Diabetes Mellitus and CKD Awareness: The Kidney Early Evaluation Program (KEEP) and National Health and Nutrition Examination Survey (NHANES)

Adam Whaley-Connell, DO, MSPH,[1] James R. Sowers, MD,[1] Peter A. McCullough, MD, MPH,[2] Tricia Roberts, MS,[3] Samy I. McFarlane, MD, MPH,[4] Shu-Cheng Chen, MS,[3] Suying Li, PhD,[3] Changchun Wang, MS,[3] Allan J. Collins, MD,[3] and George L. Bakris, MD,[5] on behalf of the KEEP Investigators

Background: Diabetes contributes to increased morbidity and mortality in patients with chronic kidney disease (CKD). We sought to describe CKD awareness and identify factors associated with optimal glycemic control in diabetic and nondiabetic individuals both aware and unaware of CKD.

Methods: This cross-sectional analysis compared Kidney Early Evaluation Program (KEEP) and National Health and Nutrition and Examination Survey (NHANES) 1999 to 2006 participants with diabetes and CKD. CKD was defined and staged using glomerular filtration rate (estimated by using the 4-variable Modification of Diet in Renal Disease Study equation) and urine albumin-creatinine ratio. NHANES defined diabetes as self-reported diabetes or fasting plasma blood glucose level of 126 mg/dL or greater, and KEEP as self-reported diabetes or diabetic retinopathy, use of diabetes medications, fasting blood glucose level of 126 mg/dL or greater, or nonfasting glucose level of 200 mg/dL or greater.

Results: Of 77,077 KEEP participants, 20,200 (26.2%) were identified with CKD and 23,082 (29.9%) were identified with diabetes. Of 9,536 NHANES participants, 1,743 (18.3%) were identified with CKD and 1,127 (11.8%) were identified with diabetes. Of KEEP participants with diabetes and CKD (n = 7,853), 736 (9.4%) were aware of CKD. Trends in lack of CKD awareness were similar for KEEP participants with and without diabetes. Unaware participants with and without diabetes identified with stages 1 and 2 CKD were less likely to reach target glucose levels, defined as fasting glucose level less than 126 mg/dL or nonfasting glucose level less than 140 mg/dL, than those with stages 3 to 5 (odds ratio, 0.69; 95% confidence interval, 0.62 to 0.78; odds ratio, 0.69; 95% confidence interval, 0.58 to 0.81; $P < 0.001$, respectively).

Conclusion: Our data support that KEEP, as a targeted screening program, is a more enriched population with CKD and comorbid diabetes than NHANES. In addition, our findings highlight the relationship between dysglycemia and early stages of unidentified CKD.

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INDEX WORDS: Chronic kidney disease; diabetes; health screening.

Diabetes mellitus, types 1 and 2, is the leading cause of incident and prevalent chronic kidney disease (CKD), accounting for about 30% to 40% of CKD and up to 45% of end-stage renal disease.[1,2] The hallmark of diabetic kidney disease is microalbuminuria, defined as a spot urine protein-creatinine ratio of 30 to 299 mg/g and found in approximately 45% of patients with diabetes.[1] Diabetes mellitus is associated with several comorbid conditions, including excess adiposity and traditional Framingham cardiovascular disease (CVD) risk factors (hypertension, dyslipidemia, tobacco use, and increasing age) that collectively predict high mortality.[3,4]

A relationship between visceral adiposity, insulin resistance, other metabolic risk factors, and microalbuminuria has been established.[5-8] This association has been attributed largely to cardiovascular inflammation and oxidative stress, hypertension, and dyslipidemia, which collectively increase the comorbid risk associated with CKD.[9] In addition, there is sufficient evidence to sug-

From the [1]University of Missouri-Columbia School of Medicine and Harry S. Truman VA Medical Center, Columbia, MO; [2]William Beaumont Hospital, Royal Oak, MI; [3]Chronic Disease Research Group, Minneapolis Medical Research Foundation, Minneapolis, MN; [4]SUNY Downstate, Brooklyn, NY; and [5]University of Chicago School of Medicine, Chicago, IL.

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Address correspondence to Adam Whaley-Connell, DO, MSPH, University of Missouri-Columbia School of Medicine, Department of Internal Medicine, Division of Nephrology, MA436, DC043.0, One Hospital Dr, Columbia, MO 65212. E-mail: whaleyconnella@health.missouri.edu

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gest a role for glycemic control in improving the morbidity and mortality associated with diabetes.[3,4] Optimal glucose control reduces the risk of adverse kidney outcomes.[10-12] Insulin resistance and overt diabetes in kidney disease are increasingly recognized as public health problems, highlighting the need for early awareness and detection.

CKD often is silent until advanced stages. Because many people with CKD are unaware of its presence, it often is identified in its later stages, when opportunities to prevent adverse outcomes are limited.[1,13,14] Detection of CKD at earlier stages would allow more time for evaluation and treatment. To identify individuals at greatest risk of CKD, the Kidney Early Evaluation Program (KEEP) was developed by the National Kidney Foundation to provide screening for early CKD.[15,16] KEEP is a free voluntary community-based kidney health screening program designed to raise awareness and improve detection of kidney disease in high-risk individuals, those with diabetes mellitus or hypertension, or a first-order relative with diabetes, hypertension, or kidney disease. Participants are recruited based on their perceived risk.

In this report of the KEEP data, we sought to examine the presence of diabetes mellitus in participants with CKD and compare it with National Health and Nutrition Examination Survey (NHANES) 1999 to 2006 data. We further sought to describe CKD awareness and identify factors associated with optimal glycemic control in individuals with and without diabetes both aware and unaware of CKD.

METHODS

KEEP and NHANES Study Participants

The study population included eligible KEEP participants from August 2000 through December 31, 2007, from 47 National Kidney Foundation affiliates and 1,966 screening programs in 49 states and the District of Columbia. This KEEP study cohort includes 77,077 eligible participants with nonmissing values for CKD stage and diabetic status, whereas the NHANES 1999 to 2006 cohort used in this study was limited to participants with fasting plasma glucose values to define diabetes (n = 9,536). These NHANES data included participants 18 years or older, and for all analyses using smoking status, self-reported CVD, or self-reported high cholesterol level, included participants were 20 years or older. A complete description of the KEEP study and NHANES database has been previously published.[17]

Definitions

We applied common definitions for comorbid conditions across analyses and data sets, with some exceptions as noted in the tables. Diabetes was primarily defined in the KEEP data as recognized history of diabetes (participant self-report or retinopathy), use of medications to treat diabetes, or fasting blood glucose level of 126 mg/dL or greater or nonfasting blood glucose level of 200 mg/dL or greater in the absence of self-report or medication use (labeled "newly diagnosed diabetes" for the purpose of this article). Diabetes was defined in NHANES data as self-reported diabetes or fasting plasma blood glucose level of 126 mg/dL or greater. Unlike the KEEP definition, the NHANES definition does not use nonfasting serum glucose values because this is not recommended by the NHANES investigators. Although these definitions in the 2 data sets are not identical, they are closer than the previous approach of using only self-reported diabetes in NHANES. However, alternative diabetes definitions were used in some KEEP analyses, and these are indicated in the tables. For example, in select KEEP analyses, diabetes was defined as history of diabetes (self-report or retinopathy) or use of diabetic medications. A modified definition was applied to analyses restricted to patients with a fasting plasma blood glucose value: history of diabetes (self-report or retinopathy), use of medications to treat diabetes, or fasting blood glucose level of 126 mg/dL or greater.

Estimated glomerular filtration rate (eGFR) was calculated using the isotope dilution mass spectrometry–traceable 4-variable Modification of Diet in Renal Disease (MDRD) Study equation[18] after serum creatinine had been calibrated to the Cleveland Clinic Research Laboratory.[19] In NHANES, GFR was estimated by using the MDRD Study equation and based on standardized creatinine values for NHANES 1999-2000, 2001-2002, 2003-2004, and 2005-2006 separately, according to National Center for Health Statistics recommendations. Urine albumin-creatinine ratio (ACR) was categorized as less than 30, 30 to 300, or greater than 300 mg/g. CKD stages were defined as follows: stage 1, eGFR of 90 mL/min/1.73 m^2 or greater and ACR of 30 mg/g or greater; stage 2, eGFR of 60 to 89 mL/min/1.73 m^2 and ACR of 30 mg/g or greater; stage 3, eGFR of 30 to 59 mL/min/1.73 m^2; stage 4, eGFR of 15 to 29 mL/min/1.73 m^2; and stage 5, eGFR less than 15 mL/min/1.73 m^2. Target blood glucose was defined as fasting blood glucose level less than 126 mg/dL or nonfasting blood glucose level less than 140 mg/dL.[20]

Hypertension was defined as self-reported history of hypertension, use of medications to treat hypertension, or, based on the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) guidelines,[21] systolic blood pressure of 130 mm Hg or greater or diastolic blood pressure of 80 mm Hg or greater for participants with a history of diabetes or CKD or as systolic blood pressure of 140 mm Hg or greater or diastolic blood pressure of 90 mm Hg or greater for participants without diabetes or CKD. NHANES defined hypertension as self-reported history of hypertension or newly diagnosed hypertension using the JNC 7 definition as described.

CVD history was defined as self-reported history of heart attack, heart angioplasty, bypass surgery, heart failure, abnormal heart rhythm, or stroke. NHANES defined CVD history as self-reported history of coronary heart disease, angina/angina pectoris, heart attack, congestive heart failure, or stroke.

Obesity was defined as body mass index of 30 kg/m^2 or greater (based on fasting weight in NHANES), proteinuria as ACR of 30 mg/g or greater, and dyslipidemia as cholesterol level greater than 200 mg/dL or triglyceride level greater than 150 mg/dL (fasting or nonfasting). Awareness of CKD was defined as an affirmative response to the KEEP questionnaire question "Have you ever been told you have kidney disease?" (the questionnaire includes additional yes/no questions about kidney stones, bladder infections, and polycystic kidney disease) or the NHANES question "(Have you/Has SP [sample person]) ever been told by a doctor or other health professional that (you/she/he) had weak or failing kidneys? Do not include kidney stones, bladder infections, or incontinence."

Prescription medication cost and medical practitioner data were available for only the KEEP cohort and defined according to the KEEP screening questionnaire. Monthly prescription medication cost included self-reported average monthly out-of-pocket costs for prescription medications. Medical practitioner information included self-reports of the types of physicians a participant was seeing; each participant could indicate several types.

Statistical Analysis

Participant demographic characteristics were described in the KEEP and NHANES cohorts according to CKD and diabetic status. To obtain national estimates of each statistic in NHANES, sampling weights and survey design were implemented using SUDAAN (Research Triangle Institute, Research Triangle Park, NC). Diabetic KEEP participants with CKD also were characterized by CKD stage and awareness.

In participants with stages 1 and 2 CKD with fasting blood glucose values, clinical variables were described according to deciles of fasting blood glucose levels and diabetic status. Variables included measurements of systolic blood pressure, diastolic blood pressure, body mass index, cholesterol, triglycerides, and eGFR.

Using logistic regression models by groups aware and unaware of CKD, odds ratios were computed for diabetic and nondiabetic KEEP participants for the outcome of target blood glucose levels. These models compared CKD stages 1 and 2 versus a composite of stages 3 to 5 after adjusting for age, sex, race, current smoking status, hypertension, family history of diabetes, family history of hypertension, and obesity. *P* less than 0.05 indicated statistical significance.

RESULTS

Of 77,077 KEEP participants, 20,200 (26.2%) were identified with CKD and 23,082 (29.9%) were identified with diabetes. Of 9,536 NHANES participants, 1,743 (18.3%) were identified with CKD and 1,127 (11.8%) were identified with diabetes. The age distribution was similar for KEEP and NHANES participants with and without diabetes; white men were underrepresented in the diabetic KEEP population compared with the NHANES population with CKD (53.0% versus 66.3% white, 33.7% versus 53.7% men; Tables 1 and 2). Diabetes prevalence was greater in participants classified as having CKD in both cohorts than in those without CKD (40.7% and 26.1% in KEEP, 29.7% and 7.8% in NHANES, respectively). Educational achievement was higher (77.3% versus 62.9% with high school or higher) and tobacco use was lower (8.9% versus 19.9%) for diabetic KEEP participants with CKD than for diabetic NHANES participants with CKD, but percentages of obesity, hypertension, and CVD were similar. Of note, fewer participants with diabetes were identified with dyslipidemia and CKD in KEEP than NHANES; however, this result was influenced by missing values for lipid panels in nearly half the KEEP participants. Diabetic participants with and without CKD spent more on prescription medications than their nondiabetic counterparts in the KEEP population. Moreover, most KEEP participants were followed by a family physician, and more participants with diabetes were followed by an endocrinologist than participants without identifiable diabetes. A greater percentage of participants with identified CKD stages 3 to 5, even those with diabetes, were followed by a nephrologist than participants at stages 1 to 2. However, this was still a relatively small percentage of screened participants, suggesting a role for increased CKD awareness, even for participants receiving nephrologist care.

Of KEEP participants with diabetes and CKD (n = 7,853), 736 (9.4%) were aware of CKD (Table 3). We found generally similar trends in demographic percentages between aware and unaware participants for advancing age, female sex, white race, health insurance coverage, and seeing family practitioners (Table 3). Of participants with diabetes who were aware they had CKD, 29.6% were followed by nephrologists, whereas 2.7% of those who were unaware of CKD were followed by nephrologists. For participants aware of CKD, greater percentages were followed by nephrologists at stages 3 to 5 than at stages 1 to 2. Percentages of aware diabetic participants with self-reported CVD and dyslipi-

Table 1. Demographic Characteristic Distribution by Diabetes and CKD Status, KEEP and NHANES, Stages 1 to 2 and 3 to 5 CKD

	Stages 1-2 CKD				Stages 3-5 CKD			
	KEEP		NHANES		KEEP		NHANES	
Characteristics	Diabetes	No Diabetes	Diabetes	No Diabetes	Diabetes	No Diabetes	Diabetes	No Diabetes
No. of participants	2,703	3,377	286	593	5,528	8,592	232	632
Age (y)								
18-30	3.4	10.9	—	20	0.2	1.3	0	—
31-45	15.0	25.5	22.4	25.9	3.3	8.7	—	6.6
46-60	38.3	32.4	39.3	24.8	22.0	27.2	15.2	20.2
61-75	33.6	22.2	21.7	18.4	50.2	39.1	49.2	33.4
>75	9.6	9.0	12.9	10.9	24.2	23.7	33.0	39.1
Sex								
Men	37.8	27.6	59.4	37.1	31.6	28.2	45.3	35.5
Women	62.2	72.4	40.6	62.9	68.4	71.8	54.7	64.5
Race								
White	40.1	38.9	57.4	63.7	59.4	63.9	79.1	87.3
African American	35.7	39.9	17.0	15.8	24.3	22.8	11.7	6.7
Others	24.2	21.2	25.5	20.6	16.3	13.3	—	6.0
Ethnicity								
Hispanic	13.5	11.2	20.4	13.9	7.5	7.0	—	—
Non-Hispanic	86.5	88.8	79.6	86.1	92.5	93.0	92.3	95.6
Education								
<High school	22.9	15.3	37.9	23.8	22.6	16.8	36.1	22.8
≥High school	77.1	84.7	62.1	76.2	77.4	83.2	63.9	77.2
Health insurance coverage								
Yes	77.4	77.4	87.5	83.5	88.9	88.6	98.3	94.3
No	22.6	22.6	12.5	16.5	11.1	11.4	—	5.7
Risk factors								
Current smoker	13.8	15.1	25.9	24.8	6.4	8.7	11.2	13.4
Obesity	59.6	42.7	56.4	37.5	55.0	37.0	54.0	26.7
Hypertension	92.5	81.5	89.0	65.5	94.3	87.4	92.0	83.4
Self-reported CVD	33.7	19.6	23.2	11.7	43.0	26.8	43.5	28.4
Proteinuria	100.0	100.0	100.0	100.0	30.2	15.8	34.9	22.6
Dyslipidemia	38.7	32.3	74.3	59.7	36.9	35.3	64.6	65.0
Missing	42.6	48.9			44.2	49.9		
Monthly prescription medication cost* ($)								
<20	15.9	21.3			11.6	14.6		
20-40	9.6	10.2			8.9	10.7		
41-75	9.2	5.9			8.4	8.4		
76-100	6.4	3.4			7.2	5.1		
101-250	7.9	3.2			9.9	4.9		
>250	3.8	1.3			4.8	1.9		
Missing value	47.2	54.6			49.2	54.4		
Medical practitioner*								
Family practice	63.0	59.6			66.5	64.8		
Internist	17.7	14.7			22.7	20.7		
Endocrinologist	11.7	1.3			11.5	1.6		
Obstetrician/gynecologist	11.9	21.4			11.4	16.9		
Nephrologist	2.3	2.9			6.6	4.2		
Cardiologist	10.0	4.9			15.1	9.1		
Gerontologist	0.9	0.8			1.5	1.2		
Physician assistant	2.3	1.8			2.8	1.6		
Nurse practitioner	3.5	2.4			3.5	1.9		
None	2.4	4.1			1.0	2.0		
Other/unknown	12.4	12.2			15.4	13.9		

Note: Values expressed as percent unless noted otherwise.

Abbreviations: CKD, chronic kidney disease; CVD, cardiovascular disease; KEEP, Kidney Early Evaluation Program; NHANES, National Health and Nutrition Examination Survey.

*Not available in NHANES data.

Table 2. Demographic Characteristic Distribution by Diabetes and CKD Status, KEEP and NHANES, All CKD and Non-CKD

	All CKD				Non-CKD			
	KEEP		NHANES		KEEP		NHANES	
Characteristic	Diabetes	No Diabetes	Diabetes	No Diabetes	Diabetes	No Diabetes	Diabetes	No Diabetes
No. of participants	8,231	11,969	518	1,225	14,851	42,026	609	7,184
Age (y)								
18-30	1.3	4.0	—	10.0	2.7	11.0	3.0	27.9
31-45	7.2	13.5	14.3	15.9	15.9	27.2	19.9	34
46-60	27.4	28.7	29.5	22.4	39.8	36.5	39	25.5
61-75	44.7	34.3	32.9	26.2	34.1	20.2	32.5	10.2
>75	19.4	19.5	21.1	25.5	7.4	5.0	5.7	2.5
Sex								
Men	33.7	28.0	53.7	36.3	32.9	31.6	52.3	49.4
Women	66.3	72.0	46.3	63.7	67.1	68.4	47.7	50.6
Race								
White	53.0	56.8	66.3	75.9	48.8	45.6	67.4	72.2
African American	28.1	27.6	14.9	11.1	31.3	34.3	13.5	10.6
Others	18.9	15.5	18.8	13.0	19.9	20.1	19.1	17.1
Ethnicity								
Hispanic	9.5	8.2	15.2	9.0	11.9	12.7	13.3	12.8
Non-Hispanic	90.5	91.8	84.8	91.0	88.1	87.3	86.7	87.2
Education								
<High school	22.7	16.4	37.1	23.3	17.4	12.6	24.9	18.6
≥High school	77.3	83.6	62.9	76.7	82.6	87.4	75.1	81.4
Health insurance coverage								
Yes	85.1	85.4	91.9	89.1	81.5	79.6	87.7	80
No	14.9	14.6	8.1	10.9	18.5	20.4	12.3	20
Risk factors								
Current smoker	8.9	10.5	19.9	18.8	10.5	12.6	21.7	25.6
Obesity	56.5	38.6	55.4	31.9	55.9	39.5	56.3	29.3
Hypertension	93.7	85.7	90.3	75.1	84.6	56.1	76.4	27.9
Self-reported CVD	40.0	24.8	31.5	20.5	27.2	15.7	16.8	4.7
Proteinuria	54.7	41.6	74.1	60.9	0.0	0.0	0.0	0.0
Dyslipidemia	37.5	34.4	70.4	62.5	38.7	34.4	67.5	55.2
Missing	43.6	49.6			36.7	44.7		
Monthly prescription medication cost* ($)								
<20	13.0	16.5			17.0	25.0		
20-40	9.2	10.6			12.3	11.2		
41-75	8.6	7.7			10.5	6.3		
76-100	6.9	4.6			7.4	3.5		
101-250	9.2	4.4			8.2	2.8		
>250	4.5	1.7			3.0	1.0		
Missing value	48.5	54.5			41.7	50.2		
Medical practitioner*								
Family practice	65.4	63.4			65.0	61.0		
Internist	21.1	19.0			18.8	14.8		
Endocrinologist	11.5	1.5			10.2	1.4		
Obstetrician/gynecologist	11.6	18.2			17.0	23.9		
Nephrologist	5.2	3.8			1.4	1.0		
Cardiologist	13.4	7.9			8.7	4.3		
Gerontologist	1.3	1.1			0.8	0.5		
Physician assistant	2.7	1.7			2.6	1.6		
Nurse practitioner	3.5	2.1			3.9	2.5		
None	1.4	2.6			2.5	4.7		
Other/unknown	14.4	13.4			12.8	10.8		

Note: Values expressed as percent unless noted otherwise.

Abbreviations: CKD, chronic kidney disease; CVD, cardiovascular disease; KEEP, Kidney Early Evaluation Program; NHANES, National Health and Nutrition Examination Survey.

*Not available in NHANES data.

Table 3. Demographic Characteristic Distribution of KEEP Participants With Diabetes by CKD Stage and Awareness

	Stages 1-2 CKD			Stages 3-5 CKD			All CKD		
Characteristic	All	Unaware	Aware	All	Unaware	Aware	All	Unaware	Aware
No. of participants	2,548	2,394	154	5,305	4,723	582	7,853	7,117	736
Age (y)									
18-30	3.3	3.4	2.6	0.2	0.1	0.9	1.2	1.2	1.2
31-45	14.6	14.5	14.9	3.4	3.1	5.3	7.0	7.0	7.3
46-60	38.2	38.3	37.7	22.0	21.9	23.0	27.3	27.4	26.1
61-75	34.3	34.0	37.7	50.3	50.2	50.7	45.1	44.8	48.0
>75	9.6	9.8	7.1	24.1	24.6	20.1	19.4	19.6	17.4
Sex									
Men	37.3	37.4	35.7	31.6	30.4	41.8	33.5	32.8	40.5
Women	62.7	62.6	64.3	68.4	69.6	58.2	66.5	67.2	59.5
Race									
White	40.9	40.5	47.4	59.4	59.8	56.2	53.4	53.3	54.3
African American	35.2	36.0	23.4	24.3	24.4	23.7	27.9	28.3	23.6
Others	23.8	23.5	29.2	16.3	15.8	20.1	18.7	18.4	22.0
Ethnicity									
Hispanic	13.5	12.8	24.0	7.5	7.1	10.8	9.4	9.0	13.6
Non-Hispanic	86.5	87.2	76.0	92.5	92.9	89.2	90.6	91.0	86.4
Education									
<High school	22.8	22.4	29.1	22.5	22.5	22.3	22.6	22.5	23.7
≥High school	77.2	77.6	70.9	77.5	77.5	77.7	77.4	77.5	76.3
Health insurance coverage									
Yes	77.9	78.5	68.7	89.0	89.4	86.2	85.4	85.7	82.5
No	22.1	21.5	31.3	11.0	10.6	13.8	14.6	14.3	17.5
Risk factors									
Current smoker	13.5	13.5	14.1	6.3	6.3	6.5	8.6	8.7	8.1
Obesity	59.6	59.5	60.3	55.2	55.2	55.7	56.6	56.6	56.6
Hypertension	92.8	93.0	89.6	94.4	94.2	96.2	93.9	93.8	94.8
Self-reported CVD	34.5	34.0	42.2	43.3	41.5	57.4	40.4	39.0	54.2
Proteinuria	100.0	100.0	100.0	30.1	27.3	51.6	54.4	53.6	62.3
Dyslipidemia	38.7	38.2	46.1	36.7	35.5	46.4	37.3	36.4	46.3
Missing	42.9	43.3	35.7	44.5	46.5	28.2	44.0	45.5	29.8
Medical practitioner									
Family practice	63.8	64.5	53.2	66.7	66.8	66.0	65.8	66.1	63.3
Internist	18.1	18.2	16.9	22.7	22.7	22.7	21.2	21.2	21.5
Endocrinologist	12.2	12.0	14.9	11.8	10.7	21.0	11.9	11.1	19.7
Obstetrician/gynecologist	12.0	12.0	11.7	11.4	11.6	10.3	11.6	11.7	10.6
Nephrologist	2.4	1.5	16.2	6.6	3.3	33.2	5.2	2.7	29.6
Cardiologist	10.2	9.9	16.2	15.1	13.9	25.1	13.5	12.5	23.2
Gerontologist	0.8	0.9	0.0	1.5	1.5	1.5	1.3	1.3	1.2
Physician assistant	2.4	2.3	2.6	2.9	2.8	3.6	2.7	2.6	3.4
Nurse practitioner	3.5	3.5	4.5	3.6	3.5	4.1	3.6	3.5	4.2
None	2.1	2.0	3.2	0.9	0.9	1.2	1.3	1.3	1.6
Other/unknown	12.2	12.2	13.0	15.5	15.6	14.6	14.4	14.5	14.3
Albumin-creatinine ratio (mg/g)									
<30				69.9	72.7	48.4	45.6	46.4	37.7
30-300	89.3	90.0	78.6	22.5	21.3	31.6	45.7	46.1	41.9
>300	10.7	10.0	21.4	7.6	6.0	20.1	8.7	7.5	20.4
eGFR (mL/min/1.73 m^2)	86.9 ± 20.5	87.1 ± 20.4	83.6 ± 20.4	47.0 ± 10.5	48.1 ± 9.5	38.4 ± 13.3	60.0 ± 23.6	61.2 ± 23.3	47.9 ± 23.8

Note: Values expressed as percent or mean ± SD unless noted otherwise. Diabetes defined as self-reported history of diabetes or receiving medications for diabetes.

Abbreviations: CKD, chronic kidney disease; CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate; KEEP, Kidney Early Evaluation Program.

demia were greater than percentages of those unaware. This finding is similar to other KEEP reports, an indication that CKD awareness may increase in the presence of existing comorbidity.[22] Percentages of hypertension were high in participants both aware and unaware of CKD at stages 1 to 2 and 3 to 5. Based on our definition of CKD stage, all participants with stages 1 to 2 had proteinuria; however, at stages 3 to 5, a greater percentage of aware than unaware participants had proteinuria.

The presence of diabetes is associated with multiple comorbid conditions, including hypertension, obesity, and dyslipidemia, all of which have been associated with proteinuria. In measured clinical variables for KEEP participants

with CKD stages 1 and 2, we found a general trend toward greater mean systolic blood pressure, body mass index, and triglyceride levels in diabetic than nondiabetic participants across glycemia levels (Table 4). Interestingly, this effect was not observed for total cholesterol level.

To assess factors associated with glycemia in diabetic and nondiabetic groups both aware and unaware of CKD, we then examined the association between risk factors and target blood glucose levels less than 126 mg/dL fasting or less than 140 mg/dL nonfasting. In both aware and unaware participants with diabetes, men were less likely than women to meet optimal blood glucose levels (Table 5). Participants with diabetes who were aware they had CKD who also had comorbid obesity or a family history of diabetes were less likely than those without these conditions to meet glucose targets. Of note, unaware diabetic participants with comorbid hypertension or obesity or a family history of diabetes were also less likely to meet the target. Importantly, both diabetic and nondiabetic participants unaware of CKD who were defined as having stages 1 and 2 CKD were less likely to meet target glucose levels than unaware participants with stages 3 to 5. For unaware nondiabetic participants, factors associated with the likelihood of increased glucose levels were increasing age, male sex, African American or other race, comorbid obesity, and family history of diabetes.

DISCUSSION

This report of KEEP data highlights the relative similarities of diabetic participants with CKD in the KEEP and NHANES populations, as well as CKD awareness in participants with diabetes and prevalent CKD. Our observations are consistent with previous reports of KEEP data and other reports regarding awareness in patients with CKD.[23,24] Our collective findings in this and previous reports, that overt diabetes is associated with increased prevalence of CKD stages 1 to 2, corroborate previous reports of diabetes in patients with CKD.[25] Our data further complement previous investigations using general population screenings, such as NHANES,[26,27] regarding diabetes and CKD prevalence. Our report suggests that the KEEP health screening population is a more enriched CKD population than NHANES, with comorbid diabetes mellitus and CKD, largely because of the targeted nature of the screening program.

Importantly, regarding prevalence of comorbid risk factors in the diabetic populations in both KEEP and NHANES, age distribution was similar, but white men were underrepresented in KEEP compared with NHANES. Obesity (a major determinant of dysglycemia), hypertension (a frequent comorbid condition), and self-reported CVD were similar in KEEP and NHANES. Diabetic participants with and without CKD spent more on prescription medications than their nondiabetic counterparts in KEEP. Relatively few KEEP participants with self-reported or identifiable diabetes were receiving endocrinologist care, and most were cared for by family physicians. Overall, these data are consistent with our previously published articles and prior KEEP data reports.[28-32]

Diabetes prevalence is highest in the age group 65 years and older, although the largest increase in the last decade, corresponding to the obesity pandemic, is in the age group younger than 45 years.[33] The disproportionately greater diabetes prevalence and rate of increase in African Americans and Hispanics is well recognized.[34] Although the proportion of diabetic patients remains highest in the United States, the rapid increase in diabetes prevalence is occurring globally, and soon more than 300 million people worldwide will be affected as overnutrition and obesity become more likely than undernutrition.[33] Data from this report extend our understanding of the association of diabetes and CKD in the United States. CKD awareness was similar for diabetic and nondiabetic participants; our finding of an association between CKD awareness and such comorbid conditions as dyslipidemia, proteinuria, and CVD is novel[22] and emphasizes the notion that multiple comorbid conditions may be necessary to achieve the needed recognition to increase awareness and ultimately attention to individual medical care. Programs such as KEEP that deliver early aggressive CKD screening and promote awareness represent a timely and important public health care initiative.

We found it noteworthy that compared with CKD stages 3 to 5, unawareness of CKD status in participants defined as CKD stages 1 and 2 was associated with increased blood glucose levels regardless of diabetes status. The strength

Table 4. Clinical Variables by Deciles of Fasting Blood Glucose Levels and Diabetic Status (n = 1,265)

Variable	Fasting Blood Glucose (g/dL)			
	<83		83-<90	
	Diabetes*	No Diabetes	Diabetes*	No Diabetes
Systolic blood pressure (mm Hg)	148.2 ± 22.6	133.1 ± 22.4	139.2 ± 22.1	133.1 ± 22.7
Diastolic blood pressure (mm Hg)	86.5 ± 16.5	82.3 ± 11.9	82.1 ± 10.3	82.8 ± 13.6
Body mass index (kg/m^2)	30.9 ± 7.6	28.1 ± 7.1	31.7 ± 6.1	28.5 ± 7.3
Cholesterol (mg/dL)	194.3 ± 53.4	207.7 ± 47.1	187.3 ± 33.5	203.2 ± 43.1
Triglycerides (mg/dL)	100.9 ± 58.1	140.8 ± 305.7	137.8 ± 66.9	103.0 ± 49.1
eGFR (mL/min/1.73 m^2)	88.3 ± 18.2	92.4 ± 25.4	96.2 ± 20.6	89.2 ± 19.2
	90-<95		95-<100	
	Diabetes*	No Diabetes	Diabetes*	No Diabetes
Systolic blood pressure (mm Hg)	140.2 ± 20.0	135.5 ± 22.5	134.9 ± 19.5	137.0 ± 23.2
Diastolic blood pressure (mm Hg)	81.9 ± 13.4	83.1 ± 13.1	82.0 ± 13.5	84.5 ± 14.8
Body mass index (kg/m^2)	32.2 ± 8.5	30.0 ± 7.2	28.4 ± 5.3	29.7 ± 7.6
Cholesterol (mg/dL)	197.7 ± 56.1	204.4 ± 38.3	196.5 ± 42.6	205.7 ± 39.3
Triglycerides (mg/dL)	117.3 ± 39.9	108.7 ± 70.0	162.6 ± 144.9	133.9 ± 111.8
eGFR (mL/min/1.73 m^2)	88.1 ± 15.3	88.4 ± 18.6	87.1 ± 15.9	94.0 ± 24.2
	100-<105		105-<113	
	Diabetes*	No Diabetes	Diabetes*	No Diabetes
Systolic blood pressure (mm Hg)	129.5 ± 11.5	136.8 ± 28.1	138.4 ± 17.6	141.1 ± 24.7
Diastolic blood pressure (mm Hg)	81.8 ± 5.9	82.9 ± 14.1	80.0 ± 9.0	84.1 ± 13.0
Body mass index (kg/m^2)	32.4 ± 6.7	30.1 ± 7.6	32.3 ± 7.4	31.7 ± 8.4
Cholesterol (mg/dL)	185.7 ± 42.6	206.3 ± 41.3	193.6 ± 40.3	194.8 ± 34.8
Triglycerides (mg/dL)	128.6 ± 81.6	114.5 ± 71.6	149.1 ± 76.6	121.5 ± 64.1
eGFR (mL/min/1.73 m^2)	82.8 ± 15.4	91.2 ± 21.4	94.3 ± 30.6	90.4 ± 23.8
	113-<128		128-<152	
	Diabetes*	No Diabetes	Diabetes*	No Diabetes
Systolic blood pressure (mm Hg)	146.2 ± 22.2	141.8 ± 21.7	145.2 ± 23.8	
Diastolic blood pressure (mm Hg)	83.6 ± 9.8	85.3 ± 11.7	84.5 ± 13.1	
Body mass index (kg/m^2)	32.0 ± 7.0	30.7 ± 7.0	33.4 ± 7.6	
Cholesterol (mg/dL)	201.7 ± 47.0	221.6 ± 47.9	190.7 ± 44.8	
Triglycerides (mg/dL)	158.1 ± 124.1	139.9 ± 72.9	157.9 ± 84.5	
eGFR (mL/min/1.73 m^2)	87.5 ± 22.4	84.7 ± 19.8	87.0 ± 21.1	
	152-<213		≥213	
	Diabetes*	No Diabetes	Diabetes*	No Diabetes
Systolic blood pressure (mm Hg)	145.8 ± 19.6		142.0 ± 20.8	
Diastolic blood pressure (mm Hg)	85.0 ± 12.5		85.7 ± 12.1	
Body mass index (kg/m^2)	34.2 ± 7.6		33.1 ± 8.0	
Cholesterol (mg/dL)	205.0 ± 54.3		221.4 ± 53.2	
Triglycerides (mg/dL)	205.2 ± 138.0		251.5 ± 313.0	
eGFR (mL/min/1.73 m^2)	86.8 ± 20.7		96.5 ± 24.2	

Note: Values expressed as mean ± SD. Includes patients with stages 1 and 2 chronic kidney disease with fasting blood glucose values. Conversion factor for units: fasting blood glucose in mg/dL to mmol/L, ×0.05551; cholesterol in mg/dL to mmol/L, ×0.02586; triglycerides in mg/dL to mmol/L, ×0.01129; eGFR in mL/min/1.73 m^2 to mL/s/1.73 m^2, ×0.01667.

Abbreviation: eGFR, estimated glomerular filtration rate.

*Defined as self-reported history of diabetes, receiving medications for diabetes, or fasting blood glucose level of 126 mg/dL or greater.

Table 5. Odds of Diabetic and Nondiabetic KEEP Participants With CKD Having Target Blood Glucose Level (<126 mg/dL fasting or <140 mg/dL nonfasting) by CKD Awareness

	Diabetes*				No Diabetes			
	Aware CKD (n = 630)		Unaware CKD (n = 5,972)		Aware CKD (n = 753)		Unaware CKD (n = 9,502)	
	Odds Ratio (95% CI)	*P*	Odds Ratio (95% CI)	*P*	Odds Ratio (95% CI)	*P*	Odds Ratio (95% CI)	*P*
Age (y; reference, 46-60)								
18-30	1.51 (0.34-6.75)	0.6	0.89 (0.57-1.40)	0.6	2.11 (0.25-18.18)	0.5	2.63 (1.50-4.61)	<0.001
31-45	1.40 (0.72-2.72)	0.3	0.99 (0.80-1.23)	0.9	1.49 (0.49-4.52)	0.5	1.38 (1.05-1.81)	0.02
61-75	1.32 (0.88-1.98)	0.2	1.11 (0.97-1.26)	0.1	0.48 (0.23-0.99)	0.05	0.66 (0.54-0.80)	<0.001
>75	0.89 (0.52-1.53)	0.7	1.14 (0.96-1.34)	0.1	0.71 (0.30-1.69)	0.4	0.56 (0.44-0.71)	<0.001
Sex (reference, women)								
Men	0.50 (0.35-0.70)	<0.001	0.83 (0.74-0.93)	<0.001	0.94 (0.52-1.70)	0.8	0.80 (0.68-0.94)	0.007
Race (reference, white)								
African American	0.85 (0.57-1.28)	0.4	0.96 (0.85-1.09)	0.5	0.40 (0.21-0.75)	0.004	0.80 (0.67-0.95)	0.01
Others	0.61 (0.40-0.93)	0.02	0.71 (0.62-0.82)	<0.001	0.69 (0.32-1.50)	0.4	0.63 (0.51-0.77)	<0.001
Risk factors (reference, without)								
Current smoker	0.75 (0.41-1.38)	0.4	1.00 (0.83-1.20)	0.9	0.66 (0.28-1.54)	0.3	0.87 (0.68-1.11)	0.3
Hypertension	1.12 (0.55-2.26)	0.8	0.68 (0.54-0.84)	<0.001	1.83 (0.70-4.79)	0.2	0.82 (0.63-1.05)	0.1
Family history of diabetes	0.72 (0.50-1.04)	0.08	0.83 (0.74-0.93)	0.002	0.57 (0.32-1.00)	0.05	0.82 (0.70-0.95)	0.009
Family history of hypertension	0.97 (0.65-1.44)	0.9	1.15 (1.02-1.30)	0.03	0.61 (0.27-1.35)	0.2	1.26 (1.06-1.50)	0.009
Obesity	0.63 (0.45-0.89)	0.008	0.85 (0.77-0.95)	0.004	1.00 (0.55-1.81)	0.9	0.66 (0.56-0.77)	<0.001
CKD stage (reference, stages 3-5)								
1-2	0.83 (0.55-1.25)	0.4	0.69 (0.62-0.78)	<0.001	1.64 (0.68-3.96)	0.3	0.69 (0.58-0.81)	<0.001

Abbreviations: CI, confidence interval; CKD, chronic kidney disease; KEEP, Kidney Early Evaluation Program.
*Defined as self-reported history of diabetes or receiving medications for diabetes.

of the association at CKD stages 1 and 2 highlights the association of CKD in the insulin-resistant state and excess visceral adiposity. Insulin resistance has been associated with CKD in general population observational studies. In a report of 6,453 nondiabetic NHANES III participants, odds of CKD increased as levels of serum insulin, serum C peptide, hemoglobin A_{1c}, and insulin resistance increased.[26] Furthermore, recent evidence from the ARIC (Atherosclerosis Risk in Communities) Study, including 10,096 nondiabetic participants with normal baseline kidney function, showed that insulin-resistant participants have greater odds for incident CKD.[6] After adjustment for the subsequent development of diabetes and hypertension, during the 9 years of follow-up, these participants still had a greater risk of incident CKD.

Tight glycemic control in patients with both type 1 and type 2 diabetes is now widely accepted to reduce the risk of microvascular complications in the general population.[35,36] Observational studies suggest that tighter glycemic control is associated with reduced risk of these outcomes in patients with CKD.[10-12] The present report extends earlier observations and suggests that in diabetic KEEP participants with CKD, systolic blood pressure, obesity, and triglyceride levels are higher than for nondiabetic participants. In addition, in unaware diabetic participants, those with comorbid hypertension, obesity, or a family history of diabetes are less likely than those without these conditions to reach optimal blood glucose levels. Lack of CKD awareness with increased blood glucose levels in diabetic and nondiabetic KEEP participants emphasizes the relationship between dysglycemia and early stages of unidentified CKD.

Although the strength of our investigation is in the large sample size and generalizable data regarding a targeted CKD population compared with NHANES, its limitations are common to population studies, and conclusions for population-attributable risk may be limited. Screened participants are volunteers who likely were motivated by their recognized risk of CKD. Thus, diabetes rates were greater, possibly influencing other results. Comparisons between KEEP and NHANES data are limited to be qualitative rather than statistical because of differences in recruitment, design, and questionnaires. However, we believe the targeted nature of the KEEP screening program and the large sample size with clinical characteristics similar to the NHANES database allow for accurate definition of the diabetic CKD population in the United States. In

addition, our findings highlight the relationship between dysglycemia and early stages of unidentified CKD.

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