Evaluation of the Modification of Diet in Renal Disease Study Equation in a Large Diverse Population

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ABSTRACT

Glomerular filtration rate (GFR) estimates facilitate detection of chronic kidney disease. Performance of the Modification of Diet in Renal Disease (MDRD) Study equation varies substantially among populations. To describe the performance of the equation in a large, diverse population, estimated GFR (eGFR) was compared to measured GFR (mGFR) in a cross-sectional analysis of 5504 participants in 10 studies that included measurements of standardized serum creatinine and urinary clearance of iothalamate. At eGFR <60 ml/min per 1.73 m^2, the MDRD Study equation had lower bias and higher precision than at eGFR ≥ 60 ml/min per 1.73 m^2. The accuracy of the equation, measured by the percent of estimates that fell within 30% of mGFR, was similar for eGFR values above or below 60 ml/min per 1.73 m^2 (82% and 84%, respectively). Differences in performance among subgroups defined by age, sex, race, diabetes, transplant status, and body mass index were small when eGFR was <60 ml/min per 1.73 m^2. The MDRD Study equation therefore provides unbiased and reasonably accurate estimates across a wide range of subgroups when eGFR is <60 ml/min per 1.73 m^2. In individual patients, interpretation of GFR estimates near 60 ml/min per 1.73 m^2 should be interpreted with caution to avoid misclassification of chronic kidney disease in the context of the clinical setting.

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Chronic kidney disease (CKD) is a recently recognized public health problem. Current guidelines define CKD as kidney damage or GFR <60 ml/min per 1.73 m^2 for 3 months or more, irrespective of cause.[1–3] CKD is classified into stages according to the level of GFR, and stage-specific action plans facilitate evaluation and management of CKD. Kidney damage is usually ascertained from markers, most commonly albuminuria. GFR can be estimated using estimating equations that incorporate serum creatinine concentration with demographic and clinical variables such as age, gender, race, and body size. GFR estimating equations provide a more accurate assessment of the level of kidney function than serum creatinine alone. National and international organizations recommend that clinical laboratories report estimated GFR (eGFR) and that clinicians use eGFR to evaluate kidney function for all patients.[1–4]

The most commonly used equation is the Modification of Diet in Renal Disease (MDRD) Study equation. There is a now a considerable body of literature demonstrating variation in performance of these equations among study populations.[5–25] In

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part, this variation is due to differences among studies in range of GFR, methods for GFR measurement, and serum creatinine assays.[26] We pooled individual patient data from six research studies and four clinical populations, with similar GFR measurements protocols and serum creatinine assays calibrated to a reference standard, to describe the performance of the MDRD Study equation, with particular attention to the level of GFR and participant clinical characteristics.

RESULTS

Figure 1 shows the search and selection process for studies that used urinary clearance of iothalamate to measure GFR. Ten studies were selected as category 1 studies. The study population for this report includes 5504 people in the development data set. Table 1 summarizes the clinical characteristics of the study cohort for the overall pooled data set as well as by study. Mean (SD) measured GFR (mGFR) and serum creatinine concentrations were 68 (39) ml/min per 1.73m^2 and 1.65 (1.07) mg/dl, (146 [94] μmol/L), respectively.

Table 2 and Figure 2 show the performance of the MDRD Study equation for the overall data set and by level of eGFR. The MDRD Study equation had a median (interquartile range [IQR]) difference of 2.7 (16.4) ml/min per 1.73 m^2, median percentage (IQR) difference of 5.8% (27.6), and a percentage of estimates within 30% of mGFR (P_{30}) of 83%. The MDRD Study equation had little bias for eGFR <60 ml/min per 1.73 m^2, underestimated mGFR for levels of eGFR between 60 and 119 ml/min per 1.73 m^2, and overestimated mGFR for levels of eGFR >120 ml/min per 1.73 m^2

Table 3 and Figure 3 compare the performance of the MDRD Study equation by subgroups defined by clinical characteristics according to eGFR >and <60 ml/min per 1.73m^2. At eGFR <60 ml/min per 1.73 m^2, the median (IQR) difference was 0.9 (9.6) ml/min per 1.73 m^2, P_{30} was 82%, and differences in performance among subgroups were small. At eGFR >60 ml/min per 1.73 m^2, the median (IQR) difference

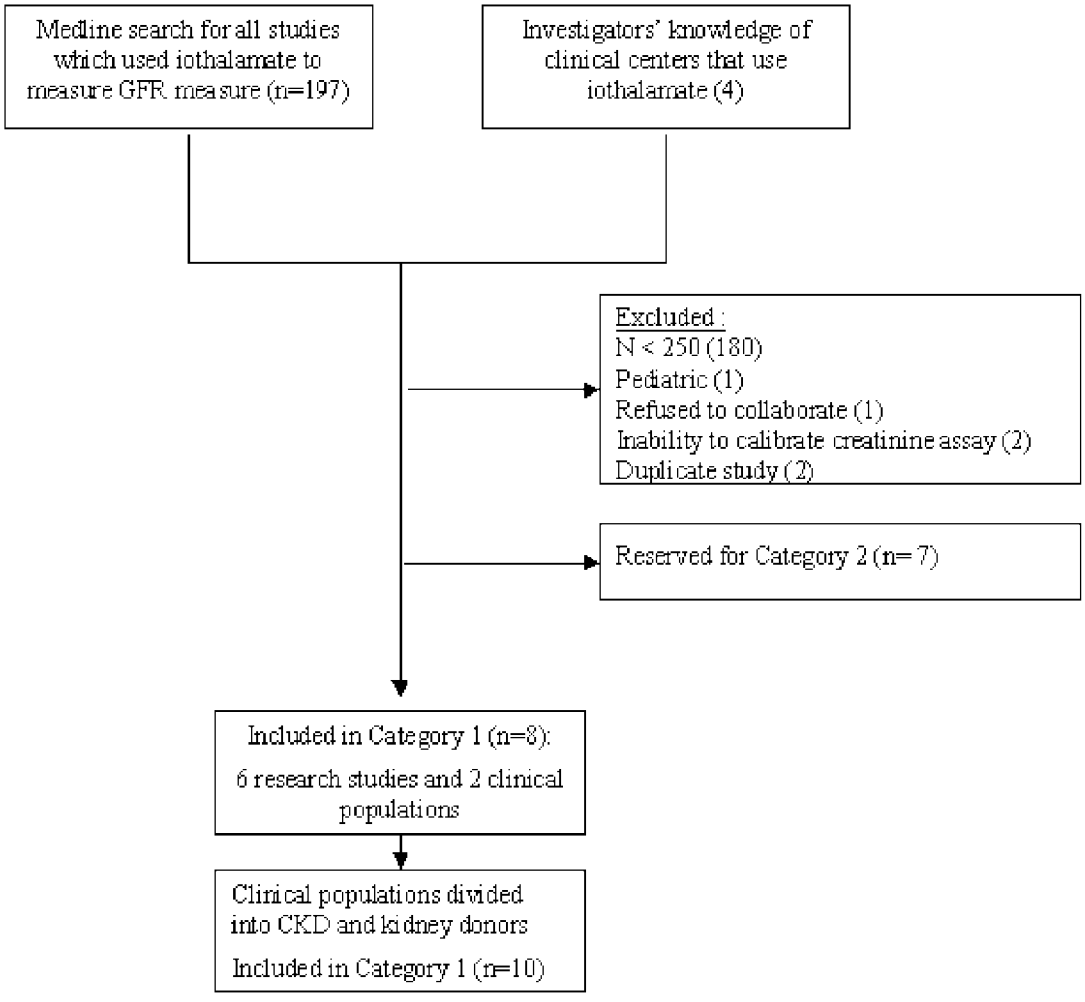

Figure 1. Study selection and assignment to category 1 or category 2 data set. The clinical populations were divided into patients with CKD and people who were being evaluated as potential kidney donors. Consideration of the timing of the availability of the data and the goal to include similar populations in both data sets determined specific assignments of a study to category 1 or category 2.

Table 1. Study and participant characteristics[a]

Characteristic	Overall[b]	Study[c]									
		MDRD Study[28c]	AASK[6]	DCCT[18]	DRDS[40]	CSG[41]	CRIC[42]	CCF CKD[5]	CCF Donors[5]	Mayo CKD[7]	Mayo Donors[7]
Study											
type	—	RS	RS	RS	RS	RS	RS	CP	CP	CP	CP
center	—	MC	MC	MC	SC	MC	MC	SC	SC	SC	SC
N	5504	1085	1205	787	126	266	446	695	301	221	372
dates	—	1989 to 1992	1995 to 1998	1987 to 1989	1988 to 1993	1987 to 1992	2003 to 2005	1996 to 2003	1996 to 2003	1999 to 2000	1996 to 2002
Clinical											
age (mean [SD])	47 (15)	51 (13)	54 (11)	29 (6)	42 (11)	34 (8)	55 (14)	54 (16)	42 (10)	54 (14)	41 (11)
<40 (*n* [%])	2029 (37)	259 (13)	136 (7)	787 (39)	51 (3)	210 (1)	78 (4)	138 (7)	149 (7)	41 (2)	180 (9)
40 to 65 (*n* [%])	2739 (50)	663 (24)	864 (32)	0 (0)	75 (3)	56 (2)	231 (8)	368 (13)	173 (6)	126 (5)	183 (7)
>65 (*n* [%])	736 (13)	163 (22)	205 (28)	0 (0)	0 (0)	0 (0)	137 (19)	168 (23)	0 (0)	54 (7)	9 (1)
female (*n* [%])	2397 (44)	427 (39)	414 (34)	356 (45)	75 (60)	129 (48)	214 (48)	299 (43)	191 (64)	79 (36)	214 (58)
race (*n* [%])											
white and other	3462 (63)	875 (25)	0	764 (22)	0	235 (7)	205 (6)	563 (16)	242 (7)	217 (6)	361 (10)
black	1737 (32)	128 (7)	1205 (69)	10 (0.6)	0	21 (1)	194 (11)	122 (7)	50 (3)	0	7 (0.4)
Asian	62 (1)	11 (18)	0	2 (3)	0	1 (2)	33 (53)	6 (10)	3 (5)	3 (5)	3 (5)
Native American	243 (4)	71 (29)	0	11 (5)	126 (52)	9 (4)	14 (6)	4 (2)	6 (2)	1 (0.4)	1 (0.4)
diabetes (*n* [%])	1580 (29)	68 (6)	0	787 (100)	104 (83)	266 (100)	290 (43)	148 (21)	0 (0)	16 (7)	0
type		Type 2	None	Type 1	Type 2	Type 1	Type 1 and type 2	Type 1 and type 2[b]		Type 1 and type 2	
transplant (*n* [%])	251 (5)	0	0	0	0	0	0	146 (21)	0	105 (48)	0
BMI (mean [SD])	28 (6)	27 (5)	31 (7)	24 (3)	35 (4)	25 (4)	32 (8)	28 (7)	27 (4)	29 (6)	28 (5)
<20 (*n* [%])	189 (3)	32 (17)	28 (15)	30 (16)	0	18 (10)	11 (6)	40 (21)	14 (7)	4 (2)	12 (6)
20 to 25 (*n* [%])	1671 (30)	343 (21)	200 (12)	456 (27)	12 (1)	137 (8)	72 (4)	193 (12)	95 (6)	58 (3)	105 (6)
26 to 30 (*n* [%])	1922 (35)	421 (22)	414 (22)	269 (14)	24 (1)	88 (5)	131 (7)	221 (12)	116 (6)	83 (4)	155 (8)
<30 (*n* [%])	1722 (31)	289 (17)	563 (33)	32 (2)	90 (5)	23 (1)	232 (13)	241 (14)	76 (4)	76 (4)	100 (6)
GFR (mean [SD])	68 (39)	40 (21)	57 (24)	124 (20)	115 (27)	78 (33)	51 (21)	36 (30)	106 (19)	48 (25)	100 (16)
original Scr (mean [SD])	1.79 (1.25)	2.22 (1.13)	1.90 (0.88)	0.83 (0.14)	0.81 (0.19)	1.34 (0.45)	1.81 (0.68)	3.20 (2.05)	0.83 (0.18)	1.97 (0.97)	1.04 (0.15)
standardized Scr (mean [SD])	1.65 (1.07)	2.11 (1.07)	1.72 (0.81)	0.75 (0.13)	0.67 (0.17)	1.26 (0.41)	1.72 (0.60)	2.93 (1.82)	0.83 (0.16)	1.76 (0.96)	0.84 (0.15)

[a]To convert Scr to SI units, multiply by 88.4. AASK, African American Study of Kidney Diseases and Hypertension; CCF, Cleveland Clinic Foundation; CRIC, Chronic Renal Insufficiency Cohort Study; CSG, Collaborative Study Group: Captopril in Diabetic Nephropathy Study; DCCT, Diabetes Control and Complications Trial; DRDS, Diabetic Renal Disease Study; MC, multicenter; RS, research study; SC, single center; Scr, serum creatinine.
[b]Column percentage.
[c]Row percentages.

Table 2. Comparison of performance of MDRD Study equation by level of eGFR[a]

eGFR	*N*	Difference		% Difference		P_{30} (CI)
		Median (CI)	IQR	Median (CI)	IQR	
Overall	5504	2.7 (2.4 to 3.1)	16.4	5.8 (5.1 to 6.4)	27.6	83 (83 to 84)
>120	325	−9.0 (−12.3 to −5.9)	31.2	−7.1 (−10.1 to −4.6)	26.6	82 (80 to 84)
90 to 119	941	11.1 (9.7 to 12.6)	25.6	9.9 (8.6 to 11)	20.8	89 (88 to 90)
60 to 89	1364	9.5 (8.3 to 10.7)	25.4	11.7 (10.2 to 12.7)	28.0	82 (81 to 83)
30 to 59	1782	1.7 (1.1 to 2.3)	13.0	3.5 (2.4 to 4.9)	27.4	84 (83 to 85)
16 to 29	793	0.0 (−0.4 to 0.5)	6.7	0.0 (−1.8 to 2.4)	31.4	81 (80 to 82)
<15	299	0.8 (0.3 to 1.4)	5.0	6.3 (2.5 to 11.1)	34.5	72 (69 to 75)

[a]Units of GFR are in ml/min per 1.73 m^2. Difference is calculated as mGFR − eGFR. Percentage difference is calculated as (mGFR − eGFR)/mGFR. Median values measure bias, and IQR measure precision. mGFR ranges in the rows correspond to GFR cutoffs for CKD stages: Stage 1, GFR >90; stage 2, GFR 60 to 89; stage 3, GFR 30 to 59; stage 4, GFR 15 to 29; stage 5, GFR <15. CI, confidence interval.

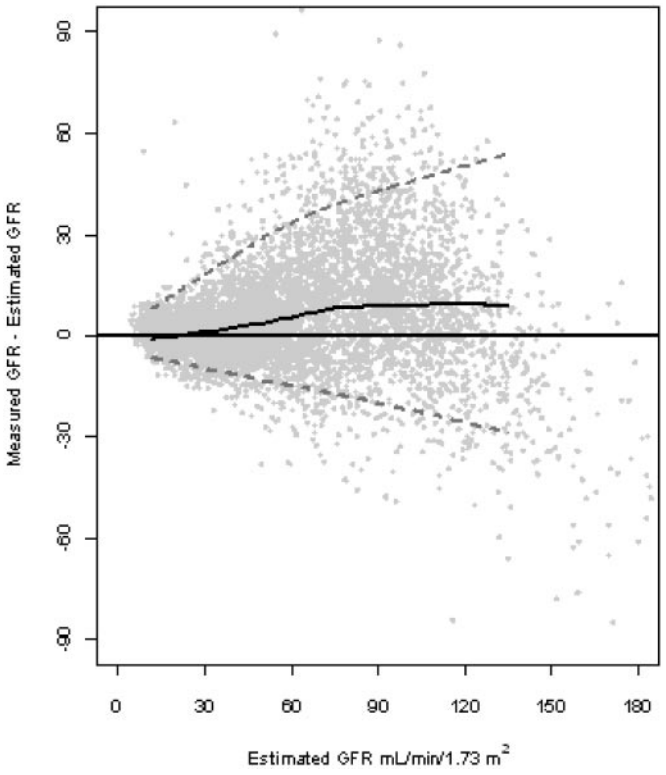

Figure 2. Difference of the MDRD Study equation by level of eGFR. Difference is calculated as (mGFR − eGFR). Solid horizontal line indicates no difference. Solid black curve is a nonlinear regression of the mean difference, which measures bias. Black curved line is a smooth curve through the points and was created using 95% of the data. Dashed gray lines are quantile regressions of the 5th and 90th percentiles of the differences, which measures precision.

was 8.3 (26.6) ml/min per 1.73 m^2, the P_{30} was 84%, and there was substantial variation in performance among subgroups. As noted in Figure 3, in some of the subgroups, bias begins to increase at levels of eGFR <60 ml/min per 1.73 m^2.

DISCUSSION

GFR estimating equations are important tools in clinical practice. We pooled research studies and clinical populations to form a data set of individuals of diverse demographic and clinical characteristics, including people with or without diabetes, with or without organ transplants, of various racial and ethnic backgrounds, and across the range of age and GFR. The strengths of the analysis include a larger and more diverse population than previous publications and use of similar GFR measurement protocols and calibrated serum creatinine in all studies. This pooled database allows evaluation of the performance of GFR estimating equations in important subgroups of the clinical population and should facilitate interpretation of GFR estimates in clinical practice.

The MDRD Study equation showed little bias for GFR estimates <60 ml/min per 1.73 m^2 in the pooled database and in subgroups defined by demographic and clinical characteristics. In contrast, GFR estimates ≥60 ml/min per 1.73 m^2 had greater bias, and bias varied substantially among subgroups. In the subgroup of patients in the pooled database with GFR estimates <60 ml/min per 1.73 m^2 (mean mGFR 37 ml/min per 1.73 m^2), performance of the MDRD Study equation was not as accurate as in the MDRD Study database (mean mGFR 40 ml/min per 1.73 m^2); P_{30} was 82% compared with 90%, respectively.[27,28]

Possible explanations for the greater errors at higher eGFR, as well as relatively poorer performance of the MDRD Study equation in the pooled data set compared with the MDRD Study database, include unresolved differences in the calibration of serum creatinine, error in measurement of GFR, short-term biologic variation in mGFR, distribution of mGFR among the studies, and variation among populations in clinical characteristics that are not incorporated into the MDRD Study equation and affect the association of serum creatinine with mGFR (*e.g.*, muscle mass, diet).[26] These effects are greater at higher levels of GFR.

Our study demonstrates good performance in subgroups at GFR <60 ml/min per 1.73 m^2. Previous studies reported conflicting results in the performance of the MDRD Study equation among subgroups on the basis of age, diabetes, transplant status, or body mass index (BMI).[5,8,9,18,20,25,29,30] The conflicting results may be due, in part, to differences in GFR measurement methods, differences in creatinine calibration, or inclusion of individuals with higher GFR in some of these studies.

Table 3. Performance of the MDRD Study equation in subgroups[a]

Parameter	eGFR <60 (mGFR 37 [18])				eGFR ≥60 (mGFR 101 [28])			
	N	Difference (Median [95% CI])	% Difference (Median [95% CI])	P_{30} (95% CI)	*N*	Difference (Median [95% CI])	% Difference (Median [95% CI])	P_{30} (95% CI)
Overall	2874	0.9 (0.6 to 1.1)	3.0 (2 to 3.7)	82 (81 to 83)	2630	8.3 (7.4 to 9.2)	8.7 (7.5 to 9.7)	84 (83 to 85)
Age (yr)								
<40	585	0.7 (0.1 to 1.5)	2.9 (0.2 to 4.9)	84 (83 to 86)	1473	10.6 (9.2 to 12.2)	9.8 (8.6 to 10.8)	83 (82 to 84)
40 to 65	1709	1.3 (1.0 to 1.8)	4.1 (3.1 to 5.7)	82 (81 to 83)	1042	6.4 (5.2 to 7.8)	7.5 (6.0 to 7.5)	85 (84 to 86)
>65	580	−0.4 (−0.8 to 0.4)	−1.2 (−2.9 to 1.2)	82 (80 to 84)	115	−0.3 (−5.3 to 2.3)	−0.4 (−9.2 to 3.0)	88 (85 to 91)
Gender								
female	1212	1.0 (0.7 to 1.7)	3.8 (2.4 to 5.5)	81 (80 to 82)	1179	11.3 (9.9 to 12.6)	11.4 (9.9 to 12.8)	82 (81 to 83)
male	1662	0.7 (0.4 to 1.1)	2.4 (1.1 to 3.4)	83 (82 to 84)	1451	6.2 (5.2 to 7.5)	6.6 (5.6 to 7.8)	86 (85 to 87)
Race								
white and other	1668	0.6 (0.3 to 0.9)	2.3 (1 to 3.4)	82 (81 to 83)	1799	12.1 (10.9 to 12.9)	11.7 (10.5 to 12.6)	83 (82 to 84)
black	1085	1.2 (0.7 to 1.9)	3.4 (1.9 to 5.1)	82 (81 to 83)	643	0.1 (−1.4 to 1.5)	0.2 (−2 to 2)	88 (87 to 89)
Asian	44	4.2 (1.2 to 7.3)	10.8 (3.7 to 20.9)	89 (84 to 94)	18	8.5 (−3.2 to 15.0.2)	11.8 (−3.6 to 18)	83 (74 to 92)
Native American/Pacific Islander/Hispanic	77	1.5 (−1 to 2.5)	5.9 (−3.2 to 10.1)	91 (88 to 94)	170	1.0 (−2.8 to 5.3)	1.0 (−2.6 to 5.5)	82 (79 to 85)
Diabetes								
yes	510	1.7 (0.8 to 2.4)	5.1 (2.5 to 7.8)	74 (72 to 76)	1071	10.8 (8.7 to 12.5)	9.6 (8 to 10.9)	83 (82 to 84)
no	2364	0.7 (0.4 to 1.1)	2.5 (1.4 to 3.5)	84 (83 to 85)	1559	6.8 (5.7 to 8.1)	7.8 (6.5 to 9.5)	85 (84 to 86)
Transplant								
yes	169	0.4 (−1.3 to 2.1)	1.2 (−3.6 to 5.8)	78 (75 to 81)	72	−7.6 (−11.7 to −2.9)	−11.1 (−20.2 to −3.9)	75 (70 to 80)
no	2705	0.9 (0.6 to 1.2)	3.1 (1.9 to 3.9)	83 (82 to 84)	2558	8.7 (7.9 to 9.6)	9.1 (8 to 9.9)	84 (83 to 85)
BMI								
<20	96	−1.4 (−2.4 to 2)	−4.7 (−10.9 to 8.3)	74 (70 to 79)	90	4.8 (−0.9 to 7.3)	4.5 (−0.9 to 8.8)	79 (75 to 83)
20 to 25	740	−0.2 (−0.6 to 0.4)	−0.6 (−2.4 to 1.7)	80 (79 to 82)	927	9.6 (8.2 to 11)	9.5 (7.5 to 10.6)	83 (82 to 84)
26 to 30	999	1.3 (0.8 to 1.9)	4.0 (2.6 to 5.5)	85 (84 to 86)	938	9.0 (7.6 to 10.8)	9.6 (8 to 11)	87 (86 to 88)
>30	1039	1.3 (0.9 to 2)	4.1 (2.7 to 5.8)	82 (81 to 83)	675	6.6 (4.2 to 8.1)	6.7 (5 to 9)	83 (82 to 84)

[a]Units of GFR are in ml/min per 1.73 m^2. Difference is calculated as mGFR − eGFR. Percent difference is calculated as (mGFR − eGFR)/mGFR.

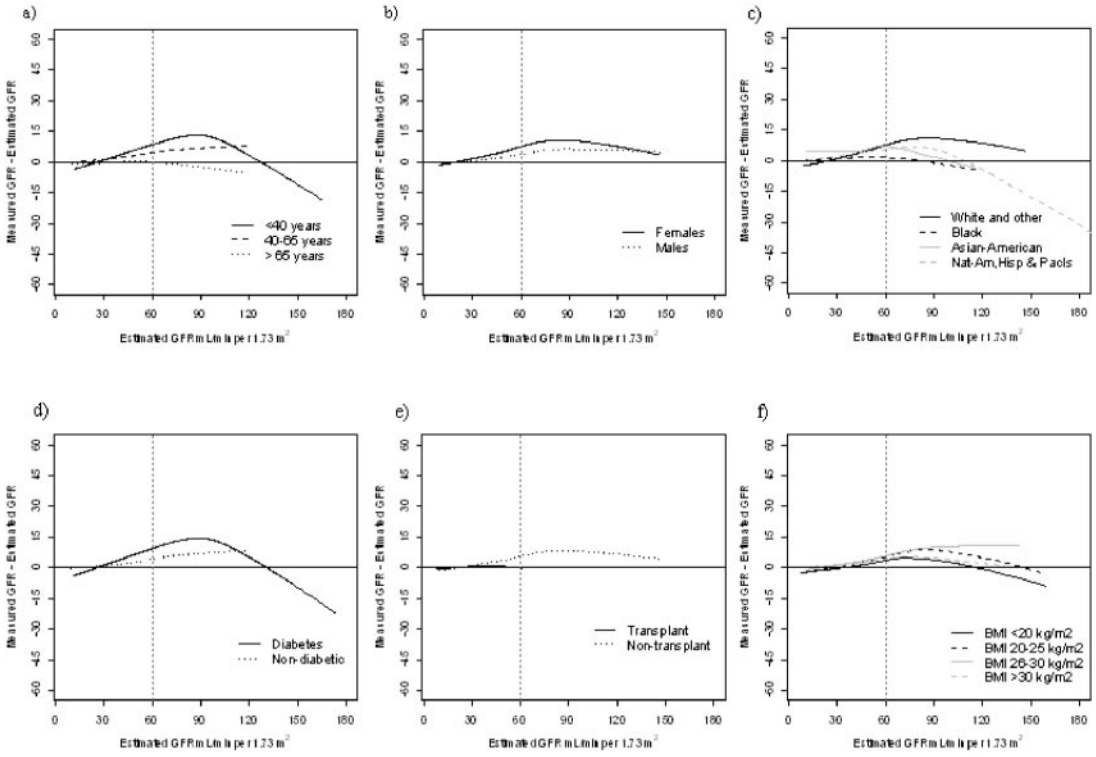

Figure 3. Difference of the MDRD Study equation by level of eGFR for subgroups. Solid horizontal line indicates no difference. Difference is calculated as (mGFR − eGFR). Curved lines are a smooth curve through the points and was created using 97.5% of the data for each subgroup. (A) Age (<40, 40 to 65, >65 yr). (B) Gender. (C) Race (white or other; black; Asian; Native American, Hispanic, or Pacific Islander). (D) Diabetes. (E) Solid organ transplant. (F) BMI (<20, 20 to 25, 26 to 30, and >30 kg/m^2). The gray dotted vertical lines indicate 60 ml/min per 1.73 m^2.

In this study, we also demonstrate differences in bias by race. These differences are small but are present even at levels of GFR <60 ml/min per 1.73 m^2. In particular, at eGFR <60 ml/min per 1.73 m^2, Asian individuals have a greater bias than black and white individuals or others. This is consistent with reports from populations in China and Japan, which both have shown inaccuracies in the performance of the MDRD Study equation.[31,32] It is interesting that the two studies show divergent results; the MDRD Study equation underestimated mGFR in the Chinese population, as shown here, whereas the MDRD Study equation overestimated mGFR in the Japanese study, suggesting population differences other than race. These differences likely represent variation in muscle mass or diet among populations that differ by descent and geography.

Differences in performance of the MDRD Study equation among subgroups, especially at higher GFR, suggest that the relationship between creatinine and GFR differs among these groups. New equations may be able to improve on the performance of the MDRD Study equation by incorporating different forms of variables that are incorporated into the current equation (*i.e.*, age, gender, race, or creatinine) or by inclusion of new variables or interactions of the new or old variables with serum creatinine. The addition of new variables, such as diabetes, may improve performance in those subgroups. The use of new forms of variables or interactions will allow for articulation of the different relationship between serum creatinine and these other variables. However, these statistical approaches may not be able to overcome the inherent limitations of serum creatinine as a filtration marker. Any new equation that substantially improves on the MDRD Study equation may require the use of new filtration markers that are not affected by muscle mass, such as cystatin C.

An important limitation of the analysis is that we pooled studies that differ from one another in their source populations. In previous reports, we showed that the relationship between mGFR and serum creatinine varies among these studies.[33–35] In this analysis, any study-related differences are averaged together, with each study population weighted in proportion to the number of patients in that study. The implications are that the results presented here may not be fully applicable to other populations whose characteristics follow different distributions than observed in this study population included in the pooled data set. For example, in populations with a lower prevalence of CKD than in the pooled Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) data set, we would expect a larger underestimation of the mGFR and a higher rate of "false positive" misclassifications of individuals without CKD as having CKD. However, there are no

large studies in the general population with GFR measurements. The pooled data set is more diverse than any of the individual studies, and the performance of the equations in this diverse population may be more representative of performance when the equations are applied in a broad range of clinical settings.

Other limitations of this study are that we cannot account for other sources of error, such as in measurement of GFR or short-term biologic variation in GFR. Therefore, the differences between mGFR and eGFR reported here reflect, in part, errors in mGFR rather than in eGFR. We also did not tested performance of the equation in populations other than in the United States, which may have different levels of creatinine generation. Finally, this cross-sectional study cannot address the use of these equations in estimating change in GFR.

Our analyses facilitate interpretation of GFR estimates in clinical practice. Current recommendations are to report specific values of eGFR only when <60 ml/min per 1.73 m^2.[4,36] Within this range, the MDRD Study equation exhibits minimal bias and reasonable accuracy for all subgroups. However, the P_{30} of 82% indicates that limited precision in the GFR estimate are important to consider when evaluating individual patients. Caution should be exercised when interpreting GFR estimates just below 60 ml/min per 1.73 m^2, because imprecision and underestimation of mGFR may lead to misclassification of CKD in some patients. Interpretation of the eGFR in this range should consider the clinical context, which is not incorporated into current equations. Patients with markers of kidney damage, such as proteinuria, have CKD, regardless of the level of eGFR. For patients without markers of kidney damage, clinical decision making will depend on other characteristics, such as the presence or absence of risk factors for CKD or complications. Clearance measurements using creatinine or exogenous markers such as iothalamate or iohexol may be necessary to obtain accurate levels for these patients or for those with reduced creatinine generation as a result of low protein intake, muscle wasting, malnutrition, or chronic illness, in whom all creatinine-based GFR estimating equations are likely to be inaccurate across the range of GFR.

The MDRD Study equation provides unbiased and reasonably accurate estimates for eGFR <60 ml/min per 1.73 m^2 and can be used in clinical practice. Clinicians should be aware of limitations of the GFR estimating equations. Education programs should be established to educate physicians and other health care providers on the proper use of GFR estimates. Clinical laboratories should be included in the educational campaign.

CONCISE METHODS

Sources of Data

CKD-EPI is a research group formed to develop and validate improved GFR estimating equations by pooling data from research studies and clinical populations (hereafter referred to as "studies"), which include individuals with diverse clinical characteristics, with and without kidney disease, and across a wide range of GFR. We identified studies by searching the Medline database and through personal knowledge of the investigators and collaborators. Inclusion criteria were as follows: GFR measured as urinary iothalamate clearance; study population >250 adults; availability of serum samples and quality control data; ability to calibrate serum creatinine assay; experience of collaborators in GFR measurement, creatinine assay, and clinical investigation; and willingness of collaborators to share individual patient data. Pooling of data from different sources is justified because of the similarity of GFR measurement methods and ability to calibrate serum creatinine assays.

The CKD-EPI pooled creatinine database was divided into two distinct data sets, referred to as category 1 and category 2, on the basis of timing of availability of data and with the goal to include similar populations in both data sets. The category 1 data set is used for model development (random selection of two thirds of data) and internal validation (remaining one third of data). Clinical populations were subdivided into people with known or suspected CKD and healthy individuals who were being evaluated for potential kidney donation. The category 2 data set is used for external validation. The population described in this study includes people from category 1 in the development data set.

Measurements

All studies measured GFR using urinary clearance of iothalamate. Serum creatinine assays were calibrated to the creatinine reference standard using Roche enzymatic method (Roche-Hitachi P-Module instrument with Roche Creatininase Plus assay) at the Cleveland Clinic Research Laboratory.[37]

Variables

Clinical characteristics were defined as follows: Age (<40, 40 to 65, and >65 yr), gender, race (black, Asian, Native American or Pacific Islander or Hispanic, and white or other), diabetes (yes, no), previous organ transplant (yes, no), and BMI (<20, 20 to 25, 26 to 30, and >30 kg/m^2). Assignment for race, diabetes status, and transplant status were based on the definitions used in the individual studies. GFR is adjusted for body surface area as ml/min per 1.73 m^2.[38] Level of eGFR was categorized in two ways: (*1*) ≥60 *versus* <60 ml/min per 1.73 m^2, the threshold value for the definition of CKD[3] and for reporting by clinical laboratories,[36] and (*2*) >120, 90 to 119, 60 to 89, 30 to 59, 15 to 29, or <15 ml/min per 1.73m^2 as used for staging the severity of CKD.[3]

GFR Estimation

GFR was estimated using the MDRD Study equation re-expressed for use with the serum creatinine values standardized to isotope dilution mass spectroscopy: GFR = 175 × standardized $S_{cr}^{-1.154}$ × $age^{-0.203}$ × 1.212 (if black) × 0.742 (if female), where S_{cr} is serum creatinine.[27]

Statistical Analyses

The study population was stratified by subgroups defined by clinical characteristics and level of eGFR. Comparison between mGFR and

eGFR was determined graphically by plotting mGFR and the difference (mGFR − eGFR) against eGFR.[39] Bias was measured as the difference (mGFR − eGFR) and percentage difference [(mGFR − eGFR)/mGFR × 100]) between mGFR and eGFR, with positive values indicating lower eGFR than mGFR (underestimation). Precision was measured as IQR for the differences. Accuracy was measured as P_{30}, which takes into account higher errors at higher values. Confidence intervals were calculated by bootstrap methods (2000 bootstraps) for difference and percentage difference and by the binomial method for P_{30}. Performance was evaluated for the overall pooled data set and for subgroups defined by age, gender, race, diabetes, transplant status, BMI, and level of eGFR.

Analyses were computed using R (version 2; Free Software Foundation, Boston, MA) and SAS software (version 9.1; SAS Institute, Cary, NC). Smooth estimates of the mean in the figures were created using the lowess function in R.

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DISCLOSURES

None.

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