Prevalence of Chronic Kidney Disease in US Adults with Undiagnosed Diabetes or Prediabetes

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Background and objectives: Prevalence of chronic kidney disease (CKD) in people with diagnosed diabetes is known to be high, but little is known about the prevalence of CKD in those with undiagnosed diabetes or prediabetes. We aimed to estimate and compare the community prevalence of CKD among people with diagnosed diabetes, undiagnosed diabetes, prediabetes, or no diabetes.

Design, setting, participants, & measurements: The 1999 through 2006 National Health and Nutrition Examination Survey is a representative survey of the civilian, noninstitutionalized US population. Participants who were aged ≥20 years; responded to the diabetes questionnaire; and had fasting plasma glucose (FPG), serum creatinine, and urinary albumin-creatinine ratio measurements were included (N = 8188). Diabetes status was defined as follows: Diagnosed diabetes, self-reported provider diagnosis (n = 826); undiagnosed diabetes, FPG ≥126 mg/dl without self-reported diagnosis (n = 299); prediabetes, FPG ≥100 and <126 mg/dl (n = 2272); and no diabetes, FPG <100 mg/dl (n = 4791). Prevalence of CKD was defined by estimated GFR 15 to 59 ml/min per 1.73 m^2 or albumin-creatinine ratio ≥30 mg/g; adjustment was performed with multivariable logistic regression.

Results: Fully 39.6% of people with diagnosed and 41.7% with undiagnosed diabetes had CKD; 17.7% with prediabetes and 10.6% without diabetes had CKD. Age-, gender-, and race/ethnicity-adjusted prevalence of CKD was 32.9, 24.2, 17.1, and 11.8%, for diagnosed, undiagnosed, pre-, and no diabetes, respectively. Among those with CKD, 39.1% had undiagnosed or prediabetes.

Conclusions: CKD prevalence is high among people with undiagnosed diabetes and prediabetes. These individuals might benefit from interventions aimed at preventing development and/or progression of both CKD and diabetes.

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The prevalence of chronic kidney disease (CKD), characterized by either albuminuria or reduced kidney function, is >40% among adults with a diagnosis of diabetes (1). Recent data indicate that 13% of US adults have diabetes and that at least 25% of these adults' diabetes is undiagnosed. An additional 30% of US adults are at high risk for developing diabetes and are considered to have prediabetes (2,3). Despite the heavy burden of undiagnosed diabetes and prediabetes, relatively little is known about CKD prevalence in affected individuals.

In this study, we estimated the prevalence of CKD among a representative sample of US adults with undiagnosed diabetes and prediabetes, compared with that in adults with diagnosed or no diabetes, using 1999 through 2006 National Health and Nutrition Examination Survey (NHANES) data. We also examined whether the CKD prevalence among those with undiagnosed diabetes or prediabetes differed by demographic factors, socioeconomic status, and clinical indicators.

Materials and Methods

Study Design

The NHANES, conducted by the National Center for Health Statistics of the Centers for Disease Control and Prevention, consists of a standardized in-home interview, followed by a physical examination and

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blood and urine collection at a mobile examination center (MEC). Data from NHANES consist of 2-year representative samples of noninstitutionalized US civilian residents. All participants give written informed consent. The protocol was approved by the National Center for Health Statistics Research Ethics Review Board.

The combined data from the 1999 through 2000, 2001 through 2002, 2003 through 2004, and 2005 through 2006 continuous NHANES were examined. The study was limited to participants who were at least 20 years of age, underwent a MEC examination, provided self-reported information on diabetes, and had measured fasting plasma glucose (FPG; $N = 8188$). Participants who were pregnant or had estimated GFR (eGFR) <15 ml/min per 1.73 m^2 were excluded ($n = 550$). NHANES had a 70% response rate for MEC examinations among adults who were aged ≥20 years (http://www.cdc.gov/nchs/nhanes/nhanes_cps_totals.htm), and 94.3% (8188 of 8682) of the eligible MEC sample were analyzed in this study.

Measurements

FPG was measured using the hexokinase method, and glycohemoglobin was measured using HPLC at the University of Missouri-Columbia (1999 through 2004) and the University of Minnesota (2005 through 2006). Appropriate regression equations were applied to both FPG (http://www.cdc.gov/nchs/data/nhanes/nhanes_05_06/glu_d.pdf) and glycohemoglobin (http://www.cdc.gov/nchs/data/nhanes/nhanes_05_06/ghb_d.pdf) to make the data comparable across survey years.

Self-reported information on demographics (age, gender, race/ethnicity), socioeconomic status (education, insurance, income), and health conditions (diagnosed diabetes, hypertension) was obtained during the interview, as was prescription medication information, with the interviewer recording the names of medications from the bottles provided by the participant. Height and weight were measured during the MEC examination. Serum creatinine was measured by the modified kinetic method of Jaffe using different analyzers in different survey years. Random spot urine samples were obtained, and urine albumin and creatinine were measured using frozen specimens. Urine albumin was measured using solid-phase fluorescence immunoassay; urine creatinine was measured using the modified Jaffe kinetic method in the same laboratory.

Definitions

Diagnosed diabetes was defined by the answer "yes" to the question, "Have you ever been told by a doctor or other health professional that you have diabetes or sugar diabetes?" Those who answered "no" or "borderline" ($n = 43$) to the same question were classified according to their measured FPG only: Undiagnosed diabetes, FPG ≥126 mg/dl; prediabetes, FPG ≥100 but <126 mg/dl; and no diabetes, FPG <100 mg/dl (4).

We defined CKD as either reduced kidney function or elevated albuminuria, because reduced kidney function may occur even in the absence of albuminuria in those with type 2 diabetes (5,6). eGFR was calculated according to the Modification of Diet in Renal Disease (MDRD) Study (7) and Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) (8) equations for calibrated creatinine. We corrected serum creatinine levels in the 1999 through 2000 and 2005 through 2006 surveys, according to NHANES documentation (9). Albuminuria was defined by a urinary albumin-creatinine ratio of 30 to 300 mg/g (microalbuminuria) and >300 mg/g (macroalbuminuria). Because urine albumin measurements in NHANES were cross-sectional, we did not have data on persistent albuminuria, and the definitions of stages were therefore modified as follows: Stage 1, eGFR >90 ml/min per 1.73 m^2 and presence of albuminuria at a single measurement; stage 2, eGFR 60 to 89 ml/min per 1.73 m^2 and presence of albuminuria at a single measurement; and stages 3 and 4, eGFR 15 to 59 ml/min per 1.73 m^2.

Self-reported hypertension was defined by the answer "yes" to the question, "Have you ever been told by a doctor or other health professional that you have hypertension, or high BP?" Self-reported hypertension was used as another identified high-risk condition for which the participant might be followed for CKD. The use of diabetes medications was defined as any prescription for any of the drugs metformin HCl, insulin, glimepiride, glipizide, glyburide, pioglitazone, or rosiglitazone. Angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin II receptor blockers (ARBs), used to treat both hypertension and CKD, were also identified.

Statistical Analysis

Selected characteristics were compared across all four diabetes status groups, using χ^2 and Kruskal-Wallis tests for categorical and continuous variables, respectively. Bonferroni correction was used for additional pairwise comparisons of interest between groups (gender and race/ethnicity *versus* diabetes status). Unadjusted and adjusted CKD prevalence was calculated by diabetes status, and variance of proportions was estimated with Taylor series linearization, a standard approach for estimation of SEs for multistage samples that consist of many sampling units. Prevalence estimates were adjusted for age, gender, and race/ethnicity using multivariable logistic regression. Sensitivity analyses, in which diagnosed diabetes was also defined by use of diabetes medications and in which CKD was defined by various cutoffs of both reduced kidney function (eGFR 15 to 59 ml/min per 1.73 m^2) and albuminuria, were also performed to estimate the effects of possible misclassification of diabetes and CKD.

All analyses were performed using the svy commands in Stata 10.0 (Stata Corp, College Station, TX) to account for the complex sample design of the survey. $P < 0.05$ was considered statistically significant.

Results

Selected Characteristics by Diabetes Status

Individuals with diagnosed or undiagnosed diabetes were older and had higher FPG and glycohemoglobin than those with prediabetes or no diabetes (Table 1). The gender distribution differed significantly across all four diabetes groups; in pairwise comparisons, those with undiagnosed diabetes were more likely to be male than those with diagnosed diabetes ($P = 0.005$), and those with prediabetes were more likely to be male than those with no diabetes ($P < 0.001$). Overall, race/ethnicity differed across diabetes groups, and, in pairwise comparisons, non-Hispanic white individuals composed a larger proportion of those with undiagnosed diabetes, prediabetes, and no diabetes, relative to diagnosed diabetes ($P = 0.015$, <0.001, and <0.001, respectively). Individuals with prediabetes or no diabetes were more likely to have a higher education level and higher income than those with diagnosed or undiagnosed diabetes; those whose diabetes was diagnosed were more likely to be insured and have a routine site for health care than the other groups. Those with diagnosed diabetes, undiagnosed diabetes, or prediabetes were less likely to be smokers but were more likely to be obese than those with no diabetes. More than half of those with diagnosed or undiagnosed diabetes reported having hypertension, whereas only approximately one fifth of those

Table 1. Population characteristics by diabetes status, NHANES 1999 through 2006

Characteristic	Diabetes Status				P[a]
	Diagnosed Diabetes	Undiagnosed Diabetes	Prediabetes	No Diabetes	
n	826	299	2272	4791	—
Mean FPG (mg/dl)	153.0	166.5	107.1	90.7	<0.001
Mean glycohemoglobin (%)	7.21	7.04	5.49	5.23	<0.001
Mean age (years)	57.7	58.8	52.0	42.4	<0.001
Gender (%)					<0.001
male	48.4	63.0	59.9	43.9	
female	51.6	37.0	40.1	56.1	
Race/ethnicity (%)[b]					<0.001
non-Hispanic white	61.7	74.0	74.2	72.3	
non-Hispanic black	15.1	11.8	7.8	11.4	
Mexican American	8.4	6.6	7.7	7.1	
Education (%)					<0.001
less than high school	29.0	31.7	22.8	16.6	
high school or more	71.0	68.3	77.2	83.4	
Household income (%)					<0.001
<$20,000	26.6	24.1	18.3	15.0	
$20,000–$44,999	35.6	43.4	29.1	28.5	
$45,000–$74,999	20.1	15.9	26.6	26.7	
≥$75,000	17.7	16.6	26.1	29.8	
Insurance (%)					<0.001
not insured	8.9	16.8	17.3	19.4	
insured	91.1	83.2	82.7	80.6	
Routine site for health care (%)					<0.001
no	2.5[c]	10.3	15.8	16.5	
yes	97.5	89.7	84.2	83.5	
Smoking (%)					0.020
every day	18.6	17.4	19.0	22.3	
sometimes/not at all	81.4	82.6	81.0	77.7	
BMI (kg/m^2; %)					<0.001
≥30	55.3	55.1	39.7	24.6	
<30	44.7	44.9	60.3	75.4	
Self-reported hypertension (%)					<0.001
yes	60.3	54.6	36.6	20.9	
no	39.7	45.2	63.4	79.1	
ACEIs/ARBs (%)					<0.001
yes	20.8	11.0	7.5	3.0	
no	79.2	89.0	92.5	97.0	

Diagnosed diabetes, self-reported of diabetes diagnosis; undiagnosed diabetes, FPG ≥126 mg/dl and no self-report of diabetes; prediabetes, FPG ≥100 and <126 mg/dl and no self-report of diabetes; no diabetes, FPG <100 mg/dl and no self-report of diabetes. BMI, body mass index.

[a]Across all four groups of diabetes status, by χ^2 (categorical variables) and Kruskal-Wallis (continuous variables) tests.

[b]Other race/ethnicity not shown because of small sample sizes, but individuals in category are included in all analyses.

[c]Unreliable estimate: Relative SE ≥30%.

with no diabetes did. Reported ACEI/ARB use was low overall but highest among those with diagnosed diabetes (Table 1).

Prevalence of CKD by Diabetes Status

The unadjusted CKD prevalence using the MDRD Study equation (7) was 39.6 and 41.7% in those with diagnosed and undiagnosed diabetes, respectively (Figure 1A). In those with prediabetes, the CKD prevalence was 17.7%, compared with 10.6% in those with no diabetes. Prevalence was slightly lower but similar with the CKD-EPI equation (Figure 2A) (8), with slightly fewer individuals in later stages of CKD. Of those with diagnosed diabetes and CKD, 39.0% had stage 3 or 4 CKD, and for those with undiagnosed diabetes and CKD, 40.6% had stage 3 or 4 CKD. For those with prediabetes and CKD, 56.2% had

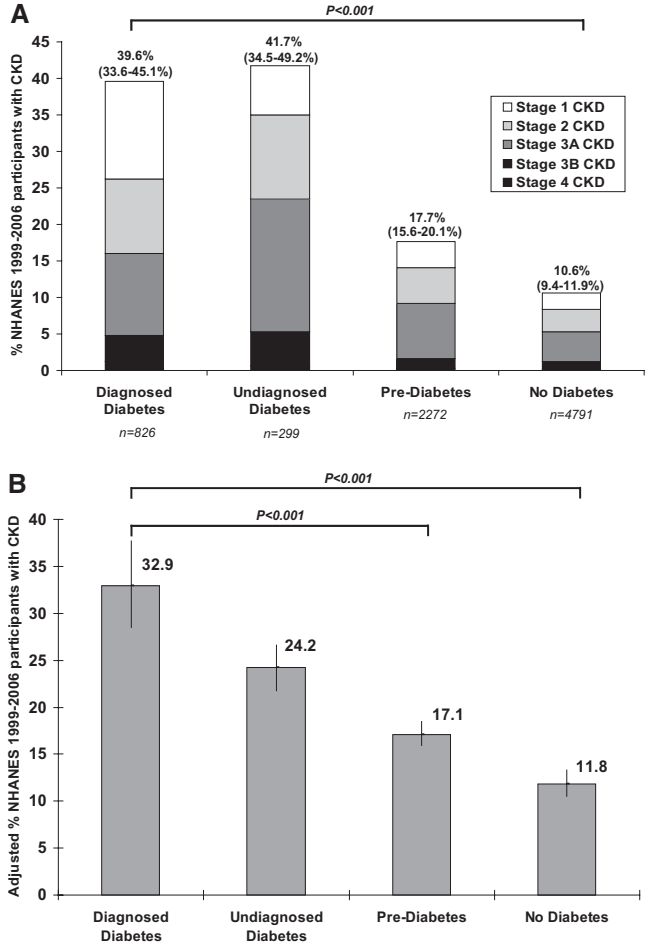

Figure 1. Unadjusted (A) and age-, gender-, and race/ethnicity-adjusted (B) population prevalence (%) of stages 1 through 4 CKD, with estimation of GFR by the MDRD Study equation, by diabetes status, NHANES 1999 through 2006. Diagnosed diabetes is defined as self-report of provider diagnosis; undiagnosed diabetes is defined as FPG ≥126 mg/ml, without a report of provider diagnosis; prediabetes is defined as FPG ≥100 and <126 mg/dl; and no diabetes is defined as FPG <100 mg/ml. CKD is defined by MDRD Study equation–calculated eGFR stage and a single determination of albuminuria (stages 1 and 2). Values in parentheses (A) and bars (B) represent 95% confidence intervals.

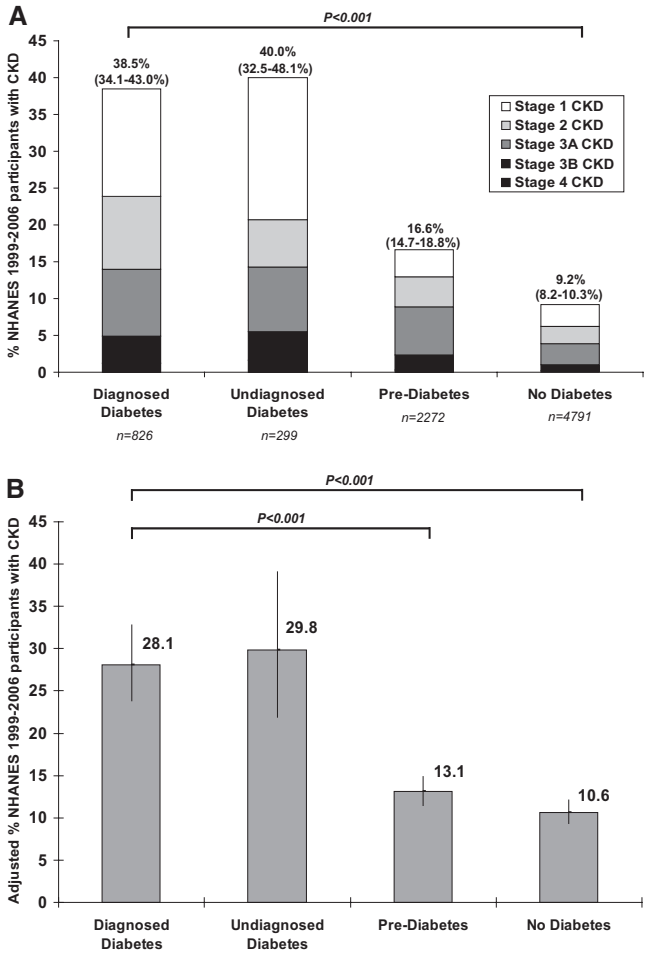

Figure 2. Unadjusted (A) and age-, gender-, and race/ethnicity-adjusted (B) population prevalence (%) of stages 1 through 4 CKD, with estimation of GFR by the CKD-EPI equation, by diabetes status, NHANES 1999 through 2006. Diagnosed diabetes is defined as self-report of provider diagnosis; undiagnosed diabetes is defined as FPG ≥126 mg/ml, without a report of provider diagnosis; prediabetes is defined as FPG ≥100 and <126 mg/dl; and no diabetes is defined as FPG <100 mg/ml. CKD is defined by CKD-EPI equation–calculated eGFR stage and a single determination of albuminuria (stages 1 and 2). Values in parentheses (A) and bars (B) represent 95% confidence intervals.

stage 3 or 4 CKD. Among those with stage 3 or 4 CKD, 19.4, 20.7, 18.0, and 14.5% of those with diagnosed diabetes, undiagnosed diabetes, prediabetes, and no diabetes, respectively, had evidence of albuminuria in addition to reduced kidney function (similar for CKD-EPI estimation; data not shown). Adjustment for estimated persistence of albuminuria (10) and for gender-specific cutoffs for albuminuria (11) resulted in slightly lower and higher prevalence, respectively, but similar patterns across diabetes categories (Tables 2 and 3). A much stricter definition of CKD (reduced kidney function and microalbuminuria, or macroalbuminuria alone (Tables 2 and 3) resulted in much lower but still substantial CKD prevalence, with similar patterns across diabetes categories. Similarly, defining CKD by reduced kidney function and albuminuria alone both resulted in lower prevalence estimates (particularly for reduced kidney function and macroalbuminuria alone) but similar patterns (Table 4).

After adjustment for age, gender, and race/ethnicity, CKD prevalence using the MDRD Study equation (7) was lower in those with undiagnosed *versus* diagnosed diabetes (24.2 *versus* 32.9%) and lower still among those with prediabetes (17.1%); adjusted prevalence was lowest among those with no diabetes (11.8%; Figure 1B). Adjusted prevalence was similar using the CKD-EPI equation (Figure 2B) (8). Age accounted for much of the difference between the unadjusted and adjusted CKD prevalence estimates. The undiagnosed and diagnosed groups had

Table 2. Unadjusted population CKD prevalence by diabetes status and CKD definition, with estimation of GFR by the MDRD Study equation, NHANES 1999 through 2006

Characteristic	Prevalence (95% CI) by Diabetes Status			
	Diagnosed Diabetes	Undiagnosed Diabetes	Prediabetes	No Diabetes
CKD defined by reduced kidney function (15 to 59 ml/min per 1.73 m^2) *or* microalbuminuria				
ACR ≥30	39.6 (35.1 to 44.3)	41.7 (34.5 to 49.2)	17.7 (15.6 to 20.1)	10.6 (9.4 to 11.9)
% with stage 1	10.4 (7.9 to 13.5)	14.1 (8.8 to 22.0)	2.7 (2.0 to 3.6)	2.0 (1.5 to 2.6)
% with stage 2	13.4 (10.4 to 17.0)	10.7 (7.4 to 15.0)	4.7 (3.8 to 6.0)	2.6 (2.2 to 3.2)
% with stage 3A	10.0 (6.9 to 14.1)	11.9 (8.3 to 16.8)	7.4 (6.1 to 8.9)	4.1 (3.4 to 5.0)
% with stage 3B	4.1 (2.7 to 6.4)	3.7 (1.9 to 6.9)	1.9 (1.4 to 2.6)	0.7 (0.5 to 1.0)
% with stage 4	1.1 (0.5 to 2.3)	1.3 (0.5 to 3.7)	0.8 (0.1 to 0.5)	0.2 (0.0 to 0.3)
estimated persistence of ACR ≥30[a]	32.5 (26.5 to 38.8)	32.3 (25.5 to 39.2)	14.8 (12.9 to 16.8)	8.0 (6.9 to 9.0)
gender-specific ACR[b]	44.3 (39.3 to 49.4)	48.7 (39.8 to 57.7)	21.5 (19.9 to 23.7)	12.9 (11.7 to 14.2)
CKD defined by reduced kidney function (15 to 59 ml/min per 1.73 m^2) *and* microalbuminuria *or* macroalbuminuria alone				
ACR ≥30, *or* ACR >300	11.1 (8.4 to 14.6)	6.6 (3.8 to 11.3)	3.7 (3.1 to 4.5)	2.4 (1.9 to 3.0)
gender-specific ACR[b]	13.0 (10.3 to 16.4)	8.4 (4.6 to 14.9)	4.4 (3.7 to 5.4)	2.6 (2.1 to 3.2)

$P < 0.001$ across diabetes categories for all definitions listed. ACR, albumin-creatinine ratio; CI, confidence interval.
[a]Estimated persistence of albuminuria based on previous study (10) from repeat sampling in a subset of NHANES III.
[b]Gender-specific cutoffs (11) were as follows: Microalbuminuria, ACR ≥17 mg/g and ≥25 mg/g, and macroalbuminuria, ACR ≥250 and ≥355 mg/g, for men and women, respectively.

greater proportions of individuals aged ≥60 years than the prediabetes and no diabetes groups (45.6 and 44.0 *versus* 31.0 and 14.4%, respectively); however, even after adjustment for the differences in age distributions among diabetes groups, CKD prevalence was higher among those with undiagnosed and diagnosed diabetes than among those with prediabetes and no diabetes. Further adjustment for gender and race/ethnicity did not change the estimates substantially, regardless of estimation equation; neither did additional adjustment for insurance, income, self-reported hypertension or cardiovascular disease, reported use of ACEI/ARBs or diuretics, or body mass index (data not shown). Among all individuals who were identified in this cohort as having CKD by the MDRD Study equation, 19.4% had diagnosed diabetes, 7.7% had undiagnosed diabetes, 31.4% had prediabetes, and 41.5% had no diabetes (19.4, 7.7, 31.4, and 41.5% for CKD-EPI).

Prevalence of CKD among Individuals with Prediabetes and No Diabetes, by Selected Characteristics

Those with prediabetes had higher adjusted CKD prevalence than those with no diabetes; for those who were aged ≥60 years, the difference was not statistically significant (Tables 5 and 6). Women with prediabetes had higher CKD prevalence than did women with no diabetes; the difference was NS for men. After adjustment for demographics, CKD prevalence was higher in those with prediabetes regardless of body mass index or self-reported hypertension, although the differences were not statistically significant using CKD-EPI (Table 6). Results were similar without adjustment: 11.6 and 8.3% of those with prediabetes and no diabetes, respectively, and no individuals with self-reported hypertension had CKD by the MDRD Study equation (9.6 and 6.5% for CKD-EPI).

Smoking, insurance status, and having a routine site for health care were not significantly associated with CKD among those with prediabetes or no diabetes, regardless of estimating equation or FPG; higher education and income were associated with lower CKD prevalence for all participants, but the associations were statistically significant only for those with no diabetes (data not shown). In sensitivity analyses in which those who were on medications for diabetes were considered to have a diagnosis regardless of self-report, 32 participants (18 with undiagnosed diabetes, 12 with prediabetes, and two with no diabetes) became participants with diagnosed diabetes; however, results using this classification were nearly identical to those in Table 2 (data not shown).

Discussion

We found that CKD prevalence, as estimated by reduced kidney function and presence of albuminuria, was high among those with diabetes, regardless of diagnosis status or GFR estimating equation; approximately 40% of those with undiagnosed diabetes showed evidence of CKD. By applying our final CKD and diabetes prevalence estimates from NHANES to available US Census data on noninstitutionalized adult civilian residents, we estimate that up to 13 million US adults may have

Table 3. Unadjusted population CKD prevalence by diabetes status and CKD definition, with estimation of GFR by the CKD-EPI equation, NHANES 1999 through 2006

Characteristic	Prevalence (95% CI) by Diabetes Status			
	Diagnosed Diabetes	Undiagnosed Diabetes	Prediabetes	No Diabetes
CKD defined by reduced kidney function (15 to 59 ml/min per 1.73 m^2) *or* microalbuminuria				
ACR ≥30	38.5 (34.1 to 43.0)	40.0 (32.5 to 48.1)	16.6 (14.7 to 18.8)	9.2 (8.2 to 10.3)
% with stage 1	14.3 (11.3 to 17.9)	19.3 (14.0 to 26.1)	3.5 (2.7 to 4.6)	2.6 (2.0 to 3.4)
% with stage 2	9.7 (7.7 to 12.1)	6.5 (3.9 to 10.4)	3.9 (3.0 to 5.2)	2.1 (1.6 to 2.7)
% with stage 3A	9.0 (6.3 to 12.7)	8.8 (5.7 to 13.2)	6.3 (5.2 to 7.6)	2.5 (2.0 to 3.1)
% with stage 3B	3.6 (2.2 to 5.8)	3.9 (2.0 to 7.1)	1.9 (1.4 to 2.6)	0.8 (0.5 to 1.1)
% with stage 4	1.2 (0.6 to 2.4)	1.6 (0.6 to 3.6)	0.3 (0.2 to 0.6)	0.2 (0.0 to 0.3)
estimated persistence of ACR ≥30[a]	30.3 (25.0 to 35.7)	33.9 (26.2 to 42.2)	14.3 (10.5 to 20.0)	6.4 (2.5 to 10.4)
gender-specific ACR[b]	42.7 (37.9 to 47.6)	47.2 (38.0 to 56.6)	20.4 (18.4 to 22.4)	11.5 (10.5 to 12.7)
CKD defined by reduced kidney function (15 to 59 ml/min per 1.73 m^2) *and* microalbuminuria *or* macroalbuminuria alone				
ACR ≥30, *or* ACR >300	10.9 (8.2 to 14.4)	6.6 (3.8 to 11.3)	3.7 (3.1 to 4.5)	2.3 (1.8 to 2.9)
gender-specific ACR[b]	12.5 (9.8 to 15.9)	8.4 (4.6 to 14.9)	4.4 (3.6 to 5.3)	2.5 (2.1 to 3.1)

$P < 0.001$ across diabetes categories for all definitions listed. ACR, albumin-creatinine ratio; CI, confidence interval.
[a]Estimated persistence of albuminuria based on previous study (10) from repeat sampling in a subset of NHANES III.
[b]Gender-specific cutoffs (11) were as follows: Microalbuminuria, ACR ≥17 mg/g and ≥25 mg/g, and macroalbuminuria, ACR ≥250 and ≥355 mg/g, for men and women, respectively.

Table 4. Unadjusted population prevalence of reduced kidney function and albuminuria by diabetes status, NHANES 1999 through 2006

Characteristic	Prevalence (95% CI) by Diabetes Status			
	Diagnosed Diabetes	Undiagnosed Diabetes	Prediabetes	No Diabetes
Reduced kidney function (15 to 59 ml/min per 1.73 m^2) only				
CKD-EPI estimation of GFR	14.0 (10.5 to 18.4)	13.8 (10.1 to 18.6)	8.5 (7.3 to 10.0)	3.4 (2.9 to 4.0)
MDRD estimation of GFR	15.7 (11.6 to 21.0)	16.3 (12.3 to 21.4)	9.7 (8.2 to 11.4)	4.9 (4.1 to 5.8)
Albuminuria only				
microalbuminuria: ACR ≥30	29.2 (25.0 to 33.8)	29.2 (23.1 to 37.6)	9.7 (8.4 to 11.2)	5.8 (5.0 to 6.7)
macroalbuminuria: ACR ≥300	7.7 (4.7 to 10.6)	3.3 (1.4 to 7.7)	1.1 (0.8 to 1.6)	0.6 (0.4 to 0.9)
microalbuminuria: gender-specific ACR[a]	35.2 (30.4 to 40.4)	39.8 (31.8 to 48.4)	14.2 (12.6 to 15.9)	8.7 (7.8 to 9.6)
macroalbuminuria: gender-specific ACR[a]	7.0 (4.8 to 9.9)	4.8 (1.8 to 12.1)	1.2 (0.9 to 1.7)	0.6 (0.4 to 0.9)

$P < 0.001$ across diabetes categories for all definitions listed. ACR, albumin-creatinine ratio; CI, confidence interval.
[a]Gender-specific cutoffs (11) were as follows: Microalbuminuria, ACR ≥17 mg/g and ≥25 mg/g, and macroalbuminuria, ACR ≥250 and ≥355 mg/g, for men and women, respectively.

undiagnosed or prediabetes and CKD. Although 42% of CKD cases occurred in those without diabetes, 39% of cases occurred in those with undiagnosed diabetes or prediabetes.

A substantial proportion of adults with undiagnosed diabetes had evidence of kidney damage and/or kidney function decline. Current standards of diabetes care recommend annual CKD screening among those with diabetes (12); however, this screening is unlikely to occur in those with undetected diabetes

Table 5. Adjusted prevalence of CKD, by MDRD Study equation estimation of GFR, among those with prediabetes *versus* no diabetes, by selected characteristics, NHANES 1999 through 2006

Characteristic	% with Stages 1 through 4 CKD (95% CI)		
	Prediabetes	No Diabetes	P[a]
Overall	17.1 (15.9 to 18.5)	11.8 (10.5 to 13.3)	<0.001
Age (years)			
20 to 59	11.7 (10.6 to 12.9)	6.3 (5.4 to 7.4)	0.001
≥60	36.9 (34.3 to 39.5)	31.5 (28.4 to 34.8)	0.164
Gender			
male	14.3 (12.9 to 15.8)	8.1 (6.9 to 9.6)	0.172
female	18.6 (17.0 to 20.4)	13.3 (11.5 to 15.4)	0.001
Race/ethnicity[b]			
non-Hispanic white	15.8 (14.4 to 17.2)	10.7 (9.3 to 12.3)	0.005
non-Hispanic black	20.4 (18.3 to 22.7)	12.9 (10.9 to 15.3)	0.036
Mexican American	14.5 (12.7 to 16.6)	7.6 (6.0 to 9.5)	0.035
BMI (kg/m^2)			
<30	14.6 (13.1 to 16.3)	9.7 (8.5 to 11.2)	0.017
≥30	17.9 (15.8 to 20.2)	11.5 (9.6 to 13.8)	0.008
Self-reported hypertension			
yes	29.5 (27.1 to 31.9)	21.6 (18.7 to 24.8)	0.011
no	10.7 (9.3 to 12.4)	7.1 (6.0 to 8.3)	0.121

CKD defined by MDRD Study equation–calculated eGFR <60 ml/min per 1.73 m^2 or single micro/macroalbuminuria measurement; prediabetes, FPG ≥100 and <126 mg/dl and no self-report of diabetes; no diabetes, FPG <100 mg/dl and no self-report of diabetes. BMI, body mass index; CI, confidence interval.

[a]Prevalence estimates adjusted for age, gender, and race/ethnicity, excluding variables being examined (*e.g.*, age-stratified prevalence adjusted for gender and race/ethnicity only). Models that produced prevalence estimates included individuals in all four categories of diabetes status; models that produced P values included only those with prediabetes or no diabetes.

[b]Prevalence for other race/ethnicity not shown because of small sample sizes, but individuals in category are included in all analyses.

unless the person has another risk factor that is being treated, such as hypertension. We showed that many in the community (approximately 10% of those with undiagnosed diabetes) do not have a routine site for health care and are likely not being followed for any CKD risk factors; however, we found that even having insurance and a routine site for health care or having a condition that is known to increase CKD risk (hypertension), which might improve preventive care as a result of increased access or earlier screening, were not associated with lower CKD prevalence among those with diabetes. Thus, greater community awareness of diabetes and its risk factors may be needed to improve detection of both diabetes and subsequent CKD among these individuals. Greater awareness of diabetes might allow for detection and treatment of both conditions to help prevent progression and complications (13).

There have been calls for CKD screening among those with prediabetes (14); however, current guidelines recommend CKD screening only among those with diabetes (10). We have shown that a substantial burden of CKD exists in those with prediabetes. This confirms previous cross-sectional studies that showed that kidney damage was detectable in individuals with undiagnosed diabetes and in those with impaired fasting glucose (15,16). Our work is consistent with a cohort study that found that those with impaired fasting glucose or newly diagnosed diabetes were at increased risk for CKD (17). In fact, we found that CKD prevalence in individuals with prediabetes and no self-reported hypertension was approximately 10%. Thus, many individuals with prediabetes and without diagnosed hypertension—a risk factor for which CKD screening is recommended—are at risk for CKD, suggesting that those with prediabetes might be appropriate for CKD screening as well (18). Although more than half of those with prediabetes and evidence of CKD had reduced kidney function, only approximately 20% of those individuals had micro- or macroalbuminuria. Thus, both urinary protein and kidney functional measurements would need to be performed to determine CKD status in adults with prediabetes, as is recommended for those with diabetes (12). Diagnosis of prediabetes might make CKD screening more effective, and campaigns to promote awareness of both kidney damage and decline in kidney function at this early stage—targeted at both physicians and the community—may be beneficial (19). In addition, screening for prediabetes in those with hypertension could be even more important, given the compounding effect of these two conditions in increasing CKD risk (20).

Although recent studies (21–23) showed improved management of various risk factors for CKD in the general US population with and without diabetes since NHANES 1988 through 1994, the prevalence of diabetes continues to increase, in large part because of increasing obesity (24,25). The proportion of

Table 6. Adjusted prevalence of CKD, by CKD-EPI equation estimation of GFR, among those with prediabetes *versus* no diabetes, by selected characteristics, NHANES 1999 through 2006

Characteristic	% with Stages 1 through 4 CKD (95% CI)		
	Prediabetes	No Diabetes	P[a]
Overall	13.1 (11.5 to 14.9)	10.6 (9.3 to 12.1)	0.012
Age (years)			
20 to 59	8.7 (7.0 to 10.9)	5.6 (4.7 to 6.7)	0.001
≥60	35.1 (32.6 to 37.6)	29.4 (26.2 to 32.8)	0.052
Gender			
male	9.9 (8.4 to 11.7)	9.0 (7.5 to 10.7)	0.580
female	17.1 (14.0 to 20.1)	12.5 (10.5 to 14.7)	0.009
Race/ethnicity[b]			
non-Hispanic white	18.9 (10.8 to 15.4)	10.6 (9.0 to 12.4)	0.042
non-Hispanic black	17.3 (13.4 to 22.1)	13.1 (10.8 to 15.9)	0.130
Mexican American	12.5 (9.5 to 16.2)	8.1 (6.0 to 10.7)	0.056
BMI (kg/m^2)			
<30	11.3 (9.6 to 13.4)	9.5 (8.0 to 11.1)	0.073
≥30	14.7 (12.0 to 17.9)	12.0 (10.0 to 14.9)	0.194
Self-reported hypertension			
yes	26.7 (22.7 to 31.0)	22.9 (19.7 to 26.5)	0.217
no	8.3 (6.7 to 10.2)	6.9 (5.8 to 8.4)	0.100

CKD defined by CKD-EPI equation–calculated eGFR <60 ml/min per 1.73 m^2 or single micro/macroalbuminuria measurement; prediabetes, FPG ≥100 and <126 mg/dl and no self-report of diabetes; no diabetes, FPG <100 mg/dl and no self-report of diabetes.

[a]Prevalence estimates adjusted for age, gender, and race/ethnicity, excluding variables being examined (*e.g.*, age-stratified prevalence adjusted for gender and race/ethnicity only). Models that produced prevalence estimates included individuals in all four categories of diabetes status; models that produced P values included only those with prediabetes or no diabetes.

[b]Prevalence for other race/ethnicity not shown because of small sample sizes, but individuals in category are included in all analyses.

those who had diabetes and developed CKD, however, remained stable during the same period (1), suggesting that the increasing incidence and/or duration of diabetes is the main driver for the increase in the number of individuals with CKD. Hence, identification of diabetes and prediabetes cases and screening recommendations for CKD may be insufficient without appropriate diabetes management to prevent onset of CKD. Indeed, the stable incidence of ESRD since 2001 suggests that treatments with ACEIs and ARBs, although slowing the progression of CKD, may not prevent the development of kidney disease as well as rigorous glycemic control (26). Further research would be useful to clarify the relative benefits of glycemic control *versus* treatment with ACEIs and ARBs with regard to CKD progression.

Even with identification of diabetes and prediabetes cases and screening recommendations, appropriate CKD management is required to prevent progression and complications. We found that the proportions of those who were treated with ACEIs/ARBs, medications that are known to prevent CKD progression, were low among those with undiagnosed diabetes and prediabetes (approximately 11% and approximately 8% in those with undiagnosed diabetes and prediabetes, respectively). Moreover, even among those with CKD and diagnosed diabetes, only approximately 21% were on a recommended ACEI/ARB, likely for hypertension or other therapeutic use, despite the confirmed antiproteinuric effect of these medicines and their cost-effectiveness in delaying the progression of CKD (27). These results are consistent with a recent study (21) that showed that the association of diabetes and CKD has not changed over time, suggesting that there may still be room for improvement in the management of diabetes in terms of CKD. Thus, physicians could further improve their understanding and use of guidelines for CKD management in the setting of diabetes (28,29) and also improve their communication with patients regarding CKD and its management.

This study is subject to several limitations. First, the study design did not allow us to follow the development of CKD. Second, the duration of diabetes is not known; longer exposure to hyperglycemia could increase the risk for CKD (30). There could be missed cases of diagnosed diabetes; sensitivity analyses that evaluated use of diabetes medications suggested that this occurred rarely. Some cases of prediabetes were likely missed, because prediabetes can be defined by either impaired fasting glucose or impaired glucose tolerance (only available in NHANES 2005 through 2006). There was also likely some misclassification of early-stage CKD as a result of limitations in GFR estimation and single spot urine measurements. Some transient albuminuria is possible (especially among women who may have urinary tract infections or be menstruating, although we found no cases of CKD among the 177 women in

our sample who self-reported menstruating at the time of examination). Sensitivity analyses that used various definitions of CKD using different estimating equations and cutoffs for eGFR and albuminuria suggested that CKD prevalence may be overestimated in general but that prevalence among those with undiagnosed diabetes and prediabetes was always significantly higher than the prevalence among those with no diabetes. Finally, causality cannot be established from a cross-sectional survey.

Conclusions

A high burden of CKD exists among individuals with undiagnosed diabetes and individuals with prediabetes. In keeping with our results, individuals with prediabetes warrant earlier detection and management efforts to prevent development, progression, and complications of both diabetes and CKD associated with diabetes. Possible interventions, perhaps first targeting obese individuals, who are most at risk for prediabetes, to prevent CKD and its progression in this population should be explored in further studies.

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Disclosures

None.

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See related editorial, "Prediabetes, Prehypertension . . . Is It Time for Pre-CKD?" on pages 557–559.