how mathematics could be made better understandable and more practical for clinical use [2].

$$\text{GFR} = \frac{150 - \text{Age (years)}}{\text{SerumCreatinine (mcmol/l)}} \cdot \text{Weight (kg)}$$

While the authors proposed to multiply by 0.85 for females [1], Luzius Dettli proposed to add +10% for males but to subtract −10% for females [3]. In case of doubt, therefore, the GFR can be estimated without sex differences.

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Reply

Sir,

There were several reasons why we did not include this equation in our work.

Firstly, there is no traceable origin of the Dettli equation: We found it printed in two publications [1,2], but in both, the references given do not contain a theoretical deduction or experimental validation. In an inquiry by phone to Luzius Dettli by Professor Thiel in 2005, he could not remember to ever having validated this equation in a substantial amount of patients. He also denied the validation in the course of an eventually unpublished doctoral thesis. Multiple inquiries written and by e-mail to Professor Galeazzi, the co-author of one publication [1], were not answered.

As we are located in Basel, we had the opportunity to review the thesis referenced by Keller [3]. It does contain the statement that the Dettli equation is intended to be a simplified form of the Cockcroft–Gault equation, but it gives no deduction or validation of the equation. There is just a reference to the Schweizer Arzneimittelkompendium [1], where, as stated above, neither a theoretical deduction nor an experimental validation is referenced. Therefore, there is no published deduction or validation of this equation. We think the merits of Professor Dettli do not lie in this equation, which is a non-validated side product, but in his work on the elimination kinetics of different substances.

Secondly, as similar to the Cockcroft–Gault equation, the Dettli formula claims to estimate creatinine clearance. As the goal of our work was to have a simple equation estimating glomerular filtration rate (GFR), we could not see a benefit including both equations and decided to include the more widespread version, which is the one by Cockcroft and Gault.

Nevertheless, as the Dettli equation is widely known in Switzerland, we also did test the results given by this equation and found it to have a significantly higher bias than inulin clearance-based estimated GFR (IB-eGFR) (Table 1) and a smaller proportion of estimations below any desired threshold (Figure 1).

Regarding the gender factor, when Keller and Hartmann state "Therefore, in doubt the GFR can be estimated without sex differences", they are mistaken twice: Firstly, when using the Dettli equation, they are not estimating GFR but creatinine clearance, a difference every nephrologist should be aware of. Secondly, the Dettli equation proposes to add 10% for males and to subtract 10% for females, which gives a sex-dependent difference of 20%. Simply omitting this gender factor will not lead to an "estimation without sex differences" but to a result giving the mean of the estimation for a male or female subject. So, this approach could also be applied to other equations, but as the gender factor is there for a reason, it will give highly biased results for both males and females.

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Table 1. Correlation and bias of IB-eGFR and Dettli equation as compared to inulin clearance

	IB-eGFR	Dettli	*P*
Correlation coefficient (*r*)	0.8484	0.8007	<0.05
Mean Bias (mL/min)	0.7 (−46.3–32.7)	2.9 (−43.3–48.5)	<0.001
Mean absolute bias (mL/min)	7.4 (0.04–46.3)	11.4 (0.02–48.5)	<0.001
Mean bias (% of GFR)	1.2 (−44.4–65.9)	5.3 (-43.3–97.2)	<0.001

Values are given as mean (range). Compared to the Dettli equation, the results of the IB-eGFR equation show a significantly smaller bias and better correlation to inulin clearance.

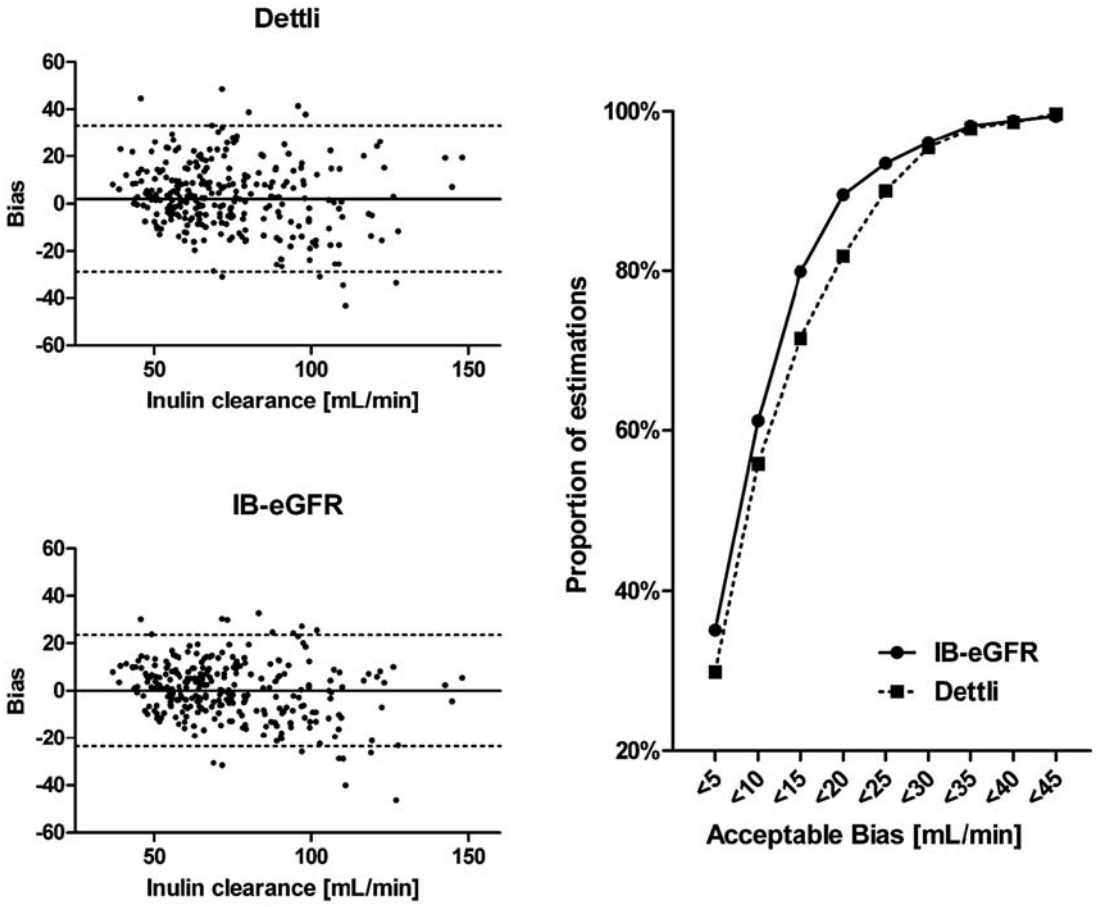

Fig. 1. On the left: Bland and Altman plot of the estimation bias plotted against inulin clearance. The solid lines indicate the mean bias, and the dotted lines ± 1.96 SD. On the right: Cumulative percentage of estimations below a certain bias. For example, if the acceptable bias is defined as up to 15 mL/min, IB-eGFR will result in 79.9% of estimations meeting this criterion as compared to 71.5% when using the Dettli equation.

Conflict of interest statement. None declared.

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The original sin of Cockcroft–Gault formula

While reading the article by Etgen and colleagues which reported that 'chronic kidney disease is associated with incident cognitive impairment in the elderly' [1] based on the renal function evaluation using the Cockcroft–Gault (C–G) formula [2], we felt it was interesting to see that the decrease of renal function in the study subjects coincided with the increase of age.

Generally in the same elderly patient group, C–G formula accurately estimates renal function in those with low creatinine clearance (Ccr) [3] while it calculates low results in those with normal Ccr [4]. In studies on young patients, it was reported that C–G formula highly evaluated renal function [4,5]. Because of all above findings, we thought it would be necessary to study how age and Ccr have any influence on C–G formula.

We divided subjects with ages of 18 years old or older into three groups of Group I, II and III, according to Ccr levels. We then calculated C–G formula in each group, and drew scatter plots between age and Ccr, and between age and C–G formula (Figure 1A and B). In all three groups, C–G formula decreased as age increased with strong correlations between age and C–G formula.

Also, the slope of regression curve decreased as Ccr decreased, and this was a predictable result when looking at the formula [2] where C–G formula = [(140 − age) × weight] / [72 × serum creatinine (Scr)]. When Scr is 1 mg/dL in the above formula, we can see that C–G formula has a negative relationship with age, and Group II from our study showed the slope as nearly 1 in negative direction. As seen in the results from our other groups, the influence