Potential implications of the 2021 KDIGO blood pressure guideline for adults with chronic kidney disease in the United States

Kathryn E. Foti[1], Dan Wang[1], Alexander R. Chang[2], Elizabeth Selvin[1], Mark J. Sarnak[3], Tara I. Chang[4], Paul Muntner[5] and Josef Coresh[1]

[1]Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland, USA; [2]Kidney Health Research Institute, Geisinger Health, Danville, Pennsylvania, USA; [3]Division of Nephrology, Tufts Medical Center, Tufts University School of Medicine, Boston, Massachusetts, USA; [4]Division of Nephrology, Department of Medicine, Stanford University School of Medicine, Stanford, California, USA; and [5]Department of Epidemiology, University of Alabama at Birmingham School of Public Health, Birmingham, Alabama, USA

The 2021 Kidney Disease: Improving Global Outcomes (KDIGO) Clinical Practice Guideline for the Management of Blood Pressure in Chronic Kidney Disease (CKD) recommends a target systolic blood pressure under 120 mmHg based on standardized office blood pressure measurement. Here, we examined the potential implications of this new guideline for blood pressure lowering with antihypertensive medication among adults in the United States with CKD compared to the 2012 KDIGO guideline (target blood pressure 130/80 mmHg or under with albuminuria or 140/90 mmHg or under without albuminuria) and the 2017 American College of Cardiology/American Heart Association (target blood pressure under 130/80 mmHg) guideline. Additionally, we determined implications of the 2021 KDIGO guideline for angiotensin converting enzyme inhibitor (ACEi) or angiotensin II-receptor blocker (ARB) use for those with albuminuria (recommended at systolic blood pressure of 120 mmHg or over) compared to the 2012 KDIGO guideline (recommended at blood pressures over 130/80 mmHg). Data were analyzed from 1,699 adults with CKD (estimated glomerular filtration rate 15-59 ml/min/1.73m^2 or a urinary albumin-to-creatinine ratio of 30 mg/g or more) in the 2015-2018 National Health and Nutrition Examination Survey and averaged up to three standardized blood pressure measurements. Among adults with CKD, 69.5% were eligible for blood pressure lowering according to the 2021 KDIGO guideline, compared with 49.8% as per 2012 KDIGO or 55.6% as per 2017 American College of Cardiology/American Heart Association guidelines. Among those with albuminuria, 78.2% were eligible for ACEi/ARB use by the 2021 KDIGO guideline compared with 71.0% by the 2012 KDIGO guideline. However, only 39.1% were taking an ACEi/ARB. Thus, our findings highlight opportunities to improve blood pressure management and reduce cardiovascular risk among adults in the United States with CKD.

Correspondence: *Kathryn E. Foti, 2024 E Monument Street, Suite 2-600, Baltimore, Maryland 21287, USA. E-mail: kfoti1@jhu.edu*

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The Kidney Disease: Improving Global Outcomes (KDIGO) 2021 Clinical Practice Guideline for the Management of Blood Pressure (BP) in Chronic Kidney Disease[1] (CKD) updated the KDIGO BP guideline published in 2012,[2] and includes recommendations for BP management for individuals with nondialysis CKD. In comparison to the systolic BP (SBP)/diastolic BP (DBP) targets of ≤130/≤80 mm Hg for those with albuminuria and ≤140/≤90 mm Hg for those without albuminuria in the 2012 KDIGO guideline, the 2021 guideline includes a recommendation that adults with CKD and high BP who are not kidney transplant recipients be treated to a target SBP <120 mm Hg based on standardized office BP measurements (Table 1).[1,2] Standardized office BP refers to measurements obtained following a guideline-recommended protocol and conducted by trained clinical staff.[3]

The evidence supporting the lower treatment target comes primarily from the Systolic Blood Pressure Intervention Trial (SPRINT), which showed targeting SBP <120 mm Hg compared with <140 mm Hg reduced the risk of cardiovascular disease (CVD) by 25% and all-cause mortality by 27%.[4] CKD was a prespecified subgroup in SPRINT, and the benefits of a target SBP <120 mm Hg versus a target SBP <140 mm Hg were similar for participants with and without CKD.[4] BP measurements in SPRINT were obtained using standardized measurement procedures and automated BP devices, the use of which is emphasized in the 2021 KDIGO guideline when applying the lower-recommended SBP target.[1,4]

Both the 2021 and 2012 KDIGO guidelines recommend use of angiotensin-converting enzyme inhibitor (ACEi) or

Table 1 | 2012 KDIGO, 2021 KDIGO, and 2017 ACC/AHA BP guideline recommendations for BP goals and use of RASi (ACEi or ARB)

Recommendation	2012 KDIGO	2021 KDIGO	2017 ACC/AHA
Blood pressure goals[a]			
No albuminuria (A1)	SBP ≤140 mm Hg and DBP ≤90 mm Hg (1B)	SBP <120 mm Hg, when tolerated, using standardized office BP measurement (2B)	SBP <130 mm Hg and DBP <80 mm Hg for all adults with CKD
Albuminuria (A2, A3),[b] no diabetes	SBP ≤130 mm Hg and DBP ≤80 mm Hg (A2: 2D; A3: 2C)		
Albuminuria (A2, A3),[b] diabetes	SBP ≤130 mm Hg and DBP ≤80 mm Hg (2D)		
RASi (ACEi/ARB) use			
No albuminuria (A1)	—	—	Treatment with ACEi (or ARB if not tolerated) may be reasonable in those with hypertension[e] and eGFR <60 ml/min per 1.73 m^2 or eGFR ≥60 ml/min per 1.73 m^2 with ACR ≥300 mg/g
Albuminuria (A2, A3),[b] no diabetes	Suggest (A2: 2D)/recommend (A3: 1B) RASi when BP-lowering drugs are indicated[c]	Suggest (A2: 2C)/recommend (A3: 1B) starting RASi for those with high BP[d]	
Albuminuria (A2, A3),[b] diabetes	Suggest (A2: 2D)/recommend (A3: 1B) RASi when BP-lowering drugs are indicated[c]	Recommend (A2, A3) RASi for people with high BP (1B)[d]	

ACC, American College of Cardiology; ACEi, angiotensin-converting enzyme inhibitor; ACR, albumin-to-creatinine ratio; AHA, American Heart Association; ARB, angiotensin II receptor blocker; BP, blood pressure; CKD, chronic kidney disease; DBP, diastolic BP; eGFR, estimated glomerular filtration rate; KDIGO, Kidney Disease: Improving Global Outcomes; RASi, renin-angiotensin-aldosterone system inhibitor; SBP, systolic BP.
Evidence grading: level 1, "We recommend"; level 2, "We suggest." Quality of evidence: A, "high"; B, "moderate"; C, "low"; D, "very low."
[a]Recommend those whose BP is consistently above the goal be treated with BP-lowering drugs to maintain a BP that is consistently below the goal.
[b]Albuminuria defined as ACR ≥30 mg/g. A2, ACR of 30 to 300 mg/g; A3, ACR >300 mg/g.
[c]BP above the goal of SBP ≤130 mm Hg and DBP ≤80 mm Hg for those with albuminuria.
[d]BP above the goal of SBP <120 mm Hg.
[e]BP above the goal of SBP <130 mm Hg and DBP <80 mm Hg.

angiotensin II receptor blocker (ARB) medications in patients with albuminuria and BP above the target who are not kidney transplant recipients.[1] However, as the target is lower in the 2021 KDIGO guideline (SBP <120 mm Hg) compared with the 2012 KDIGO guideline (SBP/DBP ≤130/≤80 mm Hg), individuals with albuminuria and SBP of 120–129 mm Hg are now recommended treatment with ACEi/ARBs.[1]

The 2021 KDIGO guideline has major implications for the management of BP in adults with CKD, a population with high CVD risk. Using nationally representative data from the 2015–2018 National Health and Nutrition Examination Survey (NHANES), the objective of the current analysis was to estimate the proportion of US adults with CKD eligible for BP lowering according to the KDIGO 2021 guideline and compare this with the proportion eligible based on the 2012 KDIGO guideline, as well as the 2017 American College of Cardiology (ACC)/American Heart Association (AHA) guideline, which recommended a SBP/DBP target of <130/<80 mm Hg for adults with CKD treated with antihypertensive medication.[5] Secondarily, we compared the proportion of adults with CKD and albuminuria recommended for treatment with an ACEi/ARB according to the 2021 and 2012 KDIGO guidelines. Finally, we described the number and classes of antihypertensive medication being taken among US adults with CKD.

METHODS

Data source

NHANES is a population-based survey conducted by the National Center for Health Statistics of the US Centers for Disease Control and Prevention, which uses stratified, multistage probability sampling to produce nationally representative estimates of the health and nutritional status of the civilian, noninstitutionalized US population. Since 1999–2000, the survey has been conducted in 2-year cycles. For the present analysis, we pooled data from the 2015–2016 and 2017–2018 survey cycles to obtain stable prevalence estimates. NHANES was approved by the National Center for Health Statistics Institutional Review Board, and written informed consent was obtained from all participants.

Data collection

NHANES data collection occurred during an in-home interview and a study visit at a mobile examination center, where physical and laboratory measurements were conducted. Covariates included in this analysis and their methods of assessment are described in Supplementary Table S1.

Study population

The study population included adults aged ≥20 years who completed the NHANES interview and examination and had laboratory data (N = 10,739). We excluded participants missing information on serum creatinine or urine albumin/creatinine ratio (N = 838), those who did not have at least 1 valid BP measurement (N = 360), as well as those missing information on other covariates (N = 122). The analytic sample included 9419 participants.

CKD assessment

CKD was defined as having a single estimated glomerular filtration rate (eGFR) of <60 ml/min per 1.73 m^2 or as having albuminuria based on a single urinary albumin-to-creatinine ratio (ACR) of ≥30 mg/g. We calculated creatinine-based eGFR using the Chronic Kidney Disease Epidemiology Collaboration equation.[6] We excluded participants with eGFR of <15 ml/min per 1.73 m^2 from the analysis as this was a small group and might not be representative of those individuals with eGFR in this range but not on dialysis. There were 1699 participants with CKD in the analytic sample.

BP measurement

BP measurements were obtained by trained study physicians using a standardized protocol during the NHANES examination.[7] After 5 minutes of seated rest, 3 BP measurements were taken using a mercury sphygmomanometer with an appropriately sized cuff. If a measurement was interrupted or incomplete, a fourth attempt was made. We used up to 3 measurements to calculate the mean SBP and DBP for each participant.[8] Study physicians were certified to measure BP following the completion of a training program, which included practice listening to Korotkoff sounds using a standardized audio-video tape presentation and practice measuring BP on volunteers. Physicians were recertified quarterly.[7]

Antihypertensive medication use

Antihypertensive medication use was determined on the basis of questionnaire responses and confirmed by a pill bottle review. Participants who responded yes to the questions, "Have you ever been told by a doctor or other healthcare professional that you had hypertension, also called high blood pressure?" and "Are you now taking prescribed medication for high blood pressure?", and had a prescription for ≥1 class of antihypertensive medication were considered to be taking antihypertensive medication. Antihypertensive medication classes were determined using the Multum Lexicon 3-level nested category system that assigns a therapeutic classification to each drug and each ingredient of the drug. Combination antihypertensive medications were classified into individual antihypertensive medication classes.

Recommended BP goals and ACEi/ARB use

Recommended BP goals were based on the 2012 KDIGO guideline, 2021 KDIGO guideline, and 2017 ACC/AHA guideline (Table 1). Those with SBP ≥120 mm Hg were considered to have BP above the 2021 KDIGO target. Those with albuminuria and SBP/DBP >130/80 mm Hg and those without albuminuria and SBP/DBP >140/90 mm Hg were considered to have BP above the 2012 KDIGO target. Those with SBP/DBP ≥130/80 mm Hg were considered to have BP above the 2017 ACC/AHA target.

Individuals were considered eligible for ACEi/ARB use by the 2021 or 2012 KDIGO guidelines if they had albuminuria and met 1 of the 2 following conditions: (i) were currently taking an ACEi/ARB regardless of their BP; or (ii) had BP above the respective KDIGO guideline target.

Analysis

We estimated the distribution of US adults with CKD across 6 groups with SBP <120 mm Hg, 120–140 mm Hg, and >140 mm Hg, according to whether they were taking antihypertensive medication. We estimated the sociodemographic (age, sex, race/ethnicity, education, and family income-to-poverty ratio) and clinical characteristics (eGFR category: G1/G2: eGFR ≥60 ml/min per 1.73 m^2; G3a: eGFR 45–59 ml/min per 1.73 m^2; G3b: eGFR 30–44 ml/min per 1.73 m^2; and G4: eGFR 15–29 ml/min per 1.73 m^2[9]; ACR category: A1: ACR <30 mg/g; A2: ACR 30–300 mg/g; and A3: ACR >300 mg/g[9]; CKD awareness; diabetes; 10-year predicted atherosclerotic CVD risk[10] or history of CVD, and 5-year predicted kidney failure risk[11]) of adults with CKD in each of these categories.

We estimated the SBP distribution among US adults with CKD, overall, and for those taking and not taking antihypertensive medication. We calculated the percentage of US adults with CKD who had BP above the 2021 KDIGO, 2012 KDIGO, and 2017 ACC/AHA guideline-recommended targets, as well as the difference in the percentage with BP above the 2021 KDIGO guideline compared with the 2012 KDIGO and 2017 ACC/AHA guidelines. These calculations were performed for the overall population with CKD and for those with CKD by sociodemographic and clinical characteristics. We examined factors associated with BP above the 2021 KDIGO guideline goal (i.e., SBP ≥120 mm Hg) among US adults with CKD using negative binomial regression to calculate adjusted prevalence ratios (PRs).

We estimated the percentage of US adults with CKD and albuminuria taking an ACEi/ARB and the percentage recommended an ACEi/ARB by the 2021 and 2012 KDIGO guidelines, separately. Calculations were conducted overall and by participant characteristics. We used negative binomial regression to calculate adjusted PRs for factors associated with ACEi/ARB use.

Finally, among those taking antihypertensive medication, we estimated the percentage taking ACEi/ARB, β-blockers, calcium channel blockers, diuretics, or other classes of medication. Also, we estimated the distribution of the number of antihypertensive medications being taken.

All analyses were conducted using Stata version 15.1 (StataCorp, College Station, TX) using survey commands to account for the complex survey design (using strata and sampling units to identify participants) and sampling weights to produce nationally representative prevalence estimates for the noninstitutionalized US population.[12,13] We estimated the number of US adults with CKD overall and by subgroup by adjusting the total weights for the NHANES participants with nonmissing data to the 2018 US census population estimates.[14] A 2-sided P value of 0.05 was used to define statistical significance.

RESULTS

In 2015–2018, 40.9% of US adults with CKD were not taking antihypertensive medication, including 15.6% with SBP <120 mm Hg, 14.8% with SBP of 120–140 mm Hg, and 10.5% with SBP >140 mm Hg (Table 2). Among those who were not taking antihypertensive medication, most had eGFR ≥60 ml/min per 1.73 m^2 and met criteria for CKD because of the presence of albuminuria alone. Adults who were taking antihypertensive medication were more likely to be older, to have diabetes, and to have high 10-year predicted atherosclerotic CVD risk or prevalent CVD compared with those who were not taking antihypertensive medication. Among those who were and were not taking antihypertensive medication, individuals with SBP >140 mm Hg were more likely to be non-Hispanic Black or non-Hispanic Asian, as well as to have lower family income-to-poverty ratio and lower education compared with their counterparts with SBP <120 and 120 to 140 mm Hg.

Among the 35.3 million US adults with CKD, 69.5% had SBP ≥120 mm Hg, 49.8% had SBP >130 mm Hg, and 34.7% had SBP >140 mm Hg (Figure 1). Among the 14.4 million US adults with CKD not taking antihypertensive medication, 61.8% had SBP ≥120 mm Hg, 39.5% had SBP >130 mm Hg, and 25.6% had SBP >140 mm Hg. Among the 20.9 million US adults with CKD taking antihypertensive medication, 74.8%, 57.0%, and 40.9% had SBP ≥120, >130, and >140 mm Hg, respectively.

Table 2 | Characteristics of US adults with CKD by SBP and antihypertensive medication use, NHANES, 2015–2018

	SBP, mm Hg					
	Not treated with antihypertensive medication			Treated with antihypertensive medication		
Characteristic	<120	120–140	>140	<120	120–140	>140
Unweighted No.	197	244	184	221	391	462
Weighted %	15.6	14.8	10.5	14.9	20.0	24.2
eGFR, median (IQR), ml/min per 1.73 m^2	98.7 (76.5–117.7)	87.4 (58.1–110.7)	80.5 (53.5–109.3)	56.1 (48.6–68.8)	58.4 (49.8–88.7)	59.4 (47.2–83.1)
eGFR category, ml/min per 1.73 m^2, % (SE)						
≥60[a]	82.5 (3.4)	67.5 (4.6)	65.9 (4.9)	33.5 (6.4)	45.0 (3.8)	49.1 (3.6)
45–59	16.5 (3.3)	28.0 (5.0)	24.1 (5.4)	51.0 (5.3)	38.5 (3.2)	30.7 (3.4)
30–44	1.0 (0.6)	4.1 (1.5)	7.8 (2.6)	14.4 (2.5)	12.0 (1.9)	15.3 (2.4)
15–29	0.0 (0.0)	0.4 (0.3)	2.2 (1.1)	1.1 (0.5)	4.5 (1.5)	4.9 (1.1)
ACR, median (IQR), mg/g	48.3 (34.8–114.5)	50.9 (17.3–110.3)	52.6 (30.6–149.3)	16.9 (8.1–60.2)	42.4 (11.0–88.0)	54.4 (18.8–154.9)
ACR category, mg/g, % (SE)						
<30[a]	13.5 (2.6)	28.5 (4.5)	22.9 (5.7)	53.4 (5.6)	37.7 (3.2)	28.8 (2.8)
30–300	77.8 (3.3)	60.6 (3.9)	61.0 (5.9)	39.1 (5.5)	53.4 (3.3)	54.7 (3.1)
>300	8.7 (2.6)	11.0 (2.6)	16.1 (4.1)	7.5 (2.9)	8.9 (1.5)	16.5 (2.5)
Age, mean (SE), yr	43.6 (1.6)	54.4 (1.8)	58.2 (1.5)	65.0 (0.9)	66.9 (0.8)	70.4 (0.8)
Age category, yr, % (SE)						
20–44	55.3 (5.2)	33.4 (5.2)	21.0 (3.9)	5.4 (2.0)	5.7 (1.8)	1.5 (0.6)
45–64	28.8 (4.5)	31.9 (4.2)	39.4 (6.7)	38.2 (6.1)	30.2 (3.0)	24.8 (3.1)
≥65	15.9 (3.9)	34.7 (3.8)	39.6 (6.5)	56.4 (5.7)	64.1 (3.2)	73.8 (3.2)
Female, % (SE)	71.2 (4.1)	49.6 (4.3)	56.9 (7.1)	47.3 (4.9)	49.3 (3.7)	59.7 (3.7)
Race/ethnicity, % (SE)						
Non-Hispanic White	61.7 (4.7)	61.3 (5.3)	62.0 (4.9)	77.0 (3.9)	67.3 (4.4)	68.0 (3.4)
Mexican American	10.5 (2.4)	13.5 (3.1)	7.4 (2.5)	5.3 (1.6)	5.5 (1.4)	5.4 (1.4)
Non-Hispanic Black	9.7 (2.4)	8.9 (2.1)	13.3 (3.2)	7.1 (1.6)	14.4 (3.0)	14.6 (2.4)
Non-Hispanic Asian	6.1 (1.7)	5.7 (1.2)	5.5 (1.6)	1.7 (0.7)	5.8 (1.3)	4.9 (1.4)
Other	11.9 (2.5)	10.7 (2.2)	11.8 (3.5)	8.9 (2.6)	7.0 (1.7)	7.0 (1.5)
Income-to-poverty ratio, % (SE)						
Tertile 1	24.0 (4.3)	26.0 (3.1)	25.8 (4.1)	17.2 (3.0)	22.6 (3.0)	23.9 (3.3)
Tertile 2	30.9 (3.9)	32.1 (4.6)	33.4 (5.1)	25.6 (4.4)	28.8 (3.3)	41.0 (3.6)
Tertile 3	36.8 (6.2)	32.9 (5.0)	27.8 (6.8)	52.9 (4.6)	38.8 (4.3)	24.3 (3.9)
Missing	8.3 (2.6)	9.0 (2.2)	13.0 (2.6)	4.3 (2.2)	9.8 (1.7)	10.9 (1.7)
Education, % (SE)						
<High school	5.6 (1.7)	7.1 (1.7)	9.2 (2.1)	3.9 (1.0)	7.7 (1.3)	8.0 (1.6)
High school degree	33.6 (4.6)	33.2 (3.6)	42.5 (4.3)	31.8 (3.5)	35.9 (3.3)	46.4 (3.3)
>High school degree	60.9 (4.5)	59.7 (4.1)	48.3 (4.4)	64.2 (3.5)	56.5 (3.7)	45.6 (3.3)
CKD awareness, % (SE)	2.7 (1.2)	7.6 (3.0)	5.3 (1.3)	14.5 (3.5)	16.1 (2.3)	16.3 (2.0)
Diabetes, % (SE)	5.7 (1.8)	20.9 (3.8)	29.6 (5.0)	46.9 (4.4)	38.8 (3.2)	38.4 (3.3)
SBP, mean (SE), mm Hg	108.8 (0.8)	128.8 (0.5)	160.3 (1.6)	110.4 (0.8)	130.2 (0.4)	158.2 (0.8)
DBP, mean (SE), mm Hg	67.3 (0.7)	72.3 (0.9)	82.6 (1.1)	63.4 (0.9)	69.0 (0.8)	73.0 (1.0)
10-yr Predicted ASCVD risk, % (SE)						
<5%	76.6 (4.1)	43.8 (4.5)	26.8 (4.6)	14.7 (3.5)	8.6 (1.8)	1.4 (0.6)
5%–<10%	10.9 (3.3)	16.2 (4.1)	17.9 (5.4)	14.9 (3.5)	10.3 (2.8)	8.6 (2.8)
10%–<20%	5.7 (2.1)	14.6 (3.4)	17.6 (3.6)	20.9 (4.0)	22.1 (3.4)	10.9 (2.4)
≥20%	2.7 (1.1)	16.5 (2.8)	25.8 (4.6)	21.1 (4.0)	28.7 (3.7)	48.0 (3.8)
Prevalent CVD	4.0 (1.3)	8.9 (2.1)	11.9 (2.7)	28.5 (4.4)	30.2 (2.8)	31.0 (3.2)
5-yr Predicted kidney failure risk, % (SE)[b]						
<2%	97.9 (1.1)	97.2 (1.0)	90.4 (3.1)	92.4 (2.1)	85.9 (2.2)	84.6 (2.0)
2%–<5%	1.3 (1.0)	1.0 (0.5)	4.9 (2.4)	3.8 (1.4)	6.5 (1.3)	7.5 (1.6)
≥5%	0.8 (0.4)	1.8 (1.0)	4.7 (1.5)	3.9 (1.1)	7.6 (1.6)	7.8 (1.5)
No. of antihypertensive medications, % (SE)						
1				43.5 (4.8)	36.6 (3.4)	33.6 (3.7)
2				18.3 (3.2)	27.9 (3.5)	28.9 (3.4)
≥3				38.2 (3.9)	35.6 (2.9)	37.5 (3.5)

ACR, albumin-to-creatinine ratio; ASCVD, atherosclerotic CVD; CKD, chronic kidney disease; CVD, cardiovascular disease; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; IQR, interquartile range; NHANES, National Health and Nutrition Examination Survey; SBP, systolic blood pressure.
[a]eGFR ≥60 ml/min per 1.73 m^2 indicates individuals defined as having CKD based on the presence of albuminuria. ACR <30 mg/g indicates individuals defined as having CKD based on reduced eGFR without albuminuria.
[b]Among those with eGFR of 15–59 ml/min per 1.73 m^2.

Overall, 69.5% (24.5 million) of US adults with CKD had BP above the 2021 KDIGO target compared with 49.8% (17.6 million) who had BP above the KDIGO 2012 target (Table 3), an increase of 19.6% or approximately 6.9 million US adults. The percentage of US adults with BP above the 2021 KDIGO target was higher in lower eGFR categories and in higher ACR

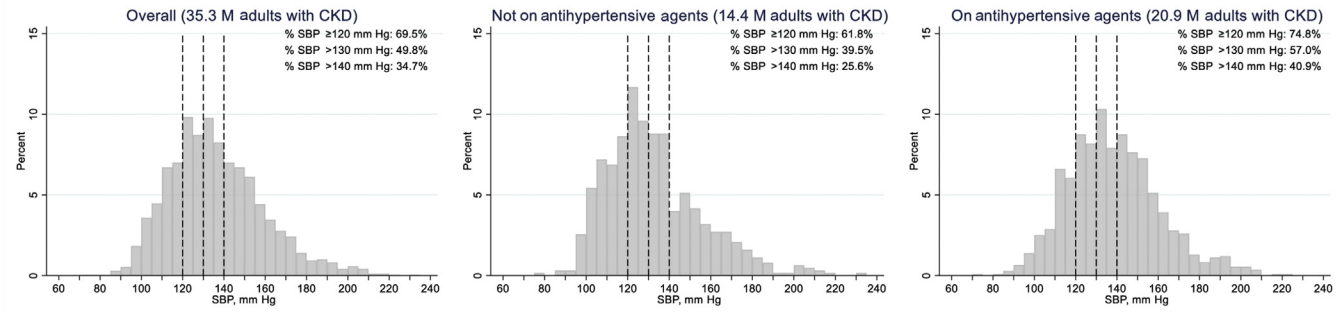

Figure 1 | Distribution of systolic blood pressure (SBP) in US adults with chronic kidney disease (CKD) overall and by antihypertensive medication use, National Health and Nutrition Examination Survey, 2015–2018. This figure shows the distribution of SBP overall among US adults with CKD, among those not taking antihypertensive medication, and among those taking antihypertensive medication. The SBP cut points shown in the figures reflect the percentage with SBP above the thresholds used in the 2021 (<120 mm Hg) and 2012 (≤130 mm Hg with albuminuria, ≤140 mm Hg without albuminuria) Kidney Disease: Improving Global Outcomes guidelines. M, million.

categories, among those who were non-Hispanic Black and non-Hispanic Asian versus non-Hispanic White, had lower income or education, were older, had diabetes, had higher atherosclerotic CVD risk or prevalent CVD, or had higher kidney failure risk. Overall, 55.6% (19.6 million) of adults with CKD had BP above the 2017 ACC/AHA BP guideline target (Supplementary Table S2). Overall, 13.9% or approximately 4.9 million US adults with CKD had BP above the target in the 2021 KDIGO guideline but not the 2017 AHA/ACC guideline.

After adjustment for sociodemographic and clinical characteristics, US adults with eGFR 15–29 versus 45–59 ml/min per 1.73 m^2 (PR, 1.19; 95% confidence interval [CI], 1.03–1.38), with ACR >300 versus <30 mg/g (PR, 1.20; 95% CI, 1.01–1.41), and who were non-Hispanic Black (PR, 1.20; 95% CI, 1.08–1.32) or non-Hispanic Asian (PR, 1.12; 95% CI, 1.02–1.23) versus non-Hispanic White were more likely to have BP above the 2021 KDIGO target (Supplementary Table S3).

Among US adults with CKD and albuminuria, 39.1% were currently taking an ACEi/ARB (Table 4). Overall, 78.2% of US adults with albuminuria were eligible for an ACEi/ARB, according to the 2021 KDIGO guideline, compared with 71.0%, according to 2012 KDIGO guideline. ACEi/ARB use was less common, and there were larger differences in recommended and current use, among those with eGFR ≥60 or 15–29 ml/min per 1.73 m^2 versus those with eGFR of 30–59 ml/min per 1.73 m^2, those aged 20–44 versus ≥45 years, those who were non-White, those in the first or second tertile of family income-to-poverty ratio, those who were not aware of their CKD, and those without diabetes. ACEi/ARB use was higher among men and among those with ACR >300 mg/g, but the difference in recommended and current ACEi/ARB use was greater than for women and those with ACR 30–300 mg/g.

After adjustment for sociodemographic and clinical characteristics, ACEi/ARB use was lower among US adults with albuminuria who had eGFR 15–29 ml/min per 1.73 m^2 versus those with eGFR of 30–59 ml/min per 1.73 m^2 (PR, 0.60; 95% CI, 0.37–0.96) and who were aged ≥65 versus 45–64 years (PR, 0.66; 95% CI, 0.46–0.96) (Supplementary Table S4). ACEi/ARB use was more common among adults with albuminuria who were in the highest versus lowest tertile of the income-to-poverty ratio (PR, 1.37; 95% CI, 1.07–1.76), who were aware of their CKD (PR, 1.32; 95% CI, 1.07–1.64), and who had diabetes (PR, 1.91; 95% CI, 1.55–2.35).

Among US adults with CKD taking antihypertensive medication, 40.5% were taking an ACEi, 31.7% were taking an ARB, 44.3% were taking a β-blocker, 41.8% were taking a diuretic (loop, thiazide-like, or K-sparing agent), 32.3% were taking a calcium channel blocker, and 0.9% were taking other medication classes (Supplementary Table S5).

DISCUSSION

According to NHANES 2015–2018, 69.5% or approximately 24.5 million US adults with CKD had BP above the 2021 KDIGO target. This represents an increase of 19.6% (~6.9 million US adults) with above target BP compared with the 2012 KDIGO guideline and 13.9% (~4.9 million US adults) compared with the 2017 ACC/AHA BP guideline. Also, 78.2% of US adults with CKD and albuminuria were recommended an ACEi/ARB by the 2021 KDIGO guideline, with only 39.1% actually taking these classes of medications. Although there was a large difference between eligible and actual ACEi/ARB use, 71.0% of US adults were previously recommended an ACEi/ARB by the 2012 KDIGO guideline.

The 2021 KDIGO guideline includes a recommendation that adults with CKD and high BP be treated to a target SBP <120 mm Hg based on standardized office BP measurement, if tolerated by the patient, based on the cardiovascular, survival, and potential cognitive benefits of more intensive BP lowering.[1] Meta-analyses of randomized trials of antihypertensive medication have suggested that treating SBP to <120 mm Hg is associated with reduced CVD risk.[15] For individuals with CKD, the evidence supporting the SBP target <120 mm Hg is largely derived from SPRINT, which included 2646 patients with CKD, defined as eGFR <60 ml/min per 1.73 m^2,

Table 3 | Percentage (SE) and millions (SE) of US adults with CKD and blood pressure above the KDIGO 2021 and KDIGO 2012 guideline targets, NHANES, 2015–2018

Characteristic	Weighted no., millions (SE)[a]	Blood pressure above 2021 KDIGO target, % (SE)	Blood pressure above 2012 KDIGO target, % (SE)	Difference between 2021 and 2012 KDIGO targets, % (SE)
Unweighted No.		1281	930	1699
Overall	35.3 (1.5)	69.5 (1.7)	49.8 (1.7)	19.6 (1.0)
eGFR category, ml/min per 1.73 m^2				
≥60[b]	19.6 (0.7)	67.7 (2.4)	55.9 (2.6)	11.8 (1.2)
45–59	11.3 (0.6)	68.0 (3.9)	37.0 (3.5)	31.0 (2.1)
30–44	3.5 (0.3)	76.4 (3.8)	49.9 (4.7)	26.5 (3.2)
15–29	0.9 (0.2)	93.4 (2.9)	70.0 (8.5)	23.4 (5.4)
ACR category, mg/g				
<30[a]	11.0 (0.6)	67.7 (3.5)	31.1 (3.1)	36.7 (2.2)
30–300	20.2 (0.6)	68.6 (2.5)	56.9 (2.5)	11.7 (1.2)
>300	4.1 (0.4)	78.6 (4.3)	65.7 (5.0)	12.9 (2.5)
Age category, yr				
20–44	6.4 (0.5)	47.7 (3.9)	35.4 (4.2)	12.3 (2.8)
45–64	11.0 (0.7)	67.2 (2.4)	53.0 (3.2)	14.2 (1.7)
≥65	17.9 (0.6)	78.6 (2.6)	53.0 (2.4)	25.5 (1.4)
Sex				
Female	19.7 (0.7)	67.4 (2.4)	47.5 (2.2)	19.9 (1.4)
Male	15.6 (0.7)	72.0 (2.5)	52.7 (2.9)	19.3 (1.5)
Race/ethnicity				
Non-Hispanic White	23.5 (1.0)	68.3 (2.2)	47.7 (2.2)	20.6 (1.6)
Mexican American	2.7 (0.5)	68.0 (4.0)	49.3 (4.1)	18.7 (2.8)
Non-Hispanic Black	4.1 (0.6)	78.0 (2.3)	59.5 (2.7)	18.5 (2.2)
Non-Hispanic Asian	1.8 (0.3)	75.8 (4.6)	59.9 (3.8)	15.9 (3.2)
Other	3.2 (0.3)	64.9 (5.0)	47.9 (4.2)	17.0 (2.8)
Income-to-poverty ratio tertile				
Tertile 1	8.2 (0.5)	72.7 (2.4)	53.4 (3.0)	19.3 (1.8)
Tertile 2	11.5 (0.5)	73.4 (2.6)	55.5 (3.2)	17.9 (1.8)
Tertile 3	12.4 (1.0)	61.1 (3.5)	39.6 (3.9)	21.4 (2.2)
Missing	3.2 (0.4)	79.0 (4.8)	59.5 (4.8)	19.5 (2.9)
Education				
<High school	2.4 (0.3)	79.0 (4.4)	59.9 (4.3)	19.0 (2.9)
High school degree	13.3 (0.5)	73.5 (2.2)	54.1 (2.6)	19.4 (1.7)
>High school degree	19.5 (0.6)	65.5 (2.5)	45.6 (2.2)	19.9 (1.5)
CKD awareness				
No	31.2 (0.4)	68.4 (1.9)	49.3 (1.9)	19.1 (1.1)
Yes	4.0 (0.4)	77.3 (4.3)	53.1 (4.7)	24.2 (2.7)
Diabetes				
No	24.3 (0.6)	67.1 (2.3)	46.2 (2.4)	20.9 (1.3)
Yes	11.0 (0.6)	74.6 (2.5)	57.9 (2.8)	16.7 (1.7)
No. of antihypertensive medications				
0	14.4 (0.6)	61.8 (2.8)	41.7 (3.4)	20.2 (1.7)
1	7.7 (0.7)	70.4 (3.6)	53.2 (3.6)	17.2 (2.3)
2	5.4 (0.3)	82.1 (3.3)	62.8 (3.9)	19.3 (2.4)
≥3	7.7 (0.5)	74.0 (2.9)	52.7 (2.9)	21.2 (2.0)
Any ACEi or ARB				
No	20.3 (0.5)	67.6 (2.6)	47.1 (3.0)	20.5 (1.4)
Yes	14.9 (0.5)	72.0 (2.5)	53.5 (2.8)	18.5 (1.5)
10-yr Predicted ASCVD risk, %				
<5	9.0 (0.5)	44.5 (2.9)	30.4 (3.3)	14.1 (2.2)
5–<10	4.3 (0.5)	68.2 (5.6)	53.8 (6.3)	14.4 (3.5)
10–<20	5.3 (0.4)	73.4 (4.6)	48.6 (5.0)	24.8 (2.8)
≥20	9.2 (0.5)	86.3 (2.7)	64.1 (3.1)	22.2 (1.9)
Prevalent CVD	7.4 (0.4)	76.8 (3.5)	54.3 (3.8)	22.5 (2.0)
5-yr Predicted kidney failure risk, %[c]				
<2	31.9 (0.3)	67.9 (1.9)	48.5 (1.9)	19.4 (1.1)
2–<5	1.6 (0.2)	83.1 (4.9)	60.7 (5.6)	22.4 (4.4)
≥5	1.7 (0.2)	85.7 (3.3)	64.0 (5.7)	21.7 (3.4)

ACEi, angiotensin-converting enzyme inhibitor; ACR, albumin-to-creatinine ratio; ARB, angiotensin II receptor blocker; ASCVD, atherosclerotic CVD; CKD, chronic kidney disease; CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate; KDIGO, Kidney Disease: Improving Global Outcomes; NHANES, National Health and Nutrition Examination Survey. Blood pressure control by the 2021 KDIGO guideline: systolic blood pressure <120 mm Hg. Blood pressure control by the 2012 KDIGO guideline: systolic blood pressure/diastolic blood pressure ≤130/80 mm Hg for those with albuminuria, ≤140/90 mm Hg for those without albuminuria.

[a]Based on 2018 US Census population estimates.

[b]eGFR ≥60 ml/min per 1.73 m^2 indicates individuals defined as having CKD based on the presence of albuminuria. ACR <30 mg/g indicates individuals defined as having CKD based on reduced eGFR without albuminuria.

[c]Among those with eGFR of 15 to 59 ml/min per 1.73 m^2.

as a prespecified subgroup.[4] SPRINT found that the effect of intensive SBP lowering on the primary cardiovascular outcome and all-cause death was similar in those with and without CKD.[4] However, SPRINT excluded certain important subgroups, such as those with SBP <130 mm Hg, diabetes mellitus, orthostatic hypotension, frailty, and heavy proteinuria (>1 g/d).

BP in SPRINT and virtually all major outcome trials[16] was measured using a standardized approach and averaged multiple readings. Standardized office BP measurements can be obtained following a protocol such as the one from the AHA by trained clinical staff.[3] The AHA BP measurement protocol includes guidance on having the patient rest before BP is measured, the proper positioning of the patient, selecting appropriate equipment, and not talking during the procedure. On average, BP is substantially higher when measured in routine clinical practice compared with following a standardized protocol.[17,18] However, given the high degree of variability in the difference between routine office-measured BP and standardized BP, it is not possible to apply a correction factor to estimate standardized office BP from a routine BP measurement.[17,18] Most systematic errors in BP measurement can be avoided if a protocol is followed.[19] For these and other reasons, the 2021 KDIGO guideline emphasizes the importance of obtaining BP measurements following a recommended protocol and individualization of BP management, including consideration of the patient's characteristics, tolerability, and preferences when considering the optimal SBP target.[1]

Among adults with CKD and high BP, the 2021 KDIGO guideline provides a strong recommendation for ACEi/ARB use in adults who have diabetes and those without diabetes who have severely increased albuminuria. Also, the guideline provides a weak recommendation for ACEi/ARB use in those without diabetes with moderately increased albuminuria. A *post hoc* analysis of SPRINT found that the benefits of intensive BP lowering on the primary cardiovascular outcome and all-cause mortality were similar among patients with and without albuminuria.[20] Although albuminuria is a potent risk factor for adverse kidney and cardiovascular outcomes, screening for it remains suboptimal, particularly in patients with hypertension.[21–23] When albuminuria is measured, higher ACR values are associated with greater likelihood of ACEi/ARB initiation.[24] Thus, increasing adherence to recommended albuminuria testing has the potential to impact BP management among US adults with CKD.[24] In the current study, CKD awareness was low, underscoring the need to educate patients and providers. Albuminuria testing is critical early in the course of CKD to detect damage before substantial loss of glomerular filtration rate.

The current analysis identified several antihypertensive medication treatment gaps for adults with CKD. For example, we estimated that 8.9 million of the 24.5 million adults with CKD who had BP above the 2021 KDIGO target were not taking any antihypertensive medication. Of these individuals, 6.0 million had CKD based on albuminuria but an eGFR ≥60 ml/min per 1.73 m^2, a group in which the CKD diagnosis rate is low and the diagnosis cannot be made without albuminuria measurement.[25] Approximately one-third of US adults with CKD who had treated SBP ≥120 mm Hg, an estimated 5.5 million individuals, were taking only a single antihypertensive medication. The SPRINT treatment algorithm for the intensive group began with a 2 or 3 drug therapy (thiazide-type diuretic and/or an ACEi or ARB and/or a calcium channel blocker), and multiple drugs[26] may be needed to achieve the 2021 KDIGO target. β-Blockers, considered a second-line antihypertensive medication, were used more frequently in the current study than thiazide diuretics and calcium channel blockers, indicating that appropriate drug selection may be another critical point of intervention to improve BP management.

In the current study, BP control and ACEi/ARB use among those with albuminuria were lower among US adults who were non-White, had lower family income relative to poverty, and had lower education, regardless of which guideline criteria were used. Differences by sociodemographic factors in recommended BP management among adults with CKD contribute to disparities in cardiovascular and kidney disease outcomes. When implementing the 2021 KDIGO guideline recommendations, it is important to focus on health equity as a priority.

Reducing BP to the lower target recommended by the 2021 KDIGO guideline will require concerted effort, especially in the context of worsening trends in BP control in the general adult population.[27] In October 2020, the US Surgeon General released a Call to Action focused on hypertension control.[28] This document provided evidence-based approaches for improving BP control, which included using standardized treatment approaches, promoting health care teams to manage hypertension, and empowering and equipping patients to use self-measured BP monitoring and medication adherence strategies.[28] Health care teams can improve BP control by implementing protocols to ensure proper BP measurement, developing evidence-based treatment algorithms that prioritize use of recommended antihypertensive medications, including combination medications where needed,[29] and partnering with patients, families, and communities to implement both pharmacologic and nonpharmacologic approaches.[30]

The current analysis has several strengths. NHANES followed standardized procedures for examination and laboratory measurements and enrolled a large sample size. The selection of participants for NHANES allowed for the generation of nationally representative estimates. Finally, we used the 2 most recent survey cycles to provide contemporary data on BP management in adults with CKD. This analysis has several limitations. Although multiple standardized measurements were obtained, BP was measured only on one occasion, whereas the 2021 KDIGO guideline indicates an average of ≥2 readings obtained on ≥2 occasions should be used to estimate an individual's BP.[1] We relied on single measurements of serum creatinine and urinary albumin, which may result in misclassification of CKD, particularly

Table 4 | Percentage (SE) of US adults with CKD and albuminuria currently taking ACEi/ARBs and recommended ACEi/ARBs by the 2021 and 2012 KDIGO guidelines, NHANES, 2015–2018

Characteristic	Taking ACEi/ARBs, % (SE)	Recommended ACEi/ARBs, % (SE)[a]		Difference between % recommended by 2021 guideline and % currently taking ACEi/ARBs, % (SE)
		By 2021 guideline	By 2012 guideline	
Overall	39.1 (1.4)	78.2 (2.0)	71.0 (2.2)	39.1 (1.4)
eGFR category, ml/min per 1.73 m^2				
≥60	34.6 (1.7)	74.8 (2.4)	67.0 (2.6)	40.3 (1.6)
45–59	60.8 (6.0)	88.9 (5.1)	85.9 (4.8)	28.1 (4.0)
30–44	64.3 (6.6)	94.9 (2.6)	88.8 (3.3)	30.6 (5.0)
15–29	46.0 (9.2)	98.3 (1.7)	95.8 (2.7)	52.3 (7.7)
ACR category, mg/g				
30–300	38.6 (1.6)	76.8 (2.5)	70.1 (2.6)	38.2 (1.6)
>300	41.4 (3.9)	85.1 (4.0)	75.8 (5.1)	43.7 (3.3)
Age category, yr				
20–44	10.6 (2.4)	50.9 (4.0)	41.3 (4.3)	40.4 (3.2)
45–64	43.8 (3.5)	82.4 (2.8)	76.1 (3.5)	38.6 (2.4)
≥65	53.1 (2.6)	91.9 (2.6)	85.6 (2.7)	38.7 (2.1)
Sex				
Female	35.8 (2.3)	72.1 (2.3)	65.8 (2.6)	36.4 (2.0)
Male	43.0 (2.8)	85.3 (2.6)	77.3 (3.0)	42.3 (2.0)
Race/ethnicity				
Non-Hispanic White	41.7 (2.0)	78.5 (3.0)	71.5 (3.0)	36.8 (2.4)
Mexican American	32.4 (4.1)	75.5 (3.5)	64.0 (5.1)	43.1 (3.4)
Non-Hispanic Black	38.1 (2.6)	83.4 (2.3)	77.0 (2.5)	45.3 (3.0)
Non-Hispanic Asian	34.3 (5.0)	78.1 (4.5)	72.8 (4.7)	43.8 (4.3)
Other	34.6 (5.0)	72.5 (4.4)	66.4 (4.8)	37.9 (3.7)
Income-to-poverty ratio tertile				
Tertile 1	34.5 (2.5)	78.2 (2.5)	68.2 (3.2)	43.7 (2.4)
Tertile 2	38.6 (3.3)	79.9 (2.6)	75.0 (3.0)	41.3 (2.5)
Tertile 3	42.7 (4.2)	74.6 (5.3)	67.5 (5.4)	32.0 (3.0)
Missing	41.4 (5.3)	83.8 (4.4)	76.7 (4.7)	42.4 (4.1)
Education				
<High school	42.3 (4.3)	84.6 (4.6)	75.9 (4.6)	42.3 (3.7)
High school degree	39.4 (2.4)	80.5 (2.5)	72.9 (2.3)	41.2 (2.3)
>High school degree	38.4 (2.6)	75.6 (3.3)	69.0 (3.4)	37.2 (2.0)
Diabetes				
No	27.1 (1.7)	69.6 (2.9)	61.5 (2.8)	42.5 (1.9)
Yes	61.9 (2.6)	94.4 (1.6)	89.2 (2.0)	32.6 (2.1)
CKD awareness				
No	37.0 (1.5)	76.6 (2.1)	69.1 (2.4)	39.6 (1.5)
Yes	54.8 (5.3)	90.6 (4.3)	86.6 (4.3)	35.8 (3.8)
No. of antihypertensive medications in addition to ACEi/ARBs				
0	20.4 (2.5)	66.2 (2.6)	56.1 (3.1)	45.8 (2.0)
1	53.7 (3.7)	91.0 (3.3)	87.4 (3.4)	37.3 (3.2)
≥2	80.5 (3.0)	98.3 (0.7)	95.9 (1.2)	23.5 (2.3)
10-yr Predicted ASCVD risk, %				
<5	12.6 (2.2)	49.9 (3.0)	40.0 (3.4)	37.2 (2.8)
5–<10	39.3 (8.0)	82.2 (5.1)	75.1 (5.6)	42.9 (4.8)
10–<20	44.9 (5.6)	88.1 (5.7)	85.6 (5.8)	43.1 (3.8)
≥20	57.0 (3.6)	98.3 (0.7)	91.4 (2.3)	41.4 (2.7)
Prevalent CVD	60.8 (4.0)	94.8 (1.8)	88.8 (2.9)	34.0 (2.9)
5-yr Predicted kidney failure risk, %[b]				
<2	37.3 (1.5)	76.4 (2.2)	69.1 (2.4)	39.1 (1.5)
2–<5	67.7 (7.9)	93.4 (5.2)	88.4 (5.6)	25.7 (5.8)
≥5	44.7 (5.7)	92.8 (2.6)	86.2 (5.1)	48.1 (4.6)

ACEi, angiotensin-converting enzyme inhibitor; ACR, albumin-to-creatinine ratio; ARB, angiotensin II receptor blocker; ASCVD, atherosclerotic CVD; CKD, chronic kidney disease; CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate; KDIGO, Kidney Disease: Improving Global Outcomes; NHANES, National Health and Nutrition Examination Survey.

[a]Includes those currently taking ACEi/ARBs and those who have blood pressure above goal. Recommended to take ACEi/ARBs by 2021 KDIGO guideline: currently taking ACEi/ARBs or ACR ≥30 mg/g and systolic blood pressure >120 mm Hg. Recommended to take ACEi/ARBs by 2012 KDIGO guideline: currently taking ACEi/ARBs or ACR ≥30 mg/g and systolic blood pressure >130 mm Hg or diastolic blood pressure >80 mm Hg.

[b]Among those with eGFR of 15–59 ml/min per 1.73 m^2.

when albuminuria exclusively is used to define CKD.[31] Clinical practice guidelines define CKD based on reduced eGFR or presence of albuminuria for at least 3 months.[9] However, ACEi/ARB use in our study was similar across the range of elevated ACR. Finally, we excluded individuals with eGFR <15 ml/min per 1.73 m^2 not on dialysis because of

concerns about generalizability to the broader patient population with these characteristics.

Conclusion

Improving BP control is a priority for reducing CVD risk in adults with CKD. Most of the 35 million US adults with CKD have SBP ≥120 mm Hg based on standardized measurement procedures in NHANES and are recommended for initiation or intensification of antihypertensive medication by the 2021 KDIGO guideline. In addition, almost 80% of US adults with albuminuria are recommended an ACEi/ARB but <40% were taking one. If implemented successfully, reducing BP to the target recommended by the KDIGO 2021 guideline and appropriate use of ACEi/ARB among those with albuminuria have the potential to prevent a large number of cardiovascular events and deaths[32] and slow kidney disease progression among US adults with CKD.

DISCLOSURE

TIC, MJS, and PM served as members of the 2021 Kidney Disease: Improving Global Outcomes Blood Pressure Work Group. MJS attended a Bayer Advisory Board in May 2019 and serves as consultant to Cardurian. He is on the Akebia Steering Committee, with funds payed to Tufts Medical Center. TIC has received funding paid by Janssen Pharmaceuticals to Stanford University; has served as a consultant for Bayer, Janssen Pharmaceuticals, Novo Nordisk, Fresenius Medical Care, Tricida, Gilead, and AstraZeneca; and has received grant support from Satellite Healthcare. PM receives grant support and consulting fees from Amgen Inc. JC is an advisor to Healthy.io and receives grants from the National Kidney Foundation, which receives industry support for epidemiologic research.

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SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

Table S1. Variables included in the current analysis and methods of ascertainment in the National Health and Nutrition Examination Survey, 2015–2018.

Table S2. Percentage (SE) and millions (SE) of US adults with chronic kidney disease and blood pressure above the 2021 KDIGO and 2017 ACC/AHA guideline targets*, NHANES 2015–2018.

Table S3. Characteristics associated with systolic blood pressure ≥120 mm Hg in US adults with chronic kidney disease, NHANES 2015–2018.

Table S4. Characteristics associated with ACEi/ARB use in US adults with albuminuria, NHANES 2015–2018.

Table S5. Patterns of antihypertensive medication use among US adults with chronic kidney disease currently taking antihypertensive medication, NHANES 2015–2018.

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