


ORIGINAL PAPER

Sustained blood pressure control and coronary heart disease, stroke, heart failure, and mortality: An observational analysis of ALLHAT

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Achieving blood pressure (BP) control is associated with lower cardiovascular disease (CVD) risk, but less is known about CVD risk associated with sustained BP control over time. This observational analysis of the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT) was restricted to participants with four to seven visits with systolic BP (SBP) measurements during a 22-month period (n = 24 309). The authors categorized participants as having sustained BP control (SBP < 140 mm Hg) at 100%, 75% to <100%, 50% to <75%, and <50% of visits during this period. Outcomes included fatal coronary heart disease (CHD)/nonfatal myocardial infarction (MI), stroke, heart failure (HF), a composite CVD outcome (fatal CHD/nonfatal MI, stroke, or HF), and mortality. Hazard ratios (HRs) for the association of category of sustained BP control for each outcome were obtained using proportional hazards models. SBP control was present among 20.0% of participants at 100%, 16.4% at 75% to less than 100%, 27.0% at 50% to less than 75%, and 36.6% at less than 50% of visits. Compared to those with SBP control at 100% visits, adjusted HR (95% CI) among those with SBP control at <50% of visits was 1.16 (0.93-1.44) for fatal CHD/nonfatal MI, 1.71 (1.26-2.32) for stroke, 1.63 (1.30-2.06) for HF, 1.39 (1.20-1.62) for the composite CVD outcome, and 1.14 (0.99-1.30) for mortality. Sustained SBP control may be beneficial for preventing stroke, HF, and CVD outcomes in adults taking antihypertensive medication.

1 | INTRODUCTION

Treatment and control of high blood pressure (BP) is a key strategy for reducing coronary heart disease (CHD), stroke, heart failure (HF), and all-cause mortality among adults with hypertension.¹⁻³

Accordingly, clinical practice guidelines provide recommendations for accurately identifying adults with hypertension, initiating appropriate antihypertensive therapy, and achieving predefined BP goals that have been shown to be associated with lower cardiovascular disease (CVD) and all-cause mortality event rates in randomized

trials.^{4,5} However, less is known about the role of sustaining BP control over time.

In clinical practice, patients may be followed over many years and often experience times of controlled as well as uncontrolled BP.⁶ There are several reasons why BP control may change over time, including changes in patients' health status or medication adherence,^{7,8} variability in BP measurement from visit to visit, or reduction in antihypertensive medication intensity due to concerns about overtreatment on the part of the provider.^{9,10} The proportion of visits at which patients achieve BP control can easily be calculated, could be used to facilitate discussions with patients about treatment goals, and could be used as a performance measure for quality improvement. Also, data on the effects of maintaining sustained BP control could be used to support greater treatment consistency over time or conversely, to allow higher BP levels at some visits.

Findings from a limited number of studies suggest that having BP control at a greater proportion of visits over time is associated with a lower CVD risk.¹¹⁻¹³ However, prior studies included primarily white participants, those with existing coronary heart disease (CHD), or with multiple CVD risk factors.¹²⁻¹⁴ The purpose of the current study was to determine the association of sustained BP control with CHD, stroke, HF, and mortality in an observational analysis of a demographically and clinically diverse population within a large clinical trial.

2 | METHODS

2.1 | Study design and population

We conducted a cohort study using existing data from the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT), a randomized, double-blind, multicenter clinical trial sponsored by the National Heart, Lung, and Blood Institute.^{15,16} ALLHAT was designed to determine whether the occurrence of major CVD events (primary end point: fatal CHD or nonfatal myocardial infarction [MI]) is lower for high-risk patients with hypertension treated with amlodipine, lisinopril, or doxazosin, each compared with a diuretic-based treatment using chlorthalidone.¹⁵⁻¹⁷ ALLHAT enrolled 42 418 men and women aged 55 years or older between 1994 and 1998 who had hypertension and at least one additional CHD risk factor (MI, stroke, left ventricular hypertrophy, diabetes mellitus, current cigarette smoking, low high-density lipoprotein [HDL] cholesterol, or documentation of other atherosclerotic cardiovascular diseases [ASCVD]).¹⁸ This analysis of ALLHAT data was approved by the Duke University Institutional Review Board.

The current study was restricted to participants randomized to receive amlodipine, lisinopril, or chlorthalidone ($n = 33\,357$), due to early termination of the doxazosin arm.¹⁷ The current analysis was further restricted to those with systolic BP (SBP) measurements at four or more of the seven ALLHAT study visits conducted between 6 and 28 months following randomization ($n = 7508$ participants excluded) and participants who did not experience any of the following events before having four visits with SBP measurements: fatal CHD/

nonfatal MI, stroke, or HF ($n = 1540$ participants excluded). We required participants to have at least four visits in order to obtain a reliable estimate of SBP control. The 28-month study visit was chosen as the end of the assessment period to provide adequate follow-up time to identify outcomes in the remaining months of the ALLHAT study. Participants who experienced events prior to having four visits with SBP measurements were excluded because the occurrence of these conditions may impact BP or lead to changes in BP treatment goals or antihypertensive medication regimens. The final analytic cohort for the current analysis consisted of 24 309 participants.

2.2 | Sustained blood pressure control

BP was measured two times at each visit by trained staff following a standardized protocol, a description of which has been previously reported.¹⁹ Participants were asked to attend all study visits. Study visits occurred at regular intervals (ie, 6, 9, 12, 16, 20, 24, and 28 months). Follow-up visits were conducted through March 2002. At each visit, BP levels were calculated as the average of two measurements obtained with a 30-second interval separation. The BP goal in all randomization arms was SBP < 140 mm Hg and diastolic BP (DBP) < 90 mm Hg. After allowing for a 6-month period for titration of study medications toward the BP goal, we determined the proportion of visits for which SBP was <140 mm Hg from the 6-month study visit through the 28-month study visit (ie, assessment period) or the last of the available SBP measures. Defining SBP < 140 mm Hg was chosen based on the goal for ALLHAT. Sustained SBP control was then categorized into four groups defined as SBP < 140 mm Hg (a) at 100% of visits, (b) at 75% to less than 100%, (c) at 50% to less than 75%, or (d) at less than 50% of visits. The categorization of sustained SBP control provides a range of sustained SBP control, is intuitive, and is similar to prior studies that categorized SBP control based on 25% increments.¹²⁻¹⁴

2.3 | Ascertainment of outcomes

Outcomes of interest included fatal CHD or nonfatal MI, stroke, HF, a composite CVD outcome that included CHD or nonfatal MI, stroke, and HF, and all-cause mortality. Outcome ascertainment has been previously described.^{16,20} Participants were followed from the date of the last visit with an SBP measurement within the assessment period to the date of each outcome, their date of death, or the end of active follow-up. For the analysis of mortality, participants were censored at three years following their last SBP obtained during the assessment period, which approximated the median follow-up for the other outcomes.

2.4 | Covariate information

Data on covariates were collected before randomization and during the 6- to 28-month assessment period. Age, race, sex, education level, current smoking, medical history (diabetes mellitus, MI, stroke, revascularization, other ASCVD), and use of aspirin and antihypertensive medication were obtained by participant report and medical

records prior to randomization. Measurements obtained at baseline included height and weight (used to calculate body mass index [BMI]), cholesterol levels, serum creatinine (used to calculate estimated glomerular filtration rate [eGFR]), and an electrocardiogram (left ventricular hypertrophy [LVH]). Data collection at each visit during the assessment period included use of statins, SBP, DBP, pulse pressure, antihypertensive medication adherence, and changes in medication classes. We calculated mean SBP, DBP, and pulse pressure across all available BP measurements during the assessment period. Low antihypertensive medication adherence was defined as a self-report of <80% adherence at any of the study visits during the assessment period. Changes in medication classes were defined as any change in BP medications during the assessment period.

2.5 | Statistical analysis

Characteristics were calculated for participants in each of the four categories of sustained BP control (100%, 75% to <100%, 50% to <75%, and <50% of visits), separately. We computed person time and incidence (number of events divided by person time, per 100 person-years) for each of the five outcomes by category of sustained BP control. Cox proportional hazards models were used to obtain hazard ratios (HRs) for the association of sustained SBP control for five separate outcomes: fatal CHD or nonfatal MI, stroke, HF, the composite CVD outcome, and all-cause mortality. Time-to-event outcomes were censored upon loss to follow-up, death for outcomes excluding mortality, and the end of study follow-up. We conducted three progressively adjusted regression models. In Model 1, we adjusted for age, race, and sex. Model 2 included additional adjustment for education level, current smoking, BMI, aspirin use, low HDL cholesterol level, total cholesterol, eGFR, type 2 diabetes mellitus, history of MI or stroke, history of other ASCVD, history of revascularization, and LVH by electrocardiography. We further adjusted for use of antihypertensive medication prior to randomization, statin use, and low adherence at any visit during the assessment period, as well as randomization group, in Model 3. To determine the impact of mean SBP, we repeated Model 3 adding the participants' mean SBP during the assessment period. The log-linearity of hazard ratios across categories of SBP control was assessed using observation-weighted orthogonal contrasts for linear effects.

As a sensitivity analysis, models were run with and without stratification by number of visits (4, 5, 6, and 7) used to calculate SBP control. Stratification allowed separate baseline hazards for participants with a different number of SBP measures during the assessment period. We repeated the analyses for the study outcomes, within subgroups by age (<65 vs ≥65 years old), sex (men vs women), race (white vs black) and randomization group (chlorthalidone, amlodipine, lisinopril), and comorbidity (history of diabetes vs no diabetes, MI/stroke vs no MI/stroke, other ASCVD vs no ASCVD, and eGFR < 60 mL/min/1.73 m² vs ≥ 60 mL/min/1.73 m²) including adjustment for the variables in Model 3. Formal tests of interaction were conducted in analyses that included the full population, main effect terms (eg, age group, sustained SBP category), and interaction

terms (eg, age group*sustained SBP category). All analyses were performed with StataSE 15 (College Station, TX), and the statistical significance threshold was set at $\alpha = 0.05$.

3 | RESULTS

3.1 | Participant characteristics

Compared to ALLHAT participants excluded from the current analysis because they had <4 visit with SBP measurements, those included were younger (66.7 vs 67.2 years of age), more likely to be non-Hispanic white (50.8% vs 32.8%), male (54.2% vs 48.0%), taking aspirin (37.4% vs 30.7%), have low HDL cholesterol (12.5% vs 9.0%), be taking antihypertensive medication prior to randomization (90.7% vs 88.0%) and less likely to be current smokers (21.4% vs 23.5%), have diabetes (41.4% vs 45.8%), and history of MI/stroke (22.0% vs 24.3%) (Table S1).

Sustained BP control was present among 4,868 (20.0%) participants at all visits, 3,988 (16.4%) at 75% to less than 100%, 6,556 (27.0%) at 50% to less than 75%, and 8,897 (36.6%) at less than 50% of visits. Participant characteristics by category percentage of visits with BP control are displayed in Table 1. Participants with SBP control at fewer visits were older, more likely to be non-Hispanic black, have an eGFR < 60 mL/min/1.73 m², and have a history of diabetes, LVH, or to be taking antihypertensive medication prior to randomization. They were also less likely to be men, had fewer years of education, current smokers and were less likely to be taking aspirin, or have low HDL cholesterol, a history of MI, stroke, ASCVD, or revascularization prior to randomization.

During the assessment period (study months 6 to 28 post-randomization), participants who had SBP control at a smaller proportion of visits had higher mean SBP, DBP, pulse pressure, and were taking more classes of antihypertensive medication. Those with SBP control at a smaller proportion of visits were less likely to be taking a statin or be randomized to chlorthalidone and more likely to have low adherence at any visit, to have changed medications classes or be randomized to lisinopril.

3.2 | Outcomes

A total of 838 participants experienced fatal CHD or nonfatal MI (rate: 1.28, 95% confidence interval [CI]: 1.20-1.37 per 100 person-years), 450 participants had a stroke (rate: 0.68, 95% CI: 0.62-0.75 per 100 person-years), 823 participants developed HF (rate: 1.26, 95% CI: 1.17-1.35 per 100 person-years), 1859 participants developed the composite CVD outcome (rate: 2.92, 95% CI: 2.79-3.06 per 100 person-years), and 2173 participants died (rate: 3.62, 95% CI: 3.47-3.78 per 100 person-years). Overall, the cumulative percentage of participants, who had a fatal CHD/nonfatal MI, stroke, HF, or the composite CVD outcome, was lowest among those with SBP control at 100% of visits (Figure 1). This was not true for mortality.

Compared to those with sustained SBP control at all visits, multivariable-adjusted HR (95% CI) for fatal CHD/nonfatal MI was 1.07

TABLE 1 Characteristics of ALLHAT participants by percentage of visits with systolic blood pressure (SBP) <140 mm Hg

	100% (n = 4868)	≥75% to <100% (n = 3988)	≥50% to <75% (n = 6556)	<50% (n = 8897)	P-value
Before randomization					
Mean age ± SD, years	65.6 ± 7.2	66.1 ± 7.5	66.8 ± 7.4	67.4 ± 7.6	<0.001
Race, n (%)					
Non-Hispanic white	2584 (53.1%)	2087 (52.3%)	3377 (51.5%)	4305 (48.4%)	<0.001
Non-Hispanic black	1224 (25.1%)	1083 (27.2%)	1977 (30.2%)	3276 (36.8%)	
Hispanic white	685 (14.1%)	479 (12.0%)	721 (11.0%)	687 (7.7%)	
Hispanic black	107 (2.2%)	115 (2.9%)	154 (2.3%)	182 (2.0%)	
Other	268 (5.5%)	224 (5.6%)	327 (5.0%)	447 (5.0%)	
Men, n (%)	2876 (59.1%)	2260 (56.7%)	3561 (54.3%)	4483 (50.4%)	<0.001
Mean education level ± SD, years	11.5 (4.0)	11.3 (3.8)	11.2 (3.8)	10.9 (3.8)	<0.001
Current smoking, n (%)	1085 (22.3%)	878 (22.0%)	1436 (21.9%)	1813 (20.4%)	0.022
Mean BMI ± SD, kg/m ²	29.2 ± 5.5	29.5 ± 5.8	29.6 ± 5.8	29.8 ± 6.0	<0.001
Aspirin use, n (%)	1912 (39.7%)	1478 (37.4%)	2412 (37.2%)	3188 (36.3%)	0.001
Low HDL cholesterol level, %	721 (14.8%)	531 (13.3%)	816 (12.4%)	964 (10.8%)	<0.001
Mean total cholesterol level ± SD, mmol/L	212.8 ± 40.7	213.9 ± 41.4	216.5 ± 42.7	217.7 ± 43.7	<0.001
eGFR < 60 mL/min/1.73 m ²	822 (17.3%)	708 (18.3%)	1250 (19.7%)	1968 (23.1%)	<0.001
Diabetes mellitus, n (%)	1604 (35.2%)	1398 (37.2%)	2494 (40.8%)	3829 (46.3%)	<0.001
History of MI or stroke, n (%)	1228 (25.2%)	883 (22.1%)	1398 (21.3%)	1845 (20.7%)	<0.001
History of other ASCVD, n (%)	1216 (25.0%)	997 (25.0%)	1506 (23.0%)	2060 (23.2%)	0.010
History of revascularization, n (%)	725 (14.9%)	557 (14.0%)	838 (12.8%)	1007 (11.3%)	
LVH by electrocardiography, n (%)	614 (12.6%)	557 (14.0%)	1098 (16.7%)	1667 (18.7%)	<0.001
Use of antihypertension medication, % n (%)	4325 (88.8%)	3554 (89.1%)	5946 (90.7%)	8227 (92.5%)	<0.001
During assessment period					
Mean SBP ± SD, mmHg	124.3 ± 6.3	130.9 ± 4.7	136.7 ± 4.6	148.7 ± 9.0	<0.001
Mean DBP ± SD, mmHg	75.8 ± 6.3	77.8 ± 6.3	78.8 ± 6.6	81.3 ± 7.7	<0.001
Mean pulse pressure (SD), mmHg	48.5 ± 7.0	53.1 ± 6.8	57.9 ± 7.2	67.4 ± 10.2	<0.001
Mean maximum antihypertensive medications at any visit (SE), n	1.4 ± 0.6	1.5 ± 0.7	1.7 ± 0.8	2.2 ± 1.0	<0.001
Low adherence at any visit, n (%)	510 (10.5%)	563 (14.1%)	953 (14.5%)	1543 (17.4%)	<0.001
Changes in medications classes, n (%)	1499 (30.8%)	1564 (39.2%)	3237 (49.4%)	6256 (70.3%)	<0.001
Statin use, n (%)	1837 (37.7%)	1398 (35.1%)	2281 (34.8%)	6009 (32.5%)	<0.001
Randomization group, n (%)					
Chlorthalidone	2574 (52.9%)	1969 (49.4%)	3037 (46.3%)	3707 (41.7%)	<0.001
Amlodipine	1106 (22.7%)	1139 (28.6%)	1904 (29.0%)	2462 (27.7%)	
Lisinopril	1188 (24.4%)	880 (22.1%)	1615 (24.6%)	2728 (30.7%)	

(0.83-1.39) at 75% to less than 100%, 1.22 (0.97-1.52) at 50% to less than 75%, and 1.16 (0.93-1.44) at less than 50% of visits (*P* linear trend = 0.14; Table 2). Higher HRs for stroke, HF, and the composite CVD outcome were present among participants with SBP control at less than 50% of visits vs their counterparts with SBP control at 100% of visits (*P* linear trend <0.01). Adjustment for mean SBP attenuated the associations of SBP control with stroke, HF, and the composite CVD outcome. Compared to having sustained SBP control at all visits, the multivariable-adjusted HR (95% CI) for all-cause

mortality was 1.04 (0.88-1.22) at 75% to less than 100%, 1.00 (0.87-1.16) at 50% to less than 75%, and 1.14 (0.99-1.30) at less than 50% of visits (*P* linear trend = 0.06).

3.3 | Sensitivity analysis

Findings for the association between category of sustained SBP control and outcomes were similar in the analysis stratified by number of visits (Table S2).

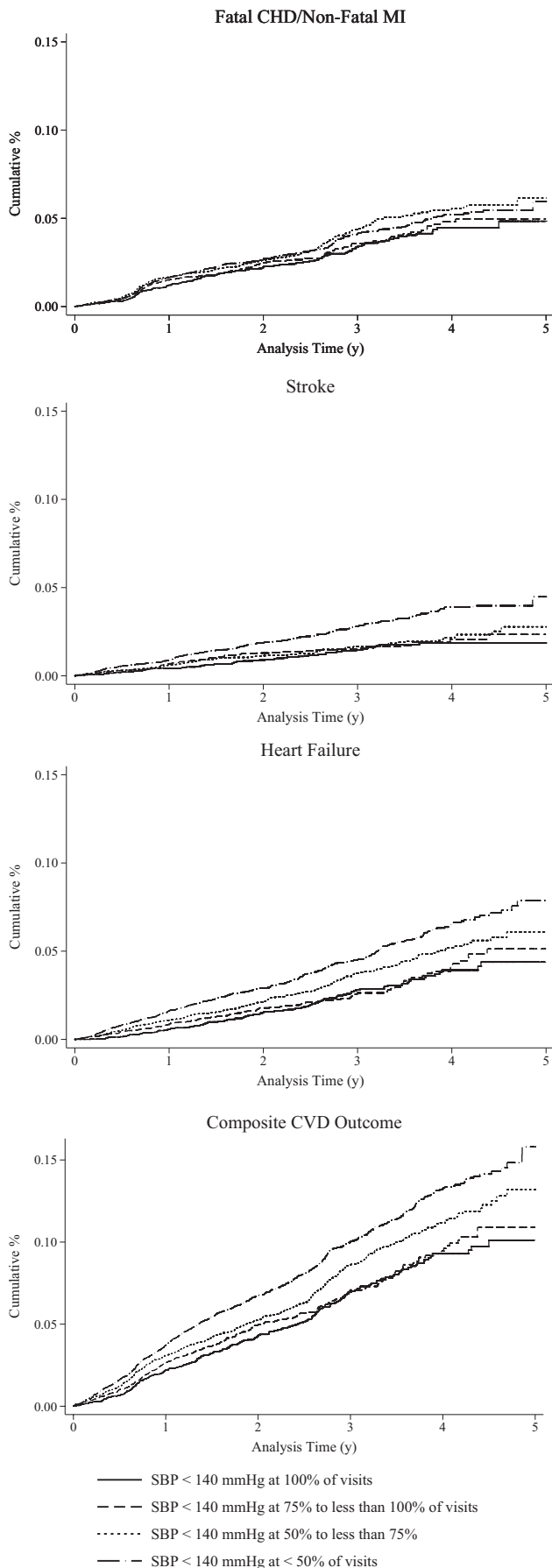


FIGURE 1 Kaplan-Meier failure function for fatal coronary heart disease (CHD)/nonfatal myocardial infarction (MI), stroke, heart failure, composite CVD, and all-cause mortality by proportion of visits with systolic blood pressure (SBP) <140 mm Hg

3.3.1 | Subgroup analysis

No statistically significant interactions were present for the association between sustained BP control and fatal CHD/nonfatal MI, stroke, or HF, the composite CVD outcome, or mortality by age (<65 vs \geq 65 years old), sex (men vs women), race (white vs black), randomization group (chlorthalidone, amlodipine, lisinopril), and comorbidity subgroups (Table S3).

4 | DISCUSSION

In this observational analysis of participants from ALLHAT, those with SBP control, defined as SBP < 140 mm Hg at <50% of study visits, were more likely to have a stroke, develop HF, or experience the combined outcome of fatal CHD/nonfatal MI, stroke, or HF. These associations were present after adjustment for potential confounders including demographic characteristics and history of CVD prior to randomization as well as medication changes and low adherence during the assessment period. While absolute differences in risk of outcomes across categories of sustained SBP control were small, a statistically significant linear trend for higher risk with a lower proportion of visits at which SBP control was achieved was present for stroke, HF, and the composite CVD outcome. These findings suggest that achieving a higher proportion of visits with SBP control may be beneficial for adults with treated hypertension.

Numerous observational studies and randomized trials have evaluated the association of BP levels with health outcomes; fewer studies have examined the association with sustained BP control over time.²¹⁻²³ Meredith and colleagues reported an association between sustained BP control and lower rates of the composite outcome (all-cause mortality, MI, refractory angina, HF requiring hospitalization, or peripheral revascularization), any CV event, MI, or debilitating stroke, in a secondary analysis of the ACTION trial (A Coronary Disease Trial Investigating Outcome with Nifedipine GITS), which included participants with stable angina.¹⁴ Statistically significant differences were only present comparing those with the highest to lowest proportion (ie, \geq 75% to <25%) of visits for all outcomes except stroke. Mancina and colleagues reported similar findings in two separate analyses, from the INVEST (International Verapamil SR-Trandolapril) trial which enrolled participants with hypertension in addition to coronary artery disease and the VALUE (Valsartan Antihypertensive Long-term Use Evaluation) trial which included those with hypertension and three or more CVD risk factors.^{12,13} In both analyses, risk of outcomes was lower among those with BP control at a greater proportion of visits which was primarily due to differences between those with BP control at <25% vs \geq 25%

of visits. Findings from the current study extend these findings to a more diverse population and to those with and without CHD.

In contrast to prior studies, there was no association between sustained SBP control and CHD/nonfatal MI and mortality. Potential explanations for the lack of association between sustained SBP control and fatal CHD/mortality outcomes in the ALLHAT study population include the likelihood that participants may have been at lower risk than those included in prior studies, in which three or more risk factors or stable angina were inclusion criteria.¹²⁻¹⁴ This corresponded to an overall lower event rate in the current analysis compared to prior studies. While the overall study population may have lower risk than previous studies, we did find that prior to randomization, a high proportion of participants in the group with SBP control at 100% of visits had already experienced a stroke, MI, or revascularization. For these participants, the advantages of sustained BP may be reduced, consistent with prior reports suggesting that the benefits of BP control are diminished for those with long-standing CVD.²⁴ In order to have a period for calculating a reliable estimate of sustained BP control (6-28 months), the follow-up time to ascertain outcomes before the end of the ALLHAT study was reduced. This

may explain the lack of association between BP control and mortality or CHD/nonfatal MI. Despite the lack of association with CHD and mortality, findings of lower risk of stroke or HF in patients with more consistent SBP control from the current analysis are clinically important.

While most research studies identify risk factors for poor health outcomes as a snapshot in time, in practice, clinicians diagnose and treat individuals with hypertension over many visits and patients live with hypertension over many years.²⁵ Considering this perspective, the findings from the current study suggest that having sustained BP control is associated with better health outcomes and that this may not be an "all-or-none" phenomenon in which treatment benefits only occur in those with SBP control at all visits, particularly for stroke and HF. Further, because the outcomes studied here are leading causes of disability and nursing home placement,²⁶ avoiding these outcomes is prioritized by both patients and providers. Possible reasons for differences in SBP from one ALLHAT study visit to another include physiologic variability, which has been previously described,²⁷ poor adherence, or changes in health status that result in changes in BP. Additionally, we found that those with sustained

TABLE 2 Incidence rates and hazard ratios for fatal coronary heart disease or nonfatal myocardial infarction, stroke, heart failure, all-cause mortality, and composite cardiovascular disease outcome associated with sustained BP control

	Percent of visits with systolic blood pressure <140 mm Hg				P-trend
	100%(n = 4868)	≥75% to <100%(n = 3988)	≥50% to <75%(n = 6556)	<50%(n = 8897)	
Fatal CHD or nonfatal MI					
N (%)	140 (3.0%)	125 (3.3%)	247 (3.9%)	326 (3.7%)	
Incidence rate, per 100 PY (95% CI)	1.11 (0.94-1.32)	1.18 (0.99-1.41)	1.40 (1.24-1.59)	1.33 (1.19-1.48)	
HR (95% CI)					
Model 1	1 (ref)	1.06 (0.83-1.35)	1.25 (1.01-1.54)	1.20 (0.98-1.46)	
Model 2	1 (ref)	1.08 (0.83-1.39)	1.21 (0.97-1.52)	1.16 (0.93-1.44)	
Model 3	1 (ref)	1.07 (0.83-1.39)	1.22 (0.97-1.52)	1.16 (0.93-1.44)	0.139
Model 3a	1 (ref)	0.98 (0.75-1.29)	1.03 (0.80-1.34)	0.85 (0.60-1.18)	0.337
Stroke					
N (%)	59 (1.3%)	59 (1.5%)	100 (1.6%)	232 (2.6%)	
Incidence rate (95% CI)	0.46 (0.36-0.60)	0.55 (0.43-0.71)	0.56 (0.46-0.68)	0.94 (0.83-1.07)	
HR (95% CI)					
Model 1	1 (ref)	1.15 (0.80-1.66)	1.14 (0.82-1.57)	1.85 (1.39-2.47)	
Model 2	1 (ref)	1.13 (0.77-1.64)	1.03 (0.73-1.45)	1.70 (1.26-2.30)	
Model 3	1 (ref)	1.13 (0.78-1.65)	1.05 (0.74-1.47)	1.71 (1.26-2.32)	<0.01
Model 3a	1 (ref)	1.07 (0.73-1.58)	0.94 (0.65-1.38)	1.40 (0.90-2.17)	0.150
Heart failure					
N (%)	110 (2.4%)	101 (2.6%)	219 (3.5%)	393 (4.4%)	
Incidence rate (95% CI)	0.87 (0.72-1.05)	0.95 (0.78-1.15)	1.23 (1.08-1.41)	1.61 (1.46-1.77)	
HR (95% CI)					
Model 1	1 (ref)	1.05 (0.80-1.38)	1.33 (1.06-1.68)	1.68 (1.36-2.08)	
Model 2	1 (ref)	1.13 (0.85-1.51)	1.32 (1.03-1.70)	1.65 (1.31-2.08)	
Model 3	1 (ref)	1.11 (0.83-1.48)	1.30 (1.01-1.67)	1.63 (1.30-2.06)	<0.01

Continues

TABLE 2 Continued

	Percent of visits with systolic blood pressure <140 mm Hg				P-trend
	100%(n = 4868)	≥75% to <100%(n = 3988)	≥50% to <75%(n = 6556)	<50%(n = 8897)	
Model 3a	1 (ref)	1.01 (0.75-1.36)	1.09 (0.83-1.44)	1.16 (0.83-1.62)	0.334
Composite CVD outcomes ^a					
N	282 (6.0%)	254 (6.6%)	497 (7.8%)	826 (9.7%)	
Incidence rate (95% CI)	2.28 (2.03-2.56)	2.44 (2.16-2.76)	2.88 (2.64-3.15)	3.49 (3.26-3.74)	
HR (95% CI)					
Model 1	1 (ref)	1.05 (0.89-1.24)	1.22 (1.05-1.41)	1.45 (1.26-1.66)	
Model 2	1 (ref)	1.08 (0.90-1.29)	1.16 (0.99-1.36)	1.39 (1.20-1.61)	
Model 3	1 (ref)	1.08 (0.90-1.29)	1.16 (0.99-1.36)	1.39 (1.20-1.62)	<0.01
Model 3a	1 (ref)	1.01 (0.84-1.21)	1.02 (0.85-1.22)	1.09 (0.87-1.35)	0.445
All-cause mortality					
N (%)	393 (8.1%)	326 (8.2%)	545 (8.3%)	909 (10.2%)	
Incidence rate (95% CI)	3.38 (3.07-3.74)	3.34 (3.00-3.72)	3.37 (3.10-3.66)	4.05 (3.80-4.33)	
HR (95% CI)					
Model 1	1 (ref)	0.95 (0.82-1.10)	0.92 (0.81-1.05)	1.06 (0.94-1.20)	
Model 2	1 (ref)	1.05 (0.89-1.23)	1.01 (0.87-1.17)	1.15 (1.01-1.32)	
Model 3	1 (ref)	1.04 (0.88-1.22)	1.00 (0.87-1.16)	1.14 (0.99-1.30)	0.064
Model 3a	1 (ref)	0.98 (0.83-1.17)	0.91 (0.77-1.08)	0.94 (0.77-1.16)	0.517

Model 1 = age, race, sex (n for CHD, CHF, stroke = 23 373; n for mortality = 24 301)

Model 2 = adjustment for the variables in Model 1 and education level, current smoking, BMI, aspirin use, low HDL cholesterol level, total cholesterol, eGFR, type 2 diabetes, history of MI or stroke, history of other ASCVD, history of revascularization, LVH by electrocardiography, (n for CHD, CHF, stroke = 19 831; n for mortality = 20 595)

Model 3 = adjustment for the variables in model 2 and use of antihypertension medication, statin use, low adherence at any visit, randomization group (n for CHD, CHF, stroke = 19 810; n for mortality = 20 574)

Model 3a = adjustment for the variables in Model 3 and mean systolic blood pressure during the assessment period

Note: Trend test was not conducted for Model 1 or Model 2.

CHD, coronary heart disease; CI, confidence interval; HR, hazard ratio; MI, myocardial infarction.

^aComposite CVD outcome includes combined occurrence of fatal CHD/nonfatal MI, stroke, and heart failure.

SBP were more likely to have been randomized to chlorthalidone. Future studies may be necessary to determine the best approach to achieving sustained SBP control.

Although ALLHAT was conducted from 1994 to 2002, the current findings may have implications for contemporary management of hypertension. Evidence from SPRINT suggests that an intensive BP goal is associated with improved outcomes.²³ Accordingly, the 2017 ACC/AHA guidelines recommend a SBP goal of <130 mm Hg for those with known CVD or 10-year ASCVD risk of 10% or higher.⁵ In the current analysis, participants who had sustained SBP control at 100% of visits within the assessment period also had a mean SBP of 124 mm Hg, nearly reaching the mean SBP achieved in the intensive arm of SPRINT. Adjustment for mean SBP suggests that the association of sustained SBP control with stroke, HF, and the composite CVD outcome is explained in part by participants achieving a lower mean SBP during the assessment period. Discussing SBP goals with patients in terms of proportion of visits controlled, not just mean SBP, may be an additional strategy to work with patients to achieve lower BP goals.

The updated 2017 ACC/AHA guidelines also suggest that performance measures in combination with quality improvement

strategies are reasonable to achieve BP control.⁵ The proportion of visits with controlled BP may represent an important performance measure that is easy to calculate and understand. Findings from the current study can be used to encourage patients and providers to achieve greater consistency in BP control, support decisions to intensify treatment when appropriate, or identify higher risk patients for tailored management strategies to improve BP control.

Strengths of our study include use of data from the ALLHAT trial, which included a large number of adults taking antihypertensive medication, availability of BP measurements over time on a large number of participants, and ascertainment of adverse outcomes. However, cautious interpretation of our findings is necessary in the context of known limitations. Although data were from a clinical trial, the current analysis had a retrospective cohort study design and potential threats to validity of the study findings exist. It is possible that confounders, such as existing disease severity, unmeasured social determinants of health, or genetic factors, may explain both participants' ability to sustain BP control and their risk of mortality and CVD outcomes. In order to assess for sustained BP control, we restricted the analytic cohort to those with four or more SBP measures and without any of the outcomes during the

assessment period. Therefore, the generalizability of the study findings may be limited to a lower risk population. Lastly, ambulatory or home blood pressure monitoring was not performed in ALLHAT.

In conclusion, among participants who were included in a large simple, clinical trial, achieving SBP control at <50% of visits was associated with higher risk of stroke, HF, or the combined outcome of fatal CHD/nonfatal MI, stroke, or HF. Along with achieving BP goals at a single time point, assessing SBP control over time may provide important risk information and this approach should be used to support care when treating patients with hypertension.

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CONFLICT OF INTEREST

The views expressed here/in this manuscript are those of the authors and do not necessarily represent the views of the National Heart, Lung, and Blood Institute; the National Institutes of Health; or the Department of Health and Human Services. Authors report no conflicts of interest.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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