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Development and Validation of a Modified Full Age Spectrum Creatinine-Based Equation to Estimate Glomerular Filtration Rate

A Cross-sectional Analysis of Pooled Data

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Background: The Chronic Kidney Disease in Children Study (CKiD) equation for children and the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation for adults are recommended serum creatinine (SCr)–based calculations for estimating glomerular filtration rate (GFR). However, these equations, as well as their combination, have limitations, notably the problem of implausible changes in GFR during the transition from adolescence to adulthood and overestimation of GFR in young adults. The full age spectrum (FAS) equation addresses these issues but overestimates GFR when SCr levels are low.

Objective: To develop and validate a modified FAS SCr-based equation combining design features of the FAS and CKD-EPI equations.

Design: Cross-sectional analysis with separate pooled data sets for development and validation.

Setting: Research and clinical studies (n = 13) with measured GFR available.

Patients: 11 251 participants in 7 studies (development and internal validation data sets) and 8378 participants in 6 studies (external validation data set).

Measurements: Clearance of an exogenous marker (reference method), SCr level, age, sex, and height were used to develop a new equation to estimate GFR.

Results: The new European Kidney Function Consortium (EKFC) equation is a FAS equation with low bias (−1.2 mL/min/1.73 m^2 [95% CI, −2.7 to 0.0 mL/min/1.73 m^2] in children and −0.9 mL/min/1.73 m^2 [CI, −1.2 to −0.5 mL/min/1.73 m^2] in adults) across the FAS (2 to 90 years) and SCr range (40 to 490 µmol/L [0.45 to 5.54 mg/dL]) and with fewer estimation errors exceeding 30% (6.5% [CI, 3.8% to 9.1%] in children and 3.1% [CI, 2.5% to 3.6%] in adults) compared with the CKiD and CKD-EPI equations.

Limitation: No Black patients were included.

Conclusion: The new EKFC equation shows improved accuracy and precision compared with commonly used equations for estimating GFR from SCr levels.

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Creatinine-based equations are commonly used in daily clinical practice to estimate glomerular filtration rate (GFR). Many equations have been developed in recent decades, often targeting specific populations (such as children, adults, older adults, or patients with chronic kidney disease [CKD]) and using correction factors for sex and ethnicity (1–10). The most commonly used estimated GFR (eGFR) formulas are the Chronic Kidney Disease in Children Study (CKiD) equation for children (2), which is also used in adolescents, and the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation for adults (4). These 2 calculations are currently recommended by the Kidney Disease: Improving Global Outcomes (KDIGO) guidelines (11); however, they have some limitations. First, the CKiD equation was designed for children (aged 1 to 16 years) with CKD and therefore does not perform well in healthy children or in adolescents (aged 16 to 18 years). It also overestimates GFR in very young children and underestimates it in those at the transition age of 18 years (12, 13). Moreover, the CKiD equation includes the "height" variable, which is frequently not available in laboratory databases but is necessary for automatic reporting of eGFR by clinical laboratories (14). Second, the CKD-EPI equation was developed in a mixed population of healthy persons and patients with CKD but overestimates GFR in young adults (13, 15, 16). Another problem arises when a patient transitions from adolescence to adulthood, because the sequential use of these 2 equations leads to an implausible rise in eGFR despite no change in serum creatinine (SCr) values (13). Although the full age spectrum (FAS) equation (9, 17) was designed to overcome the challenge in measuring GFR in patients transitioning from adolescent to adult nephrology care (13, 18), it also overestimates GFR at low SCr values and in patients with CKD (16, 18).

See also:
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The overall aim of the current study was to develop and validate a new SCr-based equation that can be applied to the full spectrum of age and renal function, by combining the properties of the FAS and CKD-EPI equations.

METHODS

Design Overview

Data from 19 629 patients in 13 cohorts were used for development and internal and external validation. Cohorts were allocated to either development–internal validation or external validation data sets to obtain distributions as similar as possible between the 2 data sets with respect to age (children and adults), the exogenous marker used for measured GFR (mGFR), and mGFR levels. Seven cohorts, comprising 11 251 participants, were used for development and internal validation. This group was randomly divided into a development (n = 8473; 75%) and an internal validation (n = 2778; 25%) data set. The remaining 6 cohorts, comprising 8378 participants, were used for external validation. Only complete data sets with no missing data for mGFR, SCr, age, sex, or height were used in the analysis. Analysis was limited to the first GFR measurement obtained for each patient (if more than 1 was available).

Data were anonymized from the source cohorts for the analysis, performed at Lund University, Sweden. All procedures involving humans and data were in agreement with the ethical principles for medical research involving human subjects established in the World Medical Association's Declaration of Helsinki. The study was reviewed and approved by the Regional Ethical Board in Lund, Sweden (registration no. 2018/220).

Figure 1. The new EKFC equation.

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

Q Values

For ages 2–25 y:
Males:
$\ln(Q) = 3.200 + 0.259 \times Age - 0.543 \times \ln(Age) - 0.00763 \times Age^2 + 0.0000790 \times Age^3$
Females:
$\ln(Q) = 3.080 + 0.177 \times Age - 0.223 \times \ln(Age) - 0.00596 \times Age^2 + 0.0000686 \times Age^3$

For ages >25 y:
Males:
Q = 80 μmol/L (0.90 mg/dL)
Females:
Q = 62 μmol/L (0.70 mg/dL)

SCr and Q in μmol/L (to convert to mg/dL, divide by 88.4)

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

Participants

Data on GFR, both for children and adults, were collected and centralized by the European Kidney Function Consortium (EKFC), which has been endorsed by the European Renal Association and European Dialysis and Transplant Association. Data were from participants (all non-Black) in previously published research studies as well as patients who had their GFR measured as part of clinical care at nephrology centers. An overview of the participating centers, the measurement methods used, and patient characteristics was published previously (16, 18).

Covariates

Age, sex, height, and SCr values were obtained from medical records. Serum creatinine was measured with assays traceable to the gold standard method of isotope dilution mass spectrometry or were corrected to that method's levels (in the case of the CRIC [Chronic Renal Insufficiency Cohort] study [19]) (20).

Outcomes

Measured GFR was obtained by using either plasma clearance (based on the decay of plasma concentrations over time) or urinary clearance (based on the urinary excretion rate divided by plasma concentration) of exogenous filtration markers (iohexol, inulin, ^{51}Cr-EDTA, or iothalamate); all methods have acceptable accuracy (21).

Statistical Analysis

Development of the New Equation

The format of the new equation is based on previous knowledge of the FAS and CKD-EPI equations. We maintained the general form of the FAS equation, which is based on a normalized SCr value calculated from SCr/Q, where SCr represents the creatinine level in an individual and Q the sex- and age-specific median creatinine value in healthy persons. With the development data set, we used least-squares linear regression to regress logarithm-transformed mGFR onto log SCr, age, and sex in a multivariable model. We considered models with fixed and varying age thresholds. Details on model development are presented in the **Supplement** (Section 3 and **Supplement Table 3**, available at Annals.org).

Internal Validation of the New Equation

Internal validation results (median bias, SD, interquartile range, and P30 accuracy [percentage of eGFRs within ±30% of mGFR]) were used to determine the final model. The development and internal validation data sets were then combined into 1 set, extreme outliers were removed, and the final coefficients were derived (see the **Supplement**, Section 3, for more details).

External Validation

The external validation data set was used to compare the new model with the FAS equation and with the KDIGO-recommended equations. In addition, the new equation was compared with the revised Lund–Malmö equation based on adjusted creatinine values for chil-

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

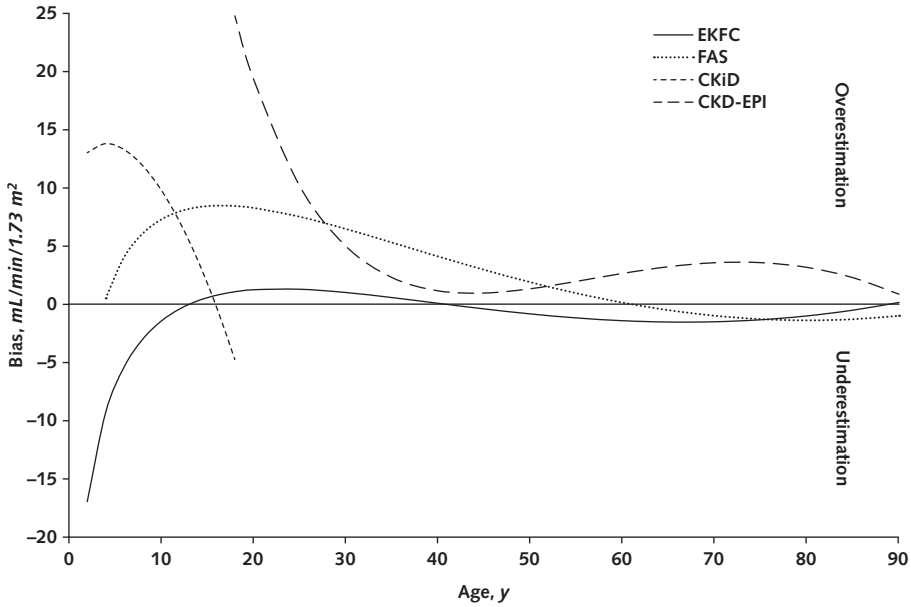
Age Group	Equation		
	EKFC	**FAS**	**CKiD**
Children (2 to <18 y)			
Median bias (95% CI), *mL/min/1.73 m²*			
All (*n* = 1254)	−1.2 (−2.7 to 0.0)	6.7 (4.8 to 8.1)	6.2 (4.6 to 7.7)
eGFR <75 mL/min/1.73 m² (*n* = 324)	−5.7 (−7.0 to −3.9)	−0.8 (−2.6 to 0.8)	−1.8 (−2.9 to −0.1)
eGFR ≥75 mL/min/1.73 m² (*n* = 930)	1.1 (−0.4 to 3.0)	10.8 (9.0 to 13.1)	11.2 (9.2 to 13.4)
Imprecision, SD (P25–P75)			
All (*n* = 1254)	27.8 (−14.9 to 11.0)	70.6 (−7.4 to 22.8)	56.6 (−7.7 to 23.6)
eGFR <75 mL/min/1.73 m² (*n* = 324)	20.3 (−18.1 to 2.3)	20.0 (−12.2 to 7.6)	18.2 (−10.2 to 7.2)
eGFR ≥75 mL/min/1.73 m² (*n* = 930)	29.6 (−14.4 to 14.3)	80.1 (−5.3 to 29.1)	63.7 (−6.5 to 30.9)
Accuracy P30 (95% CI), %			
All (*n* = 1254)	79.7 (77.4 to 81.9)	74.2 (71.7 to 76.6)	73.2 (70.8 to 75.7)
eGFR <75 mL/min/1.73 m² (*n* = 324)	73.8 (68.9 to 78.6)	77.8 (73.2 to 82.3)	80.2 (75.9 to 84.6)
eGFR ≥75 mL/min/1.73 m² (*n* = 930)	81.7 (79.2 to 84.2)	72.9 (70.0 to 75.8)	70.8 (67.8 to 73.7)
	EKFC	**FAS**	**CKD-EPI**
Adults aged 18 to <40 y			
Median bias (95% CI), *mL/min/1.73 m²*			
All (*n* = 972)	0.8 (0.0 to 2.2)	7.3 (5.9 to 8.6)	7.8 (6.3 to 9.2)
eGFR <75 mL/min/1.73 m² (*n* = 137)	2.3 (0.3 to 4.2)	7.5 (4.7 to 8.8)	3.4 (1.7 to 5.8)
eGFR ≥75 mL/min/1.73 m² (*n* = 835)	0.6 (−0.5 to 1.9)	7.2 (5.8 to 8.8)	8.7 (7.2 to 10.6)
Imprecision, SD (P25–P75)			
All (*n* = 972)	17.2 (−8.3 to 10.3)	41.7 (−3.7 to 18.2)	20.5 (−2.0 to 18.2)
eGFR <75 mL/min/1.73 m² (*n* = 137)	14.2 (−3.2 to 9.2)	14.3 (1.4 to 13.4)	14.4 (−2.1 to 12.8)
eGFR ≥75 mL/min/1.73 m² (*n* = 835)	17.6 (−8.9 to 10.8)	44.6 (−4.3 to 19.3)	21.2 (−2.0 to 19.4)
Accuracy P30 (95% CI), %			
All (*n* = 972)	89.6 (87.7 to 91.5)	82.1 (79.7 to 84.5)	84.0 (81.6 to 86.3)
eGFR <75 mL/min/1.73 m² (*n* = 137)	80.3 (73.5 to 87.0)	71.5 (63.9 to 79.2)	78.8 (71.9 to 85.8)
eGFR ≥75 mL/min/1.73 m² (*n* = 835)	91.1 (89.2 to 93.1)	83.8 (81.3 to 86.3)	84.8 (82.3 to 87.2)
Adults aged 40 to <65 y			
Median bias (95% CI), *mL/min/1.73 m²*			
All (*n* = 3585)	−1.1 (−1.6 to −0.6)	1.1 (0.5 to 1.6)	1.8 (1.3 to 2.4)
eGFR <60 mL/min/1.73 m² (*n* = 492)	1.9 (1.3 to 2.8)	4.7 (4.1 to 5.3)	1.5 (0.7 to 2.5)
eGFR ≥60 mL/min/1.73 m² (*n* = 3093)	−2.0 (−2.5 to −1.5)	−0.2 (−0.8 to 0.6)	1.9 (1.3 to 2.5)
Imprecision, SD (P25–P75)			
All (*n* = 3585)	15.1 (−9.4 to 7.4)	17.8 (−8.3 to 10.5)	15.4 (−6.1 to 10.9)
eGFR <60 mL/min/1.73 m² (*n* = 492)	9.2 (−2.5 to 7.3)	9.4 (−0.5 to 10.0)	9.2 (−2.8 to 6.9)
eGFR ≥60 mL/min/1.73 m² (*n* = 3093)	15.8 (−10.5 to 7.5)	18.7 (−9.4 to 10.6)	16.1 (−6.8 to 11.6)
Accuracy P30 (95% CI), %			
All (*n* = 3585)	89.5 (88.5 to 90.5)	85.9 (84.8 to 87.1)	88.2 (87.1 to 89.3)
eGFR <60 mL/min/1.73 m² (*n* = 492)	76.4 (72.7 to 80.2)	67.7 (63.5 to 71.8)	77.4 (73.7 to 81.1)
eGFR ≥60 mL/min/1.73 m² (*n* = 3093)	91.6 (90.6 to 92.5)	88.8 (87.7 to 89.9)	89.9 (88.9 to 91.0)
Adults aged ≥65 y			
Median bias (95% CI), *mL/min/1.73 m²*			
All (*n* = 2567)	−1.2 (−1.0 to −1.6)	−1.1 (−1.5 to −0.6)	3.0 (2.5 to 3.6)
eGFR <45 mL/min/1.73 m² (*n* = 852)	−0.5 (−0.9 to −0.1)	0.7 (0.2 to 1.2)	0.5 (0.1 to 0.9)
eGFR ≥45 mL/min/1.73 m² (*n* = 1715)	−2.0 (−2.6 to −1.3)	−2.9 (−3.7 to −2.4)	5.1 (4.3 to 6.0)
Imprecision, SD (P25–P75)			
All (*n* = 2567)	12.1 (−7.6 to 5.0)	14.3 (−8.5 to 5.3)	12.5 (−2.9 to 10.2)
eGFR <45 mL/min/1.73 m² (*n* = 852)	7.1 (−4.3 to 3.8)	7.2 (−3.5 to 5.1)	7.2 (−2.9 to 5.1)
eGFR ≥45 mL/min/1.73 m² (*n* = 1715)	13.9 (−9.6 to 6.1)	16.7 (−10.8 to 5.8)	14.3 (−2.9 to 13.1)
Accuracy P30 (95% CI), %			
All (*n* = 2567)	85.3 (83.9 to 86.7)	83.6 (82.1 to 85.0)	80.7 (79.2 to 82.2)
eGFR <45 mL/min/1.73 m² (*n* = 852)	76.8 (73.9 to 79.6)	73.9 (71.0 to 76.9)	69.6 (65.5 to 73.7)
eGFR ≥45 mL/min/1.73 m² (*n* = 1715)	89.6 (88.1 to 91.0)	88.4 (86.9 to 89.9)	83.7 (81.9 to 85.4)

CKD-EPI = Chronic Kidney Disease Epidemiology Collaboration; CKiD = Chronic Kidney Disease in Children Study; eGFR = estimated glomerular filtration rate; EKFC = European Kidney Function Consortium; FAS = full age spectrum; P25–P75 = interquartile range; P30 = accuracy within 30% of measured GFR.
* For children (aged 2 to <18 y) and adults in age subgroups 18 to <40 y, 40 to <65 y, and ≥65 y, according to the age-adapted thresholds for EKFC eGFR: 75, 60, and 45 mL/min/1.73 m², respectively.

dren (22) and the pediatric Schwartz–Lyon equation (5). We compared the performance of equations in the whole external validation data set, as well as in subgroups of age, SCr/Q, and eGFR.

To evaluate the performance of equations, we measured median bias (that is, eGFR minus mGFR) with 95% CIs, imprecision (SD of bias and interquartile range), and P30 accuracy in children (aged 2 to <18

Figure 2. Bias (eGFR minus mGFR), according to age, for the EKFC, FAS, and KDIGO-recommended equations (CKiD in children and CKD-EPI in adults).



Positive bias indicates overestimation; negative bias indicates underestimation. CKD-EPI = Chronic Kidney Disease Epidemiology Collaboration; CKiD = Chronic Kidney Disease in Children Study; EKFC = European Kidney Function Consortium; eGFR = estimated glomerular filtration rate; FAS = full age spectrum; mGFR = measured GFR.

years) and adults in age subgroups (18 to <40, 40 to <65, and ≥65 years) and in eGFR subgroups by using the age-adapted thresholds of 75, 60, and 45 mL/min/1.73 m^2, respectively (23–25), and using fixed thresholds of 60 and 90 mL/min/1.73 m^2 (**Supplement**, available at Annals.org). The target for bias is zero; imprecision should be as low as possible. The goal for P30 accuracy is 100%; however a P30 greater than 75% has been considered "sufficient for good clinical decision making" by the Kidney Disease Outcomes Quality Initiative, although its goal is to reach a P30 greater than 90% (26, 27).

Median quantiles for bias across the age spectrum (and normalized SCr in the **Supplement**) were graphically presented by using fractional polynomials (linear, square, and logarithmic). Likewise, P30 accuracy (percentage) was depicted across the age spectrum (**Supplement**) by using cubic splines with 2 free knots and by using third-degree polynomials.

We calculated the net reclassification index, which is the net total percentage of patients reclassified into a different CKD stage by the EKFC equation using the age-adapted thresholds (45, 60, and 75 mL/min/1.73 m^2) compared with the KDIGO-recommended equations (28).

All analyses were performed with SAS 9.4 (SAS Institute).

Role of the Funding Source

Dr. Björk has received funding from the Swedish Research Council to conduct large-scale epidemiologic studies linked to registered data from health care. This funding source had no involvement in the design, analysis, presentation, or interpretation of the results of the present study.

RESULTS

Characteristics of Participants

The basic participant characteristics are summarized in **Supplement Table 1a** (available at Annals.org). Further details for each cohort may be found in **Supplement Tables 1b** to **1d** (available at Annals.org). The partitioning of data into development, internal validation, and external validation sets, stratified by cohort and age (children vs. adults), is presented in **Supplement Table 2** (available at Annals.org). The mean mGFRs in the development, internal validation, and external validation data sets were 76.9 (SD, 33.1), 77.7 (SD, 32.9), and 78.9 (SD, 32.2) mL/min/1.73 m^2, respectively. Mean age was 42.4 years (SD, 25.2) in both the development and internal validation data sets, and 50.9 years (SD, 22.3) in the external validation data set. About 56% of participants in the development and internal validation data sets were male, compared with 47% in the external validation data set.

Development and Internal Validation

The results from the development and internal validation data sets are presented in **Supplement Table 3** (available at Annals.org). The final EKFC model is presented in **Figure 1**. The EKFC equation has some of the same coefficients as the FAS equation (namely, a leading coefficient of 107.3 and age threshold of 40 years), but the exponential coefficients for normalized SCr

(SCr/Q) differed when normalized SCr was less than 1 versus greater than 1. This is similar to the different exponential coefficient for creatinine according to creatinine concentration used in the CKD-EPI equation. Also, the coefficient associated with age, 0.990, lies between the FAS coefficient of 0.988 and the CKD-EPI coefficient of 0.993.

External Validation of the EKFC Equation

Table 1 presents the performance statistics for the EKFC, FAS, and KDIGO-recommended equations, overall and in subgroups of eGFR less than 75 mL/min/1.73 m^2 and 75 mL/min/1.73 m^2 and greater (for children) and in age subgroups (18 to <40, 40 to <65, and ≥65 years) according to eGFR subgroup (by using the age-adapted thresholds of 75, 60, and 45 mL/min/1.73 m^2, respectively [23–25]). Supplement Tables (available at Annals.org) present the performance statistics for each cohort (Supplement Tables 4a and 4b), age group (Supplement Tables 6a and 7a), SCr/Q interval (Supplement Tables 6b and 7b), eGFR and mGFR subgroup (Supplement Tables 6c and 7c), and eGFR subgroup based on the fixed thresholds of 60 and 90 mL/min/1.73 m^2 (Supplement Tables 9a, 9b, and 10a to 10c). To judge performance, it is important to consider the possible overlap of 95% CIs in the tables along with the charts in Figure 2 (for bias) and Supplement Figure 8 (for P30 [available at Annals.org]).

The overall median bias of the EKFC equation in children is close to zero (Table 1), whereas both the FAS and CKiD equations overestimate mGFR. Still, a split analysis by kidney function reveals that the EKFC equation has a bias of −5.7 mL/min/1.73 m^2 at reduced eGFRs, whereas bias was not different from zero at normal eGFRs (>75 mL/min/1.73 m^2). The opposite is true for the FAS and CKiD equations, with near zero bias at low eGFRs (<75 mL/min/1.73 m^2) and a bias of 11 mL/min/1.73 m^2 at normal eGFRs (>75 mL/min/1.73 m^2).

Analysis of median bias across the age range of 2 to 18 years (Figure 1 and Supplement Table 6a), reveals that bias for the CKiD equation varies considerably, between 15 mL/min/1.73 m^2 in young children to −6 mL/min/1.73 m^2 at the (transition) age of 18 years. For the EKFC equation, the median bias is about −11 mL/min/1.73 m^2 in young children (aged <5 years), between −5 and 0 mL/min/1.73 m^2 for children aged 5 to 10 years, and approximately zero in those older than 10 years. The overall median bias for the EKFC equation in adults (Table 1, Figure 1, and Supplement Table 6a) remains close to zero across the entire 18- to 90-year age span.

In nearly all age and eGFR subgroups (Table 2), bias is lower for the EKFC than the CKD-EPI equation.

The EKFC equation also shows nearly zero bias across the entire normalized SCr range, as opposed to the increasing bias at normalized SCr below 1 for the FAS and the KDIGO equations, resulting in substantial overestimation of mGFR (Supplement and Supplement Table 6b).

Imprecision is substantially reduced with the EKFC versus the CKiD and CKD-EPI equations, and accuracy (P30) is substantially improved with the EKFC com-

Table 2. Strengths and Limitations of SCr-Based eGFR Equations (in the External Validation Data Set)

Criterion	Equation		
	EKFC	**CKiD**	**CKD-EPI**
Applicable in children	Yes	Yes	No
Applicable in adults	Yes	No	Yes
Age or height based	Age and height*	Height	Age
Transition from pediatric to adult care	Continuous	Ends at 18 y	Starts at 18 y
High bias (>10 mL/min/1.73 m^2) in age subgroups*	Yes, in ages 2–4 y	Yes, in ages 2–10 y	Yes, in ages 18–25 y
High bias (>10 mL/min/1.73 m^2) in SCr/Q subgroups*	No	Yes, for Scr/Q <0.90	Yes, for Scr/Q <0.60
P30 <75% in age subgroups*	Yes, in ages 2–6 y	Yes, in ages 2–8 y	Yes, in ages 18–20 y
P30 <75% in SCr/Q subgroups*	Yes, if SCr/Q <53 μmol/L (0.60 mg/dL)	Yes, if SCr/Q <80 μmol/L (0.90 mg/dL)	Yes, if SCr/Q <53 μmol/L (0.60 mg/dL)
P30 >90% in age subgroups*	Yes, 5×†	No	Yes, 1×†
P30 >90% in SCr/Q subgroups*	Yes, if SCr/Q is 71–106 μmol/L (0.80–1.20 mg/dL)	No	No
High bias in eGFR subgroups*	No	Yes, if eGFR >90 mL/min/1.73 m^2	Yes, if eGFR >120 mL/min/1.73 m^2
P30 <75% in eGFR subgroups*	Yes, if eGFR <30 or >120 mL/min/1.73 m^2	Yes, if eGFR <30 or >90 mL/min/1.73 m^2	Yes, if eGFR <30 or >120 mL/min/1.73 m^2
Average overall P30 in children/adults, %	79.7/88.0‡	73.2/NA‡	NA/84.9‡
Average overall bias in children/adults, *mL/min/1.73 m^2*	–1.2/–0.9	6.2/NA	NA/2.9

CKD-EPI = Chronic Kidney Disease Epidemiology Collaboration; CKiD = Chronic Kidney Disease in Children Study; eGFR = estimated glomerular filtration rate; EKFC = European Kidney Function Consortium; NA = not available; P30 = percentage within 30% of measured GFR; SCr = serum creatinine; SCr/Q = normalized SCr.

* See the Supplement (available at Annals.org) for more details. eGFR subgroups are defined by the EKFC.

† Number of occurrences.

‡ Estimation errors exceeding 30%: 79.7% − 73.2% = 6.5% (95% CI, 3.8%–9.1%) in children (difference between P30 value for EKFC and CKiD) and 88.0% − 84.9% = 3.1% (CI, 2.5%–3.6%) in adults (difference between P30 value for EKFC and CKD-EPI).

Table 3. Reclassification of Participants by NRI in the External Validation Data Set With Use of the EKFC Equation Versus the KDIGO-Recommended Equations*†

Age Range	Participants, *n*	mGFR Threshold, *mL/min/1.73 m²*	Event Subgroup‡			
			Participants, *n*	Correctly Reclassified, *n (%)*	Incorrectly Reclassified, *n (%)*	Net Difference, %
<18 y	1254	75	301	22 (7.31)	15 (4.98)	2.33
18 to <40 y	972	75	158	17 (10.76)	0 (0.00)	10.76
40 to 65 y	3585	60	583	12 (2.06)	4 (0.69)	1.37
≥65 y	2567	45	887	37 (4.17)	0 (0.00)	4.17
≥18 y	7124	60	1953	90 (4.61)	5 (0.26)	4.35

CKD-EPI = Chronic Kidney Disease Epidemiology Collaboration; CKiD = Chronic Kidney Disease in Children Study; EKFC = European Kidney Function Consortium; KDIGO = Kidney Disease: Improving Global Outcomes; mGFR = measured glomerular filtration rate; NRI = net reclassification index.
* KDIGO-recommended equations: CKiD equation for children aged <18 y; CKD-EPI equation for adults aged ≥18 y.
† A further breakdown in age subgroups 18 to <40 y, 40 to <65 y, and ≥65 y is based on the age-adapted thresholds proposed by Delanaye and colleagues (24).
‡ Event subgroup is defined by mGFR below threshold; nonevent subgroup is defined by mGFR at or above threshold.

pared with the KDIGO-recommended equations (**Table 1** and **Supplement Figure 8**); the improvement is especially relevant in young children and young adults. Considering the whole age spectrum (**Supplement Table 7a**) and normalized SCr range (**Supplement Table 7b**), the accuracy of the EKFC equation was at least as good as, and sometimes better than, that of the CKiD, FAS, and CKD-EPI equations. In **Table 2**, we summarize the strengths and weaknesses of the new equation and the KDIGO-recommended equations.

Use of the new equation to classify CKD was evaluated in the external validation data set by means of the net reclassification index (**Table 3**). No significant net reclassification improvement was seen in children ($P = 0.67$) or the middle-aged adult subgroup ($P = 0.16$). The gain in reclassifying participants was significant in the young adult ($P < 0.001$) and older adult ($P = 0.003$) subgroups.

To illustrate the clinical implications of the new equation compared with the recommended equations, we consider the scenario of a child with perfectly healthy kidney function that remains as the child grows to adulthood. This healthy kidney function is reflected, on one hand, in median healthy SCr values and, on the other hand, in median mGFRs for healthy persons (which are about 105 to 110 mL/min/1.73 m^2 [29]). At the age of 5 years, the child has a normal height of 110 cm and a normal SCr level of 33.6 μmol/L (0.38 mg/dL). The CKiD equation predicts an eGFR of 120 mL/min/1.73 m^2, steadily decreasing with age to an eGFR of 82 mL/min/1.73 m^2 for a male adolescent (aged 18 years with a normal height of 179 cm and a healthy median SCr level of 79.6 μmol/L [0.90 mg/dL]), which would implausibly jump to a CKD-EPI eGFR of 124 mL/min/1.73 m^2 at age 18. Likewise a CKiD eGFR of 99 mL/min/1.73 m^2 for a female adolescent (aged 18 years with a normal height of 167 cm and a median SCr value of 61.9 μmol/L [0.70 mg/dL]) would jump implausibly to an eGFR of 127 mL/min/1.73 m^2 at age 18 on the basis of the CKD-EPI equation. This CKD-EPI eGFR would then decrease between ages 18 and 40 to 106 mL/min/1.73 m^2. Alternatively, the EKFC equation will predict a stable value of 107.3 mL/min/1.73 m^2 for persons with median healthy SCr values, both before and after age 18, with a decline starting at about age 40.

DISCUSSION

In the current work, we present a new equation combining the strengths of the CKD-EPI and FAS equations, resulting in generally lower bias across the spectrum of age and kidney function. It was developed and externally validated in a large set of mGFRs and corresponding SCr values. The EKFC equation showed higher P30 accuracy and precision than the currently recommended equations. The difference in P30 values in the external validation data set indicates that the EKFC equation has about 6.5 fewer estimation errors exceeding 30% per 100 children and 3.1 fewer per 100 adults than the CKiD and CKD-EPI equations, respectively. Further, the new equation provides continuity across the entire age range, avoiding transition problems between adolescent and adult nephrology care (13). Another finding was that the EKFC equation allows automatic reporting of eGFR, not only for adults but also for children (whereas the CKiD equation requires height, a parameter not available in the laboratory) (30). If height is available for an individual patient, the EKFC equation can be transformed easily to a height-based equation by using height-based rather than age-based normalized SCr values, which may be advantageous in very young children (**Supplement**, Section 5).

The EKFC equation shows no difference in bias or P30 accuracy across the entire age range between males and females (**Supplement**, Section 5). Like the FAS equation, the EKFC model accounts for the age dependency of GFR (GFR is fairly constant until about age 40, after which a decline is evident) (29). Incorporating the age dependency of GFR into the EKFC equation may have helped improve its performance across the whole age range. Therefore, the main clinical advantage of the EKFC equation is that normal kidney function, reflected by SCr levels close to the median value for health, lead to an eGFR that approximates

Table 3–Continued

Nonevent Subgroup‡				Total Reclassified, *n* (%)	NRI (95% CI), %	*P* Value
Participants, *n*	Correctly Reclassified, *n* (%)	Incorrectly Reclassified, *n* (%)	Net Difference, %			
953	16 (1.68)	47 (4.93)	−3.25	100 (8.0)	−0.9 (−5.2 to 3.3)	0.6705
814	0 (0.00)	8 (0.98)	−0.98	25 (2.6)	9.8 (4.9 to 14.7)	0.00009
3002	4 (0.13)	16 (0.53)	−0.40	36 (1.0)	1.0 (−0.4 to 2.3)	0.1648
1680	0 (0.00)	33 (1.96)	−1.96	70 (2.7)	2.2 (0.7 to 3.7)	0.0034
5171	5 (0.10)	74 (1.43)	−1.33	174 (2.4)	3.0 (2.0 to 4.0)	<0.0001

mGFR (zero bias). As in the CKD-EPI– but not the FAS–equation, a different coefficient is applied when the SCr level is greater or less than the median value for healthy persons. This overcomes the overestimation of eGFR by the FAS equation at low normalized SCr values and in patients with CKD (**Supplement Table 6b**). Thus, the newly proposed equation incorporates key concepts of the FAS and CKD-EPI equations.

Precision is improved with the EKFC equation compared with the recommended equations, with R^2 values up to 0.88 (for detailed information, see **Supplement Tables 8a** and **8b**, available at Annals.org). However, like other eGFR equations, the new equation is limited by imprecision, which is notably higher when SCr values are within the normal reference interval. Indeed, in patients with normal kidney function, SCr levels more closely reflect interindividual variation in muscle mass than in mGFR (31, 32). Therefore, the lack of precision of creatinine-based eGFR equations may still require the direct measurement of GFR in some clinical settings (33, 34).

Like all creatinine-based GFR estimation equations, the EKFC equation will also overestimate GFR in persons with reduced muscle mass due to, for example, anorexia, paralysis, or malnourishment, and thus erroneously indicate hyperfiltration (31, 35). Because cystatin C is less influenced by muscle mass, using a cystatin C–based equation or averaging between the EKFC and cystatin C–based equations might provide a more accurate estimate of GFR in these settings (31, 35, 36).

Our analysis has other limitations. First, the EKFC equation was developed and validated in White populations. Therefore, it may not be valid for Black people or those of other ethnicities but may be adaptable if appropriate normalized SCr levels are established on the basis of the median SCr concentration for healthy persons of other ethnicities. Such data may be generated in large patient databases, as done previously in Europe and Africa (8, 22, 37). Second, like the CKD-EPI consortium, we developed and validated the new equation by using separate development, internal validation, and external validation data sets (38). This strategy is not free from criticism, notably because it could be argued that a true external validation should be performed by independent investigators. To maximize the validity of our analysis, we assigned the role of the external validation set to an age-matched sample of the participating cohorts. Third, the mGFRs were much higher (88 and 92 mL/min/1.73 m^2) in the 2 current pediatric validation cohorts than in the CKiD study (43 mL/min/1.73 m^2) used to develop the CKiD equation. Equations developed in healthier populations will inherently perform differently from those designed using data from patients with CKD (39). Fourth, the effect of proteinuria or hypoalbuminemia on the accuracy of the equations could not be evaluated, because these data were not available.

In conclusion, the new EKFC equation may have helpful properties and perform better in estimating GFR compared with the current KDIGO-recommended equations.

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References

1. **Cockcroft DW, Gault MH.** Prediction of creatinine clearance from serum creatinine. Nephron. 1976;16:31-41. [PMID: 1244564]
2. **Schwartz GJ, Muñoz A, Schneider MF, et al.** New equations to estimate GFR in children with CKD. J Am Soc Nephrol. 2009;20:629-37. [PMID: 19158356] doi:10.1681/ASN.2008030287
3. **Levey AS, Bosch JP, Lewis JB, et al; Modification of Diet in Renal Disease Study Group.** A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. Ann Intern Med. 1999;130:461-70. [PMID: 10075613]
4. **Levey AS, Stevens LA, Schmid CH, et al; CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration).** A new equation to estimate glomerular filtration rate. Ann Intern Med. 2009;150:604-12. [PMID: 19414839]
5. **De Souza VC, Rabilloud M, Cochat P, et al.** Schwartz formula: is one k-coefficient adequate for all children? PLoS One. 2012;7:e53439. [PMID: 23285295] doi:10.1371/journal.pone.0053439
6. **Schaeffner ES, Ebert N, Delanaye P, et al.** Two novel equations to estimate kidney function in persons aged 70 years or older. Ann Intern Med. 2012;157:471-81. [PMID: 23027318] doi:10.7326/0003-4819-157-7-201210020-00003
7. **Pottel H, Hoste L, Martens F.** A simple height-independent equation for estimating glomerular filtration rate in children. Pediatr Nephrol. 2012;27:973-9. [PMID: 22252520] doi:10.1007/s00467-011-2081-9
8. **Hoste L, Dubourg L, Selistre L, et al.** A new equation to estimate the glomerular filtration rate in children, adolescents and young adults. Nephrol Dial Transplant. 2014;29:1082-91. [PMID: 24046193] doi:10.1093/ndt/gft277
9. **Pottel H, Hoste L, Dubourg L, et al.** An estimated glomerular filtration rate equation for the full age spectrum. Nephrol Dial Transplant. 2016;31:798-806. [PMID: 26932693] doi:10.1093/ndt/gfv454
10. **Björk J, Grubb A, Sterner G, et al.** Revised equations for estimating glomerular filtration rate based on the Lund-Malmö Study cohort. Scand J Clin Lab Invest. 2011;71:232-9. [PMID: 21391777] doi:10.3109/00365513.2011.557086
11. **Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group.** KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. Kidney Int Suppl. 2013;3:1-150.
12. **Ng DK, Schwartz GJ, Schneider MF, et al.** Combination of pediatric and adult formulas yield valid glomerular filtration rate estimates in young adults with a history of pediatric chronic kidney disease. Kidney Int. 2018;94:170-177. [PMID: 29735307] doi:10.1016/j.kint.2018.01.034
13. **Pottel H, Björk J, Bökenkamp A, et al.** Estimating glomerular filtration rate at the transition from pediatric to adult care. Kidney Int. 2019;95:1234-1243. [PMID: 30922665] doi:10.1016/j.kint.2018.12.020
14. **Levey AS, Stevens LA, Hostetter T.** Automatic reporting of estimated glomerular filtration rate–just what the doctor ordered. Clin Chem. 2006;52:2188-93. [PMID: 17068166]
15. **Selistre L, Rabilloud M, Cochat P, et al.** Comparison of the Schwartz and CKD-EPI equations for estimating glomerular filtration rate in children, adolescents, and adults: a retrospective cross-sectional study. PLoS Med. 2016;13:e1001979. [PMID: 27023756] doi:10.1371/journal.pmed.1001979
16. **Björk J, Nyman U, Courbebaisse M, et al.** Prospects for improved glomerular filtration rate estimation based on creatinine-results from a transnational multicentre study. Clin Kidney J. 2020;13:674-683. [PMID: 32905314] doi:10.1093/ckj/sfaa039
17. **Pottel H, Delanaye P, Schaeffner E, et al.** Estimating glomerular filtration rate for the full age spectrum from serum creatinine and cystatin C. Nephrol Dial Transplant. 2017;32:497-507. [PMID: 28089986] doi:10.1093/ndt/gfw425
18. **Björk J, Nyman U, Berg U, et al.** Validation of standardized creatinine and cystatin C GFR estimating equations in a large multicentre European cohort of children. Pediatr Nephrol. 2019;34:1087-1098. [PMID: 30715595] doi:10.1007/s00467-018-4185-y
19. **Feldman HI, Appel LJ, Chertow GM, et al; Chronic Renal Insufficiency Cohort (CRIC) Study Investigators.** The chronic renal insufficiency cohort (CRIC) study: design and methods. J Am Soc Nephrol. 2003;14:S148-53. [PMID: 12819321]
20. **Piéroni L, Delanaye P, Boutten A, et al; Société Française de Biologie Clinique.** A multicentric evaluation of IDMS-traceable creatinine enzymatic assays. Clin Chim Acta. 2011;412:2070-5. [PMID: 21803031] doi:10.1016/j.cca.2011.07.012
21. **Soveri I, Berg UB, Björk J, et al; SBU GFR Review Group.** Measuring GFR: a systematic review. Am J Kidney Dis. 2014;64:411-24. [PMID: 24840668] doi:10.1053/j.ajkd.2014.04.010
22. **Björk J, Nyman U, Delanaye P, et al.** A novel method for creatinine adjustment makes the revised Lund-Malmö GFR estimating equation applicable in children. Scand J Clin Lab Invest. 2020:1-8. [PMID: 32628043] doi:10.1080/00365513.2020.1774641
23. **Pottel H, Hoste L, Delanaye P.** Abnormal glomerular filtration rate in children, adolescents and young adults starts below 75 mL/min/1.73 m(2). Pediatr Nephrol. 2015;30:821-8. [PMID: 25403744] doi:10.1007/s00467-014-3002-5

24. **Delanaye P, Jager KJ, Bökenkamp A, et al.** CKD: A call for an age-adapted definition. J Am Soc Nephrol. 2019;30:1785-1805. [PMID: 31506289] doi:10.1681/ASN.2019030238
25. **Delanaye P, Glassock RJ, Pottel H, et al.** An age-calibrated definition of chronic kidney disease: rationale and benefits. Clin Biochem Rev. 2016;37:17-26. [PMID: 27057075]
26. **National Kidney Foundation.** K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. Am J Kidney Dis. 2002;39:S1-266. [PMID: 11904577]
27. **Earley A, Miskulin D, Lamb EJ, et al.** Estimating equations for glomerular filtration rate in the era of creatinine standardization: a systematic review. Ann Intern Med. 2012;156:785-95. [PMID: 22312131] doi:10.7326/0003-4819-156-6-201203200-00391
28. **Pencina MJ, D'Agostino RB Sr, D'Agostino RB Jr, et al.** Evaluating the added predictive ability of a new marker: from area under the ROC curve to reclassification and beyond. Stat Med. 2008;27:157-72; discussion 207-12. [PMID: 17569110]
29. **Pottel H, Hoste L, Yayo E, et al.** Glomerular filtration rate in healthy living potential kidney donors: a meta-analysis supporting the construction of the full age spectrum equation. Nephron. 2017;135:105-119. [PMID: 27764827] doi:10.1159/000450893
30. **Schwartz GJ.** Height: the missing link in estimating glomerular filtration rate in children and adolescents. Nephrol Dial Transplant. 2014;29:944-7. [PMID: 24516232] doi:10.1093/ndt/gft530
31. **Vinge E, Lindergård B, Nilsson-Ehle P, et al.** Relationships among serum cystatin C, serum creatinine, lean tissue mass and glomerular filtration rate in healthy adults. Scand J Clin Lab Invest. 1999;59:587-92. [PMID: 10691049]
32. **Osaka T, Hamaguchi M, Hashimoto Y, et al.** Decreased the creatinine to cystatin C ratio is a surrogate marker of sarcopenia in patients with type 2 diabetes. Diabetes Res Clin Pract. 2018;139:52-58. [PMID: 29496508] doi:10.1016/j.diabres.2018.02.025
33. **Agarwal R, Delanaye P.** Glomerular filtration rate: when to measure and in which patients? Nephrol Dial Transplant. 2019;34:2001-2007. [PMID: 30520986] doi:10.1093/ndt/gfy363
34. **Delanaye P, Melsom T, Ebert N, et al.** Iohexol plasma clearance for measuring glomerular filtration rate in clinical practice and research: a review. Part 2: Why to measure glomerular filtration rate with iohexol? Clin Kidney J. 2016;9:700-4. [PMID: 27679716] doi:10.1093/ckj/sfw071
35. **Thomassen SA, Johannesen IL, Erlandsen EJ, et al.** Serum cystatin C as a marker of the renal function in patients with spinal cord injury. Spinal Cord. 2002;40:524-8. [PMID: 12235535]
36. **Grubb A, Nyman U, Björk J.** Improved estimation of glomerular filtration rate (GFR) by comparison of eGFRcystatin C and eGFRcreatinine. Scand J Clin Lab Invest. 2012;72:73-7. [PMID: 22121923] doi:10.3109/00365513.2011.634023
37. **Bukabau JB, Yayo E, Gnionsahé A, et al.** Performance of creatinine- or cystatin C-based equations to estimate glomerular filtration rate in sub-Saharan African populations. Kidney Int. 2019;95:1181-1189. [PMID: 30910379] doi:10.1016/j.kint.2018.11.045
38. **Inker LA, Schmid CH, Tighiouart H, et al; CKD-EPI Investigators.** Estimating glomerular filtration rate from serum creatinine and cystatin C. N Engl J Med. 2012;367:20-9. [PMID: 22762315] doi:10.1056/NEJMoa1114248
39. **Rule AD, Larson TS, Bergstralh EJ, et al.** Using serum creatinine to estimate glomerular filtration rate: accuracy in good health and in chronic kidney disease. Ann Intern Med. 2004;141:929-37. [PMID: 15611490]

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