

Supplemental Online Content

Vitarello JA, Fitzgerald CJ, Cluett JL, Juraschek SP, Anderson TS. Prevalence of medications that may raise blood pressure among adults with hypertension in the United States. *JAMA Intern Med*. Published online November 22, 2021. doi:10.1001/jamainternmed.2021.6819

eMethods.

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

eMethods

Study Population

NHANES is a biannual survey, designed to be nationally representative of the US non-institutionalized population.⁴ We examined five survey cycles from 2009 through 2018, and included participants who were age 18 or older, non-pregnant, and completed at least one BP recording and the medication questionnaire. Missing data for covariates were imputed using multiple imputation with chained equations. A Gibbs sampling procedure was used to generate 10 imputed datasets after a burn-in of 500 iterations.

Blood Pressure Measurement

BP recordings were performed by physicians using standardized technique: after a five-minute rest period, BP measurements were checked three times during a single visit with the participant in a seated position using the same arm.⁴ Hypertension was defined as meeting any of the following criteria: (1) an average systolic BP reading ≥ 130 mmHg, (2) an average diastolic BP reading ≥ 80 mmHg, or (3) answering 'yes' to "Have you ever been told by a doctor or other health professional that you had hypertension, also called high blood pressure?". Uncontrolled hypertension was defined as an average systolic BP reading ≥ 130 mmHg or an average diastolic BP reading ≥ 80 mmHg in accordance with 2017 ACC/AHA guidelines.²

Reported Medication Use

Medications that may cause elevated BP were identified from the 2017 ACC/AHA guideline.² When broad classes were identified by the guideline, for example antidepressants, literature review was conducted to identify whether all sub-classes

were associated with BP elevation. Antihypertensives included angiotensin-converting enzyme inhibitors, angiotensin-receptor blockers, beta blockers, calcium channel blockers, thiazide type diuretics, centrally acting antiadrenergic agents, aldosterone receptor antagonists, renin inhibitors, potassium-sparing diuretics, and combination antihypertensives.

Prescription medication use was obtained from interviews conducted in the participants' homes. Participants were asked to report all prescription medications taken within the past 30 days and to show the interviewer the medication bottle if available. Drug names were linked to the Lexicon Plus database for classification. We examined each participant's use of medications that may cause elevated BP, use of antihypertensives, and overall medication count. Over-the-counter medications, apart from pseudoephedrine, were not collected by NHANES.

Covariates

Covariates included sex, race/ethnicity, age, insurance type, routine place for healthcare, received healthcare in the past year, education, household income, medication count, antihypertensive count, and survey cycle. Race and ethnicity were included as covariates given established health disparities in hypertension control and differences in prescribing patterns.

Statistical Analysis

NHANES uses a stratified multistage probability survey design, assigning weights to account for differential probability of selection and nonresponse. Sampling weights were used to provide nationally representative estimates with 95% confidence intervals. Data

was pooled from the five cycles to provide more stable estimates, except for analyses of temporal trends. Analyses were performed using SAS v9.4 and Stata v16.1.

Our analyses consisted of multiple steps. First, we determined the prevalence of medications that may cause elevated BP for the adult population and the descriptive characteristics of adults who did and did not report BP raising medications, using descriptive statistics.

Second, we modeled the association between use medications that may raise BP and BP using two approaches. Multivariable logistic regression models were used to estimate the association between use of medications that may raise BP and uncontrolled hypertension, accounting for the aforementioned covariates. Analyses were conducted for the US population and stratified by concurrent use of any antihypertensives, as the use of antihypertensives is likely to confound the relationship between use of medications which may raise BP and blood pressure. Analyses were repeated for use of any medications that may raise BP and for use of 1 and ≥ 2 medications that may raise BP to assess for possible dose response.

Third, we examined whether adults with hypertension using medications which may raise BP were treated with a greater number of antihypertensives. Multivariable negative binomial regression models were constructed which the dependent variable was the number of antihypertensives used and the independent variables included the use of medications which may raise BP, systolic BP, diastolic BP, and aforementioned covariates. Stratified analyses were conducted for adults with controlled and uncontrolled BP. Analyses were repeated for use of any medications that may raise BP and for use of 1 and ≥ 2 medications that may raise BP.