Trends in Diabetes, High Cholesterol, and Hypertension in Chronic Kidney Disease Among U.S. Adults: 1988–1994 to 1999–2004

Citation

Published Version

Permanent link

Terms of Use

Share Your Story

Trends in Diabetes, High Cholesterol, and Hypertension in Chronic Kidney Disease Among U.S. Adults: 1988–1994 to 1999–2004

CAROLINE S. FOX, MD, MPH[1,2]
PAUL MUNTNER, PHD[3]

OBJECTIVE — The prevalence of chronic kidney disease (CKD) increased among U.S. adults from 1988–1994 to 1999–2004. We sought to explore the importance of trends in risk factors for CKD over time

RESEARCH DESIGN AND METHODS — The prevalence of cigarette smoking, obesity, hypertension, high cholesterol, and diabetes among U.S. adults with stage 3 CKD (estimated glomerular filtration rate <60 ml/min per 1.73 m^2) and albuminuria (urinary albumin-to-creatinine ratio ≥30 mg/g), separately, were determined for 1988–1994 and 1999–2004 using data from serial National Health and Nutrition Examination Surveys. The prevalence ratios (PRs) for stage 3 CKD and albuminuria by the presence of these risk factors were compared across survey periods.

RESULTS — The PR for CKD declined between 1988–1994 and 1999–2004 for obesity (PR 1.51 and 1.14 for 1988–1994 and 1999–2004, respectively; P for change = 0.010), hypertension (PR 2.60 and 1.70; P for change = 0.005), and high cholesterol (PR 1.58 and 1.20; P for change = 0.028). However, for diagnosed diabetes, the PR remained unchanged (1.64 and 1.62; P for change = 0.898). Similar results were observed for undiagnosed diabetes (PR of CKD 1.38 and 1.50; P for change = 0.373). The association of cigarette smoking was similar in each time period. Besides obesity, for which the association remained stable over time, similar patterns were observed for the PR of albuminuria.

CONCLUSIONS — In terms of CKD, improvements in hypertension and high cholesterol management have been offset by both diagnosed and undiagnosed diabetes. Further increases in CKD may occur if diabetes continues to increase.

Chronic kidney disease (CKD) is a common condition, affecting a substantial proportion of adults in the U.S. and worldwide (1). A recent analysis documented a marked increase in CKD prevalence among U.S. adults over the past decade (2). Due to its impact on quality of life, cardiovascular disease (CVD) incidence, and mortality, CKD is an important public health challenge (3–5).

Obesity, smoking, hypertension, high cholesterol, and diabetes are key risk factors for CKD (6–9). Awareness, treatment, and control of hypertension has improved over the past several decades (10,11). Significant reductions in mean cholesterol levels have occurred as well (12), likely due to dietary changes and increasing usage of cholesterol-lowering medications. However, the prevalence and incidence of diabetes continue to increase (13–16), fueled by marked increases in obesity (17).

We hypothesized that CKD related to

hypertension and high cholesterol has decreased over time, likely due to improvements in the management of these conditions. However, given an ongoing increase in the prevalence of diabetes without significant improvements in its treatment (18), we further hypothesized that CKD related to diabetes has increased. We tested these hypotheses by assessing trends in the association of cigarette smoking, obesity, hypertension, high cholesterol, and diabetes with CKD and albuminuria between 1988–1994 and 1999–2004 using data from the Third National Health and Nutrition Examination Survey (NHANES) III and NHANES 1999–2004.

RESEARCH DESIGN AND METHODS

Study sample
NHANES III and NHANES 1999–2004 are cross-sectional nationally representative surveys of the noninstitutionalized civilian population of the U.S. Briefly, each survey employs a multistage stratified probability sample based on selection of counties, blocks, households, and persons within households. Mexican-Americans, non-Hispanic blacks, and older adults were oversampled in order to improve the estimate precision for these groups. Each NHANES consisted of an in-home interview and medical evaluation and a blood sample collection in a mobile examination center. In NHANES III and NHANES 1999–2004, 18,825 and 15,332 participants, respectively, completed the medical evaluation and study interview. Exclusions for the current study included those without serum creatinine measurements, estimated glomerular filtration rate (GFR)< 30 ml/min per 1.73 m^2, and women pregnant at the examination, resulting in 15,502 and 12,453 participants from NHANES III and NHANES 1999–2004, respectively, available for analysis of stage 3 CKD. For the analysis of albuminuria, individuals missing urinary albumin or creatinine

Table 1—CVD factors among NHANES III and NHANES 1999–2004 participants 20 years of age and older with and without stage 3 CKD

	Stage 3 CKD			No stage 3 CKD		
	NHANES III	NHANES 1999–2004	Age-adjusted P for time-period difference	NHANES III	NHANES 1999–2004	Age-adjusted P for time-period difference
n	882	994	—	13,499	11,459	—
Mean age (years)	71.5 (0.8)	70.7 (0.6)	0.424	44.0 (0.4)	45.0 (0.3)	0.050
Male sex	36.6 (3.0)	36.1 (1.4)	0.839	49.1 (0.4)	49.9 (0.4)	0.552
Black race	7.0 (0.8)	6.7 (0.9)	0.792	10.4 (0.6)	10.6 (1.0)	0.878
Mean SBP (mmHg)	140.8 (1.1)	138.9 (0.9)	0.303	120.2 (0.4)	122.8 (0.4)	0.001
Mean DBP (mmHg)	72.9 (0.6)	68.3 (0.6)	<0.001	73.2 (0.3)	72.7 (0.2)	<0.001
On anti-HT medications*	71.0 (2.5)	79.0 (2.2)	0.016	50.4 (1.2)	60.0 (1.6)	<0.001
Mean BMI (kg/m^2)	27.6 (0.2)	28.7 (0.3)	0.013	26.5 (0.1)	28.0 (0.1)	<0.001
Mean total cholesterol (mg/dl)	232.1 (3.0)	206.8 (1.8)	<0.001	203.1 (0.8)	202.2 (0.7)	<0.001
On cholesterol-lowering medication†	22.9 (3.9)	61.8 (2.5)	<0.001	13.5 (1.0)	38.3 (1.4)	<0.001
Glycated hemoglobin (%)	6.03 (0.07)	5.83 (0.04)	0.013	5.35 (0.02)	5.46 (0.02)	0.405
Cigarette smokers	12.4 (1.8)	8.1 (1.5)	0.033	29.1 (0.8)	21.6 (0.7)	<0.001
Obese	31.6 (2.2)	32.2 (1.6)	0.755	22.1 (0.7)	29.8 (0.8)	<0.001
Hypertension	72.7 (2.0)	70.5 (1.8)	0.622	21.6 (0.8)	27.2 (0.8)	<0.001
High cholesterol	46.8 (2.6)	44.4 (2.0)	0.326	20.5 (0.6)	24.4 (0.6)	<0.001
Diabetes						
Diagnosed	13.0 (1.3)	16.8 (1.8)	0.093	3.3 (0.2)	5.0 (0.3)	0.039
Undiagnosed	10.6 (2.1)	10.3 (1.7)	0.583	3.2 (0.3)	3.6 (0.3)	0.882

Data are n (%) unless otherwise indicated. *Among participants with a diagnosis of hypertension; †among participants with a diagnosis of high cholesterol. All P values (except age) for comparing mean levels and prevalence between NHANES III and NHANES 1999–2004 are age adjusted. DBP, diastolic blood pressure; HT, hypertensive; SBP, systolic blood pressure.

measurements and pregnant or menstruating women were excluded, resulting in valid data from 15,216 and 12,778 participants from NHANES III and NHANES 1999–2004, respectively.

Covariate data
Of relevance to the current analysis, variables collected during the in-home interview were age, race/ethnicity, sex, cigarette smoking, a history of diabetes, and pharmacologic treatment for hypertension, high cholesterol, or diabetes. Participants who reported having smoked ≥100 cigarettes during their lifetime were classified as current or former smokers if they answered affirmatively or negatively, respectively, to the question "Do you now smoke cigarettes?" A fixed stadiometer was used to measure height; a Toledo digital scale was used to measure weight with participants clothed in underwear, a disposable gown, and foam slippers. BMI was calculated as weight in kilograms divided by the square of height in meters; obesity was defined as BMI ≥30 kg/m^2.

Three blood pressure measurements were obtained using a standard protocol (American Heart Association) during the

evaluation. While three additional blood pressure measurements were taken during the NHANES III in-home interview, for comparability, the current analyses were limited to blood pressure measurements from the medical evaluation. Using the mean of all available blood pressure measurements, systolic and/or diastolic blood pressure ≥140 mmHg and/or ≥90 mmHg, respectively, or current use of blood pressure–lowering medication was used to define hypertension.

Laboratory measurements and exposure definitions
Blood samples were stored at −20°C. For lipid analyses, samples were shipped to the Lipoprotein Analytical Laboratory (Johns Hopkins University, Baltimore, MD). Total cholesterol was measured with the Hitachi 704 Analyzer; high cholesterol was defined as levels ≥240 mg/dl or concurrent pharmacologic lipid-lowering treatment.

Glucose was measured on previously frozen plasma at the University of Missouri at Columbia. Self-report of a prior diagnosis of diabetes with current use of an oral hypoglycemic agent or insulin was used to define diagnosed diabetes. For

participants without diagnosed diabetes who attended a morning NHANES study visit after fasting 8 h or longer ($n = 7,329$ and 5,572 for NHANES III and NHANES 1999–2004, respectively), undiagnosed diabetes was defined as plasma glucose ≥126 mg/dl.

Outcome definitions
Serum creatinine was measured using the modified kinetic method of Jaffe (Hitachi 917 analyzer). Serum creatinine concentrations were calibrated to the assays used for the development of the modification of diet in renal disease (MDRD) equation (19). GFR was estimated with the simplified MDRD equation. Individuals with an estimated GFR (eGFR) of 30–59 ml/min per 1.73 m^2 were considered to have stage 3 CKD.

Urine albumin and creatinine concentrations were measured in the same laboratory during both surveys. Urinary albumin was measured using a solid-phase fluorescence immunoassay; urinary creatinine was measured using modified kinetic method of Jaffe (Astra Analyzer; Beckman Coulter Synchron). Albuminuria was defined as a urinary albumin–to–urinary creatinine ratio ≥30
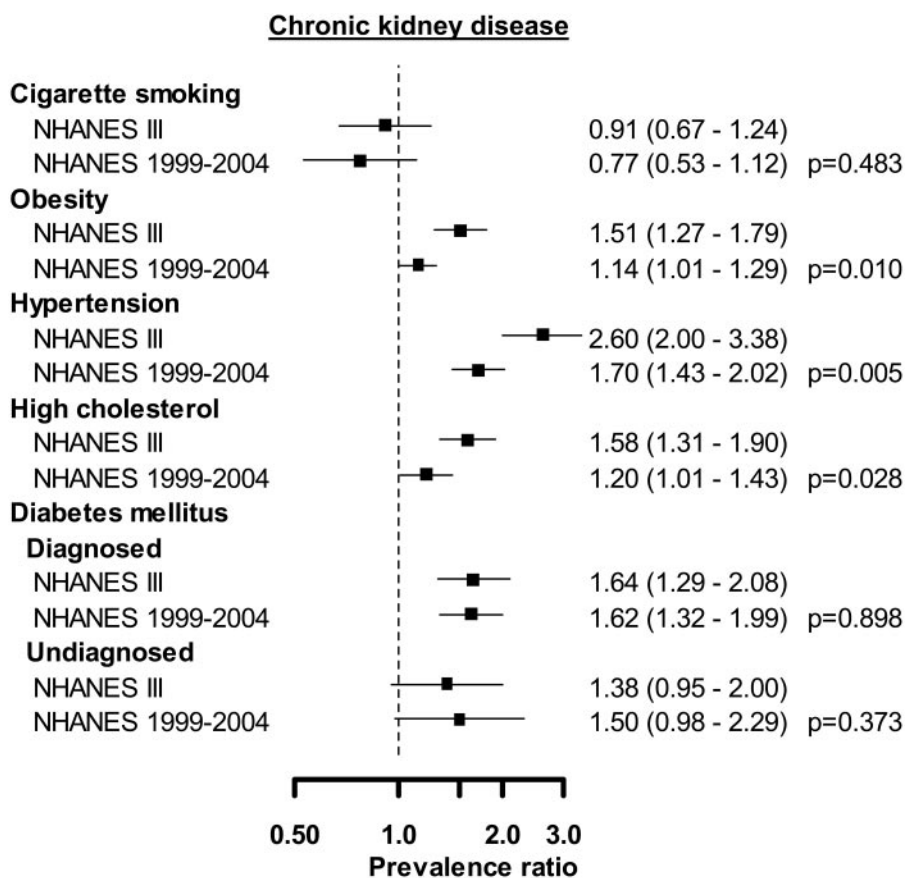
Figure 1—*PRs of CKD associated with selected risk factors in 1988–1994 (NHANES III) and in 1999–2004 (NHANES 1999–2004). Adjusted for age, race, sex, hypertension, and self-reported diabetes (except hypertension, which is adjusted for age, race, sex, and diabetes, and diabetes, which is adjusted for age, race, sex, and hypertension). P represents changes in the PRs over time.*

mg/g. The protocols for NHANES III and NHANES 1999–2004 were approved by the National Center for Health Statistics of the Centers for Disease Control and Prevention Institutional Review Board.

Statistical methods
Characteristics of the populations with and without stage 3 CKD and with and without albuminuria were calculated for each time period. Characteristics included age, race/ethnicity, sex, mean levels of systolic and diastolic blood pressure, BMI, total cholesterol, glycated hemoglobin, use of blood pressure– and cholesterol-lowering medications, and prevalence of cigarette smoking, obesity, hypertension, high cholesterol, and diagnosed and undiagnosed diabetes. The statistical significance of differences in the means and prevalence estimates across the two surveys was determined using the Wald χ^2 test. Test statistics were calculated as the difference in prevalence estimates divided by the standard error of the difference, calculated as the square root of

the sum of each estimate's variance. The prevalence ratios (PRs) of stage 3 CKD and albuminuria associated with cigarette smoking, obesity, hypertension, high cholesterol, and diagnosed and undiagnosed diabetes were estimated for each time period, separately, using log-binomial regression models including adjustment for age, race, sex, hypertension, and self-reported diabetes. The statistical significance of changes in the PRs over time was calculated using two sample t tests (i.e., the difference in the β-coefficients from the regression models divided by the square root of the sum of their variance).

Sample weights that account for the complex survey design of NHANES, including unequal probabilities of selection, over-sampling, and nonresponse, were applied for all analyses using SUDAAN (Version 9.1; Research Triangle Institute, Research Triangle Park, NC). Standard errors were estimated using the Taylor series linearization method.

RESULTS

Demographic and risk factors among individuals with and without stage 3 CKD
Demographic characteristics, risk factor levels, and the prevalence of risk factors among individuals with and without stage 3 CKD in the two time periods are shown in Table 1. Among individuals with stage 3 CKD, the prevalence of cigarette smoking declined and obesity, hypertension, and high cholesterol remained stable. However, the prevalence of diagnosed diabetes increased (13.0 and 16.8% for NHANES III and NHANES 1999–2004, respectively), although this did not reach statistical significance ($P = 0.093$). Among individuals without CKD, the prevalence of obesity, hypertension, high cholesterol, and diagnosed diabetes increased, whereas the prevalence of undiagnosed diabetes was stable.

The PR for CKD associated with cigarette smoking was similar in both time periods, while the PR for CKD associated with obesity, hypertension, and high cholesterol was significantly lower in 1999–2004 compared with 1988–1994 (Fig. 1). For example, the PR for CKD associated with hypertension was 2.60 (95% CI 2.00–3.38) in NHANES III and decreased to 1.70 (1.43–2.02) in NHANES 1999–2004 (P for change = 0.005). However, for CKD associated with diagnosed diabetes, the PR remained unchanged (1.64 in NHANES III and 1.62 in NHANES 1999–2004; P for change = 0.898). Similar results were observed for undiagnosed diabetes: the PR for CKD was 1.38 and 1.50 in NHANES III and NHANES 1999–2004, respectively; P for change = 0.373).

Risk factors among individuals with and without albuminuria
Among individuals with albuminuria, the prevalence of cigarette smoking decreased between 1988–1994 and 1999–2004. The prevalence of hypertension, high cholesterol, and undiagnosed diabetes remained stable, whereas the prevalence of obesity and diagnosed diabetes increased (Table 2). The PRs for albuminuria associated with cigarette smoking and obesity was similar for 1988–1994 and 1999–2004 (Fig. 2). However, the PRs for albuminuria associated with hypertension and high cholesterol decreased over the time period under study ($P = 0.024$ and 0.020, respectively). The PR for albuminuria associated with diag-

Table 2—CVD risk factors among NHANES III and NHANES 1999–2004 participants 20 years of age and older with and without albuminuria

	Albuminuria			No albuminuria		
	NHANES III	NHANES 1999–2004	Age-adjusted *P* for time-period difference	NHANES III	NHANES 1999–2004	Age-adjusted *P* for time-period difference
n	1,810	1,711	—	13,406	11,067	—
Mean age (years)	57.3 (0.9)	56.3 (0.7)	0.380	44.2 (0.5)	45.6 (0.3)	0.016
Male sex	43.6 (2.3)	47.9 (1.3)	0.053	51.2 (0.4)	50.3 (0.4)	0.778
Black race	15.8 (1.2)	14.3 (1.6)	0.4	10.4 (0.6)	10.4 (1.0)	1.00
Mean SBP (mmHg)	137.9 (1.1)	138.2 (0.8)	0.346	120.0 (0.4)	122.6 (0.4)	0.021
Mean DBP (mmHg)	77.0 (0.5)	74.2 (0.6)	<0.001	73.1 (0.3)	72.4 (0.2)	<0.001
On anti-HT medications	60.0 (2.2)	66.8 (2.0)	0.005	51.5 (1.3)	61.4 (1.5)	<0.001
Mean BMI (kg/m^2)	28.0 (0.3)	29.3 (0.4)	<0.001	26.5 (0.1)	27.9 (0.1)	<0.001
Mean total cholesterol (mg/dl)	220.3 (1.7)	206.3 (2.1)	<0.001	203.4 (0.9)	202.4 (0.6)	<0.001
On cholesterol lowering medications	18.0 (2.8)	51.8 (2.8)	<0.001	11.9 (1.0)	39.6 (1.6)	<0.001
Glycated hemoglobin (%)	6.24 (0.08)	6.16 (0.05)	0.267	5.31 (0.02)	5.41 (0.01)	1.00
Cigarette smokers	27.0 (1.8)	20.5 (1.4)	0.002	28.8 (0.9)	20.7 (0.7)	<0.001
Obese	32.2 (1.7)	39.3 (2.2)	0.001	22.0 (0.6)	29.0 (0.7)	<0.001
Hypertension	57.6 (2.3)	57.4 (1.8)	0.496	21.2 (0.8)	27.4 (0.8)	<0.001
High cholesterol	37.3 (1.9)	33.6 (1.7)	0.658	23.5 (0.7)	25.1 (0.6)	0.044
Diabetes						
Diagnosed	18.0 (1.3)	21.6 (1.1)	0.01	2.4 (0.2)	4.3 (0.2)	0.014
Undiagnosed	11.6 (1.9)	14.1 (2.3)	0.822	3.0 (0.3)	2.9 (0.3)	0.861

Data are *n* (%) unless otherwise indicated. All *P* values (except age) for comparing mean levels and prevalence between NHANES III and NHANES 1999–2004 are age adjusted. DBP, diastolic blood pressure; HT, hypertensive; SBP, systolic blood pressure.

nosed diabetes decreased from 3.28 to 2.69 (*P* = 0.079), whereas the PR for albuminuria associated with undiagnosed diabetes increased nonsignificantly *P* = 0.594).

Self-reported diabetes
In a secondary analysis, diagnosed diabetes was redefined to include participants who self-reported diabetes regardless of whether they were on medication. Using this definition, the prevalence of diabetes increased between 1988–1994 and 1999–2004 from 16.0 to 19.1% among those with CKD and from 4.9 to 6.2% among adults without CKD. Also, the prevalence of diabetes increased from 21.4 to 24.1% and from 3.9 to 5.3% among adults with and without albuminuria, respectively. Similar to the main results, the PRs of CKD and albuminuria associated with self-reported diabetes did not change significantly over time (each *P* > 0.30; data not shown).

CONCLUSIONS

Principal findings
The current study suggests that the association of obesity, hypertension, and high cholesterol with CKD has declined over

time. Conversely, we observed no change in the association between diabetes and CKD. With the exception of obesity, for which the association with albuminuria did not change over time, similar trend results were observed for albuminuria.

In the present study, we demonstrate significant declines in the PRs for CKD associated with obesity, hypertension, and high cholesterol, suggesting that improvements have been made in terms of risk factor management. However, we observed no change in the PR of CKD due to diabetes over time. These findings suggest that similar improvements for diabetes management have not occurred. The association between obesity and CKD declined over the time period under study. National trends data have demonstrated improvements in blood pressure and lipid values across categories of BMI over time (20). Therefore, despite increasing rates of obesity, improved risk factor management may partially account for the present findings.

In the context of the current literature
Diabetes is a critical risk factor for CKD and albuminuria (6,21,22) and accounts for nearly half of all incident cases of end-

stage renal disease in the U.S. (8). Numerous studies have shown that the prevalence and incidence of diabetes continue to increase (13–16). The increase in number of U.S. adults with diabetes has lead to an increase in the attributable risk for diabetes as a CVD risk factor relative to other traditional risk factors (23). Rates of treatment and control of CVD risk factors among people with diabetes remains poor (18). Although U.S. vital statistics document a marked decline in cardiovascular mortality over the past several decades, recent data suggest that individuals with diabetes have not experienced the same mortality reductions (24). We extend these findings to relations between diabetes and CKD and show that the PR for CKD did not decline over the past decade.

In contrast, results for hypertension and high cholesterol are more encouraging. While hypertension has increased among U.S. adults over the past decade (11), rates of hypertension treatment and control have also increased. The improvement in overall management of hypertension, despite its increasing prevalence, is reflected in the reduced PR for hypertension as a CKD risk factor. Rates of high cholesterol have decreased over time (12). Dietary
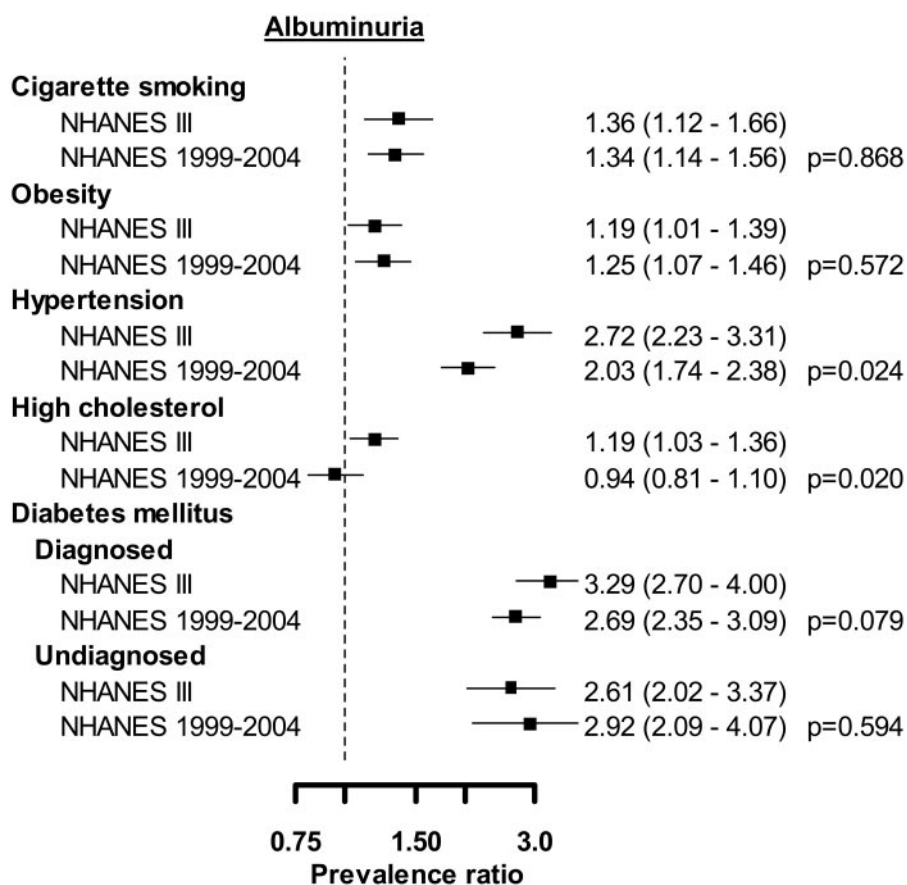
Albuminuria

Cigarette smoking		
NHANES III	1.36 (1.12 - 1.66)	
NHANES 1999-2004	1.34 (1.14 - 1.56)	p=0.868
Obesity		
NHANES III	1.19 (1.01 - 1.39)	
NHANES 1999-2004	1.25 (1.07 - 1.46)	p=0.572
Hypertension		
NHANES III	2.72 (2.23 - 3.31)	
NHANES 1999-2004	2.03 (1.74 - 2.38)	p=0.024
High cholesterol		
NHANES III	1.19 (1.03 - 1.36)	
NHANES 1999-2004	0.94 (0.81 - 1.10)	p=0.020
Diabetes mellitus		
Diagnosed		
NHANES III	3.29 (2.70 - 4.00)	
NHANES 1999-2004	2.69 (2.35 - 3.09)	p=0.079
Undiagnosed		
NHANES III	2.61 (2.02 - 3.37)	
NHANES 1999-2004	2.92 (2.09 - 4.07)	p=0.594

0.75   1.50   3.0
Prevalence ratio

Figure 2—*PRs of albuminuria associated with selected risk factors in 1988–1994 (NHANES III) and in 1999–2004 (NHANES 1999–2004). Adjusted for age, race, sex, hypertension, and self-reported diabetes (except hypertension, which is adjusted for age, race, sex, and diabetes, and diabetes, which is adjusted for age, race, sex, and hypertension). P represents changes in the PRs over time.*

improvements are likely partially responsible for these trends as well. Similar to the results for hypertension, our results indicate that an added benefit of these interventions may be the reduced risk of CKD and albuminuria associated with high cholesterol.

Strengths and limitations

Strengths of the current study include the well-characterized NHANES datasets, large sample size, and nationally representative data. We were able to examine CKD as defined by reduced eGFR as well as albuminuria, a well-established risk factor for CKD (25,26). Further, albuminuria identifies different subsets of individuals at risk for CVD and all-cause mortality as compared with CKD alone (27). Limitations include the use of the MDRD equation to estimate GFR instead of a direct measurement (28), which would not be feasible in a large population-based study. Further, the MDRD equation underestimates eGFR in healthy

individuals (29); how this impacts the dichotomous classification of CKD is uncertain. We used a study design that incorporated serial cross-sectional studies and therefore cannot infer causality between risk factors and CKD. However, we believe that this study design is the most powerful for determining overall trends in disease burden. Our sample was limited to individuals with stage 3 CKD due to small numbers of individuals with more severe CKD. Measures of albuminuria were based on a spot-urine collection. However, the correlation between 24-h collections and spot urine is acceptable (30). We relied on fasting plasma glucose and not an oral glucose tolerance test to define diabetes. Therefore, we may have underestimated the prevalence of undiagnosed diabetes in our sample. However, it is unlikely that this occurred differentially between NHANES III and NHANES 1999–2004. Therefore, this is unlikely to account for the observed findings.

Implications

Increases in obesity have lead to rises in the prevalence of diabetes. As diabetes continues to increase, the prevalence and incidence of CKD may continue to increase as well. Currently, individuals with diabetes are suboptimally managed with respect to CVD risk factors and overall glucose management (18). Less than half of individuals with CKD in the Framingham Heart Study had optimal A1C levels (31). Further, among individuals with CKD, diabetes, hypertension, and dyslipidemia, less than 10% of participants had optimal management of all of their risk factors. Improvement in CVD risk factor management, particularly diabetes, will be necessary to prevent further increases in CKD prevalence. Whether interventions focusing on weight loss and cholesterol reduction will reduce the risk of CKD require further study.

In conclusion, improvements in hypertension and high cholesterol management have been offset by both diagnosed and undiagnosed diabetes. Further increases in CKD may occur if diabetes continues to increase.

References
1. Coresh J, Astor BC, Greene T, Eknoyan G, Levey AS: Prevalence of chronic kidney disease and decreased kidney function in the adult US population: Third National Health and Nutrition Examination Survey. *Am J Kidney Dis* 41:1–12, 2003
2. Coresh J, Selvin E, Stevens LA, Manzi J, Kusek JW, Eggers P, Van LF, Levey AS: Prevalence of chronic kidney disease in the United States. *JAMA* 298:2038–2047, 2007
3. Go AS, Chertow GM, Fan D, McCulloch CE, Hsu CY: Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. *N Engl J Med* 351: 1296–1305, 2004
4. Anavekar NS, McMurray JJ, Velazquez EJ, Solomon SD, Kober L, Rouleau JL, White HD, Nordlander R, Maggioni A, Dickstein K, Zelenkofske S, Leimberger JD, Califf RM, Pfeffer MA: Relation between renal dysfunction and cardiovascular outcomes after myocardial infarction. *N Engl J Med* 351:1285–1295, 2004
5. Fried LF, Katz R, Sarnak MJ, Shlipak MG, Chaves PH, Jenny NS, Stehman-Breen C, Gillen D, Bleyer AJ, Hirsch C, Siscovick D, Newman AB: Kidney function as a predic-

tor of noncardiovascular mortality. *J Am Soc Nephrol* 16:3728–3735, 2005

6. Brancati FL, Whelton PK, Randall BL, Neaton JD, Stamler J, Klag MJ: Risk of end-stage renal disease in diabetes mellitus: a prospective cohort study of men screened for MRFIT: Multiple Risk Factor Intervention Trial. *JAMA* 278:2069–2074, 1997

7. Klag MJ, Whelton PK, Randall BL, Neaton JD, Brancati FL, Ford CE, Shulman NB, Stamler J: Blood pressure and end-stage renal disease in men. *N Engl J Med* 334: 13–18, 1996

8. U.S. Renal Data System: *USRDS 2006 Annual Data Report: Atlas of End-Stage Renal Disease in the United States*. Bethesda, MD, National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, 2006

9. Muntner P, Coresh J, Smith JC, Eckfeldt J, Klag MJ: Plasma lipids and risk of developing renal dysfunction: the atherosclerosis risk in communities study. *Kidney Int* 58:293–301, 2000

10. Ong KL, Cheung BM, Man YB, Lau CP, Lam KS: Prevalence, awareness, treatment, and control of hypertension among United States adults 1999–2004. *Hypertension* 49:69–75, 2007

11. Hajjar I, Kotchen TA: Trends in prevalence, awareness, treatment, and control of hypertension in the United States, 1988–2000. *JAMA* 290:199–206, 2003

12. Carroll MD, Lacher DA, Sorlie PD, Cleeman JI, Gordon DJ, Wolz M, Grundy SM, Johnson CL: Trends in serum lipids and lipoproteins of adults, 1960–2002. *JAMA* 294:1773–1781, 2005

13. Mokdad AH, Ford ES, Bowman BA, Nelson DE, Engelgau MM, Vinicor F, Marks JS: The continuing increase of diabetes in the U.S. *Diabetes Care* 24:412, 2001

14. Burke JP, Williams K, Gaskill SP, Hazuda HP, Haffner SM, Stern MP: Rapid rise in the incidence of type 2 diabetes from 1987 to 1996: results from the San Antonio Heart Study. *Arch Intern Med* 159: 1450–1456, 1999

15. Stovring H, Andersen M, Beck-Nielsen H, Green A, Vach W: Rising prevalence of diabetes: evidence from a Danish pharmaco-epidemiological database. *Lancet* 362:537–538, 2003

16. Fox CS, Pencina MJ, Meigs JB, Vasan RS, Levitzky YS, D'Agostino RB Sr: Trends in the incidence of type 2 diabetes mellitus from the 1970s to the 1990s: the Framingham Heart Study. *Circulation* 113: 2914–2918, 2006

17. Flegal KM, Carroll MD, Ogden CL, Johnson CL: Prevalence and trends in obesity among US adults, 1999–2000. *JAMA* 288:1723–1727, 2002

18. Saydah SH, Fradkin J, Cowie CC: Poor control of risk factors for vascular disease among adults with previously diagnosed diabetes. *JAMA* 291:335–342, 2004

19. Coresh J, Astor BC, McQuillan G, Kusek J, Greene T, Van Lente F, Levey AS: Calibration and random variation of the serum creatinine assay as critical elements of using equations to estimate glomerular filtration rate. *Am J Kidney Dis* 39:920–929, 2002

20. Gregg EW, Cheng YJ, Cadwell BL, Imperatore G, Williams DE, Flegal KM, Narayan KM, Williamson DF: Secular trends in cardiovascular disease risk factors according to body mass index in US adults. *JAMA* 293:1868–1874, 2005

21. Fox CS, Larson MG, Leip EP, Culleton B, Wilson PW, Levy D: Predictors of new-onset kidney disease in a community-based population. *JAMA* 291:844–850, 2004

22. Fox CS, Larson MG, Leip EP, Meigs JB, Wilson PW, Levy D: Glycemic status and development of kidney disease: the Framingham Heart Study. *Diabetes Care* 28: 2436–2440, 2005

23. Fox CS, Coady S, Sorlie PD, D'Agostino RB Sr, Pencina MJ, Vasan RS, Meigs JB, Levy D, Savage PJ: Increasing cardiovascular disease burden due to diabetes mellitus: the Framingham Heart Study. *Circulation* 115:1544–1550, 2007

24. Gregg EW, Gu Q, Cheng YJ, Narayan KM, Cowie CC: Mortality trends in men and women with diabetes, 1971–2000. *Ann Intern Med* 147:149–155, 2007

25. Nelson RG, Bennett PH, Beck GJ, Tan M, Knowler WC, Mitch WE, Hirschman GH, Myers BD: Development and progression of renal disease in Pima Indians with non-insulin-dependent diabetes mellitus: Diabetic Renal Disease Study Group. *N Engl J Med* 335:1636–1642, 1996

26. Hostetter TH, Rennke HG, Brenner BM: The case for intrarenal hypertension in the initiation and progression of diabetic and other glomerulopathies. *Am J Med* 72: 375–380, 1982

27. Foster MC, Hwang SJ, Larson MG, Parikh NI, Meigs JB, Vasan RS, Wang TJ, Levy D, Fox CS: Cross-classification of microalbuminuria and reduced glomerular filtration rate: associations between cardiovascular disease risk factors and clinical outcomes. *Arch Intern Med* 167:1386–1392, 2007

28. Levey AS, Greene T, Kusek J, Beck GJ, and Group MS: A simplified equation to predict glomerular filtration rate from serum creatinine. *J Am Soc Nephrol* 11:A0828, 2000

29. Rule AD, Larson TS, Bergstralh EJ, Slezak JM, Jacobsen SJ, Cosio FG: Using serum creatinine to estimate glomerular filtration rate: accuracy in good health and in chronic kidney disease. *Ann Intern Med* 141:929–937, 2004

30. Nathan DM, Rosenbaum C, Protasowicki VD: Single-void urine samples can be used to estimate quantitative microalbuminuria. *Diabetes Care* 10:414–418, 1987

31. Parikh NI, Hwang SJ, Larson MG, Meigs JB, Levy D, Fox CS: Cardiovascular disease risk factors in chronic kidney disease: overall burden and rates of treatment and control. *Arch Intern Med* 166:1884–1891, 2006