaboration equation ($CKD\text{-}EPI_{cysC}$) (P30 = 80.4%) and the FAS_{combi} equation (P30 = 89.9%) was also equal to the combined CKD-EPI equation (P30 = 88.2%). In older adults, FAS_{cysC} was superior (P30 = 88.2%) to $CKD\text{-}EPI_{cysC}$ (P30 = 84.4%; $P < 0.0001$) and the FAS_{combi} equation (P30 = 91.2%) showed significantly higher performance than the combined CKD-EPI equation (P30 = 85.6%) ($P < 0.0001$).

Comparaison créatinine/cystatine C

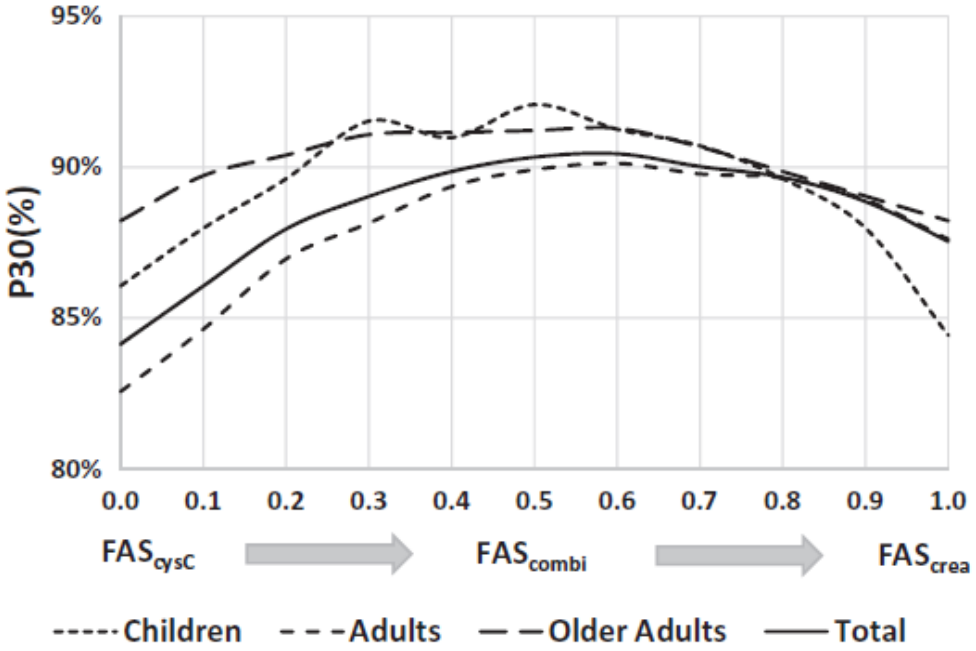

FIGURE 3: P30 as a function of the weighting factor α for the different age groups.

Cystatin C

- Combined
- Cost-effectiveness?
- At the individual level, the imprecision remains…

Conclusions: eGFR a double message ?

- For General Physicians:

  MDRD (or CKD-EPI or FAS) is probably the best and simplest way to estimate GFR

- For Nephrologists:

  MDRD (or CKD-EPI) is not “magic”, keep our critical feeling, there are several limitations we have to know

→ **Go back to measured GFR if necessary**

The applicability of eGFR equations to different populations

Pierre Delanaye and Christophe Mariat

Today the true question is maybe not about which equation is the best

- When is it necessary to measure GFR?
- « Measuring GFR is costly and cumbersome »

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

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Questions?