

Prevalence of Chronic Kidney Disease in Persons With Undiagnosed or Prehypertension in the United States

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Abstract—Hypertension is both a cause and a consequence of chronic kidney disease, but the prevalence of chronic kidney disease throughout the diagnostic spectrum of blood pressure has not been established. We determined the prevalence of chronic kidney disease within blood pressure categories in 17 794 adults surveyed by the National Health and Nutrition Examination Survey during 1999–2006. Diagnosed hypertension was defined as self-reported provider diagnosis (n=5832); undiagnosed hypertension was defined as systolic blood pressure ≥ 140 mm Hg or diastolic blood pressure ≥ 90 mm Hg, without report of provider diagnosis (n=3046); prehypertension was defined as systolic blood pressure ≥ 120 and < 140 mm Hg or diastolic blood pressure ≥ 80 and < 90 mm Hg (n=3719); and normal was defined as systolic blood pressure < 120 mm Hg and diastolic blood pressure < 80 mm Hg (n=5197). Chronic kidney disease was defined as estimated glomerular filtration rate < 60 mL/min per 1.73 m² or urinary albumin:creatinine ratio > 30 mg/g. Prevalences of chronic kidney disease among those with prehypertension and undiagnosed hypertension were 17.3% and 22.0%, respectively, compared with 27.5% with diagnosed hypertension and 13.4% with normal blood pressure, after adjustment for age, sex, and race in multivariable logistic regression. This pattern persisted with varying definitions of kidney disease; macroalbuminuria (urinary albumin:creatinine ratio > 300 mg/g) had the strongest association with increasing blood pressure category (odds ratio: 2.37 [95% CI: 2.00 to 2.81]). Chronic kidney disease is prevalent in undiagnosed and prehypertension. Earlier identification and treatment of both these conditions may prevent or delay morbidity and mortality from chronic kidney disease. (*Hypertension*. 2010;55:1102-1109.)

Key Words: epidemiology ■ albuminuria ■ renal ■ prevention ■ awareness ■ surveillance

Hypertension is the second leading cause of end-stage renal disease (ESRD) in the United States¹ and is well established as both a cause and consequence of chronic kidney disease (CKD).² An estimated 26 million adults (13%) in the United States had CKD in 1999–2004, representing a 3% increase from the previous 10 years.³ Hypertension has been estimated to affect 29% of US adults.⁴ However, many adults with hypertension are not aware that they have this condition. Between 1999 and 2004, $\approx 28\%$ of those with hypertension were not aware of their diagnosis.⁴ What is unknown is how many adults in the United States who have undiagnosed hypertension also have CKD. Understanding the burden of CKD among adults with undiagnosed hypertension could assist public health and healthcare professionals in the prevention and screening efforts for both of these conditions.

In addition to the well-known risks of cardiovascular and renal diseases posed by hypertension, extensive literature is

emerging regarding the risks associated with elevated blood pressure throughout its diagnostic continuum. Several prospective studies have shown that even modestly elevated blood pressures place individuals at increased risk of ESRD relative to those with normal blood pressures.^{5–7} Recently published prospective data have shown that, even in the absence of diabetes mellitus and atherosclerosis, “high-normal” blood pressure (defined as systolic 130 to 139 mm Hg or diastolic 85 to 89 mm Hg) is associated with an ≈ 3 -fold greater risk of future development of ESRD.⁸

Given the evidence that risk of ESRD is increased throughout the diagnostic spectrum of elevated blood pressure, it is important to understand the prevalence of pre-ESRD CKD among persons with undiagnosed or prehypertension in the United States. Such data have not been reported previously and could serve as a platform for future studies on the efficacy of screening such persons for CKD. Therefore, we

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sought to determine the prevalence of CKD stages 1 to 4⁹ in individuals with undiagnosed or prehypertension using data from the National Health and Nutrition Examination Survey (NHANES) from 1999 to 2006. In addition, we sought to describe the demographic, socioeconomic, and clinical indicators of individuals with undiagnosed or prehypertension and CKD to provide a foundation for targeted studies of individuals who may be at an increased risk of the consequences of both conditions.

Methods

Study Design

The NHANESs are currently conducted every 2 years by the National Center for Health Statistics to examine disease prevalence and trends over time in representative samples of noninstitutionalized US civilian residents.¹⁰ The survey consists of a standardized in-home interview and a physical examination and blood and urine collection at a mobile examination center (MEC). Participants gave informed consent. The protocol was approved by an institutional review board.

We examined combined data from the 1999–2000, 2001–2002, 2003–2004, and 2005–2006 NHANESs. Although the total number of participants for these study years was 41 474, our study was limited to NHANES participants from 1999 to 2006 who provided self-reported information on hypertension and had blood pressure measured (n=31 266), underwent an MEC examination (n=29 815), were ≥ 20 years old (n=18 938), had estimated glomerular filtration rate (eGFR) ≥ 15 mL/min per 1.73 m² (n=18 885), and were not pregnant (final n=17 794).

Measurements

Blood pressure was measured during the MEC visit using a standardized protocol.¹¹ Each participant was in a seated position with ≥ 5 minutes of rest before the first measurement. Up to 3 brachial systolic and diastolic blood pressures (separated by 30 seconds after a 5-minute rest period) were taken by trained physicians using appropriate cuff sizes and a mercury sphygmomanometer. The averages of all of the available measurements for systolic and diastolic blood pressures were used.

Self-reported information on demographics (age, sex, and race/ethnicity), socioeconomic status (education, insurance, and income), and health conditions (diabetes mellitus) was obtained during the interview portions of the surveys. Income was assessed using the poverty income ratio, which is a ratio of household income to household poverty level.¹² In addition, prescription medication information was obtained during the interview, with the interviewer recording the names of medications from medication containers provided by the participant. Height and weight, used in the calculation of body mass index, 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 a solid-phase fluorescence immunoassay; urine creatinine was measured using the modified Jaffe kinetic method in the same laboratory.

Definitions

Diagnosed hypertension was defined by an answer of “yes” to the question, “Have you ever been told by a doctor or other health professional that you have hypertension, also called high blood pressure?” Among those who answered “no,” undiagnosed hypertension was defined by a measured average systolic blood pressure of ≥ 140 mm Hg or by a measured average diastolic blood pressure of ≥ 90 mm Hg, and prehypertension was defined by an average systolic blood pressure of ≥ 120 mm Hg and < 140 mm Hg (with diastolic < 90 mm Hg) or by a measured average diastolic blood pressure of ≥ 80 and < 90 mm Hg (with systolic < 140 mm Hg).¹³

Normal blood pressure was defined by an average systolic blood pressure of < 120 mm Hg and a measured average diastolic blood pressure of < 80 mm Hg and an answer of “no” to the same question.

CKD was defined using eGFR and the presence of albuminuria, according to the Kidney Disease Outcomes Quality Initiative staging guidelines.⁹ eGFR was calculated according to the modified Modification of Diet in Renal Disease Study equation for calibrated creatinine: $eGFR = 175 \times [(\text{calibrated serum creatinine in milligrams/deciliter})^{-1.154}] \times \text{age}^{-0.203} \times (0.742 \text{ if female}) \times (1.210 \text{ if black})$.^{14,15} Serum creatinine was calibrated to adhere to the Cleveland Clinic protocol for survey years 1999–2000 and 2005–2006 using regression formulas provided by NHANES; no correction was required for calibrated serum creatinine in participants in the 2001–2002 or 2003–2004 surveys.¹⁶ Albuminuria was considered to be present at urinary albumin:creatinine ratios of ≥ 30 mg/g. Microalbuminuria was defined as 30 to 300 mg/g of creatinine and macroalbuminuria as > 300 mg/g of creatinine. Because urinary albumin measurements in NHANES are cross-sectional, we did not have data on persistent albuminuria, and the definitions of stages in our study were, therefore, modified as follows: (1) stage 1, eGFR > 90 mL/min per 1.73 m² and the presence of albuminuria at a single measurement; (2) stage 2, eGFR 60 to 89 mL/min per 1.73 m² and the presence of albuminuria at a single measurement; (3) stage 3, eGFR 30 to 59 mL/min per 1.73 m²; and (4) stage 4, 15 to 29 mL/min per 1.73 m².

Self-reported diabetes mellitus was defined by an answer of “yes” to the question, “Have you ever been told by a doctor that you have diabetes or sugar diabetes?” The use of hypertension medications was defined as any prescription for diuretics, angiotensin-converting enzyme inhibitors, α - and/or β -blockers, calcium channel blockers, angiotensin II receptor blockers, central α -2 agonists, aldosterone receptor blockers, or direct vasodilators, either prescribed alone or in combination. CKD awareness was defined by an answer of “yes” to the question, “Have you ever been told by a doctor or other health professional that you have weak or failing kidneys?”

Statistical Methods

Participant characteristics were compared by hypertension status, as were the unadjusted proportions with CKD both overall and by patient characteristics. Variance of proportions was estimated with Taylor series linearization. These characteristics were examined in logistic models predicting CKD, with adjustment for age, sex, and race/ethnicity. Odds ratios and adjusted percentages were obtained from these models; only adjusted percentages are shown, because the odds ratios are likely to overestimate the relative risk here. Sensitivity analyses, in which diagnosed hypertension was also defined by use of hypertension medications, were also performed to estimate the effect of possible misclassification of medication-controlled hypertension. Additional sensitivity analyses were performed wherein various cutoffs of both reduced kidney function and albuminuria were also performed, as was an analysis using the Chronic Kidney Disease Epidemiology Collaboration equation¹⁷ to estimate glomerular filtration rate.

To estimate nationally representative population results, all of the analyses were performed using the svy commands in Stata version 10.0 to account for NHANES study design weights, strata, and pseudostrata. Appropriate NHANES 8-year MEC weights were used; 8-year weights were calculated as follows: 8-year weight = $1/2 \times 4$ -year weight (if survey year = 1999–2002); and 8-year weight = $1/4 \times 2$ -year weight (if survey year = 2003–2004 or 2005–2006).¹⁸ Estimates of the proportion of US adults with undiagnosed or prehypertension and CKD were calculated using 2006 US Census estimates of the number of individuals > 20 years of age (111 440 340) and the burden of undiagnosed hypertension, prehypertension, and CKD found in the present study.

Results

There were 17 794 NHANES participants from the 1999–2006 surveys who were ≥ 20 years old, underwent MEC examinations (including measurement of serum creatinine and urinary albumin:creatinine ratio), provided self-reported

Table 1. Characteristics of Adults Age ≥ 20 Years by Hypertension Status, NHANES 1999–2006

Characteristic	Hypertension Status			
	Diagnosed Hypertension (Self-Reported Diagnosis)	Undiagnosed Hypertension (SBP ≥ 140 mm Hg or DBP ≥ 90 mm Hg and No Self-Reported Diagnosis)	Prehypertension (SBP ≥ 120 and < 140 mm Hg or DBP ≥ 80 and < 90 mm Hg)	Normal (SBP < 120 mm Hg and DBP < 80 mm Hg)
N	5832	3046	3719	5197
Mean SBP, mm Hg	135.0 (0.39)	149.3 (0.62)	125.4 (0.17)	108.4 (0.15)
Mean DBP, mm Hg	73.5 (0.31)	80.6 (0.67)	74.4 (0.23)	66.6 (0.18)
Mean age, y	56.9 (0.44)	49.4 (0.52)	44.6 (0.35)	38.2 (0.27)
Sex, %				
Female	54.4 (52.5 to 56.3)	50.9 (48.6 to 53.1)	37.4 (35.6 to 39.3)	57.8 (56.1 to 59.4)
Race/ethnicity, %				
Non-hispanic white	74.0 (70.7 to 77.0)	68.4 (64.8 to 71.9)	72.9 (69.7 to 75.8)	71.1 (67.8 to 74.2)
Non-hispanic black	13.9 (11.6 to 16.5)	12.4 (10.4 to 14.7)	9.9 (8.3 to 11.9)	8.5 (7.1 to 10.1)
Hispanic	4.3 (3.2 to 5.7)	7.7 (6.3 to 9.3)	7.4 (6.0 to 9.1)	9.4 (8.0 to 11.1)
Education, %				
High school or more	76.2 (74.3 to 78.1)	77.4 (75.0 to 79.6)	81.7 (80.0 to 83.4)	83.4 (81.7 to 85.1)
Income quartiles*				
Q1 (low)	11.6 (10.5 to 12.8)	13.0 (11.0 to 15.2)	10.5 (9.3 to 11.9)	13.1 (11.6 to 14.7)
Q2	20.5 (18.8 to 22.2)	19.2 (17.4 to 21.3)	16.1 (14.3 to 18.2)	18.3 (16.7 to 20.1)
Q3	29.6 (27.6 to 31.6)	29.1 (26.6 to 31.8)	28.4 (26.3 to 30.7)	26.3 (24.8 to 28.0)
Q4 (high)	38.4 (35.7 to 41.1)	38.7 (35.8 to 41.6)	44.9 (41.8 to 48.0)	42.3 (39.4 to 45.3)
Insurance, %				
Insured	89.0 (87.3 to 90.5)	82.3 (80.3 to 84.2)	79.6 (77.2 to 81.8)	77.8 (76.0 to 79.4)
Routine site for health care, %				
Yes	94.3 (93.2 to 95.1)	84.0 (81.5 to 86.3)	80.8 (79.2 to 82.4)	80.8 (78.9 to 82.6)
Smoking, %				
Current	31.9 (29.6 to 34.2)	40.1 (37.0 to 43.3)	45.3 (42.6 to 48.1)	49.8 (46.6 to 53.0)
Past	5.5 (4.4 to 6.8)	7.2 (5.7 to 9.1)	7.9 (6.7 to 9.1)	9.7 (8.2 to 11.5)
Never	62.6 (60.3 to 64.9)	52.7 (49.5 to 55.9)	46.8 (44.4 to 49.3)	40.5 (37.4 to 43.6)
Body mass index, %				
≥ 30 kg/m ²	46.2 (44.6 to 47.9)	30.4 (28.1 to 32.9)	31.1 (29.0 to 33.4)	20.8 (19.3 to 22.4)
Self-reported diabetes mellitus, %				
Yes	16.7 (15.6 to 17.8)	6.1 (5.4 to 6.9)	4.4 (3.7 to 5.4)	2.5 (2.0 to 3.1)

SEs are reported in parentheses after continuous variables, and 95% CIs are reported for categorical variables. $P < 0.001$ for each comparison of characteristics across hypertension categories (using ANOVA). SBP indicates systolic blood pressure; DBP, diastolic blood pressure.

*Income was assessed using the poverty income ratio, which is a ratio of household income to household poverty level.

information on hypertension, and had measured blood pressures, excluding pregnant individuals and those with eGFR < 15 mL/min per 1.73 m². Among these participants, 5832 had diagnosed hypertension, 3046 had undiagnosed hypertension, 3719 had prehypertension, and 5197 had normal blood pressure. Participant characteristics by hypertension status are shown in Table 1. Mean systolic and diastolic blood pressures were highest in those with undiagnosed hypertension. Women composed the majority of those with diagnosed hypertension, whereas men were the majority in prehypertension. The proportion of individuals who were Hispanic was larger in undiagnosed hypertension and prehypertension than in diagnosed hypertension. High school graduates composed a greater percentage of participants with prehypertension and normal blood pressure than they did diagnosed and undiag-

nosed hypertension. Those participants whose annual household income (relative to household size) fell in the highest quartile were more likely to have prehypertension or normal blood pressure rather than diagnosed or undiagnosed hypertension. The presence of health insurance increased across the diagnostic spectrum of blood pressure, and individuals with health insurance composed the majority of those with diagnosed hypertension. The overwhelming majority of participants in all of the diagnostic groups reported having a regular site for health care, including 84% of those with undiagnosed hypertension. Those individuals with diagnosed hypertension were the least likely to report current or past cigarette smoking. Obese participants (body mass index ≥ 30 kg/m²) composed a greater percentage of those with diagnosed hypertension than they did undiagnosed and prehypertension.

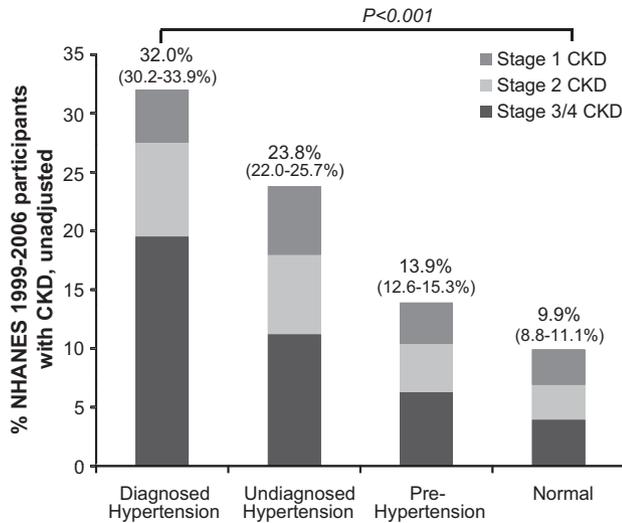


Figure 1. Population prevalence (%) of CKD stages 1 to 4, by hypertension status, NHANES 1999–2006. Diagnosed hypertension is defined as self-report of provider diagnosis; undiagnosed hypertension is defined as systolic blood pressure ≥ 140 mm Hg or diastolic blood pressure ≥ 90 mm Hg, without a report of provider diagnosis; prehypertension is defined as systolic blood pressure ≥ 120 and < 140 mm Hg or diastolic blood pressure ≥ 80 and < 90 mm Hg; and normal is defined as systolic blood pressure < 120 mm Hg and diastolic blood pressure < 80 mm Hg. CKD is defined by eGFR 15 to 59 mL/min per 1.73 m² or a single determination of albuminuria measurement. CKD stages were defined as stage 1, eGFR > 90 mL/min per 1.73 m² and presence of albuminuria at a single measurement; stage 2, eGFR 60 to 89 mL/min per 1.73 m² and presence of albuminuria at a single measurement; stage 3, eGFR 30 to 59 mL/min per 1.73 m²; and stage 4, 15 to 29 mL/min per 1.73 m². Values in parentheses represent 95% CIs.

Finally, self-reported diabetes mellitus increased across the diagnostic spectrum of blood pressure, with persons with diabetes mellitus composing 16.7% of those with diagnosed hypertension.

Figure 1 reveals that the unadjusted prevalence of CKD increases throughout the diagnostic spectrum of blood pressure, with 9.9%, 13.9%, 23.8%, and 32.0% having CKD in the normal blood pressure, prehypertension, undiagnosed hypertension, and diagnosed hypertension groups, respectively. In the same figure, examination of the stages of CKD revealed that the unadjusted prevalences of CKD stages 3/4 (eGFR 15 to 59 mL/min per 1.73 m²) were 3.9%, 6.3%, 11.2%, and 19.6% for the normal blood pressure, prehypertension, undiagnosed hypertension, and diagnosed hypertension groups, respectively. Notably, a greater proportion of CKD stage 3/4 was found among those with diagnosed hypertension than among the other groups (composing 61.0% of those with CKD and diagnosed hypertension).

Table 2 shows that even after adjustment for age, race/ethnicity, and sex the prevalence of CKD increases throughout blood pressure categories, with 13.4%, 17.3%, 22.0%, and 27.5% having CKD in the normal blood pressure, prehypertension, undiagnosed hypertension, and diagnosed hypertension groups, respectively. In addition, persons with either prehypertension or undiagnosed hypertension accounted for 35.0% of all cases of CKD, whereas those with diagnosed hypertension accounted for 52.2% of cases (data

not shown). These findings suggest that there are as many as 8 million US adults with undiagnosed hypertension or prehypertension who also have CKD (data not shown).

Increasing age and female sex were associated with greater prevalence of CKD in all of the hypertension groups (Table 2). Hispanics had the highest adjusted prevalence of CKD (39.8%) among those with diagnosed hypertension, and a similar, but nonsignificant, trend was present among those with undiagnosed hypertension and prehypertension. Lack of high school diploma was associated with a greater prevalence of CKD among those with prehypertension, undiagnosed hypertension, and diagnosed hypertension; and decreasing household income was associated with a greater prevalence of CKD in all of the blood pressure groups. Obesity was associated with a greater prevalence of CKD among those with diagnosed hypertension, and a similar (but nonsignificant) trend was seen among those with undiagnosed hypertension and prehypertension. Self-reported diabetes mellitus was associated with very high adjusted prevalence of CKD in all of the hypertension groups, including 43.4% of those with diabetes mellitus and undiagnosed hypertension and 21.0% of those with diabetes mellitus and prehypertension. Smoking history, insurance status, and having a routine healthcare site had no relationship with CKD in any category of blood pressure.

CKD awareness was assessed across blood pressure groups. Awareness was 2.0%, 2.2%, 3.5%, and 9.1%, among those with CKD and normal blood pressure, prehypertension, undiagnosed hypertension, and diagnosed hypertension, respectively (Figure 2). A sensitivity analysis examining the inclusion of reported antihypertensive medication use in the definition of diagnosed hypertension (n = 17 794), regardless of measured blood pressure or self-report, revealed similar results to the primary definition used above (data not shown).

Sensitivity analyses of various measures of kidney disease revealed that the presence of microalbuminuria was more common across the diagnostic continuum of hypertension than was the presence of decreased eGFR (Table 3). Microalbuminuria or macroalbuminuria was more common among younger persons (mean age: 42.5 years), whereas eGFR < 60 mL/min per 1.73 m² was more common among older persons (mean age: 72.4 years). Stricter definitions of kidney disease (eGFR < 45 mL/min per 1.73 m² or macroalbuminuria) resulted in much lower, but still substantial, CKD prevalence, with similar patterns across blood pressure categories (Table 3). Compared with other measures of kidney disease, macroalbuminuria had the strongest association with increasing blood pressure category. The use of the Chronic Kidney Disease Epidemiology Collaboration equation yielded similar but slightly attenuated estimates to our primary analysis (CKD prevalence of 26.0%, 20.5%, 16.0%, and 12.3% for the diagnosed, undiagnosed hypertension, prehypertension, and normal blood pressure groups, respectively). Adjustment for estimated persistence of albuminuria¹⁹ also resulted in slightly lower CKD prevalence across categories (24.5%, 14.8%, 14.9%, and 4.9%, respectively).

Discussion

We found the prevalence of CKD to be high among individuals with undiagnosed or prehypertension in the United

Table 2. Adjusted Prevalence of CKD by Participant Characteristics and Hypertension Status, NHANES 1999–2006

Characteristic	Percentage of Participants With CKD Stages 1 to 4			
	Diagnosed Hypertension (Self-Reported Diagnosis) (n=5832), % (95% CI)	Undiagnosed Hypertension (SBP ≥140 mm Hg or DBP ≥90 mm Hg, and No Self-Reported Diagnosis) (n=3046), % (95% CI)	Prehypertension (SBP ≥120 and <140 mm Hg or DBP ≥80 and <90 mm Hg) (n=3719), % (95% CI)	Normal (SBP <120 mm Hg and DBP <80 mm Hg) (n=5197), % (95% CI)
Overall	27.5 (25.7 to 29.4)	22.0 (20.8 to 23.2)	17.3 (16.3 to 18.3)	13.4 (12.3 to 14.6)
Age, y				
20 to 39	13.3 (11.1 to 15.8)	13.5 (11.3 to 16.0)	9.0 (7.7 to 10.5)	7.0 (5.9 to 8.3)
40 to 59	23.8 (21.6 to 26.1)	21.1 (19.3 to 23.2)	14.3 (13.0 to 15.6)	12.5 (11.1 to 14.0)
60 to 69	38.9 (37.1 to 40.1)	31.5 (29.4 to 33.7)	21.8 (19.8 to 24.0)	21.3 (18.5 to 24.4)
≥70	56.4 (53.7 to 59.1)	44.1 (39.9 to 48.5)	32.0 (27.9 to 36.4)	33.8 (27.9 to 40.3)
<i>P</i> _{trend}	<0.001	<0.001	<0.001	<0.001
Sex				
Male	33.6 (31.3 to 36.0)	22.7 (20.6 to 25.0)	10.5 (9.3 to 11.9)	8.4 (7.1 to 10.0)
Female	37.3 (34.9 to 39.8)	27.7 (24.9 to 30.8)	14.3 (12.1 to 16.9)	11.0 (9.5 to 12.7)
<i>P</i>	0.015	0.010	0.001	0.008
Race/ethnicity				
Non-hispanic white	33.0 (31.0 to 35.0)	24.0 (21.5 to 26.7)	13.3 (11.7 to 15.1)	8.7 (7.5 to 10.2)
Non-hispanic black	36.3 (34.3 to 38.4)	25.2 (23.5 to 27.1)	14.5 (13.2 to 15.9)	9.9 (8.7 to 11.2)
Hispanic	39.8 (36.5 to 43.2)	26.5 (23.5 to 29.7)	15.8 (13.7 to 18.2)	11.2 (9.5 to 13.2)
<i>P</i>	<0.001	0.280	0.083	0.014
Education				
Less than high school	42.8 (39.7 to 46.0)	30.7 (26.6 to 35.0)	16.8 (14.4 to 19.5)	10.4 (8.3 to 13.0)
High school or more	32.6 (30.4 to 35.0)	23.1 (20.9 to 25.5)	13.7 (12.2 to 15.3)	9.7 (8.4 to 11.1)
<i>P</i>	<0.001	0.005	0.030	0.546
Income quartiles*				
Q1 (low)	45.4 (41.9 to 48.9)	30.7 (25.6 to 36.5)	20.1 (16.5 to 24.3)	12.2 (10.1 to 14.6)
Q2	39.6 (37.6 to 41.6)	26.9 (24.1 to 29.8)	16.6 (14.7 to 18.5)	10.5 (9.2 to 11.9)
Q3	34.1 (32.0 to 36.3)	23.3 (21.4 to 25.4)	13.5 (12.2 to 15.0)	9.0 (7.9 to 10.3)
Q4 (high)	29.0 (25.7 to 32.5)	20.1 (17.1 to 23.5)	11.0 (9.0 to 13.3)	7.7 (6.3 to 9.4)
<i>P</i> _{trend}	<0.001	0.007	0.001	0.003
Insurance				
Yes	35.6 (33.7 to 37.6)	24.2 (22.1 to 26.5)	14.5 (13.0 to 16.1)	9.6 (8.2 to 11.1)
No	32.6 (27.4 to 38.3)	27.0 (22.0 to 32.7)	13.0 (10.3 to 16.3)	10.1 (8.2 to 12.4)
<i>P</i>	0.304	0.365	0.414	0.661
Smoking, %				
Current	36.5 (32.0 to 41.2)	29.9 (24.2 to 36.3)	14.4 (11.8 to 17.4)	9.1 (7.3 to 11.1)
Past	35.1 (32.9 to 37.4)	28.2 (25.2 to 31.4)	14.3 (12.6 to 16.2)	8.6 (7.3 to 10.1)
Never	33.8 (30.3 to 37.3)	26.6 (22.5 to 31.0)	14.3 (11.6 to 17.5)	8.2 (6.3 to 10.7)
<i>P</i> _{trend}	0.424	0.419	0.970	0.583
Routine site for health care, %				
Yes	36.6 (34.3 to 38.9)	25.6 (23.1 to 28.2)	14.4 (12.4 to 16.7)	9.6 (8.0 to 11.4)
No	34.3 (25.3 to 44.6)	30.2 (24.0 to 37.1)	15.1 (11.5 to 19.6)	9.1 (6.9 to 11.7)
<i>P</i>	0.657	0.242	0.798	0.727
Body mass index				
<30 kg/m ²	33.2 (30.9 to 35.6)	23.2 (21.0 to 25.5)	13.2 (11.7 to 14.8)	9.4 (8.2 to 10.8)
≥30 kg/m ²	37.2 (34.5 to 40.0)	27.0 (23.5 to 30.7)	16.2 (13.4 to 19.4)	10.4 (8.3 to 12.9)
<i>P</i>	0.018	0.094	0.074	0.387
Self-reported diabetes mellitus				
Yes	55.1 (51.5 to 58.6)	43.4 (34.1 to 53.2)	21.0 (15.3 to 28.1)	22.7 (15.5 to 32.0)
No	31.0 (28.9 to 33.2)	23.6 (21.8 to 25.5)	13.8 (12.5 to 15.2)	9.4 (8.2 to 10.7)
<i>P</i>	<0.001	<0.001	0.014	<0.001

CKD is defined by eGFR 15 to 59 mL/min per 1.73 m² or a single albuminuria measurement (stage 1, eGFR >90 mL/min per 1.73 m² and presence of albuminuria at a single measurement; stage 2, eGFR 60 to 89 mL/min per 1.73 m² and presence of albuminuria at a single measurement; stage 3, eGFR 30 to 59 mL/min per 1.73 m²; stage 4, 15 to 29 mL/min per 1.73 m²). Prevalence estimates for each covariate were adjusted for age, sex, and race/ethnicity in individual logistic regression models. *P*_{trend} values represent statistical significance across ordinal categorical variables within blood pressure categories.

*Income was assessed using the poverty income ratio, which is a ratio of household income to household poverty level.

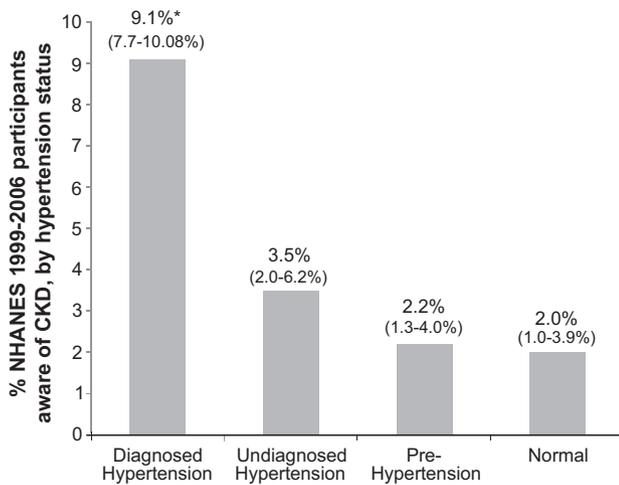


Figure 2. Prevalence of CKD awareness (%), by hypertension status, NHANES 1999–2006. Diagnosed hypertension is defined as self-report of provider diagnosis; undiagnosed hypertension is defined as systolic blood pressure ≥ 140 mm Hg or diastolic blood pressure ≥ 90 mm Hg, without a report of provider diagnosis; prehypertension is defined as systolic blood pressure ≥ 120 and < 140 mm Hg or diastolic blood pressure ≥ 80 and < 90 mm Hg; and normal is defined as systolic blood pressure < 120 mm Hg and diastolic blood pressure < 80 mm Hg. CKD is defined by eGFR 15 to 59 mL/min per 1.73 m² or a single determination of albuminuria. Values in parentheses represent 95% CIs. *Statistically different from other awareness estimates ($P < 0.001$).

States. Although CKD was most prevalent among those with diagnosed hypertension, persons with either undiagnosed or prehypertension accounted for more than one third of all cases of CKD, representing an estimated 8 million US adults. In addition, we found that such individuals are largely unaware of their kidney disease.

Prevalence of CKD was found to be increased across the spectrum of blood pressure, with those with normal blood pressure having the lowest prevalence of CKD and those with diagnosed hypertension having the greatest prevalence. Microalbuminuria was the most commonly noted marker of kidney disease across all of the blood pressure categories, far more common than reduced eGFR or macroalbuminuria. Importantly, our study provides evidence that the risk factors

for CKD are similar across blood pressure categories. We noted that certain demographic (increasing age, female sex, and Hispanic ethnicity), socioeconomic (limited education and low income), and clinical (diabetes mellitus and obesity) factors were each associated with an increased prevalence of CKD irrespective of blood pressure category.

Our finding that the prevalence of CKD was lower among the undiagnosed as compared with those with diagnosed hypertension may be because of a number of patient, physician, and healthcare system factors. For example, patients with greater kidney disease severity may be more likely to have received blood pressure measurements by their physician, potentially leading to a diagnosis of hypertension. This idea is supported by our finding of a greater proportion of CKD stage 3/4 among those with diagnosed hypertension than among other blood pressure groups.

Individuals with both undiagnosed hypertension and CKD represent a population uniquely in need of improved screening efforts. The Seventh Report of the Joint National Committee recommends screening persons on antihypertensive therapy with creatinine measures ≥ 1 to 2 times annually. Also, the report recommends aggressive blood pressure control to $< 130/80$ mm Hg in persons with hypertension and CKD or diabetes mellitus.¹³ Individuals with undiagnosed hypertension may not be receiving these recommended evaluation and treatment measures. In addition, in the absence of traditional risk factors for CKD (eg, younger persons, nonobese, and those without diabetes mellitus), providers who see these persons may not be screening them for CKD or aiming for treatment targets appropriate for CKD patients. Our analysis demonstrated that 17.7% of adults with undiagnosed hypertension lack health insurance, and 16.0% do not have a routine site for health care. In addition, we found that the greatest burden of CKD in the setting of undiagnosed hypertension is among those with very low income, again suggesting that healthcare resources may be very limited in this population. Also, CKD awareness was extremely low in this population, as has been shown in the general population,²⁰ underscoring the need for improved education both in the community and among healthcare providers, especially because awareness of hypertension has also been shown to be suboptimal but improving.⁴

Table 3. Adjusted Prevalence of Various Measures of Kidney Disease by Hypertension Status, NHANES 1999 to 2006

Measure of Kidney Disease	Percentage of Participants With Each Measure of Kidney Disease				Odds of Kidney Disease as Hypertension Category Increases (Normal to Diagnosed), Odds Ratio, (95% CI)
	Diagnosed Hypertension (Self-Reported Diagnosis) (n=5832), % (95% CI)	Undiagnosed Hypertension (SBP ≥ 140 mm Hg or DBP ≥ 90 mm Hg, and No Self-Reported Diagnosis) (n=3046), % (95% CI)	Prehypertension (SBP ≥ 120 and < 140 mm Hg or DBP ≥ 80 and < 90 mm Hg) (n=3719), % (95% CI)	Normal (SBP < 120 mm Hg and DBP < 80 mm Hg) (n=5197), % (95% CI)	
Microalbuminuria*	12.5 (11.5 to 13.6)	9.5 (8.8 to 10.2)	7.1 (6.6 to 7.7)	5.3 (4.7 to 5.9)	1.37 (1.30 to 1.44)
Macroalbuminuria†	3.3 (2.7 to 4.0)	1.4 (1.1 to 1.7)	0.6 (0.4 to 0.8)	0.2 (0.2 to 0.4)	2.37 (2.00 to 2.81)
eGFR < 60 ‡	7.8 (6.6 to 9.2)	5.6 (4.9 to 6.4)	4.0 (3.4 to 4.6)	2.8 (2.3 to 3.4)	1.43 (1.33 to 1.53)
eGFR < 45 ‡	1.4 (1.0 to 2.0)	0.8 (0.6 to 1.1)	0.5 (3.7 to 6.8)	0.3 (0.2 to 0.4)	1.69 (1.43 to 2.00)

Prevalence estimates for each measure of kidney disease were adjusted for age, sex, and race/ethnicity in individual logistic regression models.

*Microalbuminuria is defined as 30 to 300 mg/g of creatinine.

†Macroalbuminuria is defined as > 300 mg/g of creatinine.

‡eGFR was measured in milliliters per minute per 1.73 meters squared.

We found that the prevalence of CKD among persons with prehypertension is higher than that of those with normal blood pressure. This finding complements previous studies recognizing the risk of ESRD throughout the continuum of hypertension.⁵ Thus, persons with prehypertension may warrant increased screening and preventive efforts toward identifying and reducing the risk of CKD. Such efforts have been encouraged in the Kidney Disease Improving Global Outcomes position statement, wherein it is recommended that CKD screening be targeted at those who would derive the most benefit.²¹ However, screening for CKD using urinary albumin testing has only been estimated to be cost-effective in high-risk patient populations, including individuals with hypertension.²² Little is known about the cost-effectiveness of screening those with prehypertension for CKD. Such individuals may have other well-established indications for CKD screening, such as diabetes mellitus, which may lead their physician to evaluate them for CKD. In our study, we found that 21% of individuals with prehypertension and CKD also had diabetes mellitus. Additional study of the most appropriate patient populations to undergo CKD screening is needed.

To our knowledge, this is the first report of population-based CKD prevalence estimates across the diagnostic spectrum of blood pressure classification in the United States. Our study does have certain limitations, however. First, given the cross-sectional design of NHANES, we were not able to follow the relationship between hypertension status and CKD over time, and blood pressures were measured on a single day as opposed to on ≥ 2 separate days as guidelines for the diagnosis of hypertension recommend.¹³ CKD was also defined on the basis of a single laboratory measure, as opposed to measures separated by ≥ 3 months, as the Kidney Disease Outcomes Quality Initiative guidelines recommend.⁹ We attempted to address this by estimating the persistence of albuminuria and found slightly attenuated prevalence estimates. Third, NHANES participants are a representative sample of the noninstitutionalized civilian US population; therefore, we may have missed some individuals with greater disease severity, such as nursing home residents. We were also limited to those participants in NHANES who completed the MEC examination, which may represent a more highly motivated population than those who only completed the survey. Fourth, some cases of hypertension may have been misclassified because of the definitions that were used in our study. For example, persons with well-controlled hypertension may have been classified as having prehypertension or normal blood pressure if they did not report knowledge of their diagnosis. We attempted to address this issue by performing a sensitivity analysis evaluating the use of antihypertensive medications as the defining factor for diagnosed hypertension and found largely similar results to our primary definition. Fifth, because our blood pressure cutoff for diagnosed hypertension was that recommended for the general adult population by the Seventh Report of the Joint National Committee, we may have misclassified persons with diabetes mellitus whose physicians may have “diagnosed” them with hypertension when their blood pressure reached $>130/80$ mm Hg, which may have resulted in an overestimate of the proportion with diagnosed hypertension. Finally, our measure

of CKD awareness may not have captured all of the participants who were aware of their kidney disease, because many physicians may not communicate CKD as being the presence of “weak or failing kidneys.”

Perspectives

The prevalence of CKD is high among individuals with undiagnosed hypertension or prehypertension in the United States. The presence of macroalbuminuria has the strongest relationship with increasing blood pressure category; however, the prevalence of CKD increases across the diagnostic spectrum of hypertension regardless of how kidney disease is defined. CKD awareness is low among individuals with undiagnosed hypertension or prehypertension and CKD. Risk factors for CKD are similar across blood pressure categories. Persons with undiagnosed hypertension or prehypertension warrant further study of appropriate CKD education, screening, and prevention programs, because they are likely at high risk for the detrimental effects of both conditions.

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Disclosures

None.

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Prevalence of Chronic Kidney Disease in Persons With Undiagnosed or Prehypertension in the United States

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Title: Prevalence of Chronic Kidney Disease in Persons with Undiagnosed or Pre-Hypertension in the U.S.

Running Title: Kidney Disease in Undiagnosed or Pre-Hypertension

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