

Comparison of CKD Awareness in a Screening Population Using the Modification of Diet in Renal Disease (MDRD) Study and CKD Epidemiology Collaboration (CKD-EPI) Equations

Manjula Kurella Tamura, MD, MPH,¹ Shuchi Anand, MD,¹ Suying Li, PhD,²
Shu-Cheng Chen, MS,² Adam T. Whaley-Connell, DO, MSPH,³
Lesley A. Stevens, MD, MS,⁴ and Keith C. Norris, MD⁵

Background: Low awareness of chronic kidney disease (CKD) may reflect uncertainty about the accuracy or significance of a CKD diagnosis in individuals otherwise perceived to be low risk. Whether reclassification of CKD severity using the CKD Epidemiology Collaboration (CKD-EPI) equation to estimate glomerular filtration rate (GFR) modifies estimates of CKD awareness is unknown.

Methods: In this cross-sectional study, we used data collected from 2000-2009 for 26,213 participants in the Kidney Early Evaluation Program (KEEP), a community-based screening program, with CKD based on GFR estimated using the 4-variable Modification of Diet in Renal Disease (MDRD) Study equation and measurement of albuminuria. We assessed CKD awareness after CKD stage was reclassified using the CKD-EPI equation.

Results: Of 26,213 participants with CKD based on GFR estimated using the MDRD equation ($eGFR_{MDRD}$), 23,572 (90%) also were classified with CKD based on $eGFR_{CKD-EPI}$. Based on $eGFR_{MDRD}$, 9.5% of participants overall were aware of CKD, as were 4.9%, 6.3%, 9.2%, 41.9%, and 59.2% with stages 1-5, respectively. Based on $eGFR_{CKD-EPI}$, 10.0% of participants overall were aware of CKD, as were 5.1%, 6.6%, 10.0%, 39.3%, and 59.4% with stages 1-5, respectively. Reclassification to a less advanced CKD stage using $eGFR_{CKD-EPI}$ was associated with lower odds for awareness (OR, 0.58; 95% CI, 0.50-0.67); reclassification to a more advanced stage was associated with higher odds for awareness (OR, 1.50; 95% CI, 1.05-2.13) after adjustment for confounding factors. Of participants unaware of CKD, 10.6% were reclassified as not having CKD using $eGFR_{CKD-EPI}$.

Conclusions: Using $eGFR_{CKD-EPI}$ led to a modest increase in overall awareness rates, primarily due to reclassification of low-risk unaware participants.

Am J Kidney Dis. 57(3)(S2):S17-S23. © 2011 by the National Kidney Foundation, Inc.

INDEX WORDS: Awareness; chronic kidney disease; Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI); estimated glomerular filtration rate.

Chronic kidney disease (CKD) is common in US adults, and it contributes to increased risks of death, end-stage renal disease, and cardiovascular events.^{1,2} Although awareness of CKD has improved modestly over time, it remains low. For example, in the 2000-2004 National Health and Nutrition Examination Survey (NHANES), 6% of individuals with CKD were aware of the condition.³ In those with stage 4 CKD, less than half were aware, and in those with stage 3 CKD, less than 15% were aware.³ Early detection and treatment of CKD may slow progression, prevent complications, and increase preparedness for end-stage renal disease. Thus, improving CKD awareness in patients and providers is a key step toward improving CKD care.

Low CKD awareness may reflect poor provider recognition and communication of CKD and uncertainty about the accuracy of a CKD diagnosis in certain individuals. The 4-variable Modification of Diet in Renal Disease (MDRD) Study equation used to estimate glomerular filtration rate (GFR) has gained broad acceptance in clinical care, yet controversy remains about the implications of its widespread use.

In particular, because the MDRD Study equation systematically underestimates GFR, especially in individuals with $GFR > 60 \text{ mL/min/1.73 m}^2$, it may lead to false-positive diagnoses of CKD.⁴ The prognostic significance of mild decreases in estimated GFR ($eGFR$) in the absence of other CKD risk factors in older individuals also has been questioned.^{5,6} Concerns about these issues may lead providers to under-

From the ¹Department of Medicine, Division of Nephrology, Stanford University, Palo Alto, CA; ²Chronic Disease Research Group, Minneapolis Medical Research Foundation, Minneapolis, MN; ³Harry S. Truman VA Medical Center and University of Missouri-Columbia School of Medicine, Columbia, MO; ⁴Division of Nephrology, Tufts Medical Center, Boston, MA; and ⁵Department of Medicine, Charles Drew University, Los Angeles, CA.

Received August 20, 2010. Accepted in revised form November 8, 2010.

Address correspondence to Manjula Kurella Tamura, MD, MPH, Division of Nephrology, Stanford University, 780 Welch Rd, Ste 106, Palo Alto, CA 94304. E-mail: mktamura@stanford.edu

© 2011 by the National Kidney Foundation, Inc.

0272-6386/\$36.00

doi:10.1053/j.ajkd.2010.11.008

report CKD diagnoses to patients they consider at low risk of progression or other complications.

The newly developed CKD Epidemiology Collaboration (CKD-EPI) equation is reported to have greater precision and less bias for estimating GFR.^{7,8} Its application has led to a downwardly revised estimated US prevalence of CKD, attributable primarily to a lower prevalence of stage 3 CKD (eGFR, 30-59 mL/min/1.73 m²).⁷ Preliminary reports suggest that the CKD-EPI equation also may be more accurate for mortality risk prediction than the MDRD Study equation.^{9,10} We used data collected as part of the Kidney Early Evaluation Program (KEEP), a community-based convenience health screening sample, to compare estimates of CKD awareness using the CKD-EPI and MDRD Study equations. We hypothesized that the high prevalence of CKD unawareness would be attenuated by reclassification of CKD severity using CKD-EPI estimates of GFR.

METHODS

Study Population

KEEP is a free community-based voluntary screening program launched in August 2000, designed to identify individuals at increased risk of kidney disease and encourage follow-up care.¹¹ KEEP screenings are conducted in urban and rural locations throughout the United States through each state's National Kidney Foundation affiliate. In this study, we included eligible KEEP participants screened from August 2000 through December 2009 (n = 123,704) aged at least 18 years with a diagnosis of CKD based on National Kidney Foundation guidelines using the MDRD Study equation to estimate GFR (n = 28,109). From this sample, we excluded individuals receiving maintenance dialysis or with a previous kidney transplant, leaving 27,987 individuals in the analytic cohort. We further excluded individuals with missing values for CKD awareness and other covariates, resulting in a final sample size of 26,213.

KEEP Screening Procedures

During KEEP screening, participants complete a questionnaire to assess demographic characteristics, personal and family medical history, and health behaviors. Blood pressure, height, and weight

Table 1. Characteristics of KEEP Participants Classified as Having CKD Using the MDRD Study Equation and Reclassification Using the CKD-EPI Equation

Characteristics	GFR Estimating Equation				
	MDRD Study		No CKD	CKD-EPI	
	CKD Stages 1-2	CKD Stages 3-5		CKD Stages 1-2	CKD Stages 3-5
No.	8,134	18,079	2,641	8,421	15,151
eGFR (mL/min/1.73 m ²)	87.3 ± 22.4	48.7 ± 9.7	62.8 ± 2.1	89.8 ± 18.8	47 ± 10.2
Age category					
18-30 y	580 (7.1)	132 (0.7)	49 (1.9)	589 (7.0)	74 (0.5)
31-45 y	1,630 (20.0)	992 (5.5)	444 (16.8)	1,694 (20.1)	484 (3.2)
46-60 y	2,867 (35.3)	4,211 (23.3)	1,218 (46.1)	3,029 (36.0)	2,831 (18.7)
61-75 y	2,305 (28.3)	8,029 (44.4)	915 (34.6)	2,409 (28.6)	7,010 (46.3)
>75 y	752 (9.3)	4,715 (26.1)	15 (0.6)	700 (8.3)	4,752 (31.4)
Men	2,650 (32.6)	5,436 (30.1)	588 (22.3)	2,705 (32.1)	4,793 (31.6)
Race					
White	3,297 (40.5)	11,786 (65.2)	1,910 (72.3)	3,466 (41.2)	9,707 (64.1)
African American	3,108 (38.2)	3,970 (22.0)	302 (11.4)	3,133 (37.2)	3,643 (24.0)
Other	1,729 (21.3)	2,323 (12.8)	429 (16.2)	1,822 (21.6)	1,801 (11.9)
Hispanic	1,024 (12.6)	1,206 (6.7)	256 (9.7)	1,074 (12.8)	900 (5.9)
High school graduate	6,658 (81.8)	14,871 (82.3)	2,361 (89.4)	6,911 (82.1)	12,257 (80.9)
Insured	6,226 (76.5)	16,104 (89.1)	2,198 (83.2)	6,427 (76.3)	13,705 (90.5)
Access to physician	5,498 (66.8)	13,012 (72.0)	1,810 (68.2)	5,684 (67.5)	11,016 (72.7)
Diabetes	3,701 (45.5)	7,379 (40.8)	750 (28.4)	3,841 (45.6)	6,489 (42.8)
Hypertension	7,031 (86.4)	16,424 (90.9)	2,124 (80.4)	7,275 (86.4)	14,056 (92.8)
Cardiovascular disease	2,194 (27.0)	6,331 (35.0)	618 (23.4)	2,262 (26.9)	5,645 (37.3)
Current tobacco use	1,087 (13.3)	1,210 (6.7)	272 (10.3)	1,131 (13.4)	894 (5.9)
Family history of kidney disease	1,580 (19.4)	3,104 (17.2)	520 (19.7)	1,659 (19.7)	2,505 (16.5)

Note: Unless otherwise indicated, values shown are mean ± standard deviation or number (percentage). CKD stages are defined as follows: stage 1, eGFR ≥90 mL/min/1.73 m² with ACR ≥30 mg/g; stage 2, eGFR of 60-89 mL/min/1.73 m² with ACR ≥30 mg/g; stage 3, eGFR of 30-59 mL/min/1.73 m²; and stages 4-5, eGFR <30 mL/min/1.73 m².

Abbreviations: ACR, albumin-creatinine ratio; CKD, chronic kidney disease; CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; eGFR, estimated glomerular filtration rate; KEEP, Kidney Early Evaluation Program; MDRD, Modification of Diet in Renal Disease.

are recorded, and blood and urine specimens are collected for determination of serum creatinine level, fasting glucose level, and urine albumin-creatinine ratio (ACR). KEEP laboratory procedures have been described in detail previously.¹²

Definitions

CKD was categorized into stages¹³ as follows using eGFR calculated using both the isotope-dilution mass spectrometry-traceable MDRD Study equation (eGFR_{MDRD}) and the CKD-EPI equation (eGFR_{CKD-EPI}): stage 1, eGFR ≥ 90 mL/min/1.73 m² with ACR ≥ 30 mg/g; stage 2, eGFR of 60-89 mL/min/1.73 m² with ACR ≥ 30 mg/g; stage 3, eGFR of 30-59 mL/min/1.73 m²; and stages 4-5, eGFR < 30 mL/min/1.73 m². CKD awareness was defined as an affirmative answer to the question, "Have you ever been told by a doctor or health care professional you have kidney disease (do not include kidney stones, bladder infections, or incontinence)?" Age was categorized as 18-30, 31-45, 46-60, 61-75, and > 75 years. Education was categorized as high school graduate versus not. Diabetes was defined as self-report, use of medications for diabetes, fasting glucose values ≥ 126 mg/dL, or nonfasting glucose values ≥ 200 mg/dL. Hypertension was defined as self-report, use of medications for hypertension, systolic blood pressure ≥ 130 mm Hg, or diastolic blood pressure ≥ 80 mm Hg. Cardiovascular disease was defined as self-report of heart angioplasty, heart bypass surgery, heart attack, heart failure, abnormal heart rhythm, stroke, or peripheral vascular disease (peripheral vascular disease information was collected until only May 2005).

Statistical Analysis

Participant baseline characteristics and CKD awareness are described by CKD stage and eGFR equation using proportions. We used logistic regression, expressed as odds ratio (OR) and 95% confidence interval (CI), to describe the association of CKD stage and other clinical characteristics with CKD awareness. Separate models were constructed using eGFR_{MDRD} and eGFR_{CKD-EPI} to categorize CKD stage. Adjusted models accounted for age, sex, race, education, and diabetes plus all other variables significant at the $P < 0.1$ level in unadjusted analyses. To determine the relation between reclassification of CKD severity using eGFR_{CKD-EPI} and CKD awareness, we first determined the reclassification rate in

unaware and aware participants. Next, we classified participants into 3 categories as follows: unchanged CKD stage using eGFR_{CKD-EPI} versus eGFR_{MDRD}, less advanced CKD stage using eGFR_{CKD-EPI} versus eGFR_{MDRD}, and more advanced CKD stage using eGFR_{CKD-EPI} versus eGFR_{MDRD}. These categories were used to determine the unadjusted and multivariable-adjusted associations between CKD reclassification and awareness. We further stratified analyses by CKD stage to assess whether findings were consistent. Analyses were conducted using SAS, version 9.2 (www.sas.com).

RESULTS

Using eGFR_{MDRD}, 26,213 participants were classified with CKD: 8,134 (31%) with stages 1-2 and 18,079 (69%) with stages 3-5 (Table 1). Using eGFR_{CKD-EPI}, 23,572 participants were classified with CKD: 8,421 (32%) with stages 1-2 and 15,151 (58%) with stages 3-5. Thus, 2,641 participants (10%) were classified with CKD using eGFR_{MDRD}, but not eGFR_{CKD-EPI}. Of participants with CKD using eGFR_{MDRD}, 9.5% were aware of CKD; 4.9%, 6.3%, 9.2%, 41.9%, and 59.2% with stages 1-5, respectively, were aware (Fig 1). Of participants with CKD using eGFR_{CKD-EPI}, 10.0% were aware of CKD; 5.1%, 6.6%, 10.0%, 39.3%, and 59.4% with stages 1-5, respectively, were aware. An association between more advanced CKD stages and higher odds for awareness remained after adjustment for clinical characteristics (Table 2). Odds for awareness were slightly higher for CKD stages based on eGFR_{CKD-EPI} than for CKD stages based on eGFR_{MDRD}. The association between other clinical characteristics and awareness was not changed substantially when eGFR_{CKD-EPI} was substituted for eGFR_{MDRD}. In participants with eGFR_{CKD-EPI} < 60 mL/min/1.73 m², albuminuria (ACR ≥ 30 mg/g) was associated with higher odds for aware-

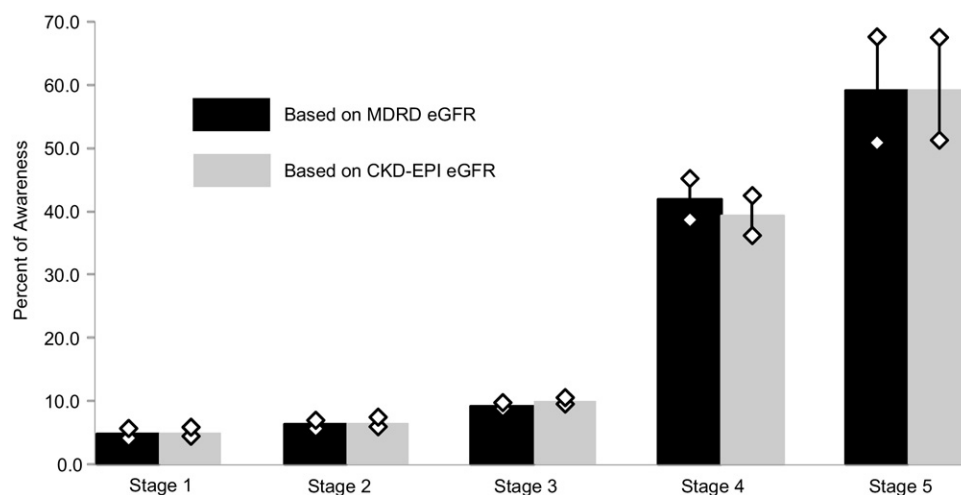


Figure 1. Prevalence of chronic kidney disease (CKD) awareness by Modification of Diet in Renal Disease (MDRD) Study estimated glomerular filtration rate (eGFR; $n = 26,213$) and CKD Epidemiology Collaboration (CKD-EPI) eGFR ($n = 23,572$) stages. Bars indicate 95% confidence intervals. CKD stages are defined as follows: stage 1, eGFR ≥ 90 mL/min/1.73 m² with albumin-creatinine ratio (ACR) ≥ 30 mg/g; stage 2, eGFR of 60-89 mL/min/1.73 m² with ACR ≥ 30 mg/g; stage 3, eGFR of 30-59 mL/min/1.73 m²; and stages 4-5, eGFR < 30 mL/min/1.73 m².

Table 2. Association of CKD Stage and Other Participant Characteristics With CKD Awareness

Characteristics	Unadjusted OR (95% CI)	Adjusted Model 1 ^a OR (95% CI)	Adjusted Model 2 ^a OR (95% CI)
MDRD Study CKD stage			
1	1.00 (reference)	1.00 (reference)	—
2	1.31 (1.07-1.60)	1.32 (1.07-1.63)	—
3	1.99 (1.67-2.37)	2.29 (1.89-2.78)	—
4	14.12 (11.40-17.50)	17.32 (13.61-22.04)	—
5	28.43 (19.31-41.87)	32.78 (21.64-49.66)	—
CKD-EPI CKD stage			
None	0.98 (0.78-1.23)	—	1.11 (0.87-1.41)
1	1.00 (reference)	—	1.00 (reference)
2	1.32 (1.10-1.59)	—	1.53 (1.25-1.87)
3	2.07 (1.78-2.42)	—	2.90 (2.41-3.47)
4	12.07 (9.93-14.67)	—	18.58 (14.76-23.40)
5	27.31 (18.89-39.47)	—	38.40 (25.69-57.41)
Age (/decade)	1.05 (1.02-1.08)	0.91 (0.87-0.94)	0.83 (0.80-0.87)
Men (vs women)	1.33 (1.22-1.45)	1.29 (1.18-1.42)	1.24 (1.12-1.36)
White race (vs other)	1.30 (1.19-1.41)	1.21 (1.09-1.33)	1.29 (1.17-1.43)
High school graduate (vs less)	0.87 (0.79-0.97)	0.86 (0.77-0.97)	0.88 (0.78-0.99)
Insured (vs uninsured)	0.73 (0.66-0.81)	0.67 (0.59-0.77)	0.67 (0.59-0.76)
Access to physician	0.89 (0.75-1.06)	—	—
Diabetes	1.22 (1.12-1.33)	1.03 (0.94-1.14)	1.02 (0.93-1.12)
Hypertension	1.89 (1.60-2.24)	1.59 (1.33-1.91)	1.55 (1.29-1.86)
Cardiovascular disease	1.74 (1.60-1.89)	1.48 (1.35-1.63)	1.48 (1.34-1.63)
Current smoking	0.97 (0.84-1.13)	—	—
Family history of kidney disease	1.72 (1.56-1.90)	1.86 (1.67-2.06)	1.87 (1.68-2.07)
Screening year			
2000-2002	1.00 (reference)	1.00 (reference)	1.00 (reference)
2003	1.26 (0.97-1.62)	1.45 (1.10-1.91)	1.52 (1.15-2.00)
2004	1.10 (0.86-1.40)	1.31 (1.01-1.70)	1.37 (1.05-1.77)
2005	1.66 (1.33-2.07)	2.00 (1.58-2.53)	2.09 (1.65-2.65)
2006	2.15 (1.73-2.67)	2.79 (2.20-3.53)	2.89 (2.28-3.66)
2007	2.57 (2.07-3.19)	3.13 (2.48-3.96)	3.24 (2.56-4.09)
2008	2.55 (2.06-3.16)	3.23 (2.56-4.08)	3.42 (2.71-4.32)
2009	2.87 (2.33-3.54)	3.70 (2.94-4.65)	3.86 (3.07-4.86)

Note: CKD stages are defined as follows: stage 1, eGFR ≥ 90 mL/min/1.73 m² with ACR ≥ 30 mg/g; stage 2, eGFR of 60-89 mL/min/1.73 m² with ACR ≥ 30 mg/g; stage 3, eGFR of 30-59 mL/min/1.73 m²; and stages 4-5, eGFR < 30 mL/min/1.73 m².

Abbreviations: ACR, albumin-creatinine ratio; CI, confidence interval; CKD, chronic kidney disease; CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; eGFR, estimated glomerular filtration rate; MDRD, Modification of Diet in Renal Disease; OR, odds ratio.

^aAdjusted models include all covariates listed.

ness (OR, 1.85; 95% CI, 1.64-2.08) after adjustment for eGFR and other confounders.

Although prevalence estimates of awareness changed only modestly, CKD severity classification changed considerably, especially in CKD-unaware participants (Table 3). Of 23,733 unaware participants with CKD using eGFR_{MDRD}, 2,863 (12.1%) were reclassified to a less advanced CKD stage using eGFR_{CKD-EPI}, including 2,509 (10.6%) who were reclassified to no CKD, and 158 (<1%) who were reclassified to a more advanced CKD stage. Mean age of unaware participants who were reclassified to no CKD was 55 years, and mean eGFR_{CKD-EPI} was 62 mL/min/1.73 m². All had eGFR_{MDRD} ≥ 45 mL/min/

1.73 m²; 77% were women, 72% did not have diabetes, and 80% had hypertension. Of 2,480 aware participants with CKD using eGFR_{MDRD}, 35 (1.4%) were reclassified to a more advanced stage, and 188 (7.5%), to a less advanced stage.

Relative to unchanging CKD stage using eGFR_{MDRD} and eGFR_{CKD-EPI}, reclassification to a less advanced stage using eGFR_{CKD-EPI} was associated with 40% lower odds for CKD awareness (OR, 0.58; 95% CI, 0.50-0.67), and reclassification to a more advanced stage, with 50% higher odds for CKD awareness (OR, 1.50; 95% CI, 1.05-2.13; Table 4). These findings persisted after adjustment for age, sex, race, education, and other potential confounders. Results were

Table 3. Reclassification of Participants Unaware and Aware of CKD Using the CKD-EPI and MDRD Study Equations

CKD by MDRD Study Equation	CKD-EPI Equation					No. Reclassified	
	No CKD	Stage 1-2	Stage 3	Stage 4	Stage 5	More Advanced	Less Advanced
Unaware (n = 23,733)							
CKD stages 1-2	0	7,601	65	0	0	65	0
CKD stage 3	2,509	322	12,600	88	0	88	2,831
CKD stage 4	0	0	30	460	5	5	30
CKD stage 5	0	0	0	2	51	—	2
Total no. reclassified						158	2,863
Aware (n = 2,480)							
CKD stages 1-2	0	463	5	0	0	5	0
CKD stage 3	132	35	1,390	21	0	21	167
CKD stage 4	0	0	17	331	9	9	17
CKD stage 5	0	0	0	4	73	—	4
Total no. reclassified						35	188

Note: CKD stages are defined as follows: stage 1, eGFR ≥ 90 mL/min/1.73 m² with ACR ≥ 30 mg/g; stage 2, eGFR of 60-89 mL/min/1.73 m² with ACR ≥ 30 mg/g; stage 3, eGFR of 30-59 mL/min/1.73 m²; and stages 4-5, eGFR < 30 mL/min/1.73 m².

Abbreviations: ACR, albumin-creatinine ratio; CKD, chronic kidney disease; CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; eGFR, estimated glomerular filtration rate; MDRD, Modification of Diet in Renal Disease.

consistent across all CKD stages, although most pronounced for stages 3-5 using eGFR_{MDRD} (Table 4).

DISCUSSION

We found that classification of CKD severity using eGFR_{CKD-EPI} aligned more closely with CKD awareness than classification of severity using eGFR_{MDRD}. Application of eGFR_{CKD-EPI} to KEEP data led to a modest increase in overall awareness rates, primarily

due to reclassification of low-risk unaware participants as not having CKD. These findings suggest that eGFR_{CKD-EPI} is a better indicator of the perceived accuracy and prognostic importance of a CKD diagnosis than eGFR_{MDRD}.

Awareness of CKD in the United States is low, especially compared with awareness of chronic conditions associated with CKD, such as hypertension or diabetes, for which awareness rates are $>70\%$.^{14,15}

Table 4. ORs for CKD Awareness in KEEP Participants With Reclassified Versus Unchanged CKD Stage

CKD Stage Reclassification From MDRD Study to CKD-EPI eGFR	Unadjusted OR (95% CI)	Adjusted OR (95% CI) ^a
Full analytic cohort (n = 23,572)		
Reclassified as less advanced	0.58 (0.51-0.66)	0.58 (0.50-0.67)
Unchanged	1.00 (reference)	1.00 (reference)
Reclassified as more advanced	1.48 (1.05-2.10)	1.50 (1.05-2.13)
MDRD Study stages 1-2 CKD (n = 8,134)		
Reclassified as less advanced	0.99 (0.74-1.33)	0.92 (0.68-1.23)
Unchanged	1.00 (reference)	1.00 (reference)
Reclassified as more advanced	0.96 (0.47-1.96)	1.13 (0.54-2.38)
MDRD Study stage 3 CKD (n = 14,456)		
Reclassified as less advanced	0.54 (0.45-0.63)	0.45 (0.38-0.54)
Unchanged	1.00 (reference)	1.00 (reference)
Reclassified as more advanced	2.16 (1.34-3.49)	2.56 (1.56-4.19)
MDRD Study stages 4-5 CKD (n = 982)		
Reclassified as less advanced	0.83 (0.47-1.46)	0.56 (0.30-1.04)
Unchanged	1.00 (reference)	1.00 (reference)
Reclassified as more advanced	2.28 (0.76-6.85)	3.38 (1.05-10.83)

Note: CKD stages are defined as follows: stage 1, eGFR ≥ 90 mL/min/1.73 m² with ACR ≥ 30 mg/g; stage 2, eGFR of 60-89 mL/min/1.73 m² with ACR ≥ 30 mg/g; stage 3, eGFR of 30-59 mL/min/1.73 m²; and stages 4-5, eGFR < 30 mL/min/1.73 m².

Abbreviations: ACR, albumin-creatinine ratio; CI, confidence interval; CKD, chronic kidney disease; CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; eGFR, estimated glomerular filtration rate; KEEP, Kidney Early Evaluation Program; MDRD, Modification of Diet in Renal Disease; OR, odds ratio.

^aAdjusted for age, sex, race, education, insurance, diabetes, hypertension, cardiovascular disease, and screening year.

As for other chronic conditions, awareness of CKD is dependent on several patient and provider factors. Patients must have access to health care services to be tested for CKD. Providers must identify at-risk individuals, decide to evaluate kidney function, and interpret these results. KEEP screenings, promotion of CKD clinical practice guidelines, and automated eGFR reporting by laboratories aim to facilitate several of these factors. Increased CKD awareness over time in KEEP and nationally and a recent increase in nephrology referrals suggest that these efforts may be having some impact.^{3,16,17}

Providers also must consider the accuracy and prognostic significance of test results and communicate the findings to patients. Concern about provoking anxiety with a potentially inaccurate or inconsequential CKD diagnosis may deter provider communication.^{4,18} Our findings are consistent with this hypothesis. In KEEP, CKD awareness decreased dramatically below stage 4, rather than decreasing stepwise. Furthermore, 10.6% of participants labeled as CKD unaware were reclassified as not having CKD using eGFR_{CKD-EPI}. These participants all had eGFR_{MDRD} of 45-59 mL/min/1.73 m² and no albuminuria; most did not have diabetes. Recent findings would suggest that they are a group at lower risk of adverse outcomes.^{5,6,19} In addition, the cost-effectiveness of early CKD diagnosis has been challenged, primarily due to the potential decrease in quality of life caused by a false-positive diagnosis.^{20,21} Although the potential effects of a true-positive or false-positive diagnosis cannot be inferred from our findings, they suggest that providers are relying on additional markers of risk beyond eGFR, such as albuminuria or family history, to communicate diagnostic and prognostic information about CKD.

These controversies should not obscure disappointingly low rates of CKD awareness in individuals with eGFR <30 mL/min/1.73 m², a group for whom CKD awareness is universally considered important for preventing CKD-related complications and prompting preparation for renal replacement therapy. In KEEP, only 39.3% and 59.4% of individuals with eGFR_{CKD-EPI} of 15-30 and <15 mL/min/1.73 m² were aware of CKD, respectively. Correlates of CKD awareness in KEEP were similar to NHANES results; younger patients, men, whites, and patients with hypertension were more likely to be aware of CKD.³ Curiously, high school education, health insurance, and access to a physician were associated with lower rather than higher odds for awareness, suggesting that poor health literacy and lack of access to care are not major factors preventing awareness. Additional studies are needed to understand the barriers to detection and communication of CKD in this high-risk group.

By showing its relation to CKD awareness, our study also provides indirect evidence of the validity of estimating GFR using the CKD-EPI equation. After the initial validation study, subsequent reports have confirmed that the CKD-EPI equation reduces bias across patient subgroups thought to be at low risk of CKD complications and in those with eGFR >60 mL/min/1.73 m² compared with the MDRD Study equation.⁸ Two large cohort studies have noted that eGFR_{CKD-EPI} performs better than eGFR_{MDRD} in predicting risk of death, cardiovascular events, and end-stage renal disease.^{9,10} Future studies may be able to determine whether improved accuracy and risk prognostication using eGFR_{CKD-EPI} encourage providers to communicate a diagnosis of CKD more often.

Our study has several limitations common to large studies that use creatinine-based estimating equations for renal filtration function. First, CKD awareness (or lack of) may influence participation in a KEEP screening. Compared with the general US population, KEEP is enriched with individuals at higher risk of CKD-related morbidity.^{22,23} Second, because we did not have repeated assessments of eGFR, some individuals with acute changes in kidney function may have been misclassified. Finally, the questionnaire item we used to assess awareness may have been misinterpreted by participants, possibly causing underestimates of overall awareness rates. For example, participants may have been told they had “low kidney function” rather than “kidney disease.”

In summary, eGFR_{CKD-EPI} more strongly correlated with CKD awareness than eGFR_{MDRD}, and its application to KEEP data led to a modest increase in CKD awareness due to upward reclassification of unaware participants with mild decrements in eGFR. Improvements in GFR estimation, such as with the creatinine-based CKD-EPI equation or other biomarkers of kidney damage, may help increase CKD awareness by reducing provider uncertainty about the accuracy and prognostic significance of a CKD diagnosis.

ACKNOWLEDGEMENTS

The authors thank Shane Nygaard, BA, and Nan Booth, MSW, MPH, ELS, of the Chronic Disease Research Group for manuscript preparation and editing, respectively.

Support: The KEEP is a program of the National Kidney Foundation Inc and is supported by Amgen, Abbott, Siemens, Astellas, Fresenius Medical Care, Genzyme, LifeScan, Nephroceuticals, and Pfizer. Dr Kurella Tamura receives support from the National Institute of Aging (K23AG028952). Dr Whaley-Connell receives support from the Veteran's Affairs Career Development Award-2. Dr Stevens receives grant support from Gilead Inc.

Financial Disclosure: Dr Norris has consulted with Amgen, King Pharmaceuticals, and Abbott. The remaining authors declare that they have no relevant financial interests.

REFERENCES

1. Coresh J, Selvin E, Stevens LA, et al. Prevalence of chronic kidney disease in the United States. *JAMA*. 2007;298:2038-2047.
2. Go AS, Chertow GM, Fan D, McCulloch CE, Hsu CY. Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. *N Engl J Med*. 2004;351:1296-1305.
3. Plantinga LC, Boulware LE, Coresh J, et al. Patient awareness of chronic kidney disease: trends and predictors. *Arch Intern Med*. 2008;168:2268-2275.
4. Glasscock RJ. Referrals for chronic kidney disease: real problem or nuisance? *JAMA*. 2010;303:1201-1203.
5. Hemmelgarn BR, Manns BJ, Lloyd A, et al. Relation between kidney function, proteinuria, and adverse outcomes. *JAMA*. 2010;303:423-429.
6. O'Hare AM, Hailpern SM, Pavkov ME, et al. Prognostic implications of the urinary albumin to creatinine ratio in veterans of different ages with diabetes. *Arch Intern Med*. 2010;170:930-936.
7. Levey AS, Stevens LA, Schmid CH, et al. A new equation to estimate glomerular filtration rate. *Ann Intern Med*. 2009;150:604-612.
8. Stevens LA, Schmid CH, Greene T, et al. Comparative performance of the CKD Epidemiology Collaboration (CKD-EPI) and the Modification of Diet in Renal Disease (MDRD) Study equations for estimating GFR levels above 60 mL/min/1.73 m². *Am J Kidney Dis*. 2010;56:486-495.
9. Matsushita K, Selvin E, Bash LD, Astor BC, Coresh J. Risk implications of the new CKD Epidemiology Collaboration (CKD-EPI) equation compared with the MDRD Study equation for estimated GFR: the Atherosclerosis Risk in Communities (ARIC) Study. *Am J Kidney Dis*. 2010;55:648-659.
10. White SL, Polkinghorne KR, Atkins RC, Chadban SJ. Comparison of the prevalence and mortality risk of CKD in Australia using the CKD Epidemiology Collaboration (CKD-EPI) and Modification of Diet in Renal Disease (MDRD) Study GFR estimating equations: the AusDiab (Australian Diabetes, Obesity and Lifestyle) Study. *Am J Kidney Dis*. 2010;55:660-670.
11. Brown WW, Peters RM, Ohmit SE, et al. Early detection of kidney disease in community settings: the Kidney Early Evaluation Program (KEEP). *Am J Kidney Dis*. 2003;42:22-35.
12. Stevens LA, Stoycheff N. Standardization of serum creatinine and estimated glomerular filtration rate in the National Kidney Foundation Kidney Early Evaluation Program (KEEP). *Am J Kidney Dis*. 2008;51(suppl 2):S77-S82.
13. National Kidney Foundation. K/DOQI Clinical Practice Guidelines for Chronic Kidney Disease: evaluation, classification, and stratification. *Am J Kidney Dis*. 2002;39(suppl 1):S1-S266.
14. Egan BM, Zhao Y, Axon RN. US trends in prevalence, awareness, treatment, and control of hypertension, 1988-2008. *JAMA*. 2010;303:2043-2050.
15. Cowie CC, Rust KF, Byrd-Holt DD, et al. Prevalence of diabetes and high risk for diabetes using A1C criteria in the U.S. population in 1988-2006. *Diabetes Care*. 2010;33:562-568.
16. Hemmelgarn BR, Zhang J, Manns BJ, et al. Nephrology visits and health care resource use before and after reporting estimated glomerular filtration rate. *JAMA*. 2010;303:1151-1158.
17. Saab G, Whaley-Connell AT, McCullough PA, Bakris GL. CKD awareness in the United States: the Kidney Early Evaluation Program (KEEP). *Am J Kidney Dis*. 2008;52:382-383.
18. Mann SJ. Pitfalls in diagnosing chronic kidney disease from eGFR. *Arch Intern Med*. 2009;169:1168-1169.
19. Matsushita K, van der Velde M, Astor BC, et al. Association of estimated glomerular filtration rate and albuminuria with all-cause and cardiovascular mortality in general population cohorts: a collaborative meta-analysis. *Lancet*. 2010;375:2073-2081.
20. den Hartog JR, Reese PP, Cizman B, Feldman HI. The costs and benefits of automatic estimated glomerular filtration rate reporting. *Clin J Am Soc Nephrol*. 2009;4:419-427.
21. Hallan SI, Dahl K, Oien CM, et al. Screening strategies for chronic kidney disease in the general population: follow-up of cross sectional health survey. *BMJ*. 2006;333:1047. doi:10.1136/bmj.39001.657755.BE
22. Stevens LA, Li S, Wang C, et al. Prevalence of CKD and comorbid illness in elderly patients in the United States: results from the Kidney Early Evaluation Program (KEEP). *Am J Kidney Dis*. 2010;55(suppl 2):S23-S33.
23. Whaley-Connell AT, Sowers JR, Stevens LA, et al. CKD in the United States: Kidney Early Evaluation Program (KEEP) and National Health and Nutrition Examination Survey (NHANES) 1999-2004. *Am J Kidney Dis*. 2008;51(suppl 2):S13-S20.