Patterns of Antihypertensive Drug Utilization among US Adults with Diabetes and Comorbid Hypertension: The National Health and Nutrition Examination Survey 1999-2014

Clinical Medicine Insights: Cardiology
Volume 13: 1–9
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DOI: 10.1177/1179546819839418

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ABSTRACT

BACKGROUND: Diabetes and hypertension are the 2 leading risk factors for suboptimal cardiovascular and renal outcomes. These 2 conditions often coexist and can benefit from antihypertensive therapy, which may lead to blood pressure control and reduced risk for nephropathy (as evidenced by albuminuria).

OBJECTIVE: To quantify the trends of antihypertensive drug use and to assess the impact of antihypertensive treatment on the prevalence of blood pressure control and albuminuria, among US adults with coexisting diabetes and hypertension.

METHODS: In this serial cross-sectional study, we analyzed data from the 1999-2014 National Health and Nutrition Examination Survey (N = 3586). We determine the prevalence of antihypertensive use, drug classes used, and their association with blood pressure control and albuminuria.

RESULTS: During the study period, the study population experienced substantial increase in antihypertensive treatment (from 84.6% in 1999-2002 to 90.1% in 2011-2014, $P_{trend} < .01$) and blood pressure control (from 37.1% to 46.9%, $P_{trend} < .01$) and decrease in albuminuria (from 39.1% to 31.3%, $P_{trend} = .02$). These trends were particularly pronounced in the subgroups using angiotensin-converting-enzyme inhibitors or angiotensin II receptor blockers. In multivariate analysis, Blacks, Hispanics, and males were found more likely to have albuminuria than their respective counterparts. Achieving blood pressure control (odds ratio = 0.40, 95% confidence interval [CI]: 0.32-0.49) was associated with lower rates of albuminuria.

CONCLUSION AND RELEVANCE: Despite continued improvement in antihypertensive therapy, the burden of uncontrolled blood pressure and albuminuria remains substantial among US adults with diabetes and hypertension. Tailoring pharmacotherapy based on patient characteristics and comorbidities is needed to further improve these outcomes.

KEYWORDS: hypertension, diabetes mellitus, blood pressure, albuminuria, drug therapy

RECEIVED: June 9, 2018. **ACCEPTED:** March 1, 2019.

TYPE: Original Research

FUNDING: The author(s) received no financial support for the research, authorship, and/or publication of this article.

DECLARATION OF CONFLICTING INTERESTS: The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Introduction

Hypertension and diabetes are 2 leading risk factors for atherosclerotic cardiovascular disease (ASCVD), heart failure, and microvascular complications. Atherosclerotic cardiovascular disease (ASCVD), including acute coronary syndromes, myocardial infarction, stable or unstable angina, coronary or other arterial revascularization, stroke, transient ischemic attack, or peripheral arterial disease presumed to be of atherosclerotic origin, is the leading contributor to the clinical and economic burdens of diabetes.[1]

According to the American Heart Association, hypertension affects 86 million adults in the United States. Unfortunately, its prevalence is expected to rise drastically due to the aging population and other factors. It is estimated that hypertension will affect 41% of the US population in 2030, which represents an increase of 8.4% since 2012.[2] Prevalence of hypertension among people with diabetes varies from 20% to 60%, depending on factors such as age, sex, race/ethnicity, duration of diabetes, the extent of kidney damage, *and definitions of hypertension*.[3] In recent years, a number of well-designed studies have demonstrated the effectiveness of aggressive treatment of hypertension in reducing ASCVD, heart failure, and microvascular complications in people with diabetes.[4–7] Current clinical guidelines recommend blood pressure (BP) goal to be set at systolic blood pressure (SBP) less than 130 mm Hg and diastolic blood pressure (DBP) less than 80 mm Hg in patients with diabetes or persistent albuminuria.[8,9] Albuminuria, which is an independent predictor of cardiovascular (CV) events, CV

mortality, and all-cause mortality,[10] is particularly prevalent in patients with diabetes and essential hypertension. Data from large population-based studies in the Western countries show that the prevalence of albuminuria is 5% to 15% in the general adult population and 20% to 30% in adults with diabetes or essential hypertension.[11,12] Studies suggest that appropriate antihypertensive therapy, particularly angiotensin-converting enzyme (ACE) inhibitor or angiotensin II receptor blocker (ARB) containing regimens, is able to lower albuminuria in patients with essential hypertension.[13] However, the prevalence and the impact on albuminuria by antihypertensive therapy remains unclear in patients with coexistent hypertension and diabetes.

A recent analysis of national data shows that between 2003 and 2012, Blacks (79.1%), Whites (82.3%), and Mexican Americans (79.1%) with diabetes and hypertension had similar utilization rates of "recommended therapy," defined as any given regimen that included an ACE Inhibitor, ARB, β-blockers, thiazide diuretics, and/or calcium channel blocker (CCB).[14] Among hypertensive patients with and without diabetes in recent years, antihypertensive treatment rates are comparable between Whites and Blacks, while the latter more likely to receive thiazide diuretics and combination regimens.[15–17] Overall, Hispanics tend to be under treatment with antihypertensive medications, especially combination therapies.[16,18] While these data are important, very few population studies have systematically examined hypertension treatment patterns in diabetes population and their impact on control of BP and albuminuria. Based on the latest available national data, the aims of this study are threefold: (1) To evaluate time trends and utilization patterns of antihypertensive pharmacotherapy among US adults with comorbid hypertension and diabetes; (2) To study the prevalence and trends in BP control and albuminuria by types of antihypertensive regimens; and (3) To assess the impact of antihypertensive medication use on BP control and albuminuria.

Methods

Study design and participants

The National Health and Nutrition Examination Survey (NHANES) is conducted by the Centers for Disease Control and Prevention (CDC)/National Center for Health Statistics (NCHS) and uses a complex, multistage, clustered probability sampling method of noninstitutionalized US civilians to provide nationally representative estimates.[19] This study was restricted to nonpregnant adult participants (aged ⩾20 years) from the 1999-2000 to 2013-2014 NHANES cycles (n = 43 793). Participants were included if they had diagnosed diabetes (defined as (1) reported physician-diagnosed diabetes or (2) *an affirmative answer to 1 or both of the questions "Are you now taking insulin" and "Are you now taking diabetic pills to lower your blood sugar?"*) and diagnosed hypertension (defined as (1) mean SBP ⩾130 mm Hg or mean DBP ⩾80 mm Hg, combined with a reported physician-diagnosed hypertension or (2) *an affirmative answer to the question "Are you now taking prescribed medicine for high BP"* or (3) told twice by a physician he or she had hypertension).[16,17,20] All participants provided written informed consent. The study protocol was approved by the NCHS Institutional Review Board.

Outcomes

Antihypertensive medications were categorized into the following classes: (1) diuretics, (2) β-blockers, (3) calcium-channel blockers (CCBs), (4) ARBs, (5) angiotensin-converting enzyme inhibitors (ACE inhibitors), and (6) others (direct vasodilators, renin inhibitors, α_1-blockers, and other centrally acting drugs). Monotherapy was defined as a person who only reported taking 1 antihypertensive agent. Combination therapy (polytherapy) was defined as a person who reported taking >1 antihypertensive agents, including fixed-dose combination agents and combinations of different diuretics. Antihypertensive utilization rates (overall and class-specific) were calculated based on the reported use of specific drug of interest divided by the number of total subjects in the sample. Systolic BP and diastolic BP were calculated by using NHANES reporting guidelines. A detailed description of the procedures for BP measurement in NHANES has been published elsewhere.[21] *Hypertension control* was defined as SBP <130 mm Hg and DBP <80 mm Hg. *Albuminuria* was defined as urine albumin-to-creatinine ratio ⩾30 mg/g creatinine.[3]

Covariates

We used the following self-reported information: age, sex, race/ethnicity, educational attainment, health insurance status, medical visits over the past year, use of statins and diabetes medications, and history of physician-diagnosed CVD (including stroke, congestive heart failure, angina pectoris, myocardial infarction, or coronary artery disease). Chronic kidney disease was defined as either an estimated glomerular filtration rate <60 mL/min per 1.73 m^2 or a urinary albumin concentration of >200 mg/g of urinary creatinine, where glomerular filtration rate was estimated using the Modification of Diet in Renal Disease equation.[15] Serum creatinine values from NHANES 2005 to 2006 data were recalibrated according to the recommended standards.[22]

Statistical analysis

We used descriptive statistics to identify the following patient characteristics: (1) sociodemographic, clinical, and health care utilization factors; (2) antihypertensive utilization rates; (3) hypertension control; and (4) albuminuria. Linear trends in these characteristics were assessed with regression models with a 4-year combined survey period treated as a continuous variable. Prevalence of antihypertensive medication use (by class

and regimen) was compared by patient sex, race/*ethnicity*, and the presence of comorbidities, using multivariate regression models adjusting for potential confounders. We conducted logistic regressions to model the probability of BP control and albuminuria among patients treated with antihypertensive medications. In the fully adjusted models, we adjusted for 3 categories of patient-level variables: patient demographics, insurance status and educational attainment, and clinical characteristics. Demographics included age, sex, and race/*ethnicity* (White, Black, and Hispanic). Variables with a clinical rationale included chronic kidney disease, CVD, time since diagnoses of diabetes, statin use, and types of antihypertensive drug (ACE inhibitor/ARB containing regimens vs other regimens). In previous studies, these variable were associated with the likelihood of receiving antihypertensive treatment, and they were all at least moderately associated with BP control and albuminuria (2-sided, $P < .25$) from χ^2 tests.

Appropriate sample weights were used to account for differential probabilities of selection and the complex multistage sample survey design. Taylor linearization was used for variance estimation, and domain analysis was used for subpopulation analysis, since selection of subpopulations may be unrelated to sample design. The analyses were performed only for subgroups with sample sizes large enough to produce reliable estimates according to the NCHS standards (sample size ⩾30 and relative standard error <0.30).[19] Examination of the hypertensive patient sample in our study indicated that the distributions of age were similar across survey years ($P = .47$). Hence, we present estimates of antihypertensive prescribing rates, hypertension control, and albuminuria among US adults with diabetes and hypertension without age standardization.

Results

Baseline characteristics

A total of 3586 US adults were included in the study. Over the 16-year study period, the proportion of adults who achieved BP goal increased from 37.1% in 1999-2002 to 46.9% in 2013-2014 ($P_{trend} < .01$) and the prevalence of albuminuria decreased from 39.1% to 31.3% ($P_{trend} = .02$). Prevalence of statin use nearly doubled (from 31.5% to 60.3%, $P_{trend} < .001$), which was paralleled by a steady decrease in mean low-density lipoprotein cholesterol (LDL-C) values (from 110.8 mg/dL to 97.1 mg/dL, $P_{trend} < .001$). No significant changes were observed in the use of antidiabetic medications and HbA1c control (Supplemental Table 1).

Trends in utilization patterns

Overall, ACE inhibitors were the most commonly prescribed antihypertensive drug class accounting for 48.1% (either in combination or monotherapy) of all prescriptions throughout the study period, followed by diuretics (42.7%) and β-blockers (36.0%). The utilization of ARBs increased from 8.7% in 1999-2002 to 26.3% in 2013-2014 ($P_{trend} < .001$), and the upward trends were also observed in thiazide diuretics and β-blockers. Over the study period, the prevalence of antihypertensive medication use in US adults with diabetes and hypertension increased from 84.6% to 90.1% ($P_{trend} < .01$) and the increasing trends were particularly prominent in the utilization of combination regimens (from 54.2% to 62.5%, $P_{trend} < .01$; Table 1).

Difference in utilization patterns

More than 60% of the study population used combination regimens. Angiotensin-converting enzyme (ACE) inhibitor/diuretics (7.6%), ACE inhibitor/β-blocker (4.6%), and ACE inhibitor/β-blocker/diuretics (4.5%) were the most commonly used combination regimens. Among monotherapy users (27.9%), more than half (14.2%) used an ACE inhibitor. Men were more likely to use ACE inhibitors (53.5% vs 43.7%, $P_{diff} < .001$) and less likely to use ARBs (20.3% vs 25.2%, $P_{diff} < .01$) and diuretics (37.6% vs 47.0%, $P_{diff} < .001$) than women. The overall rate of antihypertensive pharmacotherapy was substantially lower in Hispanics (81.6%) than in Whites (89.8%) and Blacks (89.5%; $P_{diff} = .01$), particularly in combination regimens (Hispanic vs Whites vs Blacks: 47.5% vs 62.2% vs 66.0%, $P_{diff} < .001$). The presence of comorbidities (albuminuria, CVD, and chronic kidney disease) was associated with high utilization rates of combination regimens and certain antihypertensive drug classes, such as ARBs in chronic kidney disease and diuretics in CVD and chronic kidney disease (Supplemental Table 2 and Table 2).

Trends in prevalence of albuminuria and BP control

Overall, during the study period, US adults with diagnosed diabetes and hypertension experienced significant decrease in prevalence of albuminuria and improvement in BP control. These improvements were particularly pronounced among those treated with ACE inhibitors or ARBs—from 1999-2002 to 2011-2014, the prevalence of albuminuria decreased from 40.4% to 29.2% ($P_{trend} = .01$) and BP control increased from 39.7% to 51.6% ($P_{trend} < .001$) in this subgroup. At the same time, these outcomes remained fairly unchanged in untreated individuals and those treated with antihypertensive regimens not containing ACE inhibitors and ARBs (Figure 1 and Supplemental Figure 1).

Factors associated with the presence of albuminuria and BP control

As shown in Table 3, male sex, Black, and Hispanic race/ethnicity were all positively associated with the presence of albuminuria. *The presence of CVD increased the odds of albuminuria by* more than 50% (odds ratio = 1.57, 95% confidence interval

Table 1. Prevalence of antihypertensive medication use among adults with diagnosed diabetes and hypertension, NHANES, 1999-2014.

	1999-2014	1999-2002	2003-2006	2007-2010	2011-2014	P_{TREND}
Angiotensin-converting enzyme inhibitors	48.1 (1.0)	47.6 (2.6)	49.8 (2.0)	47.1 (1.9)	48.2 (2.0)	.71
Monotherapy	14.2 (0.8)	15.4 (2.2)	14.4 (1.8)	13.0 (1.4)	14.7 (1.4)	.53
Polytherapy	33.9 (1.1)	32.2 (2.8)	35.4 (2.3)	34.1 (1.7)	33.5 (2.2)	.92
Angiotensin receptor blockers	23.0 (1.0)	8.7 (1.1)	20.4 (2.1)	28.7 (1.7)	26.3 (1.9)	<.001
Monotherapy	4.4 (0.5)	2.1 (0.6)	4.0 (1.1)	5.6 (1.0)	4.6 (0.9)	.24
Polytherapy	18.6 (0.9)	6.6 (1.1)	16.4 (1.6)	23.1 (1.4)	21.7 (2.0)	<.001
Calcium channel blockers	28.3 (1.1)	32.9 (2.9)	27.0 (2.0)	26.6 (1.9)	28.5 (2.0)	.34
Monotherapy	3.0 (0.4)	7.4 (1.5)	1.9 (0.6)	2.3 (0.7)	2.5 (0.5)	.010
Polytherapy	25.3 (1.0)	25.5 (2.4)	25.1 (1.9)	24.3 (1.8)	26.1 (1.8)	.98
Diuretics	42.7 (1.1)	40.2 (2.6)	43.5 (2.4)	45.7 (2.1)	40.9 (1.9)	.63
Monotherapy	1.7 (0.2)	2.5 (0.7)	2.6 (0.6)	1.1 (0.3)	1.2 (0.3)	.04
Polytherapy	41.0 (1.1)	37.7 (2.4)	40.9 (2.6)	44.6 (2.1)	39.6 (1.9)	.35
Thiazide diuretics	28.5 (1.0)	22.6 (2.4)	27.3 (2.3)	31.5 (1.4)	29.3 (1.9)	.04
Monotherapy	1.0 (0.1)	1.3 (0.4)	0.9 (0.2)	0.7 (0.2)	1.1 (0.3)	.87
Polytherapy	27.5 (1.0)	21.4 (2.4)	26.5 (2.3)	30.8 (1.4)	28.2 (2.0)	.04
β-blockers	36.0 (1.1)	22.4 (2.1)	33.3 (2.6)	39.6 (2.0)	40.8 (2.1)	<.001
Monotherapy	3.8 (0.4)	1.2 (0.5)	5.0 (1.3)	3.8 (0.7)	4.2 (0.9)	.29
Polytherapy	32.2 (1.0)	21.2 (2.1)	28.2 (2.2)	35.7 (2.0)	36.6 (1.9)	<.001
Monotherapy	27.9 (1.0)	30.5 (2.3)	28.5 (2.4)	26.4 (1.9)	27.7 (1.8)	.12
Polytherapy	60.9 (1.1)	54.2 (2.9)	58.3 (2.2)	64.7 (1.8)	62.5 (2.1)	<.01
Single-pill combination	20.3 (1.0)	14.6 (2.1)	18.3 (2.3)	24.8 (1.8)	20.5 (1.6)	.02
Multiple-pill combination	40.6 (1.0)	39.5 (2.7)	40.0 (2.4)	40.0 (1.5)	42.0 (1.7)	.40
Any antihypertensive drug use	88.8 (0.7)	84.6 (1.5)	86.8 (2.0)	91.1 (1.0)	90.1 (1.2)	<.01

Abbreviations: NHANES, National Health and Nutrition Examination Survey.
Data are presented as mean and standard error (SE).

[CI]: 1.24-1.98). Time since diagnoses of diabetes was positively associated with albuminuria. The use of statin and antidiabetic medications both reduced the occurrence of albuminuria. Blacks were less likely than their White counterparts to achieve BP goal. Statin use and ACE inhibitor/ARB-containing regimens were both associated with increased likelihood of achieving BP goal. The presence of albuminuria *was associated with decreased likelihood of* BP control (odds ratio = 0.39, 95% CI: 0.31-0.49) and vice versa.

Discussion

This study fills the research gap in recent trends and patterns of antihypertensive medication use and its impact on BP control and albuminuria among individuals with coexisting diabetes and hypertension. Our data show that in the 16-year study period, the prevalence of antihypertensive medication use significantly increased among nonpregnant adults with diabetes and hypertension. These increases appear to be almost exclusively driven by a significant increase in the proportion of combination therapy use. The use of ARBs dramatically increased during the study period, possibly due to availability of their less expensive generic versions. In concert with the upward trends in antihypertensive drug use, the rates of BP control and albuminuria prevention improved substantially over the 16-year time period. By 2011-2014 time period, 90.1% of US adults with diabetes and hypertension used at least 1 antihypertensive medication. More than two-thirds of them were taking multiple antihypertensive agents. Among treated individuals, 48.2% achieved BP goal (<130/80 mm Hg) and 69.5% were free of albuminuria. Although clinical outcomes of hypertension

Table 2. Prevalence of antihypertensive drug use among US adults with diagnosed diabetes and hypertension by drug class and patient characteristics, NHANES, 1999-2014.

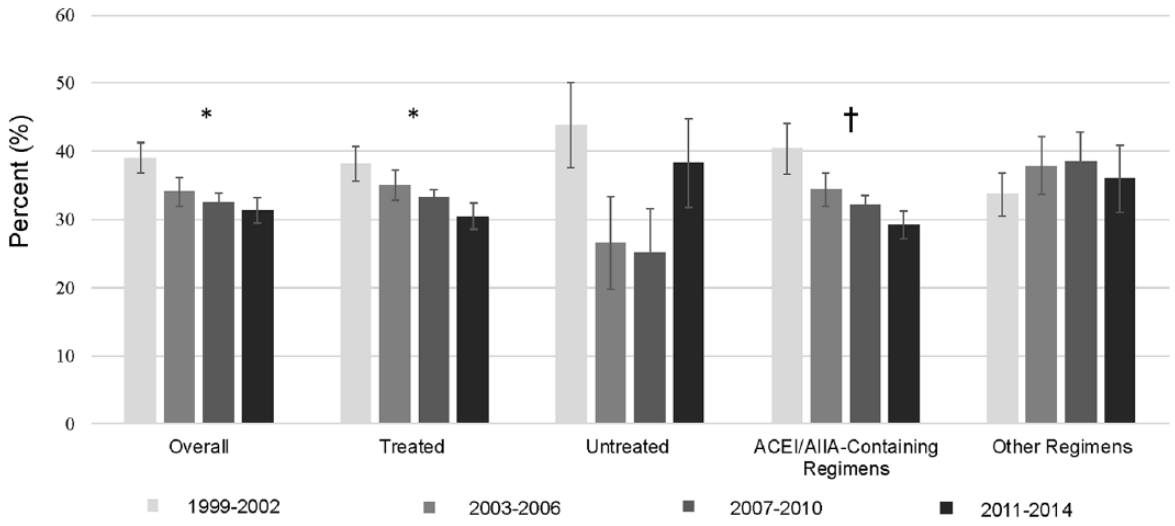
	MEN	WOMEN	P_{DIFF}	WHITE	BLACK	HISPANIC	P_{DIFF}	WITH ALBUMINURIA	WITHOUT ALBUMINURIA	P_{DIFF}	WITH CVD	WITHOUT CVD	P_{DIFF}	WITH CKD	WITHOUT CKD	P_{DIFF}
Angiotensin-converting enzyme inhibitor																
Overall	53.5 (1.6)	43.7 (1.5)	<.001	48.1 (1.6)	47.4 (1.7)	49.6 (2.1)	.56	50.7 (1.9)	48.7 (1.6)	.48	48.6 (1.9)	47.9 (1.2)	.21	46.5 (2.1)	48.8 (1.2)	.21
Monotherapy	16.3 (1.2)	12.6 (1.1)	.01	13.7 (1.0)	10.1 (1.0)	22.1 (1.8)	<.001	10.8 (1.3)	16.9 (1.1)	.04	6.7 (0.8)	17.9 (1.1)	<.001	8.3 (1.0)	16.7 (1.1)	<.01
Polytherapy	37.3 (1.5)	31.1 (1.4)	.01	34.3 (1.6)	37.4 (1.6)	27.5 (2.0)	<.001	40.0 (1.9)	31.8 (1.4)	.01	41.9 (1.8)	30.1 (1.3)	<.001	38.2 (2.2)	32.1 (1.3)	.67
Angiotensin receptor blocker																
Overall	20.3 (1.5)	25.2 (1.4)	<.01	23.6 (1.4)	20.6 (1.4)	20.0 (1.8)	.68	21.5 (1.6)	23.8 (1.4)	.11	23.2 (1.7)	22.9 (1.1)	.43	28.9 (1.9)	20.6 (1.1)	<.001
Monotherapy	4.2 (0.8)	4.5 (0.6)	.73	4.4 (0.7)	3.5 (0.7)	5.0 (0.9)	.41	3.0 (0.5)	5.2 (0.7)	.06	2.2 (0.5)	5.4 (0.7)	<.001	3.2 (0.7)	4.9 (0.6)	.30
Polytherapy	16.1 (1.4)	20.7 (1.2)	<.01	19.2 (1.2)	17.1 (1.2)	15.1 (1.7)	.46	18.5 (1.5)	18.6 (1.3)	.30	21.1 (1.7)	17.4 (1.1)	.40	25.8 (1.8)	15.7 (1.0)	<.001
Diuretics																
Overall	37.6 (1.7)	47.0 (1.5)	<.001	43.7 (1.4)	48.9 (1.6)	30.7 (1.9)	<.001	44.6 (1.9)	42.1 (1.2)	.24	53.6 (1.9)	37.6 (1.3)	<.001	54.1 (2.3)	38.1 (1.3)	<.001
Monotherapy	1.5 (0.3)	1.9 (0.4)	.78	1.5 (0.3)	2.5 (0.6)	1.4 (0.5)	.14	1.9 (0.5)	1.5 (0.3)	.65	1.6 (0.4)	1.8 (0.3)	.07	1.9 (0.6)	1.6 (0.3)	.70
Polytherapy	36.1 (1.8)	45.1 (1.5)	<.001	42.2 (1.4)	46.4 (1.7)	29.3 (1.9)	<.001	42.7 (1.9)	40.6 (1.2)	.19	52.0 (1.9)	35.8 (1.3)	<.001	52.3 (2.2)	36.4 (1.3)	<.001
Thiazide diuretics																
Overall	25.3 (1.4)	31.1 (1.3)	.02	28.2 (1.4)	34.6 (1.4)	22.1 (1.8)	<.001	25.2 (1.6)	31.4 (1.3)	<.01	25.2 (1.7)	30.0 (1.2)	.10	29.3 (2.1)	28.1 (1.3)	.24
Monotherapy	1.0 (0.2)	0.9 (0.2)	.63	0.9 (0.2)	1.7 (0.4)	0.9 (0.5)	.10	0.8 (0.2)	1.0 (0.2)	.47	0.5 (0.2)	1.2 (0.2)	.02	0.9 (0.4)	1.0 (0.2)	.94
Polytherapy	24.3 (1.5)	30.2 (1.3)	.02	27.4 (1.4)	32.9 (1.5)	21.1 (1.8)	<.001	24.5 (1.6)	30.4 (1.3)	<.01	24.7 (1.7)	28.8 (1.2)	.21	28.4 (2.1)	27.1 (1.3)	.24
Beta blocker																
Overall	35.6 (1.7)	36.3 (1.5)	.09	38.6 (1.5)	32.8 (1.5)	27.4 (2.3)	<.01	42.2 (1.9)	32.5 (1.6)	.03	57.6 (2.2)	25.6 (1.3)	<.001	47.1 (2.2)	31.4 (1.3)	.03
Monotherapy	2.9 (0.5)	4.6 (0.8)	.02	4.5 (0.7)	2.5 (0.6)	3.0 (0.7)	.06	2.7 (0.7)	4.1 (0.7)	.42	4.3 (0.9)	3.6 (0.6)	.92	3.2 (0.8)	4.1 (0.6)	.35
Polytherapy	32.8 (1.7)	31.7 (1.5)	.56	34.2 (1.4)	30.3 (1.5)	24.4 (2.2)	.07	39.5 (1.8)	28.4 (1.4)	<.01	53.3 (2.0)	22.0 (1.1)	<.001	43.9 (2.0)	27.3 (1.2)	<.01

(Continued)

Table 2. (Continued)

	MEN	WOMEN	P_{DIFF}	WHITE	BLACK	HISPANIC	P_{DIFF}	WITH ALBUMINURIA	WITHOUT ALBUMINURIA	P_{DIFF}	WITH CVD	WITHOUT CVD	P_{DIFF}	WITH CKD	WITHOUT CKD	P_{DIFF}
Calcium channel blocker																
Overall	30.2 (1.8)	26.7 (1.3)	.16	26.6 (1.5)	38.7 (1.7)	22.8 (2.0)	<.001	36.0 (1.7)	23.3 (1.2)	<.001	34.1 (1.8)	25.5 (1.3)	.08	34.7 (1.9)	25.7 (1.3)	.33
Monotherapy	2.8 (0.5)	3.2 (0.5)	.90	3.0 (0.6)	3.8 (0.6)	1.9 (0.5)	.13	3.0 (0.6)	3.0 (0.5)	.57	1.9 (0.5)	3.6 (0.5)	.02	2.4 (0.6)	3.3 (0.5)	.51
Polytherapy	27.4 (1.7)	23.5 (1.2)	.13	23.6 (1.4)	34.9 (1.7)	20.9 (1.9)	<.001	33.0 (1.7)	20.3 (1.2)	<.001	32.2 (1.8)	21.9 (1.2)	<.01	32.4 (1.9)	22.3 (1.2)	.25
Monotherapy	28.6 (1.6)	27.3 (1.5)	.40	27.6 (1.4)	23.4 (1.4)	34.1 (1.9)	<.001	22.2 (1.6)	31.3 (1.3)	<.01	17.0 (1.4)	33.1 (1.4)	<.001	19.6 (1.7)	31.3 (1.3)	.01
Polytherapy	59.4 (1.8)	62.1 (1.6)	.15	62.2 (1.5)	66.0 (1.5)	47.5 (2.5)	<.001	67.0 (1.7)	57.8 (1.3)	.06	76.8 (1.6)	53.3 (1.4)	<.001	72.8 (1.8)	56.0 (1.4)	<.01
Single-pill combination	18.3 (1.5)	22.0 (1.2)	.12	20.6 (1.4)	23.5 (1.4)	14.1 (1.6)	<.001	18.4 (1.4)	22.3 (1.3)	.13	16.6 (1.7)	22.1 (1.1)	.08	20.6 (1.8)	20.2 (1.2)	.34
Multiple-pill combination	41.1 (1.6)	40.2 (1.4)	.84	41.6 (1.5)	42.5 (1.4)	33.4 (2.2)	.01	48.6 (1.8)	35.6 (1.3)	<.001	60.3 (1.7)	31.2 (1.2)	<.001	52.2 (2.0)	35.8 (1.2)	.03
Any Antihypertensive drug use	88.0 (1.0)	89.5 (1.0)	.26	89.8 (1.0)	89.5 (0.9)	81.6 (1.9)	.01	89.1 (1.1)	89.1 (1.0)	.49	93.8 (0.8)	86.4 (0.9)	<.001	92.4 (1.1)	87.3 (0.9)	.26

Abbreviation: CKD, chronic kidney disease; CVD, cardiovascular disease; NHANES, National Health and Nutrition Examination Survey.
Data are presented as mean and standard error (SE).



* P trend <0.05; † P trend < 0.01; ACEI = angiotensin-converting-enzyme inhibitor; ARB = angiotensin receptor blocker; vertical lines mark the 95% Confidence Intervals of the estimates.

Figure 1. Prevalence of albuminuria among adults aged ⩾20 years with diagnosed diabetes and hypertension by antihypertensive medication use, NHANES 1999-2014. NHANES indicates National Health and Nutrition Examination Survey (NHANES).

treatment have improved over time, the rate of BP control in the US adults with diabetes stays lower than 50%, and the treatment of these 2 comorbidities remains to be a public health challenge for patients and health care professionals.

Effective BP control and prevention of albuminuria are paramount in reducing the risk of adverse CV events. More aggressive therapeutic approaches to hypertension are especially beneficial in patients with comorbid diabetes.[23–25] Most studies found significant increases in the attainment of BP control over the past few decades, despite the fact that reported rates of BP control may vary substantially among publications depending on study population, definitions of diabetes and hypertension, and the study time frame.[15,16,20] At the same time, it is important to note that the BP control was generally much lower among those with comorbid diabetes compared with the overall hypertensive population. Gu et al[15] analyzed recent national data and found that the presence of diabetes was associated with a more than 25% decrease in rate of BP control. Casagrande Stark et al[20] reported that the proportion of achieving BP <130/80 mm Hg ranges from 33.2% to 51.1% among US adults with diabetes between 1988 and 2010. Another recent European population-based study showed that BP control was not achieved among most hypertensive patients with diabetes mellitus and the mean BP was 142/81 mm Hg.[26] *Studies have shown that any decrease in albuminuria was strongly related to decreased risk for CV events and all-cause mortality as well as improved renal outcomes.*[10–12] Over the study period, the prevalence of albuminuria decreased by nearly 20% (from 39.1% to 31.3%, $P = .02$). However, it still remained a significant burden among US adults with comorbid diabetes and hypertension.

The selection of drugs for initial and continuing therapy of hypertension has far-reaching clinical and economic implications. In general, multiple-drug therapy is required to achieve BP targets.[3,27,28] The latest American Diabetes Association position statement recommends ACE inhibitors, ARBs, thiazide diuretics, or CCBs as first-line agents for treatment of hypertension in patients with diabetes and ACE inhibitors or ARBs for patients with albuminuria.[3] As observed in our data, the use of antihypertensive regimens containing ACE inhibitors or ARBs was an important factor for BP control and prevention of albuminuria over the 16-year study period. During the study timeframe, the use of agents containing thiazide diuretics increased by 23% and ARBs more than tripled, while ACE inhibitors and CCBs remained fairly unchanged. By the last combined survey period (2011-2014), approximately 75% of adults with diabetes and hypertension were taking agents containing either an ACE inhibitor or ARB. At the same time, the use of β-blockers remained steadily high and actually increased over time, including patients without compelling indications for their use. As an example, the proportion of individuals with self-reported history of congestive heart failure did not change appreciably over the study timeframe (from 11.4% in 1999-2002 to 11.6% in 2011-2014, $P_{trend} = .79$). This is particularly concerning because there is accumulating evidence suggests that β-blockers are inferior to other agents in treating hypertension and they are associated with elevated blood glucose levels.[29–32] Therefore, education among clinicians on best hypertension treatment practices cannot be overemphasized.

In our study, we found gaps in clinical outcomes among ethnic/racial groups. Blacks and Hispanics had substantially higher rates of albuminuria compared with Whites, which can be attributable to lower rates of diabetes diagnosis among these minority groups[33] among other reasons. Perez et al found that among US adults with diagnosed diabetes and hypertension,

Table 3. Association of patient characteristics with the likelihood of controlled for hypertension and presence of albuminuria among US adults with diabetes and hypertension, NHANES 1999-2014.

	BLOOD PRESSURE CONTROL		ALBUMINURIA	
	OR (95% CI)	*P* VALUE	OR (95% CI)	*P* VALUE
Age, ×1 year	0.97 (0.96-0.98)	<.001	1.01 (0.99-1.03)	.07
Female	0.99 (0.78-1.26)	.94	0.65 (0.51-0.82)	<.001
Race/ethnicity				
White				
Black	0.73 (0.59-0.91)	<.01	1.45 (1.15-1.82)	<.01
Hispanic	0.85 (0.66-1.09)	.19	1.87 (1.37-2.54)	<.001
Health insurance	0.87 (0.61-1.25)	.45	0.93 (0.61-1.44)	.75
College education	0.84 (0.63-1.12)	.24	0.65 (0.44-0.95)	.03
Chronic kidney disease	1.05 (0.81-1.37)	.69	3.96 (3.05-5.15)	<.001
Cardiovascular disease	1.14 (0.90-1.43)	.29	1.57 (1.24-1.98)	<.001
Albuminuria	0.39 (0.31-0.49)	<.001		
Blood pressure control			0.39 (0.31-0.49)	<.001
Time since diagnosis of diabetes				
<5 years				
5 to <10 years	1.08 (0.82-1.43)	.57	1.43 (1.04-1.97)	.03
⩾10 years	1.26 (0.97-1.52)	.12	1.96 (1.46-2.62)	<.001
Statin use	1.32 (1.05-1.56)	.02	0.76 (0.60-0.97)	.03
Diabetes medications	1.28 (0.94-1.73)	.12	0.61 (0.41-0.90)	.01
ACEI or ARB vs other regimens	1.40 (1.09-1.78)	<.01	0.85 (0.66-1.10)	.22

Abbreviations: ACEI, angiotensin-converting-enzyme inhibitor; ARB, angiotensin receptor blocker; CI, confidence interval; NHANES, National Health and Nutrition Examination Survey; OR, odds ratio.

Hispanics (68.6%) had the lowest health insurance coverage, followed by Blacks (88.6%) and Whites (94.0%). Suboptimal BP control among Blacks has been widely documented.[5,14–17] Similar to findings from Perez et al, despite comparable treatment intensity to those of Whites, Blacks were more than 25% less likely to achieve BP control than Whites. Our study also suggests that Blacks were 45% more likely to have albuminuria than their White counterparts. While biological characteristics may partially explain these discrepancies, other factors, such as low treatment adherence and suboptimal patient-provider communication, may also play a role. However, Hispanics had adjusted BP control rates only slightly lower than Whites, despite having the lowest overall prevalence of antihypertensive medication use, particularly in combination regimens. It is worth noting that at the end of the study period (2011-2014), 10% of the individuals remain untreated; minority groups, particularly Hispanics, were disproportionately represented. Previous studies suggest that the White-Hispanic disparities can be largely eliminated through improving health care access and health education in Hispanic communities.[16,33]

A strength of this study was the use of a nationally representative sample allowing generalization to the US adult noninstitutionalized population. Drug utilization information and clinical outcomes were assessed using standardized procedures, which allowed us to better characterize diabetes management. This is a serial cross-sectional study with inherent limitations due to the observational study design. Some important causal relationships such as the use of ACE inhibitors/ARBs and the presence/extent of albuminuria cannot be examined although we tried to explore some specific patient-related factors. Also, the report of drug use only includes prescription medications that have been used in the past 30 days. Another limitation is that the recordings of BP represent 1-day measurements as opposed to average measurement from several visits as recommended by 2017 American College of Cardiology/American Heart Association Guidelines. Moreover, no antihypertensive

dosing information was available for comparison and exact definition of treatment intensity.

Conclusions

Among US adults with diabetes and hypertension between 1999 and 2014, antihypertensive medication use continues to increase, with substantial improvements in BP control and prevention of albuminuria. The increased use of combination regimens, particularly ACE inhibitor or ARB-containing regimens, may have contributed to these improvements. However, suboptimal rates of BP control and albuminuria still exist, particularly in certain minority groups. More efforts are needed to close the gap between antihypertensive use and BP control, as well as to maximize the public health and clinical benefits among these high-risk subpopulations.

Author Contributions

AG and SL conceived the presented idea and supervised the project. AG developed the analytical framework and performed the analyses. SNF, YJC, and AK contributed to the literature search and participated in manuscript writing. AG and SL edited the manuscript. All authors discussed the results and contributed to the final manuscript.

Supplemental material

Supplemental material for this article is available online.

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