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ORIGINAL RESEARCH ARTICLE

Discrepancies between the Cockcroft–Gault and Chronic Kidney Disease Epidemiology (CKD-EPI) Equations: Implications for Refining Drug Dosage Adjustment Strategies

Pierre Delanaye[1] · Fabrice Guerber[2] · André Scheen[3] · Timothy Ellam[4] · Antoine Bouquegneau[1] · Dorra Guergour[5] · Christophe Mariat[6] · Hans Pottel[7]

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Abstract
Introduction The dosages of many medications require adjustment for renal function. There is debate regarding which equation, the Chronic Kidney Disease Epidemiology (CKD-EPI) equation vs. the Cockcroft–Gault (CG) equation, should be recommended to estimate glomerular filtration rate.
Methods We used a mathematical simulation to determine how patient characteristics influence discrepancies between equations and analyzed clinical data to demonstrate the frequency of such discrepancies in clinical practice. In the simulation, the modifiable variables were sex, age, serum creatinine, and weight. We considered estimated glomerular filtration rate results in mL/min, deindexed for body surface area, because absolute excretory function (rather than per 1.73 m^2 body surface area) determines the rate of filtration of a drug at a given plasma concentration. An absolute and relative difference of maximum (±) 10 mL/min and 10 %, respectively, were considered concordant. Clinical data for patients aged over 60 years ($n = 9091$) were available from one hospital and 25 private laboratories.
Results In the simulation, differences between the two equations were found to be influenced by each variable but age and weight had the biggest effect. Clinical sample data demonstrated concordance between CKD-EPI and CG results in 4080 patients (45 %). The majority of discordant results reflected a CG result lower than the CKD-EPI equation. With aging, the CG result became progressively lower than the CKD-EPI result. When weight increased, the opposite occurred.
Discussion The choice of equation for excretory function adjustment of drug dosage will have different implications for patients of different ages and body habitus.
Conclusions The optimum equation for drug dosage adjustment should be defined with consideration of individual patient characteristics.

H. Pottel and C. Mariat equally contributed as last senior author.

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✉ Pierre Delanaye
pierre_delanaye@yahoo.fr

1 Division of Nephrology, Dialysis and Transplantation, CHU Sart Tilman, University of Liège (ULg-CHU), 4000 Liège, Belgium

2 Oriade Laboratory, Vizille, France

3 Division of Clinical Pharmacology, Center for Interdisciplinary Research on Medicines, University of Liège, Liège, Belgium

4 Sheffield Kidney Institute, Northern General Hospital and Department of Infection, Immunity and Cardiovascular Science, University of Sheffield, Sheffield, UK

5 Biochemistry Laboratory, Grenoble University Hospital, Grenoble, France

6 Division of Nephrology, Dialysis, Transplantation and Hypertension, CHU Hôpital Nord, University Jean Monnet, PRES Université de LYON, Saint-Etienne, France

7 Department of Public Health and Primary Care, KU, Leuven Kulak, Kortrijk, Belgium

Key Points

There is debate regarding whether the Cockcroft–Gault (CG) equation or the Chronic Kidney Disease Epidemiology (CKD-EPI) equation should be used for drug dosage adjustment.

We illustrate both from a simulation and clinical data that age and weight are the main predictors of discrepancies between CG and CKD-EPI equation results.

Optimum dosage adjustment strategies should be defined according to age and weight.

1 Introduction

Excretory renal function plays a fundamental role both in the pharmacokinetics and pharmacodynamics of several drugs. This is particularly the case for water-soluble compounds and/or their active metabolites. Even for non-renally excreted drugs, severe chronic kidney disease can modify the pharmacokinetics by several mechanisms [1–4]. For this reason, it is now recommended that both pharmacokinetics and pharmacodynamics of every new drug be studied in the context of chronic kidney disease [5, 6]. Dosage adjustment according to excretory renal function is required for many medications. However, there is a debate in the literature regarding the best way to estimate excretory function or glomerular filtration rate (GFR) for the purpose of pharmacotherapy [7–11]. Ideally, GFR should be measured by a so-called reference method such as urinary or plasma clearance of inulin, ^{51}Cr-EDTA, or iohexol. These methods are, however, difficult to implement in daily practice and GFR is thus estimated by creatinine-based equations [12]. Several publications have illustrated potential discrepancies in estimated GFR (eGFR) results and thus in dosage prescription if different equations are used [7, 8, 10, 13–38]. For drug dosage adjustment, the sharpest debate consists in choosing between the Cockcroft–Gault (CG) equation [39], frequently promoted by clinical pharmacologists and geriatricians, and the Chronic Kidney Disease Epidemiology (CKD-EPI) equation, promoted by nephrologists [40, 41]. From the nephrological point of view, the superiority of the CKD-EPI equation over the CG equation to estimate GFR is easy to demonstrate in the general population [12, 40–42]. Moreover, this equation truly estimates GFR, whereas the CG equation estimates creatinine clearance (eClCr), which, in itself, is only a poor estimation of real GFR. Indeed, eClCr overestimates GFR because of the contribution of tubular creatinine secretion [12, 43]. Finally, sensu stricto, the CG equation cannot be used with modern and calibrated serum creatinine (SCr) values whereas the CKD-EPI equation can be used with all creatinine assays traceable to isotope dilution mass spectrometry (IDMS) [40, 44–46]. Conversely, there are arguments to support the case for applying the CG equation [2, 47–50]. Indeed, the CG equation is the equation that has been used to elaborate drug dosage adjustments for the vast majority of drugs [22, 26, 48–51]. Furthermore, the CG equation better predicts the risk of adverse events for several drugs, notably cardiovascular therapies. This may reflect the presence of the variable 'body weight' in the CG equation, not in the CKD-EPI equation [10, 48, 52]. The CG equation has been reported to give systematically lower eClCr values than are obtained for eGFR with CKD-EPI, particularly in the older population [53, 54]. This is despite the fact that eClCr (reflecting filtration plus creatinine secretion) is greater than GFR, reflecting an underestimation bias of CG in older subjects [55]. However, this underestimation will lead to a more protective behavior in terms of drug dosage in this frail population [20, 21].

The goal of this work is to define the discrepancies that would impact drug dosage adjustment if the CKD-EPI equation vs. CG equation was applied. Two complementary strategies are used: (1) a mathematical simulation relating the characteristics of patients to discrepancies between the two equations and (2) analysis of clinical data to determine both the frequency and amplitude of these discrepancies in clinical practice according to patient demographic characteristics.

2 Methods

2.1 Theoretical Simulation

We undertook a simulation study showing the differences observed between CKD-EPI and CG results when variables involved in these equations are modified. In this simulation, the modifiable variables were sex, age, SCr, weight, and height (and by consequence body surface area [BSA]) [39, 41, 56]. We modified: age from to 20 to 80 years (with 10-year intervals), weight from 25 to 125 kg (with 5-kg intervals), and SCr from 0.5 to 3.0 mg/dL (44–264 µmol/L) (with 0.1-mg/dL or 9-µmol/L intervals). Because the influence of the 'height' variable is less important from a mathematical and epidemiological point of view, we considered a constant height of 177 and 165 cm for men and women (reflecting populations means), respectively [57]. The CG and CKD-EPI equations are given in Table 1. In clinical nephrology, the results of these equations are generally used as indexed for BSA. However, in the

Table 1 Creatinine-based equations considered in the analysis: the CG and the CKD-EPI equations (without any indexation for body surface area)

CG (mL/min)	[(140-age (years))/(72×SCr)] × weight (kg) × (0.85 in female subjects)
CKD-EPI (mL/min/1.73 m^2)	k1 × $(SCr/k2)^{-\alpha}$ × 0.993^{age}
	k1 = 141, 143, 163, and 166 for white men and women and black men and women, respectively
	k2 = 0.7 and 0.9 for women and men, respectively
	α = 1.209, 1.209, 0.411, and 0.329 for men with SCr >0.9 mg/dL, women with SCr >0.7 mg/dL, men with SCr ≤0.9 mg/dL, and women with SCr ≤0.7 mg/dL, respectively
De-indexed CKD-EPI (mL/min)	eGFR in mL/min/1.73 m^2 × BSA/1.73 m^2

BSA body surface area, *CG* Cockcroft–Gault, *CKD-EPI* Chronic Kidney Disease Epidemiology, *eGFR* estimated glomerular infiltration rate, *SCr* serum creatinine (mg/dL), *Weight* actual body weight

context of drug dosing adjustment and as recommended by the International Guidelines in Nephrology (KDIGO for Kidney Disease/Improving Global Outcomes), the US Food and Drug Administration, and the European Medicines Agency, we considered the non-indexed GFR results in mL/min [5, 6, 47]. Therefore, the absolute non-indexed result is considered for the CG equation and the de-indexed value is calculated for the CKD-EPI equation (Table 1). Indeed, because drug adjustment is the quintessence of personalized medicine, it seems logical to consider the GFR of the subject and not the GFR the subject would have if his/her BSA were 1.73 m^2 [9, 58].

In this work, we consider both absolute and relative differences between equation results. We calculated absolute difference as the difference between CG results and CKD-EPI results. A negative result thus means that the CG result is lower than the CKD-EPI result. The relative difference was calculated as the absolute difference divided by the mean of the CG and CKD-EPI results. An absolute difference threshold of maximum (±) 10 mL/min and a relative difference of maximum 10 % were considered as acceptable. The choice of such thresholds is not purely arbitrary. Indeed, 10 % is the biological variation of measured GFR observed in the literature and 10 mL/min is the acceptable precision recommended for estimating GFR (when compared with measured GFR) [59, 60]. The implications of these absolute and relative thresholds will vary with GFR. Indeed, at a GFR of 10 mL/min, a relative difference of 10 % (i.e., 1 mL/min) and an absolute difference of 10 mL/min are not relevant.

In the simulation figures, red color corresponds to cases where the CG equation gives discordantly lower values than the CKD-EPI equation, blue color corresponds to cases where CG gives higher results, and green color corresponds to cases where results are concordant, i.e., within ±10 % or ±10 mL/min.

2.2 Clinical Data

In the second part of this work, we studied the prevalence of discrepancies observed from clinical data. We analyzed results from two different laboratories. The first laboratory cohort (LabU) was from a university hospital in France (Grenoble). SCr was measured by an enzymatic and IDMS-traceable method (Siemens Healthcare Diagnostics, Tarrytown, NY) [44]. Only data from hospitalized patients were considered. The second laboratory cohort (LabC) was obtained in a private laboratory (Oriade group) including 25 collecting centers in France (Grenoble and outskirts). SCr was measured by an enzymatic and IDMS traceable method (Roche Diagnostics, Mannheim, Germany) [44]. From these two laboratories, we systematically collected all data from subjects aged older than 60 years. We pooled the results from both laboratories to cover the expected creatinine range but limited the analysis of SCr results between 0.5 and 3.0 mg/dL (44–264 µmol/L) to be consistent with the simulation.

2.3 Statistics

Relative difference was calculated as the difference divided by the average of both equations. Descriptive statistics are presented as median (interquartile range). In Table 2, we used hypothesis tests (Fisher's Exact test for proportions, *t* tests for the continuous variables) to detect statistical significant differences in variables between groups of patients with relative differences between CG and CKD-EPI of less than 10 % (n = 4080, the group of patients considered with equivalent or concordant eGFR estimates) and with relative differences between CG and CKD-EPI of more than 10 % (the group of patients considered with discordant eGFR estimates), subdivided in a subgroup where CG exceeds CKD-EPI by more than 10 % (n = 438) and in a subgroup where the CG result is more than 10 % lower than CKD-EPI (n = 4573). *P* values are expressed for comparisons of the concordant group with the discordant subgroups.

A multilinear regression model was used to explain the variation in relative differences, using sex, age, weight, height, and SCr levels as independent explanatory variables. R^2 (coefficient of determination) is presented as the percentage of explained variation and as measure for the

Table 2 Clinical data: clinical characteristics of subjects with concordant vs. discordant results between CG and CKD-EPI

$N = 9091$	Relative difference within ±10 % ($n = 4080$)	Relative difference of more than 10 % (CG overestimates) ($n = 438$)	P value with ±10 % as the reference	Relative difference of less than 10 % (CG underestimates) ($n = 4573$)	P value with ±10 % as the reference
% of women	47	58	<0.0001	48	0.4504
Age (years)	67 (64;72)	65 (62;69)	<0.0001	76 (70;81)	<0.0001
Weight (kg)	78 (70;87)	95 (85;109)	<0.0001	65 (57;72)	<0.0001
Height (cm)	168 (160;174)	166 (160;173)	0.0119	165 (160;172)	<0.0001
Serum creatinine (mg/dL)	0.96 (0.8;1.18)	1.00 (0.69;1.48)	0.2446	0.94 (0.80;1.10)	<0.0001

Comparison of proportions with the Fisher Exact test. Continuous variables (age, weight, height, serum creatinine) were compared between the group of patients with relative differences between the two equations within 10 % and the groups with results outside 10 % (<−10 and >+10 %)

CG Cockcroft–Gault, *CKD-EPI* Chronic Kidney Disease Epidemiology

goodness of fit. Statistical significance was considered at the 5 % significance level.

3 Results

3.1 Theoretical Simulation

Figure 1 shows the potential discordances (1A graph is absolute difference and 1B graph is relative difference) between CKD-EPI and CG at a fixed age of 70 years for men (upper graph) and women (lower graph).

For 70-year-old male subjects, the following results were obtained: (1) when weight was above 105 kg, CG was always greater than CKD-EPI (no matter the SCr), and discordantly higher (>10 mL/min) in 75 % of the SCr range (0.5–3.0 mg/dL or 44–264 µmol/L); (2) among subjects with weight between 65 and 100 kg, 86 % of this weight range (no matter the SCr) had differences between CG and CKD-EPI within 10 mL/min, only 8 % showed discordantly higher CG and 6 % showed discordantly lower CG than CKD-EPI; (3) conversely, at low body weight (25–55 kg), CG was always lower than CKD-EPI, with about 50 % of this weight range discordantly lower (no matter the SCr), rising to nearly 100 % of the cases when SCr was in the normal range (0.6–1.2 mg/dL or 53–106 µmol/L).

For 70-year-old female subjects, similar results were obtained: (1) when body weight was above 85 kg, CG was always greater than CKD-EPI (no matter the SCr), and discordantly higher (>10 mL/min) in 74 % of the SCr range (0.5–3.0 mg/dL or 44–264 µmol/L); (2) for body weight between 50 and 80 kg, about 94 % of this weight range (no matter the SCr) had differences between CG and CKD-EPI within 10 mL/min, only 2 % showed discordantly higher CG and 4 % showed discordantly lower CG than CKD-EPI; and (3) conversely, at low weight (25–45 kg), CG was always smaller than CKD-EPI, with about 30 % of this weight range discordantly smaller (no matter the SCr), raising to nearly 100 % of this weight range when SCr was in the normal range (0.5–1.0 mg/dL or 44–88 µmol/L).

In Figs. 2 and 3, we modified age from 50 to 80 years for men and observed absolute and relative differences, respectively. Clearly, concordance between the equations increased with aging (green cases) when absolute differences were considered. The same pattern was observed in women (data not shown). If relative differences were considered, the trend was less impressive. Furthermore, with aging, we observed that the proportion of discordantly lower CG results (red cases) increased whereas the cases with discordantly higher CG results (blue cases) decreased.

In Fig. 3 (relative difference for male subjects), the yellow rectangle corresponds to subjects with normal SCr values (0.6–1.2 mg/dL or 53–106 µmol/L) and normal weights (60–85 kg). It is interesting to note that these 'normal' subjects had mostly concordant results (green cases) between the two equations at age 50 years and younger, but that discrepancies between the two equations results increased with aging, the majority of CG results being discordantly lower than the CKD-EPI equations (more red cases in these normal subjects). The same observation was made in women (data not shown).

In CKD patients (SCr 1.5–3 mg/dL or 132–264 µmol/L), the simulations showed, as expected, different results if absolute or relative differences are considered. Globally, when absolute differences were considered, the simulation showed that concordance between the two equations increased with aging, except in male subjects with low weight (<60 kg). If relative differences were considered, the higher concordance between equations with aging remained true but only in subjects with normal weight (within 60–85 kg). The concordance between relative differences was very low (between 0 and 50 %) for female subjects (independent of weight) and for male subjects with extremely low and high body weight.

A

Males																											
	Age 70		Length 177																								
	BSA	W/Scr	0,5	0,6	0,7	0,8	0,9	1	1,1	1,2	1,3	1,4	1,5	1,6	1,7	1,8	1,9	2	2,1	2,2	2,3	2,4	2,5	2,6	2,7	2,8	2,9	3
	1,20	25	-27,7	-30,3	-31,8	-32,6	-33,0	-28,5	-25,0	-22,1	-19,7	-17,8	-16,1	-14,7	-13,5	-12,4	-11,5	-10,7	-10,0	-9,3	-8,7	-8,2	-7,7	-7,3	-6,9	-6,5	-6,2	-5,9
	1,30	30	-24,2	-27,9	-30,2	-31,6	-32,4	-27,9	-24,3	-21,5	-19,1	-17,1	-15,5	-14,1	-12,9	-11,8	-10,9	-10,1	-9,4	-8,7	-8,2	-7,6	-7,2	-6,8	-6,4	-6,0	-5,7	-5,4
	1,39	35	-20,0	-25,0	-28,1	-30,1	-31,4	-26,9	-23,3	-20,5	-18,2	-16,2	-14,6	-13,2	-12,1	-11,0	-10,1	-9,3	-8,6	-8,0	-7,5	-7,0	-6,5	-6,1	-5,7	-5,4	-5,1	-4,8
	1,47	40	-15,5	-21,7	-25,6	-28,2	-30,0	-25,6	-22,1	-19,3	-17,0	-15,1	-13,6	-12,2	-11,1	-10,1	-9,2	-8,4	-7,8	-7,2	-6,6	-6,2	-5,7	-5,3	-5,0	-4,7	-4,4	-4,1
	1,54	45	-10,5	-18,0	-22,9	-26,1	-28,4	-24,0	-20,6	-17,9	-15,7	-13,9	-12,3	-11,1	-9,9	-9,0	-8,2	-7,4	-6,8	-6,2	-5,7	-5,3	-4,9	-4,5	-4,2	-3,9	-3,6	-3,4
	1,62	50	-5,3	-14,1	-19,8	-23,7	-26,5	-22,3	-19,0	-16,3	-14,2	-12,5	-11,0	-9,8	-8,7	-7,8	-7,0	-6,4	-5,8	-5,2	-4,8	-4,3	-4,0	-3,6	-3,3	-3,1	-2,8	-2,6
	1,68	55	0,2	-9,9	-16,6	-21,2	-24,4	-20,3	-17,2	-14,6	-12,6	-10,9	-9,6	-8,4	-7,4	-6,6	-5,8	-5,2	-4,6	-4,1	-3,7	-3,3	-3,0	-2,7	-2,4	-2,2	-1,9	-1,7
	1,75	60	5,9	-5,5	-13,1	-18,4	-22,2	-18,3	-15,2	-12,8	-10,9	-9,3	-8,0	-6,9	-6,0	-5,2	-4,5	-4,0	-3,5	-3,0	-2,6	-2,3	-2,0	-1,7	-1,4	-1,2	-1,0	-0,8
	1,81	65	11,8	-1,0	-9,5	-15,5	-19,8	-16,0	-13,2	-10,9	-9,1	-7,6	-6,4	-5,4	-4,5	-3,8	-3,2	-2,7	-2,2	-1,8	-1,5	-1,2	-0,9	-0,7	-0,4	-0,3	-0,1	0,1
	1,86	70	17,8	3,7	-5,8	-12,4	-17,3	-13,7	-11,0	-8,9	-7,2	-5,8	-4,7	-3,8	-3,0	-2,4	-1,8	-1,3	-0,9	-0,6	-0,3	0,0	0,2	0,4	0,6	0,8	0,9	1,0
	1,92	75	24,1	8,5	-1,9	-9,2	-14,6	-11,3	-8,8	-6,8	-5,2	-4,0	-3,0	-2,1	-1,4	-0,9	-0,4	0,0	0,4	0,7	0,9	1,2	1,4	1,5	1,7	1,8	1,9	2,0
	1,97	80	30,4	13,5	2,1	-6,0	-11,9	-8,8	-6,4	-4,6	-3,2	-2,1	-1,2	-0,4	0,2	0,7	1,1	1,5	1,7	2,0	2,2	2,4	2,5	2,7	2,8	2,9	2,9	3,0
	2,02	85	36,8	18,6	6,2	-2,6	-9,1	-6,2	-4,0	-2,4	-1,1	-0,1	0,7	1,3	1,9	2,3	2,6	2,9	3,1	3,3	3,5	3,6	3,7	3,8	3,9	3,9	4,0	4,0
	2,07	90	43,4	23,7	10,4	0,9	-6,1	-3,5	-1,5	-0,1	1,0	1,9	2,6	3,1	3,6	3,9	4,2	4,4	4,6	4,7	4,8	4,9	4,9	5,0	5,0	5,0	5,1	5,1
	2,12	95	50,1	29,0	14,7	4,5	-3,1	-0,7	1,0	2,3	3,2	4,0	4,5	5,0	5,3	5,6	5,8	5,9	6,0	6,1	6,1	6,2	6,2	6,2	6,2	6,2	6,1	6,1
	2,17	100	56,8	34,4	19,0	8,1	-0,1	2,1	3,6	4,7	5,5	6,1	6,5	6,9	7,1	7,3	7,4	7,4	7,5	7,5	7,5	7,5	7,5	7,4	7,4	7,3	7,3	7,2
	2,21	105	63,7	39,8	23,5	11,8	3,1	4,9	6,2	7,1	7,8	8,2	8,5	8,8	8,9	9,0	9,0	9,0	9,0	9,0	8,9	8,8	8,7	8,7	8,6	8,5	8,4	8,3
	2,26	110	70,6	45,3	28,0	15,5	6,3	7,9	8,9	9,6	10,1	10,4	10,6	10,7	10,7	10,7	10,7	10,6	10,5	10,4	10,3	10,2	10,0	9,9	9,8	9,7	9,5	9,4
	2,30	115	77,6	50,8	32,5	19,4	9,5	10,8	11,7	12,2	12,5	12,6	12,7	12,7	12,6	12,5	12,4	12,2	12,1	11,9	11,7	11,5	11,4	11,2	11,0	10,8	10,7	10,5
	2,34	120	84,6	56,5	37,2	23,2	12,8	13,8	14,4	14,7	14,9	14,9	14,8	14,7	14,5	14,3	14,1	13,9	13,6	13,4	13,2	12,9	12,7	12,5	12,3	12,1	11,8	11,6
	2,38	125	91,7	62,2	41,8	27,2	16,2	16,9	17,2	17,3	17,3	17,1	16,9	16,7	16,4	16,1	15,8	15,5	15,2	14,9	14,6	14,3	14,1	13,8	13,5	13,3	13,0	12,8

Females																											
	Age 70		Length 165																								
	BSA	W/Scr	0,5	0,6	0,7	0,8	0,9	1	1,1	1,2	1,3	1,4	1,5	1,6	1,7	1,8	1,9	2	2,1	2,2	2,3	2,4	2,5	2,6	2,7	2,8	2,9	3
	1,14	25	-23,7	-26,8	-28,7	-23,7	-20,0	-17,2	-14,9	-13,1	-11,6	-10,4	-9,4	-8,5	-7,8	-7,1	-6,5	-6,0	-5,6	-5,2	-4,8	-4,5	-4,2	-4,0	-3,7	-3,5	-3,3	-3,1
	1,24	30	-20,7	-24,8	-27,5	-22,5	-18,9	-16,1	-13,9	-12,1	-10,7	-9,5	-8,5	-7,7	-6,9	-6,3	-5,8	-5,3	-4,9	-4,5	-4,1	-3,8	-3,6	-3,3	-3,1	-2,9	-2,7	-2,6
	1,32	35	-17,2	-22,4	-25,8	-21,0	-17,4	-14,7	-12,6	-10,9	-9,5	-8,4	-7,4	-6,6	-6,0	-5,4	-4,9	-4,4	-4,0	-3,7	-3,4	-3,1	-2,8	-2,6	-2,4	-2,2	-2,1	-1,9
	1,40	40	-13,3	-19,7	-23,8	-19,2	-15,7	-13,1	-11,1	-9,5	-8,2	-7,1	-6,2	-5,5	-4,9	-4,3	-3,9	-3,4	-3,1	-2,8	-2,5	-2,2	-2,0	-1,8	-1,7	-1,5	-1,3	-1,2
	1,47	45	-9,1	-16,6	-21,6	-17,1	-13,8	-11,4	-9,5	-8,0	-6,7	-5,8	-4,9	-4,3	-3,7	-3,2	-2,8	-2,4	-2,1	-1,8	-1,6	-1,4	-1,2	-1,0	-0,8	-0,7	-0,6	-0,5
	1,53	50	-4,6	-13,3	-19,1	-14,8	-11,8	-9,4	-7,7	-6,3	-5,2	-4,3	-3,5	-2,9	-2,4	-2,0	-1,6	-1,3	-1,0	-0,8	-0,6	-0,4	-0,2	-0,1	0,0	0,1	0,2	0,3
	1,60	55	0,0	-9,9	-16,4	-12,4	-9,5	-7,4	-5,8	-4,5	-3,5	-2,7	-2,1	-1,5	-1,1	-0,7	-0,4	-0,1	0,1	0,3	0,4	0,6	0,7	0,8	0,9	1,0	1,1	1,1
	1,66	60	4,8	-6,2	-13,6	-9,9	-7,2	-5,3	-3,8	-2,7	-1,8	-1,1	-0,5	-0,1	0,3	0,6	0,8	1,1	1,2	1,4	1,5	1,6	1,7	1,8	1,9	1,9	2,0	2,0
	1,72	65	9,8	-2,4	-10,6	-7,2	-4,8	-3,0	-1,7	-0,8	0,0	0,6	1,0	1,4	1,7	2,0	2,1	2,3	2,4	2,5	2,6	2,7	2,7	2,8	2,8	2,8	2,9	2,9
	1,77	70	15,0	1,6	-7,5	-4,4	-2,3	-0,7	0,4	1,2	1,8	2,3	2,7	3,0	3,2	3,4	3,5	3,6	3,7	3,7	3,8	3,8	3,8	3,8	3,8	3,8	3,8	3,8
	1,82	75	20,3	5,6	-4,3	-1,5	0,4	1,7	2,6	3,3	3,8	4,1	4,4	4,6	4,7	4,8	4,9	4,9	4,9	4,9	4,9	4,9	4,9	4,8	4,8	4,8	4,7	4,7
	1,87	80	25,6	9,8	-1,0	1,4	3,0	4,1	4,9	5,4	5,7	5,9	6,1	6,2	6,3	6,3	6,3	6,2	6,2	6,2	6,1	6,0	6,0	5,9	5,8	5,8	5,7	5,6
	1,92	85	31,1	14,1	2,4	4,5	5,8	6,6	7,2	7,5	7,7	7,8	7,9	7,9	7,8	7,8	7,7	7,6	7,5	7,4	7,3	7,2	7,1	7,0	6,9	6,8	6,7	6,6
	1,97	90	36,7	18,4	5,9	7,6	8,6	9,2	9,5	9,7	9,8	9,7	9,7	9,6	9,4	9,3	9,1	9,0	8,8	8,7	8,5	8,4	8,2	8,1	7,9	7,8	7,7	7,5
	2,02	95	42,4	22,9	9,5	10,8	11,5	11,8	11,9	11,9	11,8	11,7	11,5	11,3	11,1	10,8	10,6	10,4	10,2	10,0	9,8	9,6	9,4	9,2	9,0	8,8	8,7	8,5
	2,06	100	48,1	27,4	13,1	14,0	14,4	14,5	14,4	14,2	13,9	13,6	13,3	13,0	12,7	12,4	12,1	11,8	11,6	11,3	11,0	10,8	10,5	10,3	10,1	9,9	9,7	9,5
	2,10	105	53,9	31,9	16,9	17,3	17,4	17,2	16,9	16,5	16,1	15,6	15,2	14,8	14,4	14,0	13,6	13,3	12,9	12,6	12,3	12,0	11,7	11,5	11,2	10,9	10,7	10,5
	2,15	110	59,8	36,6	20,6	20,7	20,4	19,9	19,4	18,8	18,2	17,7	17,1	16,6	16,1	15,6	15,2	14,7	14,3	14,0	13,6	13,2	12,9	12,6	12,3	12,0	11,8	11,5
	2,19	115	65,7	41,3	24,4	24,1	23,4	22,7	21,9	21,2	20,4	19,7	19,1	18,4	17,8	17,3	16,7	16,2	15,8	15,3	14,9	14,5	14,1	13,8	13,4	13,1	12,8	12,5
	2,23	120	71,7	46,0	28,3	27,5	26,5	25,5	24,5	23,6	22,7	21,8	21,0	20,3	19,6	18,9	18,3	17,7	17,2	16,7	16,2	15,8	15,3	14,9	14,6	14,2	13,9	13,5
	2,27	125	77,8	50,8	32,2	31,0	29,7	28,4	27,1	26,0	24,9	23,9	23,0	22,1	21,3	20,6	19,9	19,2	18,6	18,1	17,5	17,0	16,6	16,1	15,7	15,3	14,9	14,6

Fig. 1 Potential discordances between CKD-EPI and CG at a fixed age of 70 years for men (*upper graph*) and women (*lower graph*). Creatinine values are expressed in mg/dL. To convert in µmol/L, multiply by 88. Graphs are (**a**) absolute difference and (**b**) relative difference. *Red color* corresponds to cases where the CG equation gives discordantly lower values than the CKD-EPI equation, *blue color* corresponds to cases where the CG equation gives higher results, and *green color* corresponds to cases where results are concordant, i.e., within ±10 % or ±10 mL/min. *CG* Cockcroft–Gault, *CKD-EPI* chronic kidney disease epidemiology

3.2 Clinical Data

From the two laboratories, 9535 SCr results from subjects aged older than 60 years were available with limited anthropometric information (sex, height, weight, and age). Among these, 9091 samples had SCr measured between 0.5 and 3 mg/dL (44–264 µmol/L) and were thus included in the present analysis. Among these 9091 results, 48 % were from women. Median age was 71 [interquartile range: 66; 78] years. Median weight and height were 72 [62; 82] kg and 167 [160; 173] cm, respectively. Median SCr was 0.95 [0.80; 1.14] mg/dL (84 [70; 100] µmol/L) and median eGFR by CKD-EPI and eClCr by CG were 65 [51; 81] and 74 [59; 88] mL/min, respectively. Among these 9091 results, 4080 (45 %) had CKD-EPI and CG results within ±10 % and were thus considered concordant. The vast majority of discordant results reflected a CG equation result discordantly lower than the CKD-EPI equation ($n = 4573$, 95 %), whereas only 438 (5 %) subjects had a CKD-EPI equation result lower than the CG equation result. Table 2 shows the characteristics of these subjects. Most analyzed variables are actually significantly different for patients with discordant vs. concordant results, but the most marked difference is the median weight: 78 [70; 87] kg in subjects with concordant results, 95 [85; 109] kg in subjects with CG greater than CKD-EPI and 65 [57; 72] kg in subjects with CKD-EPI greater than CG.

We analyzed the relative difference between CG and CKD-EPI results according to the different anthropometric variables, i.e., sex, height, weight, age, and SCr. By least-

B

Males																											
	Age	70	L(cm)	177																							
	BSA	W/Scr	0,5	0,6	0,7	0,8	0,9	1	1,1	1,2	1,3	1,4	1,5	1,6	1,7	1,8	1,9	2	2,1	2,2	2,3	2,4	2,5	2,6	2,7	2,8	2,9	3
	1,20	25	-44%	-54%	-63%	-70%	-76%	-70%	-65%	-60%	-56%	-53%	-50%	-47%	-45%	-42%	-40%	-39%	-37%	-35%	-34%	-33%	-31%	-30%	-29%	-28%	-27%	-26%
	1,30	30	-34%	-45%	-53%	-60%	-67%	-61%	-56%	-52%	-49%	-46%	-43%	-41%	-38%	-36%	-35%	-33%	-31%	-30%	-29%	-28%	-26%	-25%	-24%	-24%	-23%	-22%
	1,39	35	-26%	-36%	-45%	-52%	-59%	-54%	-49%	-46%	-42%	-40%	-37%	-35%	-33%	-31%	-29%	-28%	-27%	-25%	-24%	-23%	-22%	-21%	-20%	-19%	-19%	-18%
	1,47	40	-18%	-29%	-37%	-45%	-52%	-47%	-43%	-40%	-37%	-34%	-32%	-30%	-28%	-26%	-25%	-23%	-22%	-21%	-20%	-19%	-18%	-17%	-16%	-16%	-15%	-14%
	1,54	45	-11%	-22%	-31%	-39%	-45%	-41%	-37%	-34%	-31%	-29%	-27%	-25%	-23%	-22%	-21%	-19%	-18%	-17%	-16%	-15%	-14%	-14%	-13%	-12%	-12%	-11%
	1,62	50	-5%	-16%	-25%	-33%	-39%	-35%	-32%	-29%	-27%	-24%	-23%	-21%	-19%	-18%	-17%	-15%	-14%	-13%	-13%	-12%	-11%	-10%	-10%	-9%	-8%	-8%
	1,68	55	0%	-11%	-20%	-27%	-34%	-30%	-27%	-25%	-22%	-20%	-18%	-17%	-15%	-14%	-13%	-12%	-11%	-10%	-9%	-9%	-8%	-7%	-7%	-6%	-6%	-5%
	1,75	60	5%	-6%	-15%	-22%	-29%	-26%	-23%	-20%	-18%	-16%	-15%	-13%	-12%	-11%	-10%	-9%	-8%	-7%	-6%	-6%	-5%	-4%	-4%	-3%	-3%	-2%
	1,81	65	10%	-1%	-10%	-18%	-25%	-21%	-19%	-16%	-14%	-13%	-11%	-10%	-9%	-7%	-6%	-6%	-5%	-4%	-3%	-3%	-2%	-2%	-1%	-1%	0%	0%
	1,86	70	14%	3%	-6%	-14%	-20%	-17%	-15%	-13%	-11%	-9%	-8%	-7%	-5%	-4%	-3%	-3%	-2%	-1%	-1%	0%	0%	1%	1%	2%	2%	3%
	1,92	75	18%	7%	-2%	-10%	-17%	-14%	-11%	-9%	-8%	-6%	-5%	-4%	-2%	-2%	-1%	0%	1%	1%	2%	2%	3%	3%	4%	4%	5%	5%
	1,97	80	22%	11%	2%	-6%	-13%	-10%	-8%	-6%	-4%	-3%	-2%	-1%	0%	1%	2%	3%	3%	4%	4%	5%	5%	6%	6%	6%	7%	7%
	2,02	85	25%	14%	5%	-2%	-9%	-7%	-5%	-3%	-1%	0%	1%	2%	3%	4%	4%	5%	6%	6%	7%	7%	7%	8%	8%	8%	9%	9%
	2,07	90	28%	18%	9%	1%	-6%	-4%	-2%	0%	1%	3%	4%	5%	5%	6%	7%	7%	8%	8%	9%	9%	10%	10%	10%	11%	11%	11%
	2,12	95	31%	21%	12%	4%	-3%	-1%	1%	3%	4%	5%	6%	7%	8%	9%	9%	10%	10%	11%	11%	11%	12%	12%	12%	12%	13%	13%
	2,17	100	34%	24%	15%	7%	0%	2%	4%	5%	7%	8%	9%	9%	10%	11%	11%	12%	12%	13%	13%	13%	14%	14%	14%	14%	14%	15%
	2,21	105	37%	26%	18%	10%	3%	5%	6%	8%	9%	10%	11%	12%	12%	13%	13%	14%	14%	15%	15%	15%	15%	16%	16%	16%	16%	16%
	2,26	110	40%	29%	20%	12%	5%	7%	9%	10%	11%	12%	13%	14%	14%	15%	15%	16%	16%	16%	17%	17%	17%	17%	18%	18%	18%	18%
	2,30	115	42%	32%	23%	15%	8%	10%	11%	12%	14%	14%	15%	16%	16%	17%	17%	18%	18%	18%	19%	19%	19%	19%	19%	19%	20%	20%
	2,34	120	44%	34%	25%	17%	10%	12%	14%	15%	16%	16%	17%	18%	18%	19%	19%	19%	20%	20%	20%	20%	21%	21%	21%	21%	21%	21%
	2,38	125	47%	36%	27%	20%	13%	14%	16%	17%	18%	18%	19%	20%	20%	21%	21%	21%	21%	22%	22%	22%	22%	22%	22%	23%	23%	23%

Females																											
	Age	70	L(cm)	165																							
	BSA	W/Scr	0,5	0,6	0,7	0,8	0,9	1	1,1	1,2	1,3	1,4	1,5	1,6	1,7	1,8	1,9	2	2,1	2,2	2,3	2,4	2,5	2,6	2,7	2,8	2,9	3
	1,14	25	-45%	-56%	-65%	-63%	-61%	-59%	-57%	-55%	-54%	-52%	-51%	-50%	-48%	-47%	-46%	-45%	-44%	-43%	-42%	-42%	-41%	-40%	-39%	-38%	-38%	-37%
	1,24	30	-34%	-46%	-56%	-53%	-51%	-49%	-47%	-45%	-44%	-42%	-41%	-40%	-38%	-37%	-36%	-35%	-34%	-33%	-32%	-31%	-31%	-30%	-29%	-28%	-28%	-27%
	1,32	35	-26%	-38%	-48%	-45%	-43%	-41%	-39%	-37%	-35%	-34%	-32%	-31%	-30%	-29%	-28%	-26%	-25%	-25%	-24%	-23%	-22%	-21%	-20%	-20%	-19%	-18%
	1,40	40	-18%	-30%	-40%	-38%	-35%	-33%	-31%	-29%	-28%	-26%	-25%	-23%	-22%	-21%	-20%	-19%	-18%	-17%	-16%	-15%	-14%	-13%	-13%	-12%	-11%	-10%
	1,47	45	-12%	-24%	-34%	-31%	-29%	-26%	-25%	-23%	-21%	-20%	-18%	-17%	-16%	-14%	-13%	-12%	-11%	-10%	-9%	-8%	-7%	-7%	-6%	-5%	-4%	-4%
	1,53	50	-5%	-18%	-28%	-25%	-23%	-21%	-19%	-17%	-15%	-14%	-12%	-11%	-9%	-8%	-7%	-6%	-5%	-4%	-3%	-2%	-1%	-1%	0%	1%	2%	2%
	1,60	55	0%	-12%	-22%	-20%	-17%	-15%	-13%	-11%	-10%	-8%	-7%	-5%	-4%	-3%	-2%	-1%	0%	1%	2%	3%	4%	5%	6%	6%	7%	8%
	1,66	60	5%	-7%	-18%	-15%	-12%	-10%	-8%	-6%	-5%	-3%	-2%	0%	1%	2%	3%	4%	5%	6%	7%	8%	9%	10%	11%	11%	12%	13%
	1,72	65	10%	-3%	-13%	-10%	-8%	-6%	-4%	-2%	0%	2%	3%	4%	6%	7%	8%	9%	10%	11%	12%	13%	14%	14%	15%	16%	17%	17%
	1,77	70	14%	2%	-9%	-6%	-3%	-1%	1%	3%	4%	6%	7%	9%	10%	11%	12%	13%	14%	15%	16%	17%	18%	19%	19%	20%	21%	22%
	1,82	75	18%	6%	-5%	-2%	1%	3%	5%	7%	8%	10%	11%	13%	14%	15%	16%	17%	18%	19%	20%	21%	22%	23%	23%	24%	25%	26%
	1,87	80	21%	9%	-1%	2%	4%	6%	8%	10%	12%	13%	15%	16%	17%	19%	20%	21%	22%	23%	24%	25%	25%	26%	27%	28%	28%	29%
	1,92	85	25%	13%	2%	5%	8%	10%	12%	14%	15%	17%	18%	20%	21%	22%	23%	24%	25%	26%	27%	28%	29%	30%	30%	31%	32%	33%
	1,97	90	28%	16%	6%	9%	11%	13%	15%	17%	19%	20%	22%	23%	24%	25%	26%	28%	29%	29%	30%	31%	32%	33%	34%	34%	35%	36%
	2,02	95	31%	19%	9%	12%	14%	16%	18%	20%	22%	23%	25%	26%	27%	28%	30%	31%	32%	33%	33%	34%	35%	36%	37%	37%	38%	39%
	2,06	100	34%	22%	12%	15%	17%	19%	21%	23%	25%	26%	28%	29%	30%	31%	32%	33%	34%	35%	36%	37%	38%	39%	39%	40%	41%	42%
	2,10	105	37%	25%	15%	17%	20%	22%	24%	26%	27%	29%	30%	32%	33%	34%	35%	36%	37%	38%	39%	40%	41%	41%	42%	43%	44%	44%
	2,15	110	39%	27%	17%	20%	22%	25%	27%	28%	30%	32%	33%	34%	35%	37%	38%	39%	40%	41%	42%	42%	43%	44%	45%	45%	46%	47%
	2,19	115	42%	30%	20%	23%	25%	27%	29%	31%	32%	34%	35%	37%	38%	39%	40%	41%	42%	43%	44%	45%	46%	46%	47%	48%	49%	49%
	2,23	120	44%	32%	22%	25%	27%	30%	31%	33%	35%	36%	38%	39%	40%	41%	43%	44%	44%	45%	46%	47%	48%	49%	49%	50%	51%	52%
	2,27	125	46%	35%	25%	27%	30%	32%	34%	36%	37%	39%	40%	41%	43%	44%	45%	46%	47%	48%	49%	49%	50%	51%	52%	52%	53%	54%

Fig. 1 continued

squares multiple regression, we showed that all variables explained 88 % of the variation in relative difference between the two equations (R^2-adjusted = 0.88). Among these variables, age ($r_{\text{partial}} = -0.82$) and weight are clearly the most important ($r_{\text{partial}} = 0.88$).

With aging (combining both sexes), the relative difference between CG and CKD-EPI results became more negative. In other words, the CG results were progressively lower in comparison to CKD-EPI results with aging (Fig. 4). On average, the effect was zero at the age of 60 years, but CKD-EPI exceeded CG with a nearly linear increase, reaching an overestimation of 40 % at the age of 95 years.

Regarding body weight (combining both sexes), the relative difference between CG and CKD-EPI results increased when weight increased. In other words, the CG results were lower in comparison to CKD-EPI results at low weight values. When weight increased, the difference between the two equations decreased and, in heavier subjects, the CG result was superior to CKD-EPI results (Fig. 5). On average, the effect was zero around a weight of 90 kg. The majority of subjects had a weight below 90 kg and, for them, CKD-EPI exceeded CG by 0–40 %. However, a minority of the cohort had weight above 90 kg and, in these specific patients, CKD-EPI was less than CG by 0–20 %. People with a very low weight (<50 kg) were most likely to be discordantly classified with a CKD-EPI result >20 % higher than their CG result. The effects of SCr on the discrepancy between CKD-EPI and CG were much less than those of age and weight (Fig. 6). In fact, there was no clear relationship between SCr and the CKD-EPI/CG difference.

4 Discussion

We provide a simple mathematical illustration of potential differences, absolute or relative, between the non-indexed CG equation and the de-indexed CKD-EPI equations (in

Males																											
Age 50		Length 177																									
BSA	W/Scr	0,5	0,6	0,7	0,8	0,9	1	1,1	1,2	1,3	1,4	1,5	1,6	1,7	1,8	1,9	2	2,1	2,2	2,3	2,4	2,5	2,6	2,7	2,8	2,9	3
1,20	25	-25,4	-29,4	-31,9	-33,4	-34,3	-29,5	-25,7	-22,7	-20,2	-18,1	-16,4	-14,9	-13,6	-12,5	-11,5	-10,7	-9,9	-9,2	-8,6	-8,1	-7,6	-7,1	-6,7	-6,3	-6,0	-5,7
1,30	30	-19,9	-25,6	-29,1	-31,4	-32,9	-28,2	-24,4	-21,4	-19,0	-16,9	-15,2	-13,8	-12,5	-11,4	-10,5	-9,6	-8,9	-8,3	-7,7	-7,2	-6,7	-6,3	-5,9	-5,5	-5,2	-4,9
1,39	35	-13,9	-21,1	-25,8	-28,9	-31,0	-26,3	-22,7	-19,8	-17,4	-15,4	-13,8	-12,4	-11,2	-10,1	-9,2	-8,4	-7,8	-7,1	-6,6	-6,1	-5,7	-5,3	-4,9	-4,6	-4,3	-4,0
1,47	40	-7,3	-16,2	-22,0	-25,9	-28,7	-24,2	-20,7	-17,8	-15,6	-13,7	-12,1	-10,8	-9,6	-8,7	-7,8	-7,1	-6,4	-5,9	-5,4	-4,9	-4,5	-4,1	-3,8	-3,5	-3,2	-3,0
1,54	45	-0,3	-10,9	-17,9	-22,7	-26,1	-21,7	-18,4	-15,7	-13,5	-11,8	-10,3	-9,0	-8,0	-7,1	-6,3	-5,6	-5,0	-4,5	-4,0	-3,6	-3,3	-2,9	-2,6	-2,4	-2,1	-1,9
1,62	50	7,0	-5,3	-13,4	-19,1	-23,2	-19,1	-15,9	-13,3	-11,3	-9,7	-8,3	-7,1	-6,2	-5,4	-4,6	-4,0	-3,5	-3,0	-2,6	-2,3	-1,9	-1,7	-1,4	-1,2	-1,0	-0,8
1,68	55	14,7	0,6	-8,8	-15,3	-20,1	-16,2	-13,2	-10,8	-9,0	-7,4	-6,2	-5,2	-4,3	-3,5	-2,9	-2,4	-1,9	-1,5	-1,1	-0,8	-0,6	-0,3	-0,1	0,1	0,3	0,4
1,75	60	22,5	6,7	-3,9	-11,3	-16,8	-13,1	-10,4	-8,2	-6,5	-5,1	-4,0	-3,1	-2,3	-1,6	-1,1	-0,6	-0,2	0,1	0,4	0,7	0,9	1,1	1,3	1,4	1,5	1,6
1,81	65	30,6	13,1	1,2	-7,2	-13,3	-9,9	-7,4	-5,4	-3,9	-2,7	-1,7	-0,9	-0,2	0,3	0,8	1,2	1,5	1,8	2,0	2,2	2,4	2,5	2,6	2,8	2,8	2,9
1,86	70	38,9	19,6	6,5	-2,8	-9,7	-6,6	-4,3	-2,6	-1,2	-0,2	0,7	1,4	1,9	2,4	2,7	3,0	3,3	3,5	3,7	3,8	3,9	4,0	4,1	4,1	4,2	4,2
1,92	75	47,3	26,2	11,9	1,7	-5,9	-3,2	-1,1	0,4	1,5	2,4	3,1	3,7	4,1	4,5	4,7	5,0	5,1	5,3	5,4	5,4	5,5	5,5	5,6	5,6	5,6	5,6
1,97	80	56,0	33,0	17,4	6,3	-2,0	0,4	2,1	3,4	4,4	5,1	5,7	6,1	6,4	6,6	6,8	6,9	7,0	7,1	7,1	7,1	7,1	7,1	7,1	7,0	7,0	6,9
2,02	85	64,7	39,9	23,1	11,0	2,0	4,0	5,5	6,6	7,3	7,8	8,2	8,5	8,7	8,8	8,9	8,9	8,9	8,9	8,9	8,8	8,7	8,7	8,6	8,5	8,4	8,3
2,07	90	73,6	47,0	28,8	15,8	6,1	7,8	9,0	9,7	10,3	10,6	10,9	11,0	11,0	11,0	11,0	11,0	10,9	10,8	10,7	10,5	10,4	10,3	10,2	10,0	9,9	9,8
2,12	95	82,5	54,1	34,7	20,7	10,2	11,6	12,5	13,0	13,3	13,5	13,5	13,5	13,4	13,3	13,2	13,0	12,9	12,7	12,5	12,3	12,1	11,9	11,7	11,6	11,4	11,2
2,17	100	91,6	61,4	40,6	25,7	14,5	15,5	16,0	16,3	16,4	16,4	16,3	16,1	15,9	15,6	15,4	15,1	14,9	14,6	14,3	14,1	13,8	13,6	13,3	13,1	12,9	12,7
2,21	105	100,8	68,7	46,7	30,8	18,8	19,4	19,7	19,7	19,5	19,3	19,0	18,7	18,3	18,0	17,6	17,3	16,9	16,6	16,2	15,9	15,6	15,3	15,0	14,7	14,4	14,1
2,26	110	110,1	76,1	52,8	35,9	23,2	23,5	23,4	23,1	22,7	22,3	21,8	21,3	20,8	20,4	19,9	19,4	19,0	18,5	18,1	17,7	17,3	17,0	16,6	16,3	15,9	15,6
2,30	115	119,4	83,6	59,0	41,1	27,7	27,5	27,1	26,6	26,0	25,3	24,7	24,0	23,4	22,8	22,2	21,6	21,1	20,5	20,0	19,6	19,1	18,7	18,3	17,9	17,5	17,1
2,34	120	128,9	91,2	65,2	46,4	32,3	31,7	30,9	30,1	29,2	28,4	27,5	26,7	25,9	25,2	24,5	23,8	23,2	22,6	22,0	21,4	20,9	20,4	19,9	19,5	19,1	18,6
2,38	125	138,4	98,9	71,6	51,8	36,8	35,8	34,7	33,6	32,5	31,4	30,4	29,4	28,5	27,6	26,8	26,0	25,3	24,6	23,9	23,3	22,7	22,2	21,6	21,1	20,6	20,2

Males																											
Age 60		Length 177																									
BSA	W/Scr	0,5	0,6	0,7	0,8	0,9	1	1,1	1,2	1,3	1,4	1,5	1,6	1,7	1,8	1,9	2	2,1	2,2	2,3	2,4	2,5	2,6	2,7	2,8	2,9	3
1,20	25	-26,4	-29,7	-31,6	-32,8	-33,5	-28,9	-25,2	-22,3	-19,9	-17,9	-16,2	-14,7	-13,5	-12,4	-11,4	-10,6	-9,9	-9,2	-8,6	-8,1	-7,6	-7,2	-6,8	-6,4	-6,1	-5,7
1,30	30	-21,8	-26,6	-29,5	-31,3	-32,5	-27,9	-24,2	-21,3	-18,9	-16,9	-15,3	-13,8	-12,6	-11,5	-10,6	-9,8	-9,1	-8,4	-7,9	-7,3	-6,9	-6,5	-6,1	-5,7	-5,4	-5,1
1,39	35	-16,7	-22,9	-26,7	-29,3	-31,0	-26,5	-22,9	-20,0	-17,7	-15,7	-14,1	-12,7	-11,5	-10,5	-9,6	-8,8	-8,1	-7,5	-7,0	-6,5	-6,0	-5,6	-5,3	-4,9	-4,6	-4,3
1,47	40	-11,1	-18,7	-23,6	-26,9	-29,2	-24,7	-21,2	-18,4	-16,2	-14,3	-12,7	-11,4	-10,3	-9,3	-8,4	-7,7	-7,0	-6,5	-5,9	-5,5	-5,1	-4,7	-4,4	-4,0	-3,8	-3,5
1,54	45	-5,1	-14,2	-20,1	-24,2	-27,0	-22,7	-19,3	-16,7	-14,5	-12,7	-11,2	-9,9	-8,9	-7,9	-7,1	-6,5	-5,8	-5,3	-4,8	-4,4	-4,0	-3,7	-3,4	-3,1	-2,8	-2,6
1,62	50	1,1	-9,4	-16,4	-21,2	-24,6	-20,5	-17,3	-14,7	-12,6	-10,9	-9,5	-8,4	-7,4	-6,5	-5,8	-5,1	-4,6	-4,1	-3,6	-3,2	-2,9	-2,6	-2,3	-2,1	-1,8	-1,6
1,68	55	7,7	-4,4	-12,4	-18,0	-22,0	-18,1	-15,0	-12,6	-10,6	-9,1	-7,8	-6,7	-5,7	-5,0	-4,3	-3,7	-3,2	-2,7	-2,4	-2,0	-1,7	-1,4	-1,2	-1,0	-0,8	-0,6
1,75	60	14,5	0,9	-8,2	-14,6	-19,2	-15,5	-12,6	-10,4	-8,5	-7,1	-5,9	-4,9	-4,0	-3,3	-2,7	-2,2	-1,8	-1,4	-1,0	-0,7	-0,5	-0,2	0,0	0,1	0,3	0,5
1,81	65	21,5	6,3	-3,9	-11,1	-16,3	-12,8	-10,1	-8,0	-6,3	-5,0	-3,9	-3,0	-2,3	-1,6	-1,1	-0,7	-0,3	0,1	0,3	0,6	0,8	1,0	1,2	1,3	1,4	1,6
1,86	70	28,7	11,9	0,6	-7,4	-13,2	-9,9	-7,5	-5,6	-4,1	-2,8	-1,9	-1,1	-0,4	0,1	0,6	0,9	1,3	1,5	1,8	2,0	2,1	2,3	2,4	2,5	2,6	2,7
1,92	75	36,0	17,7	5,3	-3,5	-10,0	-7,0	-4,7	-3,0	-1,7	-0,6	0,2	0,9	1,5	1,9	2,3	2,6	2,8	3,1	3,2	3,4	3,5	3,6	3,7	3,7	3,8	3,8
1,97	80	43,5	23,6	10,0	0,4	-6,7	-4,0	-1,9	-0,4	0,8	1,7	2,4	3,0	3,4	3,8	4,1	4,3	4,5	4,6	4,7	4,8	4,9	4,9	5,0	5,0	5,0	5,0
2,02	85	51,1	29,6	14,9	4,5	-3,3	-0,8	1,0	2,3	3,3	4,0	4,6	5,1	5,4	5,7	5,9	6,0	6,1	6,2	6,3	6,3	6,3	6,3	6,3	6,3	6,3	6,2
2,07	90	58,8	35,7	19,9	8,6	0,2	2,4	3,9	5,0	5,8	6,4	6,9	7,2	7,4	7,6	7,7	7,8	7,8	7,8	7,8	7,8	7,8	7,7	7,7	7,6	7,5	7,5
2,12	95	66,7	41,9	25,0	12,9	3,8	5,7	6,9	7,8	8,5	8,9	9,2	9,4	9,5	9,6	9,6	9,6	9,5	9,5	9,4	9,3	9,2	9,1	9,0	8,9	8,8	8,7
2,17	100	74,6	48,2	30,2	17,2	7,5	9,0	10,0	10,7	11,1	11,4	11,5	11,6	11,6	11,6	11,5	11,4	11,3	11,2	11,0	10,9	10,7	10,6	10,4	10,3	10,1	10,0
2,21	105	82,6	54,6	35,4	21,6	11,2	12,4	13,2	13,6	13,9	13,9	13,9	13,9	13,8	13,6	13,4	13,3	13,1	12,9	12,7	12,4	12,2	12,0	11,8	11,7	11,5	11,3
2,26	110	90,7	61,1	40,7	26,0	15,1	15,9	16,4	16,6	16,6	16,5	16,4	16,2	15,9	15,7	15,4	15,1	14,9	14,6	14,3	14,0	13,8	13,5	13,3	13,0	12,8	12,6
2,30	115	98,9	67,6	46,1	30,6	18,9	19,4	19,6	19,6	19,4	19,1	18,8	18,5	18,1	17,8	17,4	17,0	16,7	16,3	16,0	15,7	15,3	15,0	14,7	14,4	14,2	13,9
2,34	120	107,1	74,2	51,5	35,2	22,9	23,0	22,9	22,6	22,2	21,8	21,3	20,8	20,4	19,9	19,4	19,0	18,5	18,1	17,7	17,3	16,9	16,5	16,2	15,9	15,5	15,2
2,38	125	115,5	80,9	57,1	39,8	26,8	26,7	26,2	25,7	25,1	24,5	23,8	23,2	22,6	22,0	21,4	20,9	20,4	19,9	19,4	18,9	18,5	18,1	17,7	17,3	16,9	16,6

Fig. 2 Concordant (*green cases*) and discordant results (*red and blue*) when age increases from 50 to 80 years. Results are expressed as absolute difference in mL/min. Creatinine values are expressed in mg/dL. To convert in μmol/L, multiply by 88

mL/min), which are recommended for drug dosage adjustment [5, 6, 47]. Our clinical data support the conclusion that differences between the two equations are potentially influenced by each variable included in these equations: sex, age, weight, height, and SCr. Among these variables, age and weight are the most important and will systematically impact the results of the equations. The prevalence of excretory impairment in the older population and their resulting vulnerability to overdosage is a major driver for optimizing dosage adjustment strategies in this population. The assertion, frequently found in the geriatric literature, that CG must be favored because it gives systematically lower results, and thus prevents overdosage, is an oversimplification [20, 21]. We confirm using de-indexed eGFR, that CG results are lower than CKD-EPI in these subjects. However, this assertion is not true in some obese geriatric patients, even if these patients are clearly not the majority. Our clinical database was limited to subjects aged older than 60 years, but as shown by our simulation, the proportion of discordant results increases with younger age and greater body weight. This last point is important as the epidemic of obesity is well known in the general non-geriatric population. Therefore, the general recommendation to favor CG based on geriatric data would potentially have different implications for drug concentrations in younger subjects, especially if weight is high. In the context of drug dosage adjustment strategies, a personalized approach is necessary.

All creatinine-based equations have their own limitations and lack of precision to estimate true GFR [12]. They also require a steady-state situation [61]. For specific therapeutic drugs that are potentially nephrotoxic and have a tight therapeutic window such as cisplatin, it is our opinion that the measurement of real GFR with a reference method has added value, even if proof is still indirect [12, 25–27, 30, 32, 33, 35]. It is also our opinion that drugs

Males																												
	Age 70		Length 177																									
	BSA	W/Scr	0,5	0,6	0,7	0,8	0,9	1	1,1	1,2	1,3	1,4	1,5	1,6	1,7	1,8	1,9	2	2,1	2,2	2,3	2,4	2,5	2,6	2,7	2,8	2,9	3
	1,20	25	-27,7	-30,3	-31,8	-32,6	-33,0	-28,5	-25,0	-22,1	-19,7	-17,8	-16,1	-14,7	-13,5	-12,4	-11,5	-10,7	-10,0	-9,3	-8,7	-8,2	-7,7	-7,3	-6,9	-6,5	-6,2	-5,9
	1,30	30	-24,2	-27,9	-30,2	-31,6	-32,4	-27,9	-24,3	-21,5	-19,1	-17,1	-15,5	-14,1	-12,9	-11,8	-10,9	-10,1	-9,4	-8,7	-8,2	-7,6	-7,2	-6,8	-6,4	-6,0	-5,7	-5,4
	1,39	35	-20,0	-25,0	-28,1	-30,1	-31,4	-26,9	-23,3	-20,5	-18,2	-16,2	-14,6	-13,2	-12,1	-11,0	-10,1	-9,3	-8,6	-8,0	-7,5	-7,0	-6,5	-6,1	-5,7	-5,4	-5,1	-4,8
	1,47	40	-15,5	-21,7	-25,6	-28,2	-30,0	-25,6	-22,1	-19,3	-17,0	-15,1	-13,6	-12,2	-11,1	-10,1	-9,2	-8,4	-7,8	-7,2	-6,6	-6,2	-5,7	-5,3	-5,0	-4,7	-4,4	-4,1
	1,54	45	-10,5	-18,0	-22,9	-26,1	-28,4	-24,0	-20,6	-17,9	-15,7	-13,9	-12,3	-11,1	-9,9	-9,0	-8,2	-7,4	-6,8	-6,2	-5,7	-5,3	-4,9	-4,5	-4,2	-3,9	-3,6	-3,4
	1,62	50	-5,3	-14,1	-19,8	-23,7	-26,5	-22,3	-19,0	-16,3	-14,2	-12,5	-11,0	-9,8	-8,7	-7,8	-7,0	-6,4	-5,8	-5,2	-4,8	-4,3	-4,0	-3,6	-3,3	-3,1	-2,8	-2,6
	1,68	55	0,2	-9,9	-16,6	-21,2	-24,4	-20,3	-17,2	-14,6	-12,6	-10,9	-9,6	-8,4	-7,4	-6,6	-5,8	-5,2	-4,6	-4,1	-3,7	-3,3	-3,0	-2,7	-2,4	-2,2	-1,9	-1,7
	1,75	60	5,9	-5,5	-13,1	-18,4	-22,2	-18,3	-15,2	-12,8	-10,9	-9,3	-8,0	-6,9	-6,0	-5,2	-4,5	-4,0	-3,5	-3,0	-2,6	-2,3	-2,0	-1,7	-1,4	-1,2	-1,0	-0,8
	1,81	65	11,8	-1,0	-9,5	-15,5	-19,8	-16,0	-13,2	-10,9	-9,1	-7,6	-6,4	-5,4	-4,5	-3,8	-3,2	-2,7	-2,2	-1,8	-1,5	-1,2	-0,9	-0,7	-0,4	-0,3	-0,1	0,1
	1,86	70	17,8	3,7	-5,8	-12,4	-17,3	-13,7	-11,0	-8,9	-7,2	-5,8	-4,7	-3,8	-3,0	-2,4	-1,8	-1,3	-0,9	-0,6	-0,3	0,0	0,2	0,4	0,6	0,8	0,9	1,0
	1,92	75	24,1	8,5	-1,9	-9,2	-14,6	-11,3	-8,8	-6,8	-5,2	-4,0	-3,0	-2,1	-1,4	-0,9	-0,4	0,0	0,4	0,7	0,9	1,2	1,4	1,5	1,7	1,8	1,9	2,0
	1,97	80	30,4	13,5	2,1	-6,0	-11,9	-8,8	-6,4	-4,6	-3,2	-2,1	-1,2	-0,4	0,2	0,7	1,1	1,5	1,7	2,0	2,2	2,4	2,5	2,7	2,8	2,9	2,9	3,0
	2,02	85	36,8	18,6	6,2	-2,6	-9,1	-6,2	-4,0	-2,4	-1,1	-0,1	0,7	1,3	1,9	2,3	2,6	2,9	3,1	3,3	3,5	3,6	3,7	3,8	3,9	3,9	4,0	4,0
	2,07	90	43,4	23,7	10,4	0,9	-6,1	-3,5	-1,5	-0,1	1,0	1,9	2,6	3,1	3,6	3,9	4,2	4,4	4,6	4,7	4,8	4,9	4,9	5,0	5,0	5,0	5,1	5,1
	2,12	95	50,1	29,0	14,7	4,5	-3,1	-0,7	1,0	2,3	3,2	4,0	4,5	5,0	5,3	5,6	5,8	5,9	6,0	6,1	6,1	6,2	6,2	6,2	6,2	6,2	6,1	6,1
	2,17	100	56,8	34,4	19,0	8,1	-0,1	2,1	3,6	4,7	5,5	6,1	6,5	6,9	7,1	7,3	7,4	7,4	7,5	7,5	7,5	7,5	7,5	7,4	7,4	7,3	7,3	7,2
	2,21	105	63,7	39,8	23,5	11,8	3,1	4,9	6,2	7,1	7,8	8,2	8,5	8,8	8,9	9,0	9,0	9,0	9,0	9,0	8,9	8,8	8,7	8,7	8,6	8,5	8,4	8,3
	2,26	110	70,6	45,3	28,0	15,5	6,3	7,9	8,9	9,6	10,1	10,4	10,6	10,7	10,7	10,7	10,7	10,6	10,5	10,4	10,3	10,2	10,0	9,9	9,8	9,7	9,5	9,4
	2,30	115	77,6	50,8	32,5	19,4	9,5	10,8	11,7	12,2	12,5	12,6	12,7	12,7	12,6	12,5	12,4	12,2	12,1	11,9	11,7	11,5	11,4	11,2	11,0	10,8	10,7	10,5
	2,34	120	84,6	56,5	37,2	23,2	12,8	13,8	14,4	14,7	14,9	14,9	14,8	14,7	14,5	14,3	14,1	13,9	13,6	13,4	13,2	12,9	12,7	12,5	12,3	12,1	11,8	11,6
	2,38	125	91,7	62,2	41,8	27,2	16,2	16,9	17,2	17,3	17,3	17,1	16,9	16,7	16,4	16,1	15,8	15,5	15,2	14,9	14,6	14,3	14,1	13,8	13,5	13,3	13,0	12,8

Males																												
	Age 80		Length 177																									
	BSA	W/Scr	0,5	0,6	0,7	0,8	0,9	1	1,1	1,2	1,3	1,4	1,5	1,6	1,7	1,8	1,9	2	2,1	2,2	2,3	2,4	2,5	2,6	2,7	2,8	2,9	3
	1,20	25	-29,5	-31,3	-32,2	-32,6	-32,7	-28,4	-24,9	-22,1	-19,8	-17,9	-16,3	-14,9	-13,7	-12,6	-11,7	-10,9	-10,1	-9,5	-8,9	-8,4	-7,9	-7,5	-7,1	-6,7	-6,4	-6,1
	1,30	30	-26,9	-29,7	-31,3	-32,1	-32,6	-28,2	-24,7	-21,8	-19,5	-17,5	-15,9	-14,5	-13,3	-12,2	-11,3	-10,5	-9,8	-9,1	-8,6	-8,0	-7,6	-7,1	-6,7	-6,4	-6,1	-5,8
	1,39	35	-23,8	-27,6	-29,8	-31,2	-32,1	-27,6	-24,1	-21,2	-18,9	-17,0	-15,3	-13,9	-12,7	-11,7	-10,8	-10,0	-9,3	-8,6	-8,1	-7,5	-7,1	-6,7	-6,3	-5,9	-5,6	-5,3
	1,47	40	-20,2	-25,1	-28,1	-30,0	-31,2	-26,8	-23,2	-20,4	-18,1	-16,2	-14,6	-13,2	-12,0	-11,0	-10,1	-9,3	-8,6	-8,0	-7,5	-7,0	-6,5	-6,1	-5,7	-5,4	-5,1	-4,8
	1,54	45	-16,4	-22,3	-26,0	-28,4	-30,1	-25,7	-22,2	-19,4	-17,2	-15,3	-13,7	-12,4	-11,2	-10,2	-9,3	-8,6	-7,9	-7,3	-6,8	-6,3	-5,9	-5,5	-5,1	-4,8	-4,5	-4,2
	1,62	50	-12,2	-19,2	-23,7	-26,7	-28,7	-24,4	-21,0	-18,3	-16,1	-14,2	-12,7	-11,4	-10,3	-9,3	-8,5	-7,7	-7,1	-6,5	-6,0	-5,6	-5,2	-4,8	-4,5	-4,1	-3,9	-3,6
	1,68	55	-7,8	-15,9	-21,2	-24,7	-27,2	-23,0	-19,6	-17,0	-14,8	-13,1	-11,6	-10,3	-9,3	-8,3	-7,5	-6,8	-6,2	-5,7	-5,2	-4,8	-4,4	-4,0	-3,7	-3,4	-3,2	-3,0
	1,75	60	-3,3	-12,5	-18,5	-22,6	-25,5	-21,4	-18,2	-15,6	-13,5	-11,8	-10,4	-9,2	-8,2	-7,3	-6,5	-5,9	-5,3	-4,8	-4,3	-3,9	-3,6	-3,3	-3,0	-2,7	-2,5	-2,2
	1,81	65	1,5	-8,8	-15,6	-20,4	-23,7	-19,7	-16,6	-14,1	-12,1	-10,5	-9,1	-8,0	-7,0	-6,2	-5,5	-4,9	-4,3	-3,9	-3,4	-3,1	-2,7	-2,4	-2,2	-1,9	-1,7	-1,5
	1,86	70	6,4	-5,1	-12,7	-18,0	-21,8	-17,9	-14,9	-12,5	-10,6	-9,1	-7,8	-6,7	-5,8	-5,0	-4,4	-3,8	-3,3	-2,9	-2,5	-2,1	-1,8	-1,6	-1,3	-1,1	-0,9	-0,8
	1,92	75	11,5	-1,2	-9,6	-15,5	-19,7	-16,0	-13,1	-10,9	-9,1	-7,6	-6,4	-5,4	-4,6	-3,8	-3,2	-2,7	-2,2	-1,8	-1,5	-1,2	-0,9	-0,7	-0,5	-0,3	-0,1	0,0
	1,97	80	16,7	2,9	-6,4	-12,8	-17,6	-14,0	-11,3	-9,2	-7,5	-6,1	-5,0	-4,0	-3,3	-2,6	-2,0	-1,6	-1,2	-0,8	-0,5	-0,2	0,0	0,2	0,4	0,6	0,7	0,8
	2,02	85	21,9	7,0	-3,1	-10,2	-15,3	-11,9	-9,4	-7,4	-5,8	-4,5	-3,5	-2,6	-1,9	-1,3	-0,8	-0,4	0,0	0,3	0,6	0,8	1,0	1,2	1,3	1,5	1,6	1,7
	2,07	90	27,3	11,2	0,3	-7,4	-13,0	-9,8	-7,4	-5,5	-4,1	-2,9	-2,0	-1,2	-0,5	0,0	0,4	0,8	1,1	1,4	1,6	1,8	2,0	2,1	2,3	2,4	2,4	2,5
	2,12	95	32,8	15,5	3,8	-4,5	-10,6	-7,6	-5,4	-3,6	-2,3	-1,2	-0,4	0,3	0,9	1,3	1,7	2,0	2,3	2,5	2,7	2,9	3,0	3,1	3,2	3,3	3,3	3,4
	2,17	100	38,4	19,9	7,3	-1,6	-8,2	-5,4	-3,3	-1,7	-0,5	0,5	1,2	1,8	2,3	2,7	3,0	3,3	3,5	3,7	3,8	3,9	4,0	4,1	4,2	4,2	4,3	4,3
	2,21	105	44,0	24,3	10,9	1,4	-5,6	-3,1	-1,2	0,3	1,4	2,2	2,9	3,4	3,8	4,1	4,4	4,6	4,7	4,9	5,0	5,0	5,1	5,1	5,2	5,2	5,2	5,2
	2,26	110	49,7	28,8	14,6	4,5	-3,1	-0,7	1,0	2,3	3,3	4,0	4,5	5,0	5,3	5,5	5,7	5,9	6,0	6,1	6,1	6,1	6,2	6,2	6,2	6,1	6,1	6,1
	2,30	115	55,5	33,4	18,4	7,6	-0,4	1,7	3,2	4,4	5,2	5,8	6,2	6,6	6,8	7,0	7,1	7,2	7,2	7,3	7,3	7,3	7,2	7,2	7,2	7,1	7,1	7,0
	2,34	120	61,4	38,1	22,1	10,7	2,2	4,2	5,5	6,4	7,1	7,6	8,0	8,2	8,4	8,5	8,5	8,5	8,5	8,5	8,5	8,4	8,3	8,3	8,2	8,1	8,0	7,9
	2,38	125	67,3	42,7	26,0	13,9	5,0	6,6	7,8	8,6	9,1	9,5	9,7	9,9	9,9	10,0	9,9	9,9	9,8	9,8	9,7	9,6	9,5	9,3	9,2	9,1	9,0	8,9

Fig. 2 continued

that are easily monitored by plasma measurement may be favored in the context of CKD. In other cases, knowing the age, weight, height, and SCr of the patients, the Excel sheet (available in the Supplementary Material) can calculate the absolute and relative difference between the two equations, flagging up discordant cases. If results are concordant, the clinician can reasonably apply drug dosage recommendations available in the literature. If discrepancies occur, it would be important to consider the characteristics of the patients and the safety profile of the drug considered. For highly effective concentration-dependent drugs (such as antibiotics), the risk of under-dosage could be as important as the risk of over-dosage, especially if the risk of nephrotoxicity is relatively low. In such cases, it could be more efficient to consider the equation that gives the higher GFR results. Conversely, it could be better to recommend adjusting the dosage of a drug to the equation, giving the lower result if the prescription concerns potentially nephrotoxic drugs [49, 62].

There are limitations to our study. Without measured GFR data, we are not able to assert which equation must be used for a specific patient. This remains a simulation and our clinical data are probably representative neither of the French general population nor of populations from other countries. Regarding the simulation, we gave both absolute and relative differences but the general conclusions and the relevance of these differences may vary according to the GFR level. Indeed, a relative difference of 10 % is probably more relevant from a practical and clinical point of view at low GFR levels, whereas absolute and relative differences are pertinent (and in fact exactly the same for a GFR value of 100 mL/min) at relatively high GFR. At low GFR, the implications of both relative and absolute differences should be considered. By presenting absolute and relative changes in our analysis, we have illustrated the implications of demographics on CG/CKD-EPI discrepancies across the spectrum of excretory function. The choice of threshold at 10 mL/min or 10 % can be criticized

Males

Age 50 L(cm) 177

BSA	W/Scr	0,5	0,6	0,7	0,8	0,9	1	1,1	1,2	1,3	1,4	1,5	1,6	1,7	1,8	1,9	2	2,1	2,2	2,3	2,4	2,5	2,6	2,7	2,8	2,9	3
1,20	25	-34%	-44%	-53%	-60%	-66%	-61%	-56%	-52%	-48%	-45%	-43%	-40%	-38%	-36%	-34%	-33%	-31%	-30%	-28%	-27%	-26%	-25%	-24%	-23%	-22%	-22%
1,30	30	-23%	-34%	-43%	-50%	-57%	-52%	-48%	-44%	-41%	-38%	-36%	-33%	-31%	-30%	-28%	-27%	-25%	-24%	-23%	-22%	-21%	-20%	-19%	-18%	-18%	-17%
1,39	35	-15%	-25%	-34%	-42%	-48%	-44%	-40%	-37%	-34%	-32%	-29%	-27%	-26%	-24%	-23%	-21%	-20%	-19%	-18%	-17%	-16%	-15%	-15%	-14%	-13%	-13%
1,47	40	-7%	-18%	-27%	-34%	-41%	-37%	-34%	-31%	-28%	-26%	-24%	-22%	-20%	-19%	-18%	-17%	-15%	-14%	-14%	-13%	-12%	-11%	-11%	-10%	-9%	-9%
1,54	45	0%	-11%	-20%	-28%	-35%	-31%	-28%	-25%	-23%	-21%	-19%	-17%	-16%	-14%	-13%	-12%	-11%	-10%	-10%	-9%	-8%	-7%	-7%	-6%	-6%	-5%
1,62	50	6%	-5%	-14%	-22%	-29%	-25%	-22%	-20%	-18%	-16%	-14%	-13%	-11%	-10%	-9%	-8%	-7%	-7%	-6%	-5%	-5%	-4%	-3%	-3%	-2%	-2%
1,68	55	11%	1%	-9%	-16%	-23%	-20%	-17%	-15%	-13%	-11%	-10%	-9%	-7%	-6%	-5%	-5%	-4%	-3%	-2%	-2%	-1%	-1%	0%	0%	1%	1%
1,75	60	16%	6%	-4%	-11%	-18%	-15%	-13%	-11%	-9%	-7%	-6%	-5%	-4%	-3%	-2%	-1%	0%	0%	1%	1%	2%	2%	3%	3%	3%	4%
1,81	65	21%	10%	1%	-7%	-14%	-11%	-9%	-7%	-5%	-4%	-2%	-1%	0%	1%	1%	2%	3%	3%	4%	4%	5%	5%	6%	6%	6%	6%
1,86	70	25%	14%	5%	-3%	-9%	-7%	-5%	-3%	-2%	0%	1%	2%	3%	4%	4%	5%	6%	6%	7%	7%	7%	8%	8%	8%	9%	9%
1,92	75	29%	18%	9%	1%	-6%	-3%	-1%	0%	2%	3%	4%	5%	6%	7%	7%	8%	8%	9%	9%	10%	10%	10%	11%	11%	11%	11%
1,97	80	33%	22%	13%	5%	-2%	0%	2%	4%	5%	6%	7%	8%	9%	9%	10%	11%	11%	11%	12%	12%	12%	13%	13%	13%	13%	14%
2,02	85	36%	25%	16%	9%	2%	4%	5%	7%	8%	9%	10%	11%	11%	12%	13%	13%	13%	14%	14%	14%	15%	15%	15%	15%	16%	16%
2,07	90	39%	29%	20%	12%	5%	7%	8%	10%	11%	12%	13%	13%	14%	15%	15%	15%	16%	16%	16%	17%	17%	17%	17%	17%	18%	18%
2,12	95	42%	32%	23%	15%	8%	10%	11%	13%	14%	14%	15%	16%	16%	17%	17%	18%	18%	18%	19%	19%	19%	19%	19%	19%	20%	20%
2,17	100	45%	35%	26%	18%	11%	13%	14%	15%	16%	17%	18%	18%	19%	19%	20%	20%	20%	20%	21%	21%	21%	21%	21%	21%	21%	22%
2,21	105	48%	37%	28%	21%	14%	15%	17%	18%	19%	19%	20%	21%	21%	21%	22%	22%	22%	22%	23%	23%	23%	23%	23%	23%	23%	23%
2,26	110	50%	40%	31%	23%	16%	18%	19%	20%	21%	22%	22%	23%	23%	23%	24%	24%	24%	24%	25%	25%	25%	25%	25%	25%	25%	25%
2,30	115	52%	42%	34%	26%	19%	20%	22%	22%	23%	24%	24%	25%	25%	25%	26%	26%	26%	26%	26%	26%	27%	27%	27%	27%	27%	27%
2,34	120	55%	45%	36%	28%	21%	23%	24%	25%	25%	26%	26%	27%	27%	27%	28%	28%	28%	28%	28%	28%	28%	28%	28%	28%	28%	28%
2,38	125	57%	47%	38%	31%	24%	25%	26%	27%	27%	28%	28%	29%	29%	29%	29%	29%	30%	30%	30%	30%	30%	30%	30%	30%	30%	30%

Males

Age 60 L(cm) 177

BSA	W/Scr	0,5	0,6	0,7	0,8	0,9	1	1,1	1,2	1,3	1,4	1,5	1,6	1,7	1,8	1,9	2	2,1	2,2	2,3	2,4	2,5	2,6	2,7	2,8	2,9	3
1,20	25	-38%	-49%	-57%	-64%	-70%	-65%	-60%	-55%	-52%	-49%	-46%	-43%	-41%	-39%	-37%	-35%	-34%	-32%	-31%	-30%	-28%	-27%	-26%	-25%	-25%	-24%
1,30	30	-28%	-39%	-47%	-55%	-61%	-56%	-51%	-48%	-44%	-41%	-39%	-37%	-34%	-33%	-31%	-29%	-28%	-27%	-25%	-24%	-23%	-22%	-21%	-21%	-20%	-19%
1,39	35	-19%	-30%	-39%	-46%	-53%	-48%	-44%	-41%	-38%	-35%	-33%	-31%	-29%	-27%	-26%	-24%	-23%	-22%	-21%	-20%	-19%	-18%	-17%	-16%	-16%	-15%
1,47	40	-12%	-22%	-31%	-39%	-46%	-41%	-38%	-35%	-32%	-29%	-27%	-25%	-24%	-22%	-21%	-20%	-18%	-17%	-16%	-15%	-15%	-14%	-13%	-12%	-12%	-11%
1,54	45	-5%	-16%	-25%	-32%	-39%	-35%	-32%	-29%	-26%	-24%	-22%	-21%	-19%	-18%	-16%	-15%	-14%	-13%	-12%	-12%	-11%	-10%	-9%	-9%	-8%	-8%
1,62	50	1%	-10%	-19%	-26%	-33%	-30%	-27%	-24%	-22%	-20%	-18%	-16%	-15%	-14%	-12%	-11%	-10%	-10%	-9%	-8%	-7%	-7%	-6%	-6%	-5%	-5%
1,68	55	7%	-4%	-13%	-21%	-28%	-25%	-22%	-19%	-17%	-15%	-14%	-12%	-11%	-10%	-9%	-8%	-7%	-6%	-5%	-5%	-4%	-4%	-3%	-2%	-2%	-2%
1,75	60	12%	1%	-8%	-16%	-23%	-20%	-17%	-15%	-13%	-11%	-10%	-8%	-7%	-6%	-5%	-4%	-4%	-3%	-2%	-2%	-1%	-1%	0%	0%	1%	1%
1,81	65	16%	5%	-4%	-12%	-18%	-16%	-13%	-11%	-9%	-8%	-6%	-5%	-4%	-3%	-2%	-1%	-1%	0%	1%	1%	2%	2%	3%	3%	3%	4%
1,86	70	20%	10%	1%	-7%	-14%	-11%	-9%	-7%	-6%	-4%	-3%	-2%	-1%	0%	1%	2%	2%	3%	3%	4%	4%	5%	5%	6%	6%	6%
1,92	75	24%	14%	5%	-3%	-10%	-8%	-6%	-4%	-2%	-1%	0%	1%	2%	3%	4%	4%	5%	6%	6%	7%	7%	7%	8%	8%	8%	9%
1,97	80	28%	17%	8%	0%	-7%	-4%	-2%	0%	1%	2%	3%	4%	5%	6%	7%	7%	8%	8%	9%	9%	9%	10%	10%	10%	10%	11%
2,02	85	31%	21%	12%	4%	-3%	-1%	1%	3%	4%	5%	6%	7%	8%	8%	9%	10%	10%	11%	11%	11%	12%	12%	12%	12%	13%	13%
2,07	90	34%	24%	15%	7%	0%	2%	4%	6%	7%	8%	9%	10%	10%	11%	11%	12%	12%	13%	13%	13%	14%	14%	14%	14%	15%	15%
2,12	95	37%	27%	18%	10%	3%	5%	7%	8%	9%	10%	11%	12%	13%	13%	14%	14%	15%	15%	15%	16%	16%	16%	16%	16%	17%	17%
2,17	100	40%	30%	21%	13%	6%	8%	10%	11%	12%	13%	14%	14%	15%	16%	16%	16%	17%	17%	17%	18%	18%	18%	18%	18%	18%	19%
2,21	105	43%	33%	24%	16%	9%	11%	12%	13%	14%	15%	16%	17%	17%	18%	18%	18%	19%	19%	19%	19%	20%	20%	20%	20%	20%	20%
2,26	110	46%	35%	26%	19%	12%	13%	15%	16%	17%	18%	18%	19%	19%	20%	20%	20%	21%	21%	21%	21%	21%	22%	22%	22%	22%	22%
2,30	115	48%	38%	29%	21%	14%	16%	17%	18%	19%	20%	20%	21%	21%	22%	22%	22%	23%	23%	23%	23%	23%	23%	23%	24%	24%	24%
2,34	120	50%	40%	31%	24%	17%	18%	19%	20%	21%	22%	22%	23%	23%	24%	24%	24%	24%	25%	25%	25%	25%	25%	25%	25%	25%	25%
2,38	125	52%	42%	34%	26%	19%	20%	22%	22%	23%	24%	24%	25%	25%	25%	26%	26%	26%	26%	26%	26%	27%	27%	27%	27%	27%	27%

Fig. 3 Concordant (*green cases*) and discordant results (*red and blue*) when age increases from 50 to 80 years. Results are expressed as relative difference in %. Creatinine values are expressed in mg/dL. To convert in µmol/L, multiply by 88

as not relevant for every drug. Indeed, some dosage adjustments are guided simply by CKD stage. However, 10 mL/min is a difference in GFR that will have a substantial effect on plasma concentrations of some drugs. This is especially true in oncologic therapy where the dosage of cisplatin for example can be significantly (under-dosing or over-dosing) modified for a difference in GFR of 10 mL/min or 10 % [32, 33]. Moreover, it would have been impractical to propose simulations for the range of GFR discrepancies relevant to every drug.

Discordances between equations could be theoretically more important in other ethnicities, especially in African-Americans for whom an ethnic coefficient is required in the CKD-EPI equation, but not in the CG equation [63]. Finally, we did not discuss the potential interest of cystatin C-based equations in this context of drug dosage adjustment, as current data are scarce and controversial [23, 35, 64, 65].

5 Conclusion

Age and body weight are the main variables explaining discrepancies between the equations. Obviously, in the context of drug prescription, an individualization is necessary. Our mathematical tool can help physicians, alerting them when large discrepancies exist for a given patient in results calculated for CKD-EPI vs. CG results. Knowing such discrepancies, the clinician can either adjust his/her prescription to balance the risk–benefit of the drug or measure real GFR, especially if the therapeutic window of the drug is narrow. We illustrated potential discrepancies between CKD-EPI and CG with implications for drug dosage adjustment. The European Medicines Agency recommends that pharmacokinetic studies be performed for new drugs with measured GFR by a reference method in the context of CKD [5]. Our findings demonstrate the need to define pharmacokinetics in relation to estimation

Males

Age 70 L(cm) 177

BSA	W/Scr	0,5	0,6	0,7	0,8	0,9	1	1,1	1,2	1,3	1,4	1,5	1,6	1,7	1,8	1,9	2	2,1	2,2	2,3	2,4	2,5	2,6	2,7	2,8	2,9	3
1,20	25	-44%	-54%	-63%	-70%	-76%	-70%	-65%	-60%	-56%	-53%	-50%	-47%	-45%	-42%	-40%	-39%	-37%	-35%	-34%	-33%	-31%	-30%	-29%	-28%	-27%	-26%
1,30	30	-34%	-45%	-53%	-60%	-67%	-61%	-56%	-52%	-49%	-46%	-43%	-41%	-38%	-36%	-35%	-33%	-31%	-30%	-29%	-28%	-26%	-25%	-24%	-24%	-23%	-22%
1,39	35	-26%	-36%	-45%	-52%	-59%	-54%	-49%	-46%	-42%	-40%	-37%	-35%	-33%	-31%	-29%	-28%	-27%	-25%	-24%	-23%	-22%	-21%	-20%	-19%	-19%	-18%
1,47	40	-18%	-29%	-37%	-45%	-52%	-47%	-43%	-40%	-37%	-34%	-32%	-30%	-28%	-26%	-25%	-23%	-22%	-21%	-20%	-19%	-18%	-17%	-16%	-16%	-15%	-14%
1,54	45	-11%	-22%	-31%	-39%	-45%	-41%	-37%	-34%	-31%	-29%	-27%	-25%	-23%	-22%	-21%	-19%	-18%	-17%	-16%	-15%	-14%	-14%	-13%	-12%	-12%	-11%
1,62	50	-5%	-16%	-25%	-33%	-39%	-35%	-32%	-29%	-27%	-24%	-23%	-21%	-19%	-18%	-17%	-15%	-14%	-13%	-13%	-12%	-11%	-10%	-10%	-9%	-8%	-8%
1,68	55	0%	-11%	-20%	-27%	-34%	-30%	-27%	-25%	-22%	-20%	-18%	-17%	-15%	-14%	-13%	-12%	-11%	-10%	-9%	-9%	-8%	-7%	-7%	-6%	-6%	-5%
1,75	60	5%	-6%	-15%	-22%	-29%	-26%	-23%	-20%	-18%	-16%	-15%	-13%	-12%	-11%	-10%	-9%	-8%	-7%	-6%	-6%	-5%	-4%	-4%	-3%	-3%	-2%
1,81	65	10%	-1%	-10%	-18%	-25%	-21%	-19%	-16%	-14%	-13%	-11%	-10%	-9%	-7%	-6%	-6%	-5%	-4%	-3%	-3%	-2%	-2%	-1%	-1%	0%	0%
1,86	70	14%	3%	-6%	-14%	-20%	-17%	-15%	-13%	-11%	-9%	-8%	-7%	-5%	-4%	-3%	-3%	-2%	-1%	-1%	0%	0%	1%	1%	2%	2%	3%
1,92	75	18%	7%	-2%	-10%	-17%	-14%	-11%	-9%	-8%	-6%	-5%	-4%	-2%	-2%	-1%	0%	1%	1%	2%	2%	3%	3%	4%	4%	5%	5%
1,97	80	22%	11%	2%	-6%	-13%	-10%	-8%	-6%	-4%	-3%	-2%	-1%	0%	1%	2%	3%	3%	4%	4%	5%	5%	6%	6%	6%	7%	7%
2,02	85	25%	14%	5%	-2%	-9%	-7%	-5%	-3%	-1%	0%	1%	2%	3%	4%	4%	5%	6%	6%	7%	7%	7%	8%	8%	8%	9%	9%
2,07	90	28%	18%	9%	1%	-6%	-4%	-2%	0%	1%	3%	4%	5%	5%	6%	7%	7%	8%	8%	9%	9%	10%	10%	10%	11%	11%	11%
2,12	95	31%	21%	12%	4%	-3%	-1%	1%	3%	4%	5%	6%	7%	8%	9%	9%	10%	10%	11%	11%	11%	12%	12%	12%	12%	13%	13%
2,17	100	34%	24%	15%	7%	0%	2%	4%	5%	7%	8%	9%	9%	10%	11%	11%	12%	12%	13%	13%	13%	14%	14%	14%	14%	14%	15%
2,21	105	37%	26%	18%	10%	3%	5%	6%	8%	9%	10%	11%	12%	12%	13%	13%	14%	14%	15%	15%	15%	15%	16%	16%	16%	16%	16%
2,26	110	40%	29%	20%	12%	5%	7%	9%	10%	11%	12%	13%	14%	14%	15%	15%	16%	16%	16%	17%	17%	17%	17%	18%	18%	18%	18%
2,30	115	42%	32%	23%	15%	8%	10%	11%	12%	14%	14%	15%	16%	16%	17%	17%	18%	18%	18%	19%	19%	19%	19%	19%	19%	20%	20%
2,34	120	44%	34%	25%	17%	10%	12%	14%	15%	16%	16%	17%	18%	18%	19%	19%	19%	20%	20%	20%	20%	21%	21%	21%	21%	21%	21%
2,38	125	47%	36%	27%	20%	13%	14%	16%	17%	18%	18%	19%	20%	20%	21%	21%	21%	21%	22%	22%	22%	22%	22%	22%	23%	23%	23%

Males

v

BSA	W/Scr	0,5	0,6	0,7	0,8	0,9	1	1,1	1,2	1,3	1,4	1,5	1,6	1,7	1,8	1,9	2	2,1	2,2	2,3	2,4	2,5	2,6	2,7	2,8	2,9	3
1,20	25	-52%	-62%	-70%	-77%	-83%	-76%	-71%	-66%	-62%	-58%	-55%	-52%	-49%	-47%	-45%	-43%	-41%	-39%	-38%	-36%	-35%	-34%	-33%	-32%	-31%	-30%
1,30	30	-42%	-53%	-61%	-68%	-74%	-68%	-63%	-59%	-55%	-51%	-48%	-46%	-43%	-41%	-39%	-38%	-36%	-34%	-33%	-32%	-30%	-29%	-28%	-27%	-26%	-25%
1,39	35	-34%	-44%	-53%	-60%	-66%	-61%	-56%	-52%	-49%	-45%	-43%	-40%	-38%	-36%	-34%	-33%	-31%	-30%	-29%	-27%	-26%	-25%	-24%	-23%	-22%	-22%
1,47	40	-26%	-37%	-46%	-53%	-59%	-54%	-50%	-46%	-43%	-40%	-38%	-35%	-33%	-32%	-30%	-28%	-27%	-26%	-24%	-23%	-22%	-21%	-21%	-20%	-19%	-18%
1,54	45	-20%	-30%	-39%	-47%	-53%	-48%	-44%	-41%	-38%	-35%	-33%	-31%	-29%	-27%	-26%	-24%	-23%	-22%	-21%	-20%	-19%	-18%	-17%	-16%	-16%	-15%
1,62	50	-14%	-24%	-33%	-41%	-47%	-43%	-39%	-36%	-33%	-31%	-29%	-27%	-25%	-23%	-22%	-21%	-20%	-18%	-17%	-16%	-16%	-15%	-14%	-13%	-13%	-12%
1,68	55	-8%	-19%	-28%	-36%	-42%	-38%	-35%	-32%	-29%	-27%	-25%	-23%	-21%	-20%	-18%	-17%	-16%	-15%	-14%	-13%	-13%	-12%	-11%	-11%	-10%	-9%
1,75	60	-3%	-14%	-23%	-31%	-37%	-34%	-30%	-27%	-25%	-23%	-21%	-19%	-18%	-16%	-15%	-14%	-13%	-12%	-11%	-11%	-10%	-9%	-8%	-8%	-7%	-7%
1,81	65	1%	-9%	-18%	-26%	-33%	-29%	-26%	-24%	-21%	-19%	-18%	-16%	-15%	-13%	-12%	-11%	-10%	-9%	-9%	-8%	-7%	-6%	-6%	-5%	-5%	-4%
1,86	70	6%	-5%	-14%	-22%	-29%	-25%	-22%	-20%	-18%	-16%	-14%	-13%	-12%	-10%	-9%	-8%	-7%	-7%	-6%	-5%	-5%	-4%	-3%	-3%	-3%	-2%
1,92	75	10%	-1%	-10%	-18%	-25%	-22%	-19%	-17%	-15%	-13%	-11%	-10%	-9%	-8%	-7%	-6%	-5%	-4%	-3%	-3%	-2%	-2%	-1%	-1%	0%	0%
1,97	80	13%	3%	-6%	-14%	-21%	-18%	-16%	-13%	-11%	-10%	-8%	-7%	-6%	-5%	-4%	-3%	-2%	-2%	-1%	0%	0%	1%	1%	1%	2%	2%
2,02	85	17%	6%	-3%	-11%	-18%	-15%	-12%	-10%	-9%	-7%	-6%	-4%	-3%	-2%	-2%	-1%	0%	1%	1%	2%	2%	3%	3%	3%	4%	4%
2,07	90	20%	9%	0%	-8%	-14%	-12%	-9%	-7%	-6%	-4%	-3%	-2%	-1%	0%	1%	2%	2%	3%	3%	4%	4%	5%	5%	5%	6%	6%
2,12	95	23%	12%	3%	-4%	-11%	-9%	-7%	-5%	-3%	-2%	-1%	0%	1%	2%	3%	4%	4%	5%	5%	6%	6%	7%	7%	7%	8%	8%
2,17	100	26%	15%	6%	-2%	-8%	-6%	-4%	-2%	-1%	1%	2%	3%	4%	4%	5%	6%	6%	7%	7%	8%	8%	8%	9%	9%	9%	10%
2,21	105	29%	18%	9%	1%	-6%	-3%	-1%	0%	2%	3%	4%	5%	6%	7%	7%	8%	8%	9%	9%	10%	10%	10%	11%	11%	11%	11%
2,26	110	31%	21%	12%	4%	-3%	-1%	1%	3%	4%	5%	6%	7%	8%	9%	9%	10%	10%	11%	11%	11%	12%	12%	12%	12%	13%	13%
2,30	115	34%	23%	14%	7%	0%	2%	3%	5%	6%	7%	8%	9%	10%	10%	11%	12%	12%	12%	13%	13%	13%	14%	14%	14%	14%	14%
2,34	120	36%	26%	17%	9%	2%	4%	6%	7%	8%	9%	10%	11%	12%	12%	13%	13%	14%	14%	14%	15%	15%	15%	15%	16%	16%	16%
2,38	125	39%	28%	19%	11%	4%	6%	8%	9%	10%	11%	12%	13%	14%	14%	15%	15%	15%	16%	16%	16%	17%	17%	17%	17%	17%	17%

Fig. 3 continued

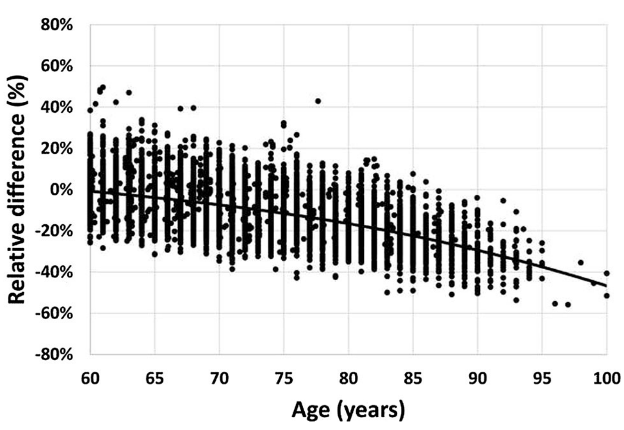

Fig. 4 Effect of age on relative difference between CG and CKD-EPI (clinical data). *CG* Cockcroft–Gault, *CKD-EPI* Chronic Kidney Disease Epidemiology

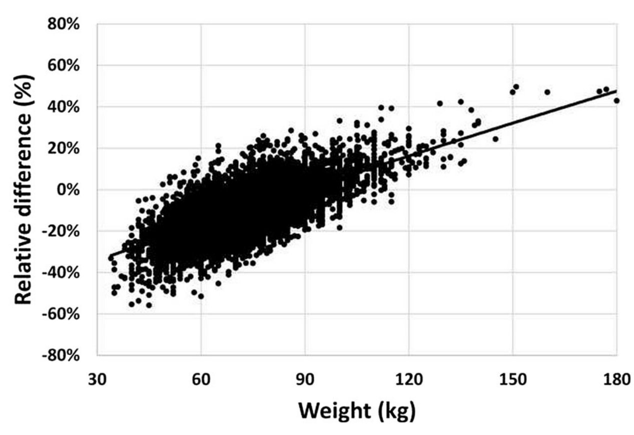

Fig. 5 Effect of weight on relative difference between CG and CKD-EPI (clinical data). *CG* Cockcroft–Gault, *CKD-EPI* Chronic Kidney Disease Epidemiology

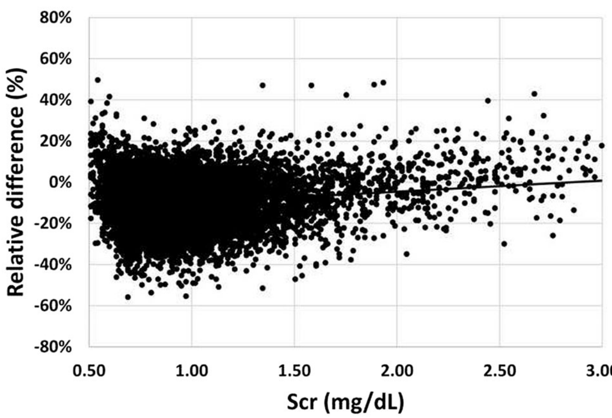

Fig. 6 Effect of SCr on relative difference between CG and CKD-EPI (clinical data). Creatinine values are expressed in mg/dL. To convert in µmol/L, multiply by 88. *CG* Cockcroft–Gault, *CKD-EPI* Chronic Kidney Disease Epidemiology, *SCr* serum creatinine

equations across the spectrum of patients' age and weight so that appropriate adjustment can be applied in clinical practice.

Compliance with Ethical Standards

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Conflict of interest Pierre Delanaye, Fabrice Guerber, André Scheen, Timothy Ellam, Antoine Bouquegneau, Dorra Guergour, Christophe Mariat, and Hans Pottel declare that they have no conflict of interest that might be relevant to the contents of this manuscript.

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