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Clinical Manifestations of Kidney Disease Among US Adults With Diabetes, 1988–2014

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Abstract

IMPORTANCE—Diabetic kidney disease is the leading cause of chronic and end-stage kidney disease in the United States and worldwide. Changes in demographics and treatments may affect the prevalence and clinical manifestations of diabetic kidney disease.

OBJECTIVE—To characterize the clinical manifestations of kidney disease among US adults with diabetes over time.

DESIGN, SETTING, AND PARTICIPANTS—Serial cross-sectional studies of adults aged 20 years or older with diabetes mellitus participating in National Health and Nutrition Examination Surveys from 1988 through 2014.

EXPOSURES—Diabetes was defined as hemoglobin A_{1c} greater than 6.5% or use of glucose-lowering medications.

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Study concept and design: Heagerty, Tuttle, Weiss, de Boer.
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Statistical analysis: Zelnick, Heagerty.
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Study supervision: Hall, de Boer.

MAIN OUTCOMES AND MEASURES—Albuminuria (urine albumin-to-creatinine ratio≥30 mg/g), macroalbuminuria (urine albumin-to-creatinine ratio≥300 mg/g), reduced estimated glomerular filtration rate (eGFR <60 mL/min/1.73m^2), and severely reduced eGFR (<30 mL/min/1.73m^2), incorporating data on biological variability to estimate the prevalence of persistent abnormalities.

RESULTS—There were 6251 adults with diabetes included (1431 from 1988–1994, 1443 from 1999–2004, 1280 from 2005–2008, and 2097 from 2009–2014). The prevalence of any diabetic kidney disease, defined as persistent albuminuria, persistent reduced eGFR, or both, did not significantly change over time from 28.4%(95% CI, 23.8%–32.9%) in 1988–1994 to 26.2% (95% CI, 22.6%–29.9%) in 2009–2014 (prevalence ratio, 0.95 [95%CI, 0.86–1.06] adjusting for age, sex, and race/ethnicity; $P = .39$ for trend). However, the prevalence of albuminuria decreased progressively over time from 20.8%(95%CI, 16.3%–25.3%) in 1988–1994 to 15.9%(95%CI, 12.7%–19.0%) in 2009–2014 (adjusted prevalence ratio, 0.76 [95%CI, 0.65–0.89]; $P < .001$ for trend). In contrast, the prevalence of reduced eGFR increased from 9.2%(95%CI, 6.2%–12.2%) in 1988–1994 to 14.1%(95%CI, 11.3%–17.0%) in 2009–2014 (adjusted prevalence ratio, 1.61 [95%CI, 1.33–1.95] comparing 2009–2014 with 1988–1994; $P < .001$ for trend), with a similar pattern for severely reduced eGFR (adjusted prevalence ratio, 2.86 [95%CI, 1.38–5.91]; $P = .004$ for trend). Significant heterogeneity in the temporal trend for albuminuria was noted by age ($P = .049$ for interaction) and race/ethnicity ($P = .007$ for interaction), with a decreasing prevalence of albuminuria observed only among adults younger than 65 years and non-Hispanic whites, whereas the prevalence of reduced GFR increased without significant differences by age or race/ethnicity. In 2009–2014, approximately 8.2 million adults with diabetes (95%CI, 6.5–9.9 million adults) had albuminuria, reduced eGFR, or both.

CONCLUSIONS AND RELEVANCE—Among US adults with diabetes from 1988 to 2014, the overall prevalence of diabetic kidney disease did not change significantly, whereas the prevalence of albuminuria declined and the prevalence of reduced eGFR increased.

Diabetes mellitus is the most common cause of chronic kidney disease in the world, leading to multiple complications including end-stage renal disease, cardiovascular disease, infection, and death.[1] Chronic kidney disease in the setting of diabetes or diabetic kidney disease (DKD), manifests clinically as albuminuria, reduced glomerular filtration rate (GFR), or both. Over the last 20 years, the prevalence of diabetes and DKD have increased.[2]

The natural history of DKD traditionally has been described as progressive albuminuria followed by a steady loss of GFR.[3] However, this natural history may have changed over the last 2 decades. In particular, GFR loss has been observed prior to the development of albuminuria,[4–6] a reduced GFR without albuminuria has been frequently described,[6–9] and albuminuria has been observed to be transient or reversible.[10–14] Changes in diabetes management over time include increased use of intensive glycemic control, improved blood pressure control, and increased use of renin-angiotensin-aldosterone system (RAAS) inhibitors.[2] In this context, the prevalence of reduced GFR was previously reported to have increased among adults with diabetes in the United States from 1988 to 2008, whereas significant changes in albuminuria were not observed.[2]

In this study, temporal trends in albuminuria and reduced GFR were evaluated through 2014. Compared with prior analyses, more advanced DKD manifestations were evaluated, subgroups defined by age, race, and ethnicity were examined, and new data on persistence of abnormalities were incorporated. The overall goal was to identify priorities for DKD screening, target implementation of existing interventions, and design clinical trials for new treatments.

Methods

Study Population

The population-based National Health and Nutrition Examination Survey (NHANES) is a program of studies conducted by the National Center for Health Statistics designed to assess the prevalence of disease, disease risk factors, and nutritional status of adults and children in the United States. It uses a probability sampling design to select participants representative of the civilian, non institutionalized US population.[15] NHANESIII took place in 1988–1994. Starting in 1999, NHANES became a continuous program, with data compiled in 2-year blocks. Health examinations including physical measurements and blood and urine collections are conducted at a mobile examination center. Each NHANES cycle oversamples persons of black race, Hispanic ethnicity, or both. The current study includes participants in NHANES III, NHANES1999–2004, NHANES 2005–2008, and NHANES 2009–2014 who were aged 20 years or older, underwent a health examination in the NHANES mobile examination center, and had available data for medication use, hemoglobin A_{1c}, serum creatinine concentration, and urine albumin and creatinine concentrations. All NHANES protocols were approved by the research ethics review board of the National Center for Health Statistics, and all participants signed written informed consent forms.

Participants with diabetes mellitus, defined as use of glucose-lowering medications (insulin or oral hypoglycemic medications), hemoglobinA_{1c} of 6.5%or greater, or both, were included in the present analyses.[16,17] HemoglobinA_{1c} was measured in all NHANES cycles using high-pressure liquid chromatography (coefficients of variation <3.0%).[15] Self-reported history of diabetes was not used to define it because temporal changes in diabetes screening and diagnosis could lead to diabetes populations with differing disease severity over time and biased estimates of DKD prevalence. Fasting glucose or glucose concentrations following anoral glucose tolerance test also were not used to define diabetes because these criteria would reduce the numbers of participants available for the analyses and the power of the study.

Diabetic Kidney Disease

During NHANES mobile examination center screenings, urine albumin concentration was measured in a random, single voided urine sample using a solid-phase fluorescent immunoassay and creatinine concentration was measured using a Jaffe rate reaction. *Albuminuria* was defined as a urine albumin to-creatinine ratio (ACR) of 30 mg/g or greater, and *macroalbuminuria* was defined as a urine ACR of 300 mg/g or greater.[4,16] Serum creatinine concentrations were measured by a kinetic rate Jaffe method, and values from NHANESIII and NHANES 1999–2000 were calibrated as previously described to account

for laboratory drift in serum creatinine across NHANES cycles.[15,18–20] Glomerular filtration rate was estimated from calibrated serum creatinine using the Chronic Kidney Disease Epidemiology Collaboration equation.[21] Reduced estimated GFR (eGFR) was defined as less than 60 mL/min/1.73 m^2 and severely reduced eGFR as less than 30 mL/min/1.73 m^2.[4] Any DKD was defined as albuminuria, reduced eGFR, or both.

To account for the biological variability inherent in urine ACR and serum creatinine measurements, the persistence of albuminuria and reduced eGFR was calculated among subsets of participants with repeat measurements of urine ACR or eGFR. Persistence was evaluated as the proportions of participants with abnormal values whose values were also abnormal on repeat testing (described in eMethods in the Supplement). Estimates of persistence were incorporated into the prevalence estimates as described below in the statistical methods section.

Other Clinical Characteristics

Age, sex, race/ethnicity, and duration of diabetes were assessed by questionnaire.[15] Race/ethnicity was categorized as non-Hispanic white, non-Hispanic black, Mexican American, other Hispanic, and other or unknown race (including multiracial). Participants of all races and ethnicities were included in the analyses, and estimates were reported for non-Hispanic white, non-Hispanic black, and Mexican American race/ethnicity only. *Type 1 diabetes* was defined for descriptive purposes only using the following criteria: (1) diagnosis prior to 30 years of age; (2) first use of insulin within 2 years of diabetes diagnosis; and (3) current insulin use. Medications taken during a 1-month period preceding the NHANES physical examination were assessed by in-person interview.[15] Medication data for 2009–2014 were based only on information from NHANES 2009–2012 because medication data were not available for NHANES 2013–2014 at the time of analysis. Body mass index was calculated as weight in kilograms divided by height in meters squared. Three or more consecutive blood pressure measurements separated by 30 seconds were made after 5 minutes of rest with the mean values used for analysis.

NHANES 2005–2008 data were used to describe clinical characteristics of US adults with diabetes by DKD status because this period included retinal photography. For this purpose, DKD status was defined by single urine and serum samples and thus did not reflect persistence. Diabetic retinopathy was defined as retinopathy or macular edema on retinal photography.

Statistical Methods

Analyses were performed using Stata version 11.1 (StataCorp) and R version 3.2.2 (RFoundation for Statistical Computing),[22] and incorporated recommended NHANES weights to account for nonresponse bias and the sampling design.[15] For each NHANES cohort, Stata *svy* commands were used to estimate the prevalence of DKD and other clinical characteristics among US adults with diabetes.

Binomial regression was used to test trends in DKD prevalence over time. NHANES III, NHANES 1999–2004, NHANES 2005–2008, and NHANES 2009–2014 were modeled primarily as non ordered independent variables. Tests for trend were performed using a

continuous variable defined by the midpoint of each study period (in years). For each outcome, participants who had the outcome were considered to have a value equal to the outcome's estimate of persistence, which allowed for estimation of DKD prevalence ratios accounting for possible misclassification of albuminuria, eGFR, or both. To account for the uncertainty in the estimate of the probability of persistence, a multiple imputation approach was used to obtain 95% CIs for adjusted prevalence ratios. The final variance of the prevalence ratios were estimated by using the rules of Rubin[23] to combine between- and within-imputation variance estimates. Models were adjusted for age (in categories of 20–39 years, 40–59 years, and ≥60 years), sex, and race/ethnicity. An age or race/ethnicity × time interaction term allowed extraction of subgroup-specific effect estimates. Significance testing for all modelswas2-sided and the significance threshold was set at $P < .05$.

Results

Characteristics of US Adults With Diabetes

The unadjusted prevalence of diabetes in the United States increased from 6.0% in 1988–1994 to 9.8% in 2009–2014(Table 1).

Over time, mean age and sex distribution of the diabetes populations were similar. However, the fraction of adults with diabetes who self-identified as Mexican American was higher and self-reported non-Hispanic white ethnicity was lower during later survey years. The mean duration of diagnosed diabetes increased in the later compared with earlier NHANES cycles. The mean body mass index also increased from 30.6 in 1988–1994 to 33.6 in 2009–2014.

Among 731 NHANES participants with diabetes who contributed 2 urine samples, ACR of greater than 30 mg/g was persistent in 58.9% of the repeat samples and an ACR of greater than 300 mg/g was persistent in 72.3% of the repeat samples (eFigure 1 and eTable 1 in the Supplement). Among 2076 NHANES participants with 2 serum samples, an eGFR of less than 60 mL/min/1.73 m^2 was persistent in 70.4% of the repeat samples and an eGFR of less than 30 mL/min/1.73 m^2 was persistent in 100% of the repeat samples (eFigure 2 and eTable 2).

The proportions of adults taking glucose-lowering medications, RAAS inhibitors, and statins were higher over time. Consistent with these changes, mean systolic and diastolic blood pressure, hemoglobin A_{1c}, total cholesterol, low-density lipoprotein cholesterol, and triglycerides were lower in later compared with earlier years. These patterns were consistent across categories of age (eFigure 3 in the Supplement) and race/ethnicity (Figure). However, older adults were more likely than younger adults to be treated with glucose-lowering medications, RAAS inhibitors, and statins and achieved lower levels of hemoglobin A_{1c} and low-density lipoprotein cholesterol (but not blood pressure) during all periods. In addition, during all periods, blacks and Mexican Americans were less likely than non-Hispanic whites to take glucose-lowering medications, RAAS inhibitors, and statins and did not achieve mean hemoglobin A_{1c} values as low as non-Hispanic whites.

Clinical Manifestations of DKD

Among US adults with diabetes, the overall prevalence of DKD did not change significantly from 1988 to 2014 (28.4% in 1988–1994 and 26.2% in 2009–2014; Table 2). However, the prevalence of albuminuria decreased from 20.8% to 15.9%, whereas the prevalence of reduced eGFR increased from 9.2% to 14.1% and the prevalence of severely reduced eGFR increased from 1.0% to 2.7%. Further adjustment for eGFR did not substantially alter results for temporal trends in the prevalence of albuminuria (eTable 3 in the Supplement). Significant heterogeneity in the temporal trend for albuminuria was noted by age ($P = .049$ for interaction) and race/ethnicity ($P = .007$ for interaction), with a decline in prevalence observed only among adults younger than 65 years and non-Hispanic whites (Table 3 and Table 4). In contrast, no significant heterogeneity in the temporal trend for reduced eGFR was observed.

Clinical Characteristics of Adults With Various Manifestations of DKD

InNHANES2005–2008, using estimates that do not take into account persistence of albuminuria or reduced eGFR, 39.3% of adults with diabetes had DKD manifested as albuminuria (21.6%), reduced eGFR (8.9%), or both (8.8%) (eTable 4 in the Supplement). Compared with participants with out reduced eGFR, those with reduced eGFR were older, had a longer duration of diabetes, were more likely to be women and white, and were more likely to take RAAS inhibitors and lipid-lowering medications, have lower hemoglobin A_{1c}, have diabetic retinopathy, and report a history of clinically diagnosed macrovascular disease regardless of whether albuminuria was also present.

Discussion

Among representative samples of adults with diabetes mellitus in the United States, there was a change in the clinical manifestations of kidney disease over the last 26 years, with a decline in the prevalence of albuminuria and an increase in the prevalence of reduced eGFR. These changes were independent of characteristics of adults with diabetes. Changes in the more severe manifestations of macro albuminuria and eGFR of less than 30 mL/min/1.73m^2 were consistent with those of albuminuria and eGFR of less than 60 mL/min/1.73 m^2, respectively.

Significant heterogeneity in the temporal trend for albuminuria prevalence was noted by age and race/ethnicity. The lower prevalence of albuminuria over time was observed only among adults younger than 65 years and non-Hispanic whites, whereas the prevalence of reduced eGFR appeared to increase without significant differences by age or race/ethnicity. The proportion of US adults with diabetes who met any criteria for DKD was stable over time, with an estimate of 26.2% (95% CI, 22.6%–29.9%) in 2009–2014. Using 2010 census data, this translates to a prevalence of approximately 8.2 million people (95% CI, 6.5–9.9 million people) with any DKD, including 4.6 million people (95% CI, 3.4–5.8 million people) with albuminuria, 1.9 million people (95% CI, 1.0–2.8 million people) with macroalbuminuria, 4.5 million people (95% CI, 3.3–5.7 million people) with reduced eGFR, and 0.9 million people (95% CI, 0.6–1.3 million) with severely reduced eGFR.

We previously reported an increase in the prevalence of reduced eGFR but no significant change in the prevalence of albuminuria among US adults with diabetes from 1988 to 2008.[2] In this study, the analyses of data collected through 2014 demonstrated a significant temporal decrease in the prevalence of albuminuria in addition to a continuation of the increase in prevalence of reduced GFR. Furthermore, we evaluated temporal trends in more advanced manifestations of DKD, observing an increase in the prevalence of severely reduced GFR that paralleled that of reduced GFR. We also examined relevant subgroups, observing significant age and race/ethnicity × time interactions and identifying older adults and racial/ethnic minorities as groups with less favorable trends for albuminuria. Repeat testing was used to more accurately define DKD based on the persistence of albuminuria and reduced eGFR. Albuminuria and eGFR have substantial biological (intra individual) variation, and current guidelines recommend that only persistent abnormalities be considered diagnostic of DKD.[1]

The lower prevalence of albuminuria observed over time maybe attributable to a higher rate of prescribed diabetes therapies (glucose-lowering medications, RAAS inhibitors, and statins). Lowering blood glucose level has consistently reduced the development of albuminuria in clinical trials,[24–26] and an increase in the use of glucose-lowering medications and lower mean hemoglobin A_{1c} values were observed over time in this study. Furthermore, RAAS inhibitors and blood pressure control reduce albuminuria through hemodynamic and other mechanisms,[27,28] and the increasing use of these agents and lower mean blood pressure levels were also noted over time. The lack of decline in albuminuria prevalence among blacks and Mexican Americans may be attributable in part to less frequent use of proven diabetes therapies, as observed herein and in other reports.[29]

Reasons for the increasing prevalence of reduced eGFR cannot be conclusively discerned from these data. Estimated GFR declines with age, but aging is not likely to be responsible for the observed trends in eGFR because the age distribution of the US adult population with diabetes did not change significantly over time and trends persisted after adjustment for demographic factors. It is possible that hemodynamic effects of RAAS inhibitors and improved blood pressure control could contribute to lower eGFR. Alternatively, an increasing duration of diabetes may be contributing to kidney damage.

There was amonotonic increase in diabetes duration from 1988 to 2014. During the same interval, there was no change in mean age, suggesting that the mean age of diabetes onset may have decreased. Earlier age at diabetes onset combined with decreased mortality due to cardiovascular disease and other diabetes complications[30] could allow adults with diabetes time to develop progressive long-term kidney damage. In NHANES 2005–2008, reduced eGFR was associated with retinopathy and macrovascular disease, regardless of whether albuminuria was present, suggesting that reduced eGFR is occurring in the setting of other long-term diabetes complications.

To reduce the prevalence of reduced GFR in diabetes, new therapies may be needed. The shift in clinical manifestations of DKD has implications for clinical trials. Clinical trials of novel DKD therapies commonly target patients with macro albuminuria because they are at high risk of GFR loss,[14] particularly when GFR is already low. However, adults with macro

albuminuria forma small and diminishing subset of those with diabetes, estimated at 5.0% in the 2009–2014 NHANES survey, and even fewer have concomitant reduced eGFR. To mitigate the large public health effect of the growing DKD population in the United States and around the world,[1,31] clinical trials will need to address a broader range of DKD presentations.

This study has limitations. First, it is possible that incomplete standardization of serum creatinine, urine albumin, and creatinine measurements over time may have contributed to the temporal drift, as previously described.[2] Second, the estimates of persistence were based on a subsample of each NHANES cohort, potentially reducing precision; however, reliance on these subsamples was unlikely to have biased the analyses of temporal trends. Third, data were not available to determine the underlying causes of DKD, and some of the identified kidney disease was likely caused by processes other than diabetes. Fourth, the proportion of adults with type 1 diabetes was small and therefore results are primarily relevant to adults with type 2 diabetes. Strengths of this study include use of nationally representative data, incorporation of persistence into the estimation of prevalence based on relevant repeat albuminuria and serum creatinine measurements, and ascertainment of both moderate and severe DKD.

Conclusions

Among US adults with diabetes from 1988 to 2014, the overall prevalence of DKD did not change significantly, whereas the prevalence of albuminuria declined and the prevalence of reduced eGFR increased.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Key Points

Question

Have the clinical manifestations of kidney disease among adults with diabetes changed over time?

Findings

In serial cross-sectional studies of US adults with diabetes mellitus participating in National Health and Nutrition Examination Surveys, no change in the prevalence of diabetic kidney disease was observed from 1988 through 2014, but there was a significant decrease in the prevalence of albuminuria and a significant increase in the prevalence of reduced glomerular filtration rate.

Meaning

The clinical manifestations of diabetic kidney disease changed from 1988 to 2014, with a lower prevalence of albuminuria and a higher prevalence of reduced glomerular filtration rate in 2014 compared with 1988.

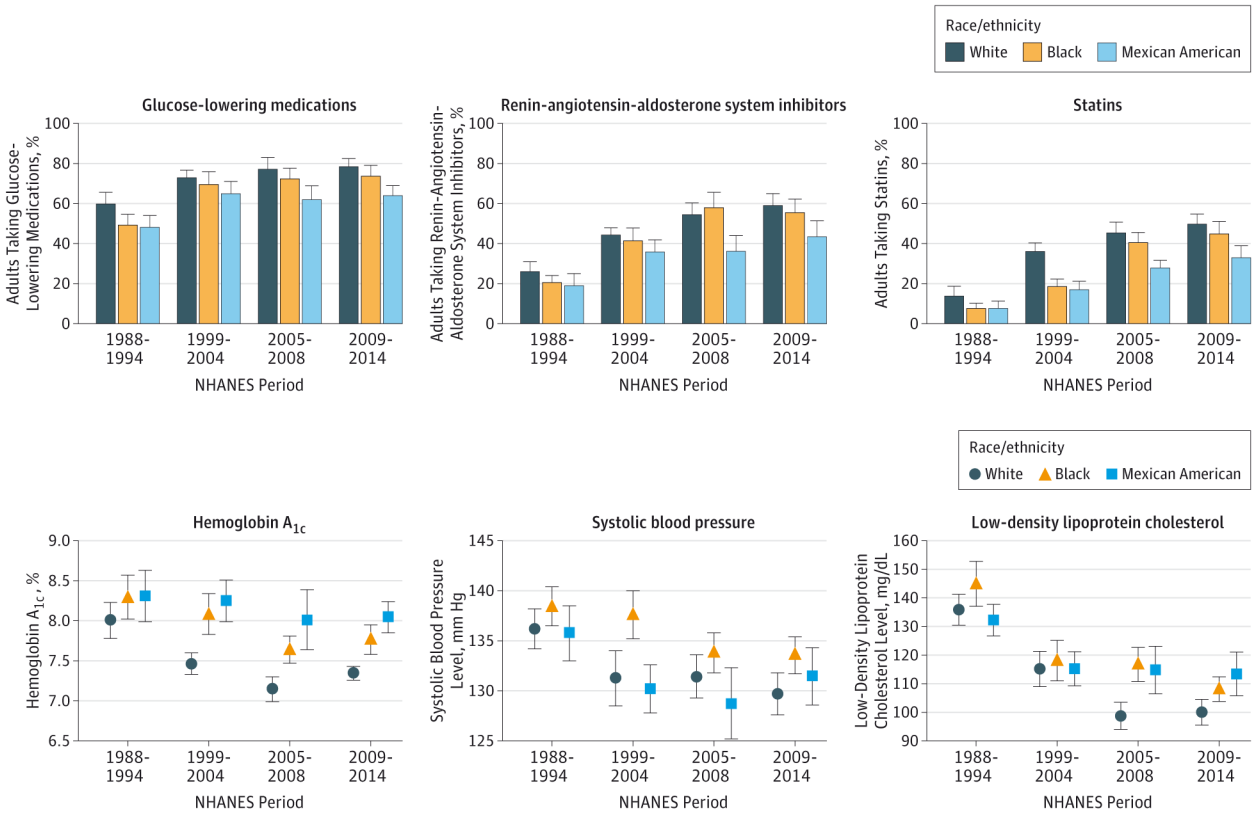

Figure. Medication Use and Trends in Clinical Targets for the Adult US Population With Diabetes by Race/Ethnicity

Error bars indicate 95% CIs; NHANES, National Health and Nutrition Examination Surveys. Participants of all races and ethnicities were included in the analyses, and estimates were reported for non-Hispanic white, non-Hispanic black, and Mexican American race/ethnicity only.

Table 1

Characteristics of US Adults With Diabetes, 1988 Through 2014

	NHANES Period							
	1988–1994 (n = 1431)		1999–2004 (n = 1443)		2005–2008 (n = 1280)		2009–2014 (n = 2097)	
	No. With Diabetes	Weighted % (95% CI)[a]	No. With Diabetes	Weighted % (95% CI)[a]	No. With Diabetes	Weighted % (95% CI)[a]	No. With Diabetes	Weighted % (95% CI)[a]
US population[b]		6.0 (5.4–6.7)		7.8 (7.2–8.5)		9.4 (8.5–10.4)		9.8 (9.2–10.4)
Demographics								
Age, mean (95% CI), y		59.7 (58.3–61.1)		58.8 (57.6–59.9)		59.1 (57.9–60.3)		59.3 (58.5–60.0)
Female sex[c]	736	48.9 (44.8–53.0)	689	47.8 (45.1–50.1)	629	50.4 (46.7–54.1)	979	46.3 (43.4–49.2)
Race/ethnicity[d]								
Non-Hispanic white	478	68.7 (63.5–73.5)	556	63.6 (57.5–69.4)	496	62.9 (54.8–70.3)	719	59.2 (54.4–63.9)
Non-Hispanic black[c]	452	16.9 (14.1–20.0)	338	14.8 (11.5–18.9)	373	17.2 (13.4–21.9)	547	15.3 (12.4–18.7)
Mexican American	451	6.6 (5.4–8.0)	430	8.1 (5.5–11.7)	257	8.7 (6.4–11.6)	373	10.4 (7.4–14.4)
Diabetes duration, y								
<5	306	25.8 (22.2–29.6)	315	25.3 (22.0–28.9)	266	22.3 (19.6–25.3)	256	17.4 (15.3–19.8)
5-<10	190	15.8 (12.4–20.0)	237	16.3 (14.2–18.7)	222	18.3 (15.4–21.5)	257	16.7 (15.1–18.5)
10-<20	243	14.7 (12.1–17.9)	267	16.6 (14.4–19.0)	275	21.6 (18.6–24.9)	315	22.8 (19.9–26.1)
≥20	157	8.9 (7.1–11.1)	258	17.4 (14.6–20.7)	175	13.0 (11.0–15.3)	227	14.9 (13.0–17.1)
Diabetes previously undiagnosed	503	34.8 (31.4–38.4)	339	24.4 (21.6–27.4)	316	24.9 (21.1–29.1)	537	28.1 (25.8–30.1)
Type 1 diabetes	18	5.8 (2.4–13.4)	17	2.4 (1.3–4.5)	28	4.6 (3.1–6.9)	41	4.5 (3.1–6.4)
Medication Use[e]								
Glucose lowering	781	56.2 (52.0–60.3)	1033	70.4 (67.0–73.5)	937	74.2 (70.2–77.8)	1125	74.5 (71.2–77.6)

	NHANES Period							
	1988–1994 (n = 1431)		1999–2004 (n = 1443)		2005–2008 (n = 1280)		2009–2014 (n = 2097)	
	No. With Diabetes	Weighted % (95% CI)[a]	No. With Diabetes	Weighted % (95% CI)[a]	No. With Diabetes	Weighted % (95% CI)[a]	No. With Diabetes	Weighted % (95% CI)[a]
Oral medications only	492	35.4 (31.7–39.3)	811	54.2 (51.0–57.3)	721	55.2 (51.4–58.9)	811	51.8 (49.4–54.3)
Insulin	289	20.8 (17.0–25.1)	222	16.2 (13.5–19.3)	216	19.0 (16.6–21.7)	314	22.7 (19.6–26.1)
RAAS inhibitors[e]	310	24.4 (21.0–28.3)	620	41.7 (38.7–44.7)	691	52.0 (47.7–56.2)	861	56.2 (52.3–59.9)
ACE inhibitors	249	19.6 (16.5–23.1)	493	32.1 (29.9–34.5)	495	37.9 (34.6–41.3)	579	36.0 (32.9–39.2)
ARBs	51	3.9 (1.9–8.0)	135	10.2 (8.1–12.8)	216	15.1 (12.2–18.5)	295	20.5 (17.9–23.4)
Aldosterone antagonists	19	1.3 (0.7–2.4)	21	1.3 (0.8–2.3)	31	2.2 (1.4–3.4)	26	1.9 (1.1–3.4)
Lipid lowering[f]	190	17.0 (13.5–21.2)	426	34.5 (31.3–37.8)	664	51.7 (47.6–55.8)	803	51.8 (48.6–55.1)
Statins	134	11.9 (8.8–15.9)	377	30.0 (27.0–33.2)	553	42.3 (38.9–45.8)	714	46.5 (43.3–49.8)
Fibrates	51	5.4 (3.8–7.8)	54	4.6 (3.5–6.0)	74	6.9 (4.9–9.7)	85	5.9 (4.3–8.1)
Physical Measurements, Mean (95% CI)								
Body mass index[g]		30.6 (30.1–31.1)		32.4 (31.8–33.1)		33.0 (32.4–33.7)		33.6 (33.0–34.1)
Systolic BP, mm Hg		136.3 (134.8–137.8)		132.4 (130.6–134.2)		131.2 (129.6–132.8)		130.1 (128.8–131.4)
Diastolic BP, mm Hg		76.2 (75.4–77.1)		70.1 (68.4–71.8)		69.3 (68.1–70.4)		68.9 (67.9–69.9)
Laboratory Measurements, Mean (95% CI)								
Hemoglobin A_{1c}, %		8.1 (7.9–8.2)		7.7 (7.6–7.9)		7.3 (7.2–7.5)		7.6 (7.5–7.7)
Total cholesterol, mg/dL		223.8 (219.1–228.5)		207.4 (203.3–211.5)		190.4 (186.8–194.0)		185.0 (182.5–187.6)
HDL cholesterol, mg/dL		44.1 (42.7–45.6)		46.3 (45.3–47.4)		47.5 (46.3–48.7)		45.9 (45.0–46.7)
LDL cholesterol, mg/dL		137.1 (132.9–141.4)		116.3 (111.8–120.7)		104.5 (100.5–108.4)		103.0 (100.0–106.0)
Triglycerides, mg/dL		198.9 (185.0–213.8)		179.0 (170.4–188.1)		152.7 (143.5–162.5)		142.3 (132.0–153.3)

Abbreviations: ACE, angiotensin-converting enzyme; ARBs, angiotensin-receptor II blockers; BP, blood pressure; HDL, high-density lipoprotein; LDL, low-density lipoprotein; NHANES, National Health and Nutrition Examination Surveys; RAAS, renin-angiotensin-aldosterone system.

SI conversion factors: To convert HDL, LDL, and total cholesterol to mmol/L, multiply by 0.0259; triglycerides to mmol/L, multiply by 0.0113.

[a] Unless otherwise indicated.

[b] Weighted percentage of the US population with diabetes regardless of kidney disease manifestations.

[c] The numbers were corrected (compared with our previous study[2]).

[d] Participants of all races and ethnicities were included in the analyses, and estimates were reported for non-Hispanic white, non-Hispanic black, and Mexican American race/ethnicity only.

[e] Data for 2009–2014 are based only on information from NHANES 2009–2012 because medication data were not available for NHANES 2013–2014.

[f] Definitions included new drugs that were not available during previous analyses.

[g] Calculated as weight in kilograms divided by height in meters squared.

Table 2

Clinical Manifestations of Kidney Disease Among US Adults With Diabetes, 1988 Through 2014

NHANES Period	No. With Diabetes	Unadjusted Prevalence, % (95% CI)		Adjusted Prevalence Ratio (95% CI)[b]	*P* Value for Trend
		Based on a Single Laboratory Value	Accounting for Persistence[a]		
Any diabetic kidney disease[c]					
1988–1994	640	42.5 (38.4–46.6)	28.4 (23.8–32.9)	1 [Reference]	.39
1999–2004	659	40.5 (37.5–43.6)	27.3 (23.1–31.4)	1.00 (0.90–1.11)	
2005–2008	573	39.3 (36.0–42.7)	27.1 (22.6–31.4)	0.99 (0.88–1.10)	
2009–2014	874	38.1 (35.3–41.0)	26.2 (22.6–29.9)	0.95 (0.86–1.06)	
Albuminuria (ACR ≥30 mg/g)					
1988–1994	534	35.2 (31.1–39.5)	20.8 (16.3–25.3)	1 [Reference]	<.001
1999–2004	531	32.1 (29.0–35.3)	18.9 (15.3–22.4)	0.93 (0.79–1.06)	
2005–2008	447	30.4 (27.6–33.4)	17.9 (14.0–21.9)	0.86 (0.75–1.01)	
2009–2014	645	27.1 (24.1–30.3)	15.9 (12.7–19.0)	0.76 (0.65–0.89)	
Macroalbuminuria (ACR ≥300 mg/g)					
1988–1994	155	7.9 (6.0–10.4)	5.6 (2.8–8.4)	1 [Reference]	.22
1999–2004	141	7.4 (5.9–9.2)	5.4 (3.1–7.7)	0.93 (0.65–1.31)	
2005–2008	111	6.9 (5.4–8.7)	4.9 (2.7–7.1)	0.86 (0.60–1.23)	
2009–2014	171	6.7 (5.6–8.2)	5.0 (3.3–6.6)	0.82 (0.59–1.14)	
Estimated GFR <60 mL/min/1.73 m^2					
1988–1994	214	13.1 (10.9–15.7)	9.2 (6.2–12.2)	1 [Reference]	<.001
1999–2004	273	16.0 (14.1–18.2)	11.6 (8.5–14.6)	1.33 (1.09–1.63)	
2005–2008	242	16.6 (14.2–19.4)	11.8 (8.4–15.1)	1.38 (1.09–1.75)	
2009–2014	450	20.1 (18.5–21.8)	14.1 (11.3–17.0)	1.61 (1.33–1.95)	
Estimated GFR <30 mL/min/1.73 m^2					
1988–1994	22	1.0 (0.5–2.0)	NA	1 [Reference]	.004
1999–2004	39	1.7 (1.1–2.6)	NA	1.86 (0.87–3.98)	
2005–2008	28	1.8 (1.2–2.7)	NA	1.93 (0.90–4.11)	
2009–2014	62	2.7 (2.0–3.7)	NA	2.86 (1.38–5.91)	

Abbreviations: ACR, albumin-to creatinine ratio; GFR, glomerular filtration rate; NA, data not applicable; NHANES, National Health and Nutrition Examination Surveys.

[a]Defined as the fraction of participants with elevated ACR, reduced estimated GFR, or both, on initial examination whose values remained abnormal during repeat testing. The estimated persistence of estimated GFR of less than 30 mL/min/1.73m^2 was 100%.

[b]Adjusted for age, sex, and race/ethnicity.

[c]Defined as urine ACR of 30 mg/g or greater or estimated GFR of less than 60 mL/min/1.73m^2, or both.

Table 3

Prevalence of Albuminuria and Reduced Estimated Glomerular Filtration Rate Among US Adults With Diabetes by Age, 1988 Through 2014

NHANES Period	No. With Diabetes	Unadjusted Prevalence, % (95% CI)		Adjusted Prevalence Ratio (95% CI)[b]	*P* Value for Trend
		Based on a Single Laboratory Value	Accounting for Persistence[a]		
Albuminuria (ACR ≥30 mg/g)[c]					
Adults aged <65 y					
1988–1994	256	33.5 (28.3–39.1)	19.5 (13.5–25.4)	1 [Reference]	.001
1999–2004	244	30.0 (25.9–34.4)	17.6 (12.9–22.3)	0.89 (0.72–1.11)	
2005–2008	224	26.6 (22.9–30.7)	15.7 (10.5–20.8)	0.80 (0.64–0.99)	
2009–2014	327	23.9 (20.6–27.6)	14.0 (10.1–18.0)	0.70 (0.57–0.87)	
Adults aged ≥65 y					
1988–1994	278	37.7 (31.7–44.2)	22.1 (15.9–28.4)	1 [Reference]	.15
1999–2004	287	35.7 (31.6–39.9)	20.7 (15.9–25.5)	0.94 (0.77–1.15)	
2005–2008	223	36.8 (33.6–40.2)	21.9 (17.0–26.8)	0.96 (0.80–1.16)	
2009–2014	318	32.3 (28.2–36.7)	19.2 (14.9–23.4)	0.84 (0.68–1.03)	
Reduced Estimated Glomerular Filtration Rate (eGFR <60 mL/min/1.73 m^2)[d]					
Adults aged <65 y					
1988–1994	40	4.0 (2.4–6.5)	2.9 (0–5.9)	1 [Reference]	.15
1999–2004	43	5.3 (3.8–7.4)	3.9 (1.3–6.5)	1.45 (0.80–2.61)	
2005–2008	53	6.0 (4.3–8.3)	4.3 (1.8–6.9)	1.62 (0.89–2.94)	
2009–2014	95	7.6 (5.9–9.9)	5.5 (2.9–8.2)	1.95 (1.12–3.39)	
Adults aged ≥65 y					
1988–1994	174	27.3 (23.3–31.8)	19.3 (13.4–25.3)	1 [Reference]	<.001
1999–2004	230	34.3 (30.1–38.8)	24.6 (18.4–30.9)	1.26 (1.04–1.54)	
2005–2008	189	34.6 (28.6–41.3)	24.4 (18.0–30.9)	1.28 (0.99–1.64)	
2009–2014	355	40.6 (36.5–44.8)	28.9 (22.9–34.9)	1.53 (1.27–1.85)	

Abbreviations: ACR, albumin-to-creatinine ratio; NHANES, National Health and Nutrition Examination Surveys.

[a]Defined as the fraction of participants with elevated urine albumin-to-creatinine ratio, reduced estimated glomerular filtration rate, or both, on initial examination whose values remained abnormal during repeat testing.

[b] Adjusted for age, sex, and race/ethnicity.

[c] The age × time interaction was $P = .049$.

[d] The age × time interaction was $P = .41$.

Table 4

Prevalence of Albuminuria and Reduced Estimated Glomerular Filtration Rate Among US Adults With Diabetes by Race/Ethnicity, 1988 Through 2014

NHANES Period	No. With Diabetes	Unadjusted Prevalence, % (95% CI)		Adjusted Prevalence Ratio (95% CI)[b]	*P* Value for Trend
		Based on a Single Laboratory Value	Accounting for Persistence[a]		
Albuminuria (ACR ≥30 mg/g)[c]					
Non-Hispanic white					
1988–1994	179	35.9 (30.6–41.5)	21.2 (14.9–27.5)	1 [Reference]	.001
1999–2004	179	28.5 (24.6–32.8)	17.1 (12.8–21.4)	0.81 (0.65–0.99)	
2005–2008	169	28.9 (25.3–32.8)	17.4 (12.8–22.1)	0.82 (0.68–1.00)	
2009–2014	204	24.1 (20.0–28.7)	14.2 (9.9–18.5)	0.67 (0.53–0.85)	
Non-Hispanic black					
1988–1994	153	32.9 (28.5–37.6)	19.4 (14.0–24.9)	1 [Reference]	.50
1999–2004	127	36.1 (31.0–41.6)	21.1 (15.6–26.6)	1.09 (0.89–1.33)	
2005–2008	131	32.7 (27.7–38.0)	19.2 (13.7–24.8)	1.00 (0.81–1.22)	
2009–2014	173	30.8 (27.4–34.4)	18.3 (13.7–22.9)	0.93 (0.78–1.11)	
Mexican American					
1988–1994	184	34.5 (29.3–40.0)	20.4 (14.2–26.6)	1 [Reference]	.95
1999–2004	179	36.0 (31.5–40.7)	20.9 (15.4–26.3)	1.03 (0.85–1.25)	
2005–2008	95	35.5 (28.8–42.8)	21.0 (14.2–27.8)	1.01 (0.79–1.30)	
2009–2014	131	35.1 (29.6–41.0)	21.0 (15.1–27.0)	1.00 (0.80–1.24)	
Reduced Estimated Glomerular Filtration Rate (eGFR <60 mL/min/1.73 m^2)[d]					
Non-Hispanic white					
1988–1994	102	14.2 (11.4–17.7)	9.8 (5.5–14.0)	1 [Reference]	<.001
1999–2004	138	18.6 (16.1–21.3)	12.9 (8.7–17.1)	1.36 (1.06–1.73)	
2005–2008	123	19.0 (15.1–23.8)	13.3 (8.1–18.6)	1.42 (1.05–1.92)	
2009–2014	206	23.4 (21.2–25.7)	16.1 (12.1–20.0)	1.65 (1.32–2.06)	
Non-Hispanic black					
1988–1994	63	12.0 (9.6–15.0)	8.2 (4.6–11.8)	1 [Reference]	<.001
1999–2004	63	14.2 (11.4–17.5)	9.6 (5.3–14.0)	1.18 (0.89–1.56)	

NHANES Period	No. With Diabetes	Unadjusted Prevalence, % (95% CI)		Adjusted Prevalence Ratio (95% CI)[b]	*P* Value for Trend
		Based on a Single Laboratory Value	Accounting for Persistence[a]		
2005–2008	70	16.4 (12.1–22.0)	11.5 (6.1–17.0)	1.39 (1.01–1.92)	
2009–2014	120	19.0 (16.1–22.4)	13.0 (9.0–17.1)	1.55 (1.20–2.01)	
Mexican American					
1988–1994	43	6.7 (4.2–10.4)	4.6 (1.5–7.7)	1 [Reference]	
1999–2004	56	7.6 (5.3–10.8)	5.3 (2.3–8.3)	1.11 (0.66–1.86)	
2005–2008	31	8.4 (5.2–13.5)	5.8 (1.8–9.8)	1.21 (0.67–2.21)	.14
2009–2014	50	10.4 (7.8–13.7)	7.2 (3.0–11.4)	1.42 (0.88–2.31)	

Abbreviations: ACR, albumin-to-creatinine ratio; NHANES, National Health and Nutrition Examination Surveys.

[a]Defined as the fraction of participants with elevated urine albumin-to-creatinine ratio, reduced estimated glomerular filtration rate, or both, on initial examination whose values remained abnormal during repeat testing.

[b]Adjusted for age, sex, and race/ethnicity.

[c]The race/ethnicity × time interaction was $P = .007$.

[d]The race/ethnicity × time interaction was $P = .99$.