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ORIGINAL ARTICLE



A novel method for creatinine adjustment makes the revised Lund–Malmö GFR estimating equation applicable in children

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ABSTRACT

The aim of this study was to establish creatinine growth curves separately for males and females that can be used to adjust childhood levels of serum creatinine to corresponding adult levels. Linear regression with fractional polynomials of age as independent variable was used to construct creatinine growth curves for a reference cohort ($n = 83,157$ samples from Belgium and Sweden, age 2–40 years). Adjusted creatinine obtained from the growth curves was used to improve accuracy of estimated glomerular filtration rate (eGFR) based on the Lund–Malmö revised (LMR) equation in children. The LMR equation based on creatinine values adjusted to age 18 years was validated against measured GFR (mGFR) in a separate cohort of 4005 children from four different European countries. Validation metrics included median bias, precision, and accuracy expressed as percentage of estimates within $\pm 30\%$ (P_{30}) of mGFR. Remarkable improvements in bias and accuracy were observed; P_{30} increased from 56% to 74% after creatinine adjustments in children with $\text{mGFR} < 75 \text{ mL/min/1.73 m}^2$ ($n = 932$), while P_{30} was relatively unchanged (89–90%) at $\text{mGFR} \geq 75 \text{ mL/min/1.73 m}^2$ ($n = 3073$). The suggested approach with adjusted creatinine makes LMR applicable in children irrespective of their renal function.

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KEYWORDS

Creatinine; glomerular filtration rate; kidney function tests; chronic kidney disease; renal failure

Introduction

The Lund–Malmö revised (LMR) equation was developed in 2011 with the explicit goal to improve accuracy of estimated glomerular filtration rate (eGFR) in adults with chronic kidney disease (CKD) [1]. Several validation studies have reported superior accuracy of LMR compared with the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation in adults with CKD [2–10]. LMR can be used with similar accuracy as dedicated paediatric equations in children with normal renal function, but yields marked overestimations in children with CKD [11]. Thus, LMR is presently not an equation for the full spectrum of age and renal function.



More recently, a novel way of developing GFR equations based on age- and sex-adjusted serum creatinine was presented [12]. This resulted in the Full Age Spectrum (FAS) equation that is applicable for all ages after normalizing creatinine for age (among children and adolescents) and sex

(among adolescents and adults) [13]. The FAS equation remedies the discontinuity problem and the implausible changes in eGFR when switching from paediatric to adult equations as children grow into adulthood [14], but overestimates GFR in children with severe CKD [11].


In the present study, we build on previous work with models for how creatinine levels increase during childhood and adolescence [12,13]. Using statistical regression, the overall aim of this study was to establish creatinine growth curves separately for males and females that can be used to adjust childhood levels of creatinine to corresponding adult levels. We demonstrate how adjusted creatinine obtained from this method can be used to improve GFR estimation accuracy based on the LMR equation in children.

Material and methods

The present study of GFR equations for children was reviewed and approved by the Regional Ethical Board in

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 Supplemental data for this article can be accessed [here](#).

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Lund, Sweden. All procedures involving subjects and data agreed with the ethical principles for medical research involving human subjects established in the World Medical Association Declaration of Helsinki of 1975, as revised in 2000.

Reference cohort for establishment of creatinine growth curves

Anonymous reference data on age, sex and plasma/serum creatinine levels for patients aged 2–40 years old were obtained from non-nephrology units at three different hospitals: (i) Kortrijk, Belgium in 2005–2007 ($n=9634$), (ii) Liege, Belgium in 2019 ($n=9123$) and (iii) Uppsala, Sweden, in 2015–2019 ($n=64,410$). All creatinine samples were analyzed in clinical routine at the hospitals with standardized assays traceable to isotope dilution mass spectrometry (IDMS) and standard reference material (SRM) 967 (National Institute of Standards and Technology, NIST, Gaithersburg, MD, USA). Creatinine was analyzed in Kortrijk on a Roche Integra 800 (Roche Diagnostics, Mannheim, Germany), in Liege on an Abbott Alinity (Abbott Laboratories, Abbott Park, IL) and in Uppsala on an Architect 8000 (Abbott Laboratories). Enzymatic creatinine reagents were used at all three sites.

Creatinine growth curves

Previous work by Hoste et al. [12] has provided mathematical expressions for how median creatinine levels grow among females and males until age 20 years. In the present study, we extended this work by allowing the growth of creatinine in the reference cohort to continue beyond 20 years, as muscle mass especially among males can be expected to continue to grow in young adulthood. We used linear regression with fractional polynomials of age as independent variable in order to construct creatinine growth curves separately for males and females:

$$\ln(Cr) = \beta_0 + \beta_1 \times \text{Age} + \beta_2 \times \ln(\text{Age}) + \beta_3 \times \text{Age}^2 + \beta_4 \times \text{Age}^3,$$

where \ln is the natural logarithm (included in order to open up for smoother associations than exponential between age and creatinine on the original scale), Cr is the observed creatinine level for each individual and β_0 – β_4 are regression coefficients estimated from data.

Adjusted GFR estimation

The creatinine growth curves can be used to recalculate childhood levels of creatinine to an equivalent level for an adult at a particular age, referred to as adjusted creatinine (\widehat{Cr}). In the present study, we used age 18 years as threshold. This means that adjusted creatinine at age 18 years is predicted for children (individuals with age <18 years). Creatinine values are left unchanged among adults (individuals with age ≥ 18 years):

Age < 18 :

$$\ln(\widehat{Cr}) = \ln(Cr) + \beta_1 \times (18 - \text{Age}) + \beta_2 \times \ln(18/\text{Age}) + \beta_3 \times (18^2 - \text{Age}^2) + \beta_4 \times (18^3 - \text{Age}^3)$$

Age ≥ 18 :

$$\ln(\widehat{Cr}) = \ln(Cr)$$

Note that the location parameter (intercept β_0) for the growth curves is cancelled out and therefore does not affect adjusted creatinine (\widehat{Cr}). This means that the adjustment is insensitive to any bias in the location of the growth curves, e.g. stemming from selection of patients into the reference cohort.

GFR estimation using the LMR equation among children is based on adjusted creatinine (\widehat{Cr}) and as though the individual had age 18 years irrespective of his or her actual age.

Lund–Malmö revised equation [1], based on creatinine adjusted to age 18 years :

$$\text{LMR18} = e^{X - 0.0158 \times \max(\text{Age}; 18) + 0.438 \times \ln(\max(\text{Age}; 18))}$$

$$\text{Female } \widehat{Cr} < 150 \mu\text{mol/L: } X = 2.50 + 0.0121 \times (150 - \widehat{Cr})$$

$$\text{Female } \widehat{Cr} \geq 150 \mu\text{mol/L: } X = 2.50 - 0.926 \times \ln(\widehat{Cr}/150)$$

$$\text{Male } \widehat{Cr} < 180 \mu\text{mol/L: } X = 2.56 + 0.00968 \times (180 - \widehat{Cr})$$

$$\text{Male } \widehat{Cr} \geq 180 \mu\text{mol/L: } X = 2.56 - 0.926 \times \ln(\widehat{Cr}/180)$$

where $\max(\text{Age}; 18)$ represents the maximum of Age (actual age of the patient) and 18 years (the applied age threshold). Actual creatinine and actual age are used among adults.

Validation cohort

The European Kidney Function Consortium (EKFC), endorsed by the ERA-EDTA, has taken the initiative to collect observational data on patients referred for GFR measurement including plasma/serum creatinine, age, sex, height and weight. Common causes for referral were congenital malformations, hereditary diseases, acquired diseases (glomerulonephritis, nephrotic syndrome, reflux nephropathy, etc.), markers of kidney injury (e.g. proteinuria), follow-up after organ transplantation and to dose drugs eliminated by the kidneys.

The children included in the EKFC database originate from six different cohorts used in cross-sectional and longitudinal studies; from the Netherlands (Amsterdam; [15–19]), Belgium (Leuven; [7]), France (Lyon; [7,13]), and Sweden (Lund; [18], Stockholm [11] and Örebro [11]). As validation cohort for the present study we selected the first available measurement of GFR for all children 2.0–17.9 years old in the EKFC database with a simultaneous creatinine measurement ($n=4005$ unique patients; Table 1). Patient data were pooled in an anonymous database for the present study at Lund University, Sweden.

Table 1. Patient characteristics.

	All (<i>n</i> = 4005)	mGFR < 75 mL/min/1.73 m ² (<i>n</i> = 932)	mGFR ≥ 75 mL/min/1.73 m ² (<i>n</i> = 3073)
Age (years)	12.0 (2.5–17.7)	12.8 (2.9–17.7)	12.0 (2.5–17.8)
Females, <i>n</i> (%)	1694 (42)	385 (41)	1309 (43)
Weight (kg)	40 (13–83)	41 (13–80)	40 (13–84)
Height (cm)	148 (90–183)	149 (89–181)	148 (90–184)
Body surface area (m ²)	1.30 (0.56–2.01)	1.31 (0.54–1.96)	1.29 (0.56–2.03)
Body mass index (kg/m ²)	18 (14–29)	18 (13–30)	18 (14–29)
Plasma/serum creatinine (μmol/L)	54 (21–139)	83 (37–275)	48 (20–91)
Measured GFR (mL/min/1.73 m ²)	96 (30–167)	58 (17–74)	104 (77–172)
Measured GFR, number (%)			
<30 mL/min/1.73 m ²	95 (2.4)	95 (10)	
30–44 mL/min/1.73 m ²	134 (3.3)	134 (14)	
45–59 mL/min/1.73 m ²	264 (6.6)	264 (28)	
60–74 mL/min/1.73 m ²	439 (11)	439 (47)	
75–89 mL/min/1.73 m ²	679 (17)		679 (22)
90–119 mL/min/1.73 m ²	1606 (40)		1606 (52)
≥120 mL/min/1.73 m ²	788 (20)		788 (26)

Descriptive measures given as median values (2.5 and 97.5 percentiles) if not stated otherwise.

Laboratory methods for the validation cohort

Details of laboratory methods are summarized in [Supplementary Table S1](#). Clearance methods for measured GFR (mGFR) included plasma and renal clearance of inulin, and plasma clearance of ⁵¹Cr-EDTA and iohexol, all considered acceptable as reference test [20]. Samples of creatinine were obtained on the day of GFR measurement in all cohorts but Stockholm, where samples within 48 h of measured GFR were accepted. All centres used standardized creatinine assays traceable to IDMS and NIST, SRM 967.

Statistical evaluation

In the validation cohort, the performance of LMR18 (i.e. the adjusted LMR equation to 18 years described above) was compared with three other equations:

- the standard LMR equation without creatinine adjustment [1]
- the Chronic Kidney Disease in Children (CKiD; bedside Schwartz) equation [21]

$$41.3 \times (\text{Height}/100)/(\text{Cr}/88.4) \approx 36.5 \times \text{Height}/\text{Cr}$$

- the Schwartz-Lyon equation [22]

Males <13 years and females <18 years:

$$36.8 \times (\text{Height}/100)/(\text{Cr}/88.4) \approx 32.5 \times \text{Height}/\text{Cr}$$

Males ≥13 years:

$$41.3 \times (\text{Height}/100)/(\text{Cr}/88.4) \approx 36.5 \times \text{Height}/\text{Cr}$$

Creatinine is expressed in μmol/L and body height in centimetre in the equation expressions above. The validation focussed on bias, precision and accuracy [23]. Bias was assessed as the median of eGFR – mGFR and precision as the interquartile range (IQR) of the differences eGFR – mGFR. Accuracy was assessed from the absolute error |eGFR – mGFR|/mGFR and summarized as the median absolute percentage difference (absolute accuracy) and as the percentage of estimates within ±10% and ±30% of

mGFR (P₁₀ and P₃₀). P₃₀ accuracy of at least 75% has been considered sufficient “for good clinical decision-making” by the National Kidney Foundation but the benchmark is to reach P₃₀ > 90% [24]. Differences in P₃₀ accuracy were evaluated statistically using 95% confidence intervals (CIs) for paired proportions.

Main results are presented stratified for mGFR below and above 75 mL/min/1.73 m², as abnormal GFR in children has been regarded to start below this threshold [25], and by sex.

Results

Creatinine growth curves

The association between age and median plasma/serum creatinine levels was for both females and males similar across the three laboratories (hospitals; [Supplementary Figure S1](#)). The pooled reference cohort included 83,157 samples in total (46,601 females and 36,556 males; median age 27 years). The serum creatinine median value (2.5, 97.5 percentile) for women (*n* = 1278) and men (*n* = 992) aged 18 years were 61 (42, 86) μmol/L and 76 (54, 107) μmol/L, respectively.

Coefficients for the sex-specific creatinine growth curves were estimated based on the reference cohort, as illustrated in [Figure 1](#). The following growth curves were obtained:

Males:

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

Females:

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

The estimated geometric means at each age obtained from the growth curves were for both boys and girls consistently within the laboratory specific reference intervals ([Supplementary Table S2](#)). The calculation of adjusted creatinine ($\widehat{\text{Cr}}$) at age 18 years based on actual creatinine (*Cr*) and actual age of the child (*Age*) was done by constructing

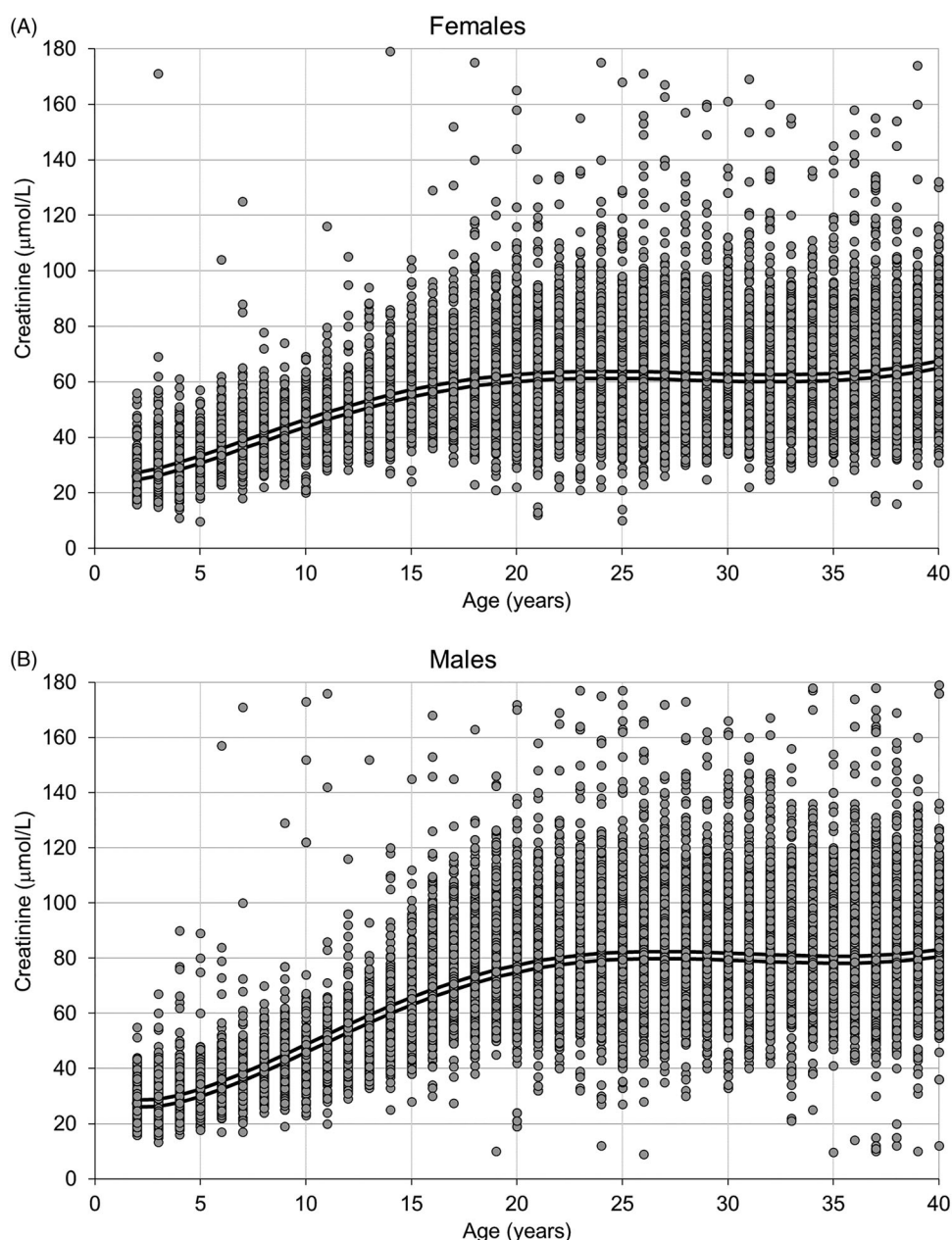


Figure 1. Plasma/serum creatinine values in 83,157 patients from the reference cohort as a function of age in (A) females ($n = 57 > 180 \mu\text{mol/L}$) and (B) males ($n = 130 > 180 \mu\text{mol/L}$). The double line represents the creatinine growth curve based on linear regression with fractional polynomials of age as independent variable (see text).

individual creatinine growth projections in the following way:

Males:

$$\ln(\widehat{Cr}) = \ln(Cr) + 0.259 \times (18 - \text{Age}) - 0.543 \times \ln(18/\text{Age}) - 0.00763 \times (18^2 - \text{Age}^2) + 0.0000790 \times (18^3 - \text{Age}^3)$$

Females:

$$\ln(\widehat{Cr}) = \ln(Cr) + 0.177 \times (18 - \text{Age}) - 0.223 \times \ln(18/\text{Age}) - 0.00596 \times (18^2 - \text{Age}^2) + 0.0000686 \times (18^3 - \text{Age}^3).$$

The calculation is outlined in Figure 2 for two hypothetical pairs of children, one pair with normal and one pair with increased creatinine levels.

Validation results

Overall validation results stratified by mGFR (<75 versus $\geq 75 \text{ mL/min/1.73 m}^2$) are presented in Table 2. Noticeable improvements at mGFR below $75 \text{ mL/min/1.73 m}^2$ were noted for LMR18 (using adjusted age and creatinine) compared with LMR (without adjustment), with decreased bias and P_{30} accuracy increasing from 56% to 74%. LMR18 thereby reached similar performance as CKiD albeit with 2.6 percentage points (pp; 95% CI 0.0–5.2 pp) higher P_{30} accuracy. However, Schwartz-Lyon was the most accurate equation at mGFR below $75 \text{ mL/min/1.73 m}^2$ ($P_{30} = 81\%$, 6.4 pp higher than for LMR18, 95% CI 4.1–8.7 pp).

Using LMR18 at mGFR above $75 \text{ mL/min/1.73 m}^2$ led to increased underestimation but improved precision compared to LMR, which kept the accuracy unchanged. Comparing

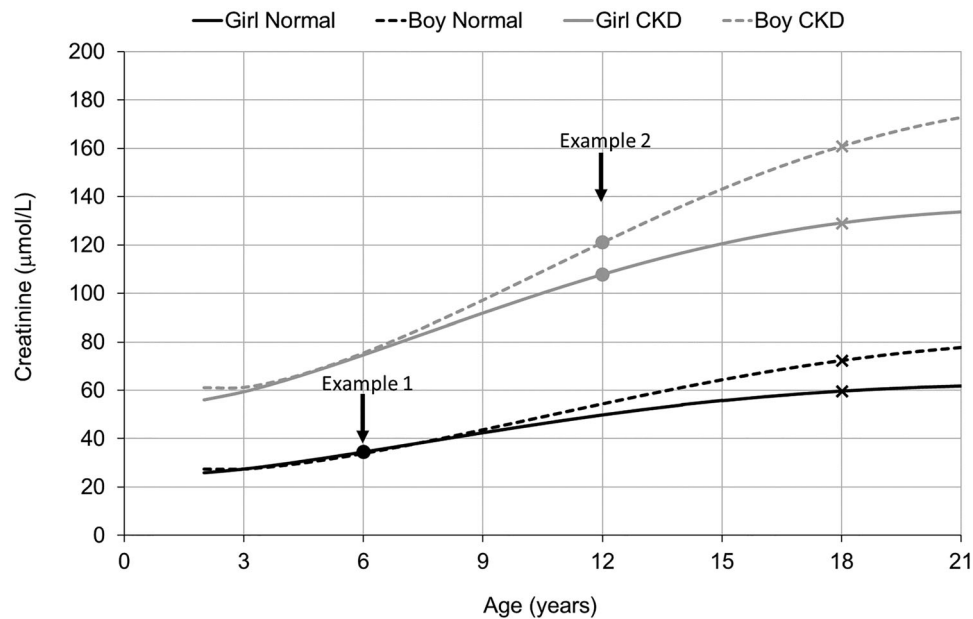


Figure 2. Individual creatinine growth projections for two hypothetical example pairs of children: (1) age 6 years and normal creatinine levels (boy 34 and girl 35 $\mu\text{mol/L}$), (2) age 12 years with elevated creatinine levels (boy 121 and girl 108 $\mu\text{mol/L}$) indicating chronic kidney disease (CKD). Adjusted creatinine for the Lund-Malmö revised equation (LMR18) is obtained by following the corresponding growth curve until age 18 years (marked with crosses).

Table 2. Bias, precision, accuracy (95% confidence intervals) of GFR estimating equations in children 2.0–17.9 years stratified for measured GFR <75 ($n = 932$) and $\geq 75 \text{ mL/min/1.73 m}^2$ ($n = 3\,073$).

Equations	Bias (mL/min/1.73 m^2)	Precision (mL/min/1.73 m^2)	Absolute percentage error	P ₁₀ (%)	P ₃₀ (%)
mGFR <75 (median 58) mL/min/1.73 m^2					
CKiD	7.4 (6.2–8.3)	18.0	16.2 (15.1–17.8)	32.7 (29.7–35.7)	71.8 (68.9–74.7)
Schwartz–Lyon	2.3 (1.5–3.1)	14.7	13.0 (12.1–14.0)	39.8 (36.7–42.9)	80.8 (78.3–83.3)
LMR	14.4 (13.2–15.8)	18.9	26.5 (24.4–28.1)	20.6 (18.0–23.2)	55.6 (52.4–58.8)
LMR18	4.8 (3.7–5.9)	18.0	16.0 (15.0–17.7)	32.7 (29.7–35.7)	74.4 (71.6–77.2)
mGFR ≥ 75 (median 104) mL/min/1.73 m^2					
CKiD	3.4 (2.4–4.4)	30.3	14.5 (13.9–15.0)	36.1 (34.4–37.8)	82.1 (80.7–83.5)
Schwartz–Lyon	–5.6 (–6.4 to –4.6)	26.2	13.8 (13.3–14.3)	37.7 (36.0–39.5)	86.7 (85.5–87.9)
LMR	–4.9 (–5.6 to –4.2)	25.4	12.4 (11.7–12.9)	41.7 (40.0–43.5)	88.9 (87.8–90.0)
LMR18	–8.2 (–9.2 to –7.4)	23.2	12.5 (11.9–12.9)	41.1 (39.3–42.8)	90.2 (89.1–91.2)

Median bias (eGFR–mGFR) and precision (interquartile range) expressed in mL/min/1.73 m^2 , and accuracy expressed as median absolute percentage error $|(eGFR - mGFR)/mGFR|$, and P₁₀ and P₃₀ accuracy (percentage of GFR estimates within $\pm 10\%$ and $\pm 30\%$ of mGFR). CKiD: Chronic Kidney Disease in Children; LMR: Lund-Malmö revised; LMR18: LMR based on creatinine values adjusted to the age of 18 years; eGFR: estimated glomerular filtration rate; mGFR: measured GFR.

P₃₀ at mGFR above 75 mL/min/1.73 m^2 , LMR18 had 8.1 pp (95% CI 6.5–9.6 pp) and 3.4 pp (95% CI 2.3–4.6 pp) higher accuracy than CKiD and Schwartz–Lyon, respectively. Validation results for a more detailed stratification by mGFR are presented in [Supplementary Table S3](#). Decreased bias for LMR18 compared with LMR was noted at all levels of mGFR below 75 mL/min/1.73 m^2 and resulted in P₃₀ of at least 75% at mGFR 45–74 mL/min/1.73 m^2 . However, Schwartz–Lyon had superior accuracy among the evaluated equations in the range 30–74 mL/min/1.73 m^2 . Validation results for children stratified by sex are presented in [Table 3](#). Substantial improvements in bias were noted for LMR18 among both girls and boys at mGFR below 75 mL/min/1.73 m^2 . Bias and accuracy of the LMR equation with and without adjustment was further compared stratified for age ([Figure 3](#), [Supplementary Table S4](#)). The improvement in bias and accuracy at mGFR below 75 mL/min/1.73 m^2 was especially evident at age below 13. Underestimation at mGFR above 75 mL/min/1.73 m^2 was noticeable for LMR also after adjustment in the youngest

age group. Validation results for individual cohorts are presented in [Supplementary Tables S5](#). Noticeable improvements in P₃₀ accuracy for LMR18 in children with mGFR below 75 mL/min/1.73 m^2 was observed in all cohorts.

Discussion

The sex-specific creatinine growth curves derived based on the reference cohort in the present study show how average creatinine levels increase during childhood and emerging adulthood. These growth curves can be used to recalculate childhood levels of creatinine to corresponding adult levels to make commonly used adult GFR equations applicable also among children. The present study demonstrated how this adjustment strategy led to marked improvements in GFR estimation accuracy for LMR when applied in children with decreased renal function and resulted in P₃₀ accuracy of at least 75% at all mGFR levels above 45 mL/min/1.73 m^2 . A practical advantage of the suggested adjustment strategy is

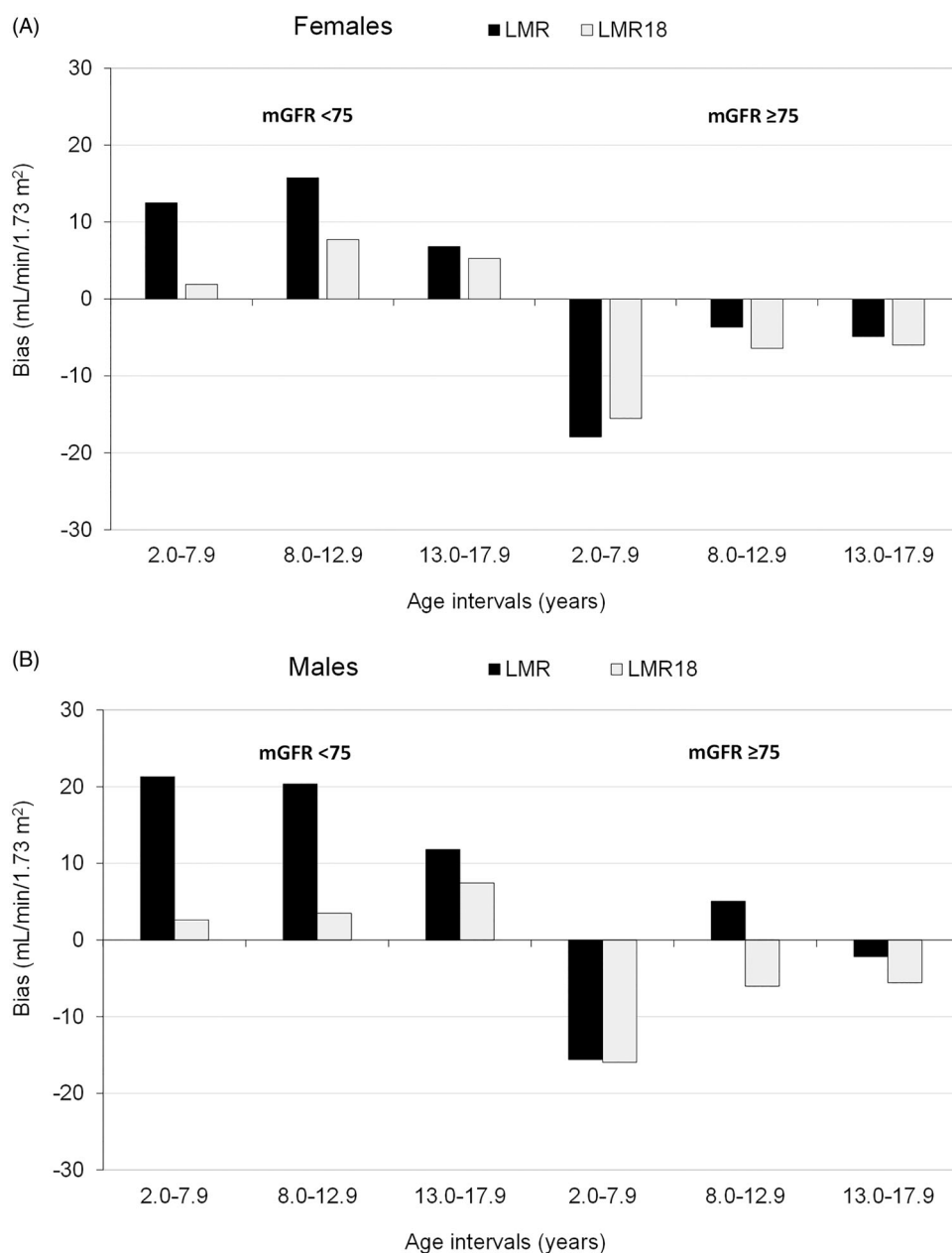


Figure 3. Associations in the validation cohort between age groups and median bias (estimated GFR – measured GFR) of the Lund–Malmö revised equation, both in the original formulation (LMR) and with creatinine adjusted to age 18 years (LMR18). Results stratified by (A) females with mGFR <75 ($n = 385$) and ≥ 75 mL/min/1.73 m² ($n = 1309$) and (B) males with measured GFR (mGFR) <75 ($n = 547$) and ≥ 75 mL/min/1.73 m² ($n = 1764$).

that there is no need for change in the original coefficients of the equation. We, therefore, expect that the same type of adjustment can be readily used also for other adult GFR equations, but the appropriate age threshold to use for each specific equation is a topic for further investigations. Another advantage of the recalculated creatinine values is that well established creatinine reference intervals for adults may be used if not available for certain childhood age intervals.

A major strength of the present study was that separate and non-overlapping cohorts were used for establishment of creatinine growth curves and validation of the GFR equations. The size of the cohorts, $n = 83,157$ to establish creatinine curves and $n = 4005$ in the validation cohort, led to narrow CIs in the overall performance metrics (e.g. the statistical uncertainty in the estimated P_{30} accuracy was at most

± 3 pp). The validation cohort included paediatric patients from four different European countries (Belgium, France, Netherlands and Sweden). Nevertheless, we do not know to what extent the creatinine growth curves and the reported improvements in estimation accuracy for LMR are broadly generalizable to patient populations of children elsewhere in Europe. Another limitation was that we were not able to study different ethnic groups. Our growth curves should therefore be used with caution in other populations, including ethnic minorities within the investigated populations, which may exhibit different patterns of growth in muscle mass and thereby in creatinine levels during childhood and emerging adulthood. On the positive side, however, is that creatinine growth curves for more specific populations can be established based on routine health care data as they do

Table 3. Bias and accuracy (P_{30}) of GFR estimating equations in children 2.0–17.9 years old stratified by sex and measured GFR <75 and ≥ 75 mL/min/1.73 m².

	N (%)	Median mGFR	CKiD	Schwartz–Lyon	LMR	LMR (18)
mGFR <75 mL/min/1.73 m ²						
Bias						
Girls	385 (41)	59	9.8	2.9	10.8	4.7
Boys	547 (59)	58	4.7	1.7	17.2	4.8
P_{30} (%)						
Girls			67	82	66	76
Boys			75	80	48	73
mGFR ≥ 75 mL/min/1.73 m ²						
Bias						
Girls	1309 (43)	103	7.5	−4.7	−6.8	−8.2
Boys	1764 (57)	104	0.7	−6.2	−3.1	−8.2
P_{30} (%)						
Girls			82	88	89	90
Boys			82	86	89	90

Median bias (eGFR – mGFR) expressed in mL/min/1.73 m² and P_{30} accuracy as percentage of GFR estimates within $\pm 30\%$ of mGFR.

CKiD: Chronic Kidney Disease in Children; LMR: Lund–Malmö revised; LMR18: LMR based on creatinine values adjusted to age 18 years; eGFR: estimated glomerular filtration rate; mGFR: measured GFR.

not require mGFR. A final limitation, as with all creatinine based GFR equations, estimates for patients with abnormally low muscle mass due to e.g. anorexia or paralysis can be expected to be systematically too high also when LMR is applied on adjusted creatinine.

The current Kidney Disease Improving Global Outcomes (KDIGO) guidelines recommend the use of the CKiD equation in children and the CKD-EPI equation in adults, unless alternative equations improve accuracy [26]. LMR18 with adjusted creatinine was in the present validation equally accurate as CKiD in children with decreased renal function, and more accurate in children with normal GFR. Previous research has highlighted how implausible intra-individual changes in eGFR may occur when switching from the height-dependent CKiD equation in paediatric care to the age-dependent CKD-EPI in adults [14]. FAS bypasses this transition problem and has so far been the only creatinine-based equation applicable for the entire lifespan [13]. However, the present study shows that LMR18 based on adjusted creatinine is an alternative that can be used irrespective of both age and renal function. Another advantage with both FAS and LMR18 compared to the paediatric equations CKiD and Schwartz–Lyon is that data on height are not necessary for valid estimations in children. As in adults, estimated GFR can thus be automatically given by the laboratories. This notwithstanding, LMR18 does not reach the KDIGO 75% limit of P_{30} accuracy (74%) in children with mGFR <75 mL/min/1.73 m² in contrast to Schwartz–Lyon (81%), which is most likely explained by the fact that height is a better marker of growth in muscle mass and creatinine than age for these patients. Still LMR18 has 80–90% P_{30} across the 75 mL/min/1.73 m² suggested CKD threshold for children [25] and 75% P_{30} down to at least 60 mL/min/1.73 m². It should also be noted that Schwartz–Lyon has a substandard accuracy (P_{30} <75%) at mGFR <45 mL/min/1.73 m².

A recent validation study using the EKFC database has provided evidence that cystatin C is a more reliable

filtration marker than creatinine for GFR estimations in children with severe CKD [11]. However, arithmetic means of the best creatinine and cystatin C equations generally led in the same study to improvements in estimation accuracy compared with both single-marker and composite equations. Future validation studies should therefore consider the possibility to use the arithmetic mean of LMR applied on adjusted creatinine and the CAPA (Caucasian, Asian, Paediatric and Adult) equation based on cystatin C [18].

In conclusion, the suggested GFR estimation strategy based on adjusted creatinine obtained from growth curves showed remarkable improvement in GFR estimation accuracy among children with CKD. The approach should be possible to extend to other GFR equations, other ethnic groups and other biomarkers of renal function such as cystatin C.

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Disclosure statement

None of the authors declare any conflict of interest.

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Data availability statement

The EKFC dataset used in the present study is hosted by the Lund University Population Research Platform (LUPOP). Legal and ethical restrictions prevent public sharing of the dataset. Data can be made available for collaborations upon request to interested researchers but would generally require a new ethical permission and the permission of each of the data-owners. You can find contact information for the data host at <https://www.lupop.lu.se/>

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