Performance of GFR Estimating Equations in Young Adults

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Supplementary Material

Supplementary File (PDF)

Figure S1, Item S1, Table S1.

Article Information

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Performance of GFR Estimating Equations in Young Adults

To the Editor:

In the United States, glomerular filtration rate (GFR) is commonly estimated using serum creatinine and the 2021 Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation for individuals older than 18 years or the 2021 Chronic Kidney Disease in Children Under 25 Study (CKiD-U25) equation for those between 1 and 25 years of age with CKD (Item S1).[1,2] These equations may result in different estimated GFR (eGFR) values at 18 years and older, leading to uncertainty in assessment of severity of disease, progression rate, and clinical decisions based on level of GFR. The CKiD-U25 has not been externally validated in a diverse population of young adults.

We compared the CKD-EPI and CKiD-U25 equations in young adults prior to the generally accepted age-related GFR decline (aged 18-40 years) in the 2023 CKD-EPI creatinine external validation dataset (1,491 participants from 21 studies) with measured GFR (mGFR) using urinary or plasma clearance of exogenous filtration markers

(Item S2, Tables S1 and S2, Fig S1).[1,2] We hypothesized that the CKiD-U25 equation would perform better in young adults with lower GFR, similar to the population in whom the CKiD-U25 equation was developed (mean GFR of 49 [SD 23.0] mL/min/1.73 m^2), compared to those of older age and higher GFR, similar to populations in whom the CKD-EPI equation was developed (mean GFR of 67.6 [SD 39.6 mL/min/1.73 m^2]). We evaluated bias and precision (median and interquartile range of the difference between mGFR and eGFR, respectively), and accuracy (percentage of eGFR within 15% or 30% of mGFR, agreement of eGFR to mGFR categories).[1,3,4] In sensitivity analyses, we calibrated mGFR to account for potential differences between measurement methods in validation versus the development datasets (Table S3).[5-21] We also evaluated performance of the European Kidney Function Consortium (EKFC) equation, which can estimate GFR across the full age spectrum, but was developed in a predominantly white population (Table S2).[22]

Mean (SD) age was 31.7 (6.0) years and mean (SD) mGFR was 92.7 (32.7) mL/min/1.73 m^2 (Table S4). Younger age was associated with higher mGFR (Fig S2). The equations provided similar estimates for participants with eGFR less than 60 mL/min/1.73 m^2. At higher values, CKD-EPI yielded generally higher GFR estimates (Fig 1, top panel). Magnitude of the difference in eGFR between equations was larger at younger age and shorter height (Fig S3).

For the CKD-EPI equation, there was minimal bias between mGFR and eGFR overall (−0.5 [95%CI −1.5 to 0.7] mL/min/1.73 m^2), with small variation by GFR (Fig 1, middle panel, Fig S4, Table S5). In contrast, the CKiD-U25 equation moderately underestimated mGFR overall (7.2 [6.1, 8.3] mL/min/1.73 m^2), with large underestimation at higher levels of eGFR (Fig 1, bottom panel, Fig S4, Table S5). There was greater variation by age groups with CKiD-U25 than CKD-EPI, with greater underestimation at younger adult ages (Table 1). The CKiD-U25 equation also had greater underestimation, compared to CKD-EPI, across sex and race groups as well as body mass index (BMI) >20 kg/m^2, but smaller bias for the BMI <20 kg/m^2 group (Table S6). P_{30} was similar for both equations in all subgroups, except for BMI <20 kg/m^2, in which P_{30} was higher for the CKiD-U25 equation. Adjustment for possible differences in measurement methods for GFR attenuated the bias in CKiD-U25 (Table S7). The EKFC equation underestimated mGFR compared to the CKD-EPI equation (Tables S6-S8 and Fig S5) and was similar to CKiD-U25.

For young adults with CKD, the transition from pediatric to adult care can occur over a wide age range. In addition, young adults without previously diagnosed CKD may have need for evaluation of GFR. Providers have choices for GFR estimation in these settings. In this study, we found that the CKiD-U25 equation, developed in children and young adults with CKD, had minimal bias in young adults with lower GFR, similar to the CKD-EPI

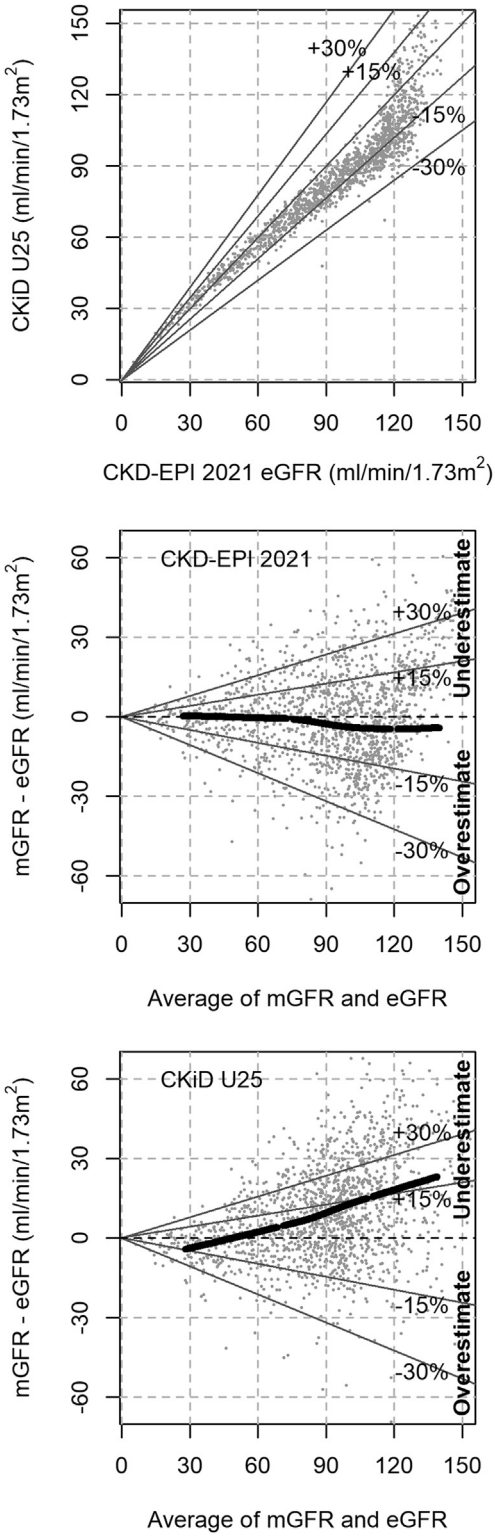

Figure 1. Difference between estimated glomerular filtration rate (eGFR) computed using the CKD-EPI and CKiD U25 equations. Top panel: Agreement between the CKD-EPI and CKiD-U25 equations in the study population. Each gray dot represents a participant. Middle and bottom panels: Comparison of the difference between measured GFR (mGFR) and eGFR creatinine and the average of the 2 for the CKD-EPI (middle) and CKiD-U25 (bottom) equations in the study population. Each gray dot represents a participant. Solid black line is a loess curve. ±30% and ±15% lines represent P_{30} and P_{15}, respectively.

Table 1. Performance of CKD-EPI 2021 and CKiD-U25 Equations by Age Groups Compared to Measured Glomerular Filtration Rate

Equation	Metric	Overall		Age, years							
	N	N = 1,491		18-25 (N = 276)		>25-30 (N = 294)		>30-35 (N = 421)		>35-40 (N = 500)	
	mGFR	95.2	(72.6, 114.0)	110	(93.0, 126.9)	100	(84.0, 117.0)	94	(71.0, 112.0)	86.5	(62.7, 106.0)
CKD-EPI	Bias	−0.5	(−1.5, 0.7)	−3.3	(−5.0, 0.0)	−3.5	(−5.5, -2.6)	1.1	(−0.5, 2.5)	1	(−0.3, 2.2)
	IQR	22.5	(21.0, 23.6)	25.9	(23.2, 29.2)	22	(19.0, 25.4)	22.8	(19.8, 25.3)	19.4	(17.0, 21.4)
	P_{15}	57.7	(55.2,60.2)	56.2	(50.0, 62.3)	61.2	(55.4, 66.7)	57.2	(52.5, 62.0)	57	(52.5, 61.2)
	P_{30}	88.9	(87.3, 90.5)	90.2	(86.6, 93.5)	90.5	(87.1, 93.5)	89.5	(86.5, 92.4)	86.6	(83.6, 89.4)
	Concordance	55.9	(53.3, 58.5)	55.4	(49.6, 61.6)	55.1	(49.3, 60.5)	56.1	(51.1, 60.8)	56.4	(52.0, 60.8)
CKiD-U25	Bias	7.2[a]	(6.1, 8.3)[a]	12.0[a]	(7.7, 15.5)[a]	8.3[a]	(6.6, 10.2)[a]	6.7[a]	(4.3, 10.7)[a]	4.8[a]	(2.8, 6.7)[a]
	IQR	23.9	(22.6, 24.9)	29.4	(24.6, 33.1)	22.7	(19.6, 26.1)	24.4	(21.6, 26.8)	20.6	(18.1, 23.5)
	P_{15}	52.3	(49.8, 54.9)	48.6	(42.8, 54.7)	53.7	(48.0, 59.5)	51.1	(46.3, 55.8)	54.6	(50.2, 58.8)
	P_{30}	87.8	(86.1, 89.4)	87	(83.0, 90.6)	87.4	(83.3, 91.2)	87.9	(84.8, 91.2)	88.4	(85.6, 91.2)
	Concordance	50.9	(48.6, 53.5)	46.7	(40.9, 52.5)	51	(45.2, 56.8)	49.4	(44.4, 54.4)	54.4	(50.0, 58.6)

mGFR is reported as median (IQR). Bias (median difference, 95% CI) was expressed as the median difference between mGFR and eGFR. A negative bias indicates overestimation of the mGFR, and a positive bias indicates underestimation of the mGFR. IQR (95% CI) is the distance between the 25th and 75th percentile of differences between mGFR and eGFR. P_{15} (95% CI) is the percentage of individuals with eGFR within 15% of measured GFR. P_{30} (95% CI) is the percentage of individuals with eGFR within 30% of mGFR. P_{30} from 75%-80% to 90% has been considered to be adequate for decision making in many clinical circumstances; P_{30} >90% is considered optimal.[24] Concordance (95% CI) was defined as the agreement between mGFR and eGFR categories (<30, 30-59, 60-89, and ≥90 mL/min/1.73 m^2). Units for bias is mL/min/1.73 m^2 and for concordance, P_{15} and P_{30} are percent.
Abbreviations: mGFR, measured glomerular filtration rate; CKD-EPI 2021, Chronic Kidney Disease Epidemiology Collaboration creatinine equation published in 2021; CKiD-25, Chronic Kidney Disease in Children Under 25 study serum creatinine equation; IQR, interquartile range; P_{30}, percentage of estimates within 30% of mGFR; eGFR = estimated glomerular filtration rate.
[a]Worse performance and non-overlapping confidence intervals (from the use of absolute values for bias) compared with the CKD-EPI equation (reference equation).

equation, but underestimated mGFR at higher values. The CKD-EPI equation had consistent performance across GFR and age subgroups. In contrast, the EKFC equation performed similarly to the CKiD-U25 equation, as was noted in a European cohort of young adults with higher GFR.[2,3] Differences between study populations in which the equations were developed, especially level of GFR, should be considered when using these equations in clinical practice.[2]

Strengths of this study are the diverse population across range of GFR, disease, and race group, separate from the population in which the equations were developed. A limitation is that the healthy individuals in CKD-EPI development and validation populations included people with type 1 diabetes or kidney donor candidates, who may differ from young adults in the general population.

The results support use of the 2021 CKD-EPI equation for reporting of eGFR by clinical laboratories in individuals older than 18 years of age. For young adults with childhood CKD, our results support continuing use of the CKiD-U25 equation to maintain consistency of eGFR. This study reinforces the need for additional research in young US adults to resolve differences observed at high levels of GFR and refine recommendations for use of eGFR equations.

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Supplementary Material

Supplementary File (PDF)

Figures S1-S5, Items S1-S3, Tables S1-S8.

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