

Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.

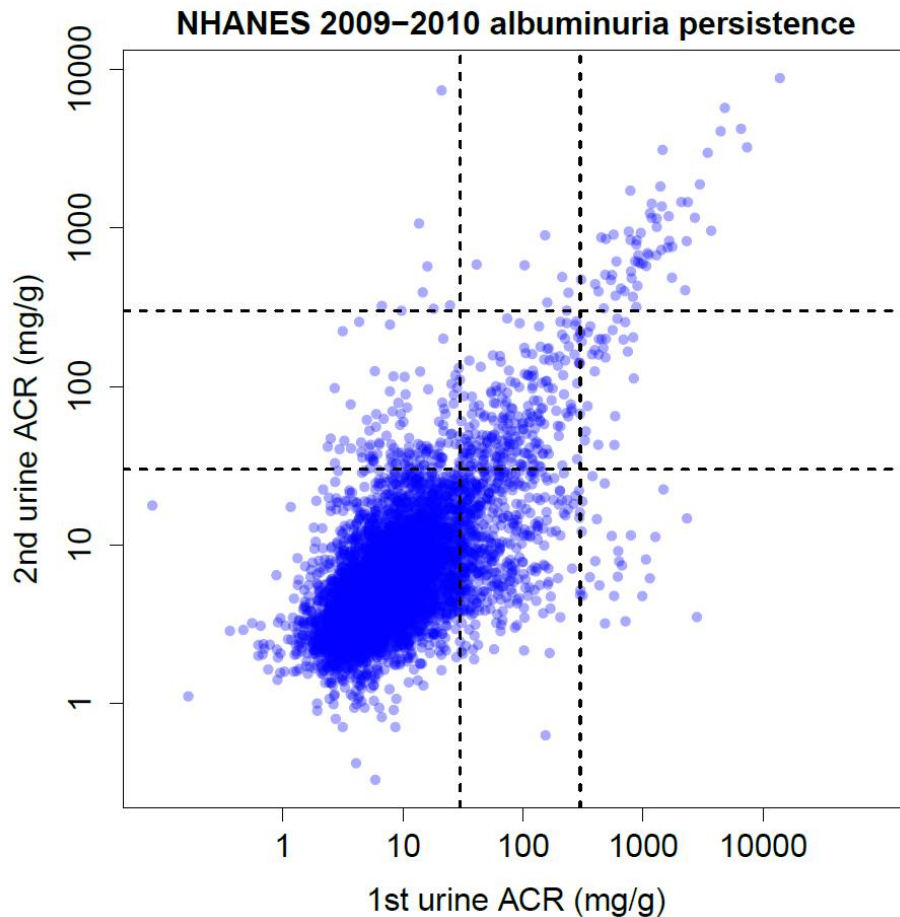
eMethods

Data from subsets of NHANES participants who donated multiple urine or serum samples were evaluated to estimate persistence of albuminuria and reduced estimated glomerular filtration rate (eGFR). In NHANES III, 2076 participants repeated blood sampling approximately two weeks after their initial Mobile Examination Center examination. The persistence of reduced eGFR was estimated among all of these NHANES III participants because there was an insufficient number with diabetes and reduced eGFR to generate reliable persistence estimates. In NHANES 2009-2010, after submitting a random urine sample at their Mobile Examination Center exam, participants were asked to collect another urine sample from a first morning void at home, within 10 days of their Mobile Examination Center exam date (http://wwwn.cdc.gov/Nchs/Nhanes/2009-2010/ALB_CR_F.htm). Persistence of albuminuria was calculated based on these samples collected by 731 participants with diabetes.

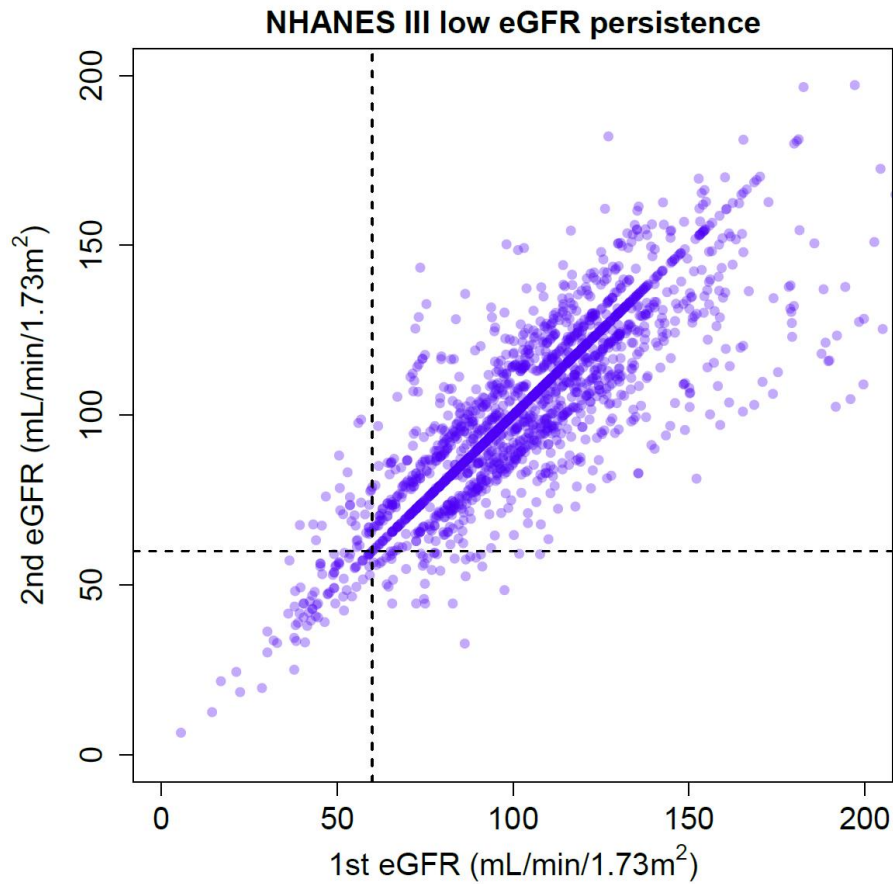
Persistence of albuminuria was defined as the fraction of participants with elevated urine ACR in the Mobile Examination Center exam whose urine ACR remained elevated in the home collection in each of forty bootstrap samples. Persistent albuminuria was estimated in each bootstrap sample by multiplying the prevalence of elevated urine ACR by the bootstrap probability of persistence to yield corresponding variance estimates. A final estimate of persistent albuminuria and 95% confidence intervals were obtained by combining across bootstrap samples using Rubin's rules. A similar process was followed to estimate the prevalence of persistently reduced GFR.

To estimate the prevalence of persistent diabetic kidney disease (DKD), each DKD subtype was calculated (albuminuria only, reduced eGFR only, or both albuminuria and reduced eGFR), and then a weighted average was used to calculate overall persistence. For participants with albuminuria only or impaired eGFR only, the respective estimates of persistence from forty bootstrap samples were calculated. For participants with both albuminuria and reduced eGFR, the probability of persistence was one minus the probability of having neither persistent albuminuria nor persistently reduced GFR. We applied prevalence estimates from NHANES 2009-2012 to 2010 census data to estimate absolute numbers of US adults with clinical manifestations of DKD during 2010.

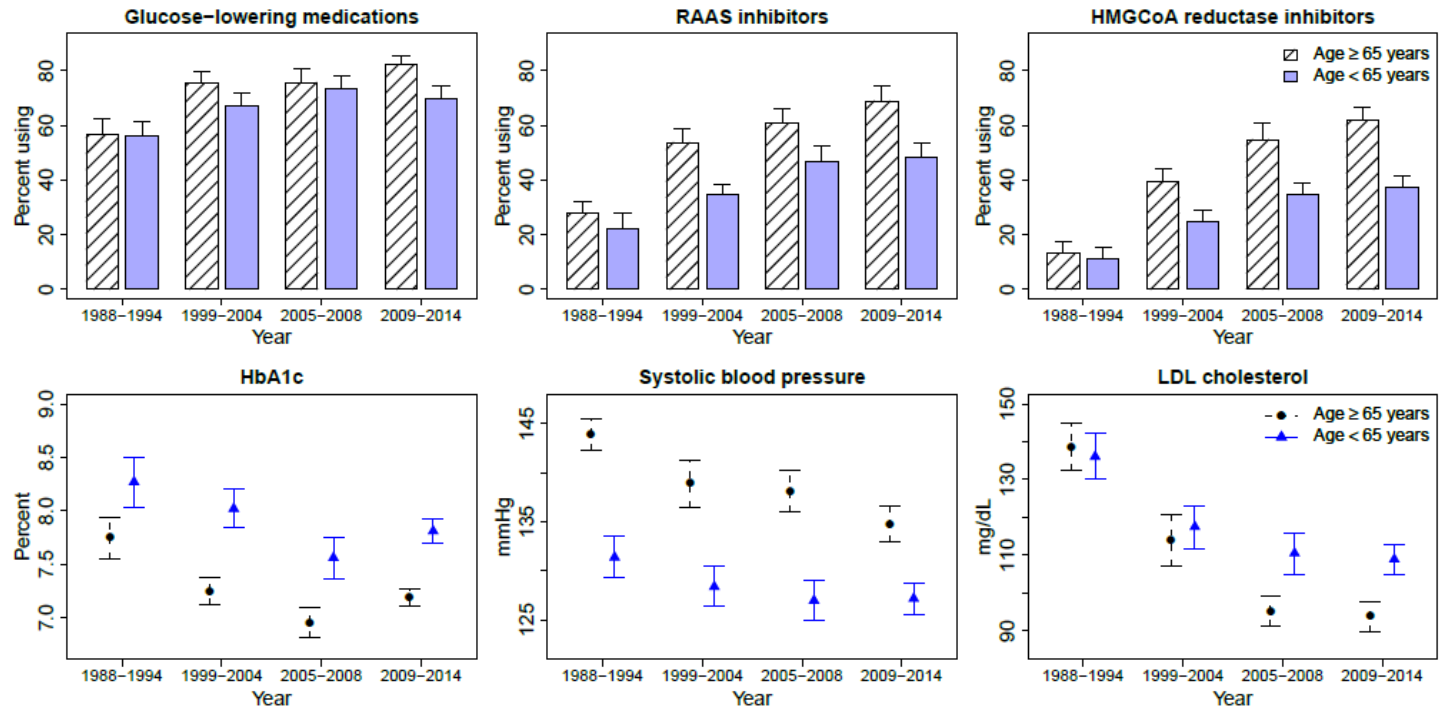
eFigure 1. Concordance of urine albumin-creatinine ratio measured twice among 731 NHANES 2009-2010 participants with diabetes. The first urine albumin-creatinine ratio (ACR) measurement was made from spot urine samples collected during the Mobile Examination Center examination at any time of day. The second urine ACR measurement was made from spot urine samples collected at home as a first-morning void. Dashed lines indicate thresholds for microalbuminuria (ACR ≥ 30 mg/g) and macroalbuminuria (ACR ≥ 300 mg/g). Units for each axis are mg albumin per gram creatinine,



eFigure 2. Concordance of estimated glomerular filtration rate (eGFR) measured twice among 2076 NHANES III (1988-1994) participants. Dashed lines indicate the threshold for reduced eGFR (<60 mL/min/1.73m²). Units for each axis are mL/min/1.73m².



eFigure 3. Use of glucose lowering medication, RAAS inhibitors and HMG-CoA reductase inhibitors and trends in their clinical targets in the US population with diabetes, by age. Proportions are displayed with upper limits of 95% confidence intervals, and means are displayed with full 95% confidence intervals. RAAS = renin-angiotensin-aldosterone system; HbA1c = hemoglobin A1c; LDL = low density lipoprotein.



eTable 1. Persistence of albuminuria in NHANES 2009-2010

		2 nd ACR measurement		
		< 30 mg/g	30 - <300 mg/g	≥ 300 mg/g
1 st ACR measurement	< 30 mg/g	507	13	2
	30 - < 300 mg/g	82	73	3
	≥ 300 mg/g	2	11	34

Cell contents are raw numbers of participants. Persistence of albuminuria was defined as the fraction of participants with elevated urine ACR in the Mobile Examination Center exam whose urine ACR remained elevated in the home collection in each of forty bootstrap samples.

eTable 2. Persistence of reduced eGFR in NHANES III (1988-1994)

		2 nd eGFR measurement		
		≥ 60 mL/min/1.73 m ²	30 – 60 mL/min/1.73 m ²	< 30 mL/min/1.73 m ²
1 st eGFR measurement	≥ 60 mL/min/1.73 m ²	1921	40	0
	30 – 60 mL/min/1.73 m ²	34	74	1
	< 30 mL/min/1.73 m ²	0	0	6

Cell contents are raw numbers of participants. Persistence of reduced eGFR was defined as the fraction of participants with reduced eGFR in the Mobile Examination Center exam whose eGFR remained reduced in the home collection in all bootstrap samples.

eTable 3. Characteristics of NHANES 2005-2008 participants with diabetes according to urine albumin-creatinine ratio and estimated glomerular filtration rate

	Urine ACR <30 mg/g & eGFR ≥60 mL/min/1.73m ² (N = 707)		Urine ACR ≥30 mg/g & eGFR ≥60 mL/min/1.73m ² (N = 311)		Urine ACR <30 mg/g & eGFR <60 mL/min/1.73m ² (N = 126)		Urine ACR ≥30 mg/g & eGFR <60 mL/min/1.73m ² (N = 136)	
	N	Proportion (95% CI) or mean (95% CI)	N	Proportion (95% CI) or mean (95% CI)	N	Proportion (95% CI) or mean (95% CI)	N	Proportion (95% CI) or mean (95% CI)
Proportion of US adults with diabetes		60.7 (57.2, 64.1)		21.6 (18.6, 25.0)		8.9 (7.6, 10.4)		8.8 (7.4, 10.4)
Demographic variables								
Age, mean, y		56.2 (54.9, 57.6)		57.2 (54.5, 59.8)		71.1 (69.2, 73.0)		71.3 (68.9, 73.7)
Female sex, %	357	50.4 (45.8, 55.1)	143	47.5 (38.5, 56.6)	65	55.5 (41.0, 69.0)	64	52.4 (42.8, 61.8)
Race/ethnicity, %								
White (non-Hispanic)	264	63.2 (53.6, 71.8)	102	54.5 (43.7, 64.9)	63	70.9 (61.3, 78.9)	67	72.9 (61.9, 81.7)
Black (non-Hispanic)	204	16.6 (12.1, 22.4)	88	19.0 (14.1, 25.2)	38	17.3 (11.9, 24.5)	43	17.3 (10.4, 27.3)
Hispanic	147	8.7 (6.2, 12.0)	78	12.3 (8.8, 17.0)	15	3.9 (1.8, 8.4)	17	4.8 (2.3, 9.7)
Diabetes duration, %								
Previously undiagnosed	208	29.2 (24.4, 34.6)	63	17.6 (12.3, 24.5)	27	25.2 (16.2, 37.0)	18	11.9 (6.8, 19.9)
< 5 years	178	26.0 (22.3, 30.0)	61	22.7 (17.0, 29.7)	15	8.9 (5.7, 13.6)	12	8.7 (5.4, 13.7)
5 years to < 10 years	116	17.7 (13.9, 22.4)	57	20.2 (15.0, 26.8)	30	20.3 (12.8, 30.7)	19	15.0 (9.4, 23.1)
10 years to < 20 years	135	18.6 (14.8, 23.1)	75	25.5 (18.7, 33.7)	26	20.7 (11.3, 34.9)	39	33.8 (25.2, 43.6)
≥ 20 years	64	7.9 (5.5, 11.2)	47	12.2 (8.3, 17.7)	21	20.6 (10.7, 36.0)	43	28.5 (18.3, 41.4)
Medication use								
Glucose-lowering medications, %	495	71.4 (66.7, 75.8)	230	76.6 (69.5, 82.5)	100	76.6 (65.7, 84.8)	112	84.9 (75.7, 91.1)
Oral medications only	396	54.3 (49.2, 59.4)	180	57.3 (48.7, 65.5)	76	56.6 (43.9, 68.5)	69	54.2 (38.8, 68.9)
Insulin	99	17.1 (14.0, 20.8)	50	19.3 (13.0, 27.6)	24	20.0 (11.7, 32.2)	43	30.7 (18.0, 47.1)
RAAS inhibitors ¹ , %	345	45.3 (39.0, 51.7)	162	56.8 (50.3, 63.0)	92	70.9 (56.3, 82.2)	92	67.6 (56.0, 77.4)
ACE inhibitors	247	32.5 (27.4, 38.1)	124	46.5 (40.7, 52.4)	56	42.6 (29.9, 56.4)	68	49.1 (37.2, 61.1)
Angiotensin receptor blockers	105	13.1 (9.7, 17.5)	49	13.5 (9.2, 19.4)	36	29.5 (21.4, 39.0)	26	18.1 (7.4, 38.0)
Aldosterone antagonists	11	1.4 (0.6, 3.1)	2	0.6 (0.1, 3.0)	10	6.4 (2.7, 14.2)	8	7.0 (3.0, 15.4)
Lipid-lowering medications ¹ , %	344	48.1 (42.7, 53.5)	144	49.4 (42.2, 56.5)	79	60.4 (48.2, 71.4)	97	74.0 (60.9, 83.8)
HMG-CoA reductase inhibitors	289	39.1 (35.5, 42.8)	118	39.9 (32.9, 47.3)	63	49.1 (37.6, 60.6)	83	63.5 (50.8, 74.6)
Fibrates	27	4.8 (2.9, 7.9)	14	5.7 (3.3, 9.8)	19	19.5 (10.8, 32.6)	8	6.3 (2.9, 13.2)
Physical measurements, (95% CI)								
Body mass index, kg/m ²		33.2 (32.2, 34.2)		33.2 (31.6, 34.8)		32.6 (30.9, 34.2)		32.2 (30.3, 34.0)
Systolic blood pressure, mmHg		127.9 (126.1, 129.6)		134.9 (131.3, 138.5)		130.7 (125.9, 135.6)		145.6 (140.1, 151.0)
Diastolic blood pressure, mmHg		70.4 (69.1, 71.7)		72.0 (69.1, 74.8)		61.1 (57.8, 64.3)		63.4 (60.4, 66.3)
Laboratory measurements								
Hemoglobin A1c, %		7.2 (7.1, 7.4)		7.8 (7.6, 8.0)		6.9 (6.6, 7.3)		7.2 (6.8, 7.6)
Serum lipids								
Total cholesterol, mg/dL		190.5 (186.2, 194.8)		197.8 (190.7, 204.8)		184.0 (174.9, 193.2)		177.8 (163.6, 191.9)
HDL cholesterol, mg/dL		47.1 (45.9, 48.4)		46.7 (44.1, 49.3)		48.6 (45.2, 52.0)		50.7 (47.6, 53.8)
LDL cholesterol, mg/dL		107.4 (102.0, 112.7)		103.4 (94.0, 112.8)		103.3 (92.2, 114.5)		88.2 (73.8, 102.7)
Triglycerides, mg/dL		145.9 (135.2, 157.4)		172.8 (146.5, 203.8)		147.8 (127.5, 171.4)		153.5 (129.6, 181.9)

Diabetes complications								
Diabetic retinopathy, %	201	27.8 (23.7, 32.4)	128	39.1 (32.9, 45.7)	49	42.5 (30.7, 55.1)	74	53.0 (38.4, 67.1)
Retinopathy on retinal photography	140	18.7 (15.3, 22.8)	88	22.3 (17.3, 28.2)	38	33.0 (21.5, 46.9)	48	33.2 (22.4, 46.2)
Macular edema on retinal photography	21	1.8 (1.1, 3.0)	13	2.7 (1.2, 6.1)	9	9.8 (4.0, 21.9)	11	6.2 (3.0, 12.5)
Cardiovascular disease, %	131	16.9 (13.6, 20.9)	74	23.5 (17.7, 30.4)	43	35.5 (25.8, 46.5)	79	60.0 (49.6, 69.0)
Self-reported congestive heart failure	41	5.0 (3.6, 7.0)	24	7.9 (4.9, 12.5)	25	20.6 (13.7, 29.8)	39	29.9 (21.3, 40.2)
Self-reported coronary heart disease	50	6.8 (4.9, 9.3)	27	9.4 (5.6, 15.2)	20	15.9 (10.1, 24.0)	34	30.7 (20.2, 43.6)
Self-reported heart attack	51	7.3 (5.6, 9.4)	27	8.0 (4.6, 13.6)	16	10.8 (5.4, 20.6)	49	38.2 (27.2, 50.5)
Self-reported stroke	48	5.7 (3.8, 8.5)	27	9.3 (5.8, 14.5)	11	13.7 (6.7, 25.8)	33	24.1 (15.2, 36.0)

Cell contents are raw numbers of participants, percentage (95% CI) of US adults with diabetes, or mean (95% CI) among US adults with diabetes.¹ These definitions of medication use included new drugs that were not available during previous analyses. Diabetic retinopathy was defined as self-reported diabetic retinopathy, or retinopathy or macular edema on retinal photography. Abbreviations: ACR = albumin-creatinine ratio; eGFR = estimated glomerular filtration rate; RAAS = renin-angiotensin-aldosterone system; ACE = angiotensin converting enzyme; HDL = high density lipoprotein, LDL = low density lipoprotein.

eTable 4. Prevalence of albuminuria among adults with diabetes in the United States, 1988-2014, with and without adjustment for estimated glomerular filtration rate.

NHANES period	Unadjusted Prevalence, accounting for persistence (95% CI)	Model 1		Model 2	
		Prevalence Ratio (95% CI)	p-value for trend	Prevalence Ratio (95% CI)	p-value for trend
1988-1994	20.8 (16.3-25.3)	1.0 (Ref.)	<0.001	1.0 (Ref.)	<0.001
1999-2004	18.9 (15.3-22.4)	0.93 (0.79-1.06)		0.87 (0.75, 1.01)	
2005-2008	17.9 (14.0-21.9)	0.86 (0.75-1.01)		0.83 (0.72, 0.96)	
2009-2014	15.9 (12.7-19.0)	0.76 (0.65-0.89)		0.73 (0.62, 0.85)	

Cell contents are proportions (%) of US adults with diabetes, adjusted prevalence ratio (95%CI), or p-value for trend across NHANES periods. Model 1 is adjusted for age, sex, and race/ethnicity. Model 2 is adjusted for age, sex, race/ethnicity, and estimated glomerular filtration rate (GFR). All prevalence values and prevalence ratios take into account information on the persistence of albuminuria.