

Disparities in Socioeconomic Context and Association With Blood Pressure Control and Cardiovascular Outcomes in ALLHAT

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Background—Observational studies demonstrate that communities of low socioeconomic status have higher blood pressure and worse cardiovascular outcomes. Yet, whether the clinical outcomes resulting from antihypertensive therapy vary by socioeconomic context in a randomized clinical trial, in which participants are treated under a standard protocol, is unknown.

Methods and Results—We used data from ALLHAT (Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial) to study the effect of socioeconomic context, defined as the county-level median household income, of study sites. We stratified sites into income quintiles and compared characteristics, blood pressure control, and cardiovascular outcomes among ALLHAT participants in the lowest- and highest-income quintiles. Among 27 862 qualifying participants, 2169 (7.8%) received care in the lowest-income sites (quintile 1) and 10 458 (37.6%) received care in the highest-income sites (quintile 5). Participants in quintile 1 were more likely to be women, to be black, to be Hispanic, to have fewer years of education, to live in the South, and to have fewer cardiovascular risk factors. After adjusting for baseline demographic and clinical characteristics, quintile 1 participants were less likely to achieve blood pressure control (<140/90 mm Hg) (odds ratio, 0.48; 95% CI, 0.37–0.63) and had greater all-cause mortality (hazard ratio [HR], 1.25; 95% CI, 1.10–1.41), heart failure hospitalizations/mortality (HR, 1.26; 95% CI, 1.03–1.55), and end-stage renal disease (HR, 1.86; 95% CI, 1.26–2.73), but lower angina hospitalizations (HR, 0.70; 95% CI, 0.59–0.83) and coronary revascularizations (HR, 0.71; 95% CI, 0.57–0.89).

Conclusions—Despite standardized treatment protocols, ALLHAT participants in the lowest-income sites experienced poorer blood pressure control and worse outcomes for some adverse cardiovascular events, emphasizing the importance of measuring and addressing socioeconomic context.

Clinical Trial Registration—URL: http://www.clinicaltrials.gov. Unique identifier: NCT00000542. (*J Am Heart Assoc.* 2019;8: e012277. DOI: 10.1161/JAHA.119.012277.)

Key Words: ALLHAT • disparities • health policy and outcomes research • high blood pressure • hypertension • randomized clinical trial • socioeconomic

L iving in a lower socioeconomic neighborhood is associated with a higher prevalence of hypertension, less hypertension control, and higher rates of secondary heart disease, renal failure, and stroke, ¹⁻⁶ even when accounting for individuals' socioeconomic status.^{7,8} In understanding the reasons for these disparities, a key question is whether antihypertensive medication therapy is associated with lower blood

pressure control and worse cardiovascular outcomes in lower socioeconomic communities. If so, then the implementation of evidence-based therapies for hypertension derived from randomized clinical trials (RCTs) may be suboptimal in achieving expected outcomes in differing socioeconomic populations.

Characterizing the socioeconomic context in which clinical care is provided can offer important insights into variation in

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Received March 7, 2019; accepted June 7, 2019.

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Accompanying Tables S1 through S17 and Figures S1 through S3 are available at https://www.ahajournals.org/doi/suppl/10.1161/JAHA.119.012277

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Clinical Perspective

What Is New?

- Whether cardiovascular outcomes resulting from antihypertensive therapy vary by socioeconomic context in a randomized clinical trial, in which participants are treated under a standard protocol, is unknown.
- We sought to determine whether socioeconomic context was associated with blood pressure control and cardiovascular outcomes in a large randomized clinical trial of antihypertensive therapy.
- ALLHAT (Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial) participants receiving care in low-income areas demonstrated worse blood pressure reduction and control and greater heart failure hospitalizations, end-stage renal disease, and overall mortality compared with participants in high-income areas.

What Are the Clinical Implications?

- Socioeconomic context is significantly associated with blood pressure control and some cardiovascular outcomes in a randomized clinical trial of antihypertensive medication therapy.
- Assessment of socioeconomic context in clinical trials is important for interpreting and translating study findings in socioeconomically diverse populations.

hypertension control and cardiovascular outcomes. Specifically, people receiving care in low socioeconomic communities (compared with high socioeconomic communities) may have fewer opportunities and resources for healthy lifestyle behaviors, including limited access to healthy foods and exercise.^{9,10} In addition, stress levels may be higher in low socioeconomic communities because of unemployment, housing conditions, financial burdens, poor social cohesion, neighborhood safety and violence, and other social ills.¹¹⁻¹⁴ These factors may exert an effect on blood pressure response to antihypertensive medication and on cardiovascular outcomes; however, this effect may be difficult to isolate because of differences in access to and guality of care. As such, the effect of community socioeconomic status, or socioeconomic context, on hypertensive outcomes may be observed in an RCT, in which participants are treated under a standard protocol with a prespecified intervention. Such uniform treatment and care, combined with randomization that is stratified by clinical site, would allow an unbiased assessment of socioeconomic context on outcomes.

Accordingly, to examine the effect of socioeconomic context on response to antihypertensive medication, we analyzed data from ALLHAT (Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial), the largest

existing RCT of hypertension treatment.¹⁵ This trial included a study population that was both demographically and geographically diverse, with treatment medications randomized within study sites. Postulating that socioeconomic context, defined herein as the area-level income of the clinical site in which ALLHAT participants were enrolled and obtained care, may impact overall treatment response in the trial, we compared blood pressure control and cardiovascular outcomes according to clinical sites' socioeconomic context.

Methods

The data that support the findings of this study are available from coauthor Dr Jeph Herrin (jeph.herrin@yale.edu) on reasonable request.

We conducted a secondary analysis of ALLHAT to examine the effect of socioeconomic context on blood pressure control and cardiovascular outcomes. As a proxy for the socioeconomic context of participants, we used the income level of the county in which the clinical site was located, assuming participants lived in nearby communities and, therefore, shared a similar socioeconomic context as the clinical site. We categorized this proxy income level into guintiles and compared baseline characteristics and outcomes of participants in quintile 1 (lowest socioeconomic status) with those of participants in quintile 5 (highest socioeconomic status). To better understand whether demographic factors, such as race and region of care, previously associated with hypertension outcomes but also associated with socioeconomic status, confounded observed differences, we assessed differences by income quintile among 2 subgroups, black participants and clinical sites in the South. Finally, we performed a sensitivity analysis to determine the impact of differences in adherence among participants in quintile 1 and quintile 5.

ALLHAT Design and Organization

ALLHAT data were obtained through the National Heart, Lung, and Blood Institute's Biologic Specimen and Data Repositories Information Coordinating Center (BioLINCC). Details of the rationale, study design, and findings for ALLHAT have been previously described.^{15,16} Conducted between 1994 and 2002, ALLHAT is the largest randomized, double-blinded clinical trial of antihypertensive medical therapy ever conducted.¹⁵ The study enrolled men and women \geq 55 years old with untreated systolic (defined as $140 \leq 180$ mm Hg) and/or diastolic (defined as $90 \leq 110$ mm Hg) hypertension present on \geq 2 visits or treated hypertension ($\leq 160/110$ mm Hg on 1-2 antihypertensive medications at visit 1 [eligibility assessment] and $\leq 180/110$ mm Hg at visit 2 [randomization after step-down from prestudy antihypertensive drugs]).¹⁶ Eligible study participants also had established cardiovascular disease or at least one additional cardiovascular risk factor (Figure S1).¹⁶ The trial population was composed of nearly 50% women and minorities; black and Hispanic participants accounted for 36% and 19% of the overall study population, respectively.¹⁷ The study was considered highly generalizable, with sampling across a broad sociogeographic distribution in North America.¹⁸ Blood pressure ascertainment by trained staff was deemed consistent and reliable.^{15,19} Participating sites acquired institutional review board approval and obtained written informed consent from all participants.

The mean follow-up was 4.9 years.²⁰ Follow-up visits were scheduled for 1, 3, 6, 9, and 12 months and, subsequently, every 4 months,²¹ which was considered usual for hypertension care.¹⁵ Participants were assigned to 1 of 4 representative antihypertensive medications, a thiazide diuretic (chlorthalidone), an angiotensin-converting enzyme inhibitor (lisinopril), a calcium channel blocker (amlodipine), or an α -adrenergic blocker (doxazosin, stopped early because of inferior treatment effect), with discouragement of mixing therapies.^{15,22} After titrating medications to the maximum titrated dose, second-line medications (atenolol, clonidine, or reserpine) and third-line medications (hydralazine) could be added.¹⁵

A total of 42 418 participants were enrolled in ALLHAT from 623 clinical sites across the United States, Puerto Rico and Virgin Islands, and Canada. For this study, we excluded participants enrolled in sites outside of the continental United States (n=5227) because of potential confounders when comparing socioeconomic context of those sites with sites in the continental United States, participants in sites lacking income data (n=304), and participants randomized to doxazosin (n=9061). Of the remaining 27 826 participants, we further restricted our analysis to the 12 627 participants in quintile 1 and quintile 5 (Figure S2).

Socioeconomic Context

We defined socioeconomic context as the median household income of the county in which a study site was located. We first mapped study site ZIP codes to their corresponding counties, hypothesizing that the county would better characterize the socioeconomic context of all participants receiving care at each clinical site. We derived county-level median household income from the 2000 US Census, the closest census year to the period in which the study was conducted. County-level incomes were adjusted for cost of living in each state in 2000. If the ZIP code mapped to >1 county, we calculated the population-weighted average median income across those counties. County-level incomes were assigned to study participants at that site. On the basis of the national distribution of county-level household median income, individuals were stratified into income quintiles. We assessed the following baseline characteristics: age, sex, race and ethnicity, level of education, geographic region, baseline systolic blood pressure and diastolic blood pressure, and qualifying risk factors for ALLHAT (body mass index, history of myocardial infarction or stroke, history of coronary revascularization, history of coronary heart disease [CHD] or other atherosclerotic cardiovascular disease, type 2 diabetes mellitus, cigarette smoking, current aspirin use, low highdensity lipoprotein, left ventricular hypertrophy, current estrogen supplementation, and participation in the lipid trial component of ALLHAT; Figure S1). We also assessed visit and medication adherence, which may correlate with baseline characteristics and outcomes. As in the original trial, we defined visit adherence as the number of attended visits divided by the protocol-determined number of expected visits in the 6-year duration of the trial.^{15,23} Adequate visit adherence was defined as attending at least 80% of expected visits. We defined adequate medication adherence as taking at least 80% of study medications at all visits, per participants' self-report.15,23

Outcomes

We assessed blood pressure control and major adverse cardiovascular events. Blood pressure control was defined as the proportion achieving the ALLHAT treatment goal of 140/ 90 mm Hg¹⁶ in years 1 to 6, regardless of age. In accordance with ALLHAT, we assessed the primary outcome of CHD (fatal CHD and nonfatal myocardial infarction combined). We assessed the following major prespecified secondary outcomes: (1) all-cause mortality, (2) stroke, (3) combined CHD (CHD, coronary revascularization, or hospitalized angina), and (4) combined cardiovascular disease (combined CHD, stroke, other treated angina, heart failure, or peripheral arterial disease [PAD]).¹⁵ Finally, we evaluated the following individual components of these outcomes: heart failure, hospitalized/ fatal heart failure, angina, coronary revascularization, PAD, and end-stage renal disease (ESRD). For secondary outcomes, we report only CIs; our results were not adjusted for multiple comparisons, but this should be considered in their interpretation.

Statistical Analysis

We compared baseline characteristics, treatment randomization, visit and medication adherence, unadjusted blood pressure response, unadjusted blood pressure control, and unadjusted cardiovascular outcomes of the study population by income quintile, using *t* tests and χ^2 tests. We then assessed the association of socioeconomic context with blood pressure control and cardiovascular outcomes in the lowest- versus highest-income quintiles, using logistic regression and Cox proportional hazards regression analysis, respectively. In these models, we adjusted for treatment group, age, sex, qualifying ALLHAT risk factors, and baseline systolic blood pressure and diastolic blood pressure, using multiple imputation if study participants had missing values for certain risk factors.

Next, we performed subgroup analyses of blood pressure control and cardiovascular outcomes across socioeconomic strata among the following: (1) black participants and (2) participants in the South. Last, we assessed whether fidelity to the protocol explained any of the differences between groups. Although visit adherence is potentially endogenous with the outcomes of interest (ie, patients with greater numbers of visits may have more opportunities to meet criteria for blood pressure control, and/or patients experiencing a cardiovascular event may be more likely to adhere to subsequent visits), we performed a sensitivity analysis, including 6-year visit adherence in the final model, to assess whether it attenuated the main findings. There were insufficient data of participants' medication adherence to include it in the model. All analyses were performed using Stata 15 (StataCorp, College Station, TX). This study was approved by the Yale Human Investigations Committee.

Results

Geographic and Economic Distribution of Clinical Sites

The 27 826 participants included in this study obtained care in clinical sites representing 372 US counties, depicted in the Figure. Nearly all (32/35, 91%) of the lowest-income counties were in the South, whereas the highest-income counties were more evenly distributed across geographic regions. Participants enrolled in the lowest-income sites (quintile 1, bottom income quintile) composed 7.8% of the study population, whereas those enrolled in the highest-income sites (quintile 5, top income quintile) composed 37.6% of the study population. The county-level cost-of-living adjusted median household income was 2.8 times higher in quintile 5, compared with quintile 1.

Baseline Characteristics

Participants in quintile 1 tended to be younger, to more often be women, to be black or Hispanic, or to live in the South; and they had attained lower levels of education than participants in quintile 5 (Table 1). Baseline clinical characteristics were similar, including blood pressure and number of antihypertensive medications taken before the trial. However, compared with quintile 5, fewer participants in quintile 1 had a history of atherosclerotic cardiovascular disease, had ever smoked, or were taking aspirin. Participants in all quintiles were equally likely to have type 2 diabetes mellitus. In addition, there were similar numbers of participants in each treatment arm across socioeconomic strata, consistent with randomization.

Visit and Medication Adherence

Participants in quintile 1 had lower visit adherence (29.7%) than those in quintile 5 (40.8%) (Table S1). Medication adherence was also lower among participants in quintile 1 (36.3%) compared with participants in quintile 5 (55.6%). Data on medication adherence were missing in 21.8% to 38.0% of participants (depending on income quintile), whereas visit adherence was only missing in 0.8% to 1.5% of participants.

Blood Pressure Control

Despite having similar baseline blood pressure, on average, blood pressure lowering was smaller among participants in quintile 1 compared with quintile 5 (systolic blood pressure, -2.6 versus -12.1 mm Hg; diastolic blood pressure, -5.8 mm Hg versus -9.9 mm Hg) (Tables S2 and S3). In comparing linear trends of blood pressure control across income guintiles, participants in guintile 1 had lower rates of blood pressure control than those in guintile 2 to guintile 5 (Figure S3). In addition, after adjusting for differences in baseline characteristics between the most disparate income groups, quintile 1 and quintile 5, participants in quintile 1 were significantly less likely than those in guintile 5 to achieve blood pressure control (<140/90 mm Hg) after 1 year in the trial (44.8% versus 57.3%; odds ratio, 0.63; 95% Cl, 0.56-0.70), a difference that progressively increased each year of the trial through year 6 (50.0% versus 69.3%; odds ratio, 0.48; 95% Cl, 0.37-0.63) (Table 2; Tables S4 through S7). We observed similar trends among black participants (Table S8) and participants living in the South (Table S9). In sensitivity analyses including visit adherence in the model, results were unchanged (Table S10).

Cardiovascular Outcomes

There was no significant difference in the primary outcome, CHD, between participants in quintile 1 and quintile 5 (Table 3, Tables S11 through S14). However, after adjusting for differences in baseline characteristics, participants in quintile 1 experienced significantly higher all-cause mortality (hazard ratio [HR], 1.25; 95% CI, 1.10–1.41), heart failure hospitalization/mortality (HR, 1.26; 95% CI, 1.03–1.55), and ESRD (HR, 1.86; 95% CI, 1.26–2.73) than those in quintile 5.



Figure. Geographic distribution and socioeconomic (income) stratification of US counties with clinical sites participating in ALLHAT (Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial) (created using mapchart.net).

Participants in quintile 1 experienced lower angina treatment/ hospitalization (HR, 0.70; 95% CI, 0.59-0.83) and coronary revascularization (HR, 0.71; 95% CI, 0.57-0.89). There were no differences in diagnosis of new-onset heart failure, PAD, or stroke. Among black participants, those in quintile 1 had higher all-cause mortality after risk adjustment (HR, 1.24; 95% Cl, 1.06-1.44) and greater (although not statistically significant) heart failure morbidity (HR, 1.29; 95% Cl, 0.99-1.68) and ESRD (HR, 1.47; 95% CI, 0.91-2.36). They also had lower angina treatment/hospitalization (HR, 0.69; 95% Cl, 0.55-0.87) and coronary revascularization (HR, 0.69; 95% Cl, 0.48-0.99) (Table S15). There were no significant differences between income groups among black participants for CHD, combined CHD, stroke, combined cardiovascular disease, new-onset heart failure, or PAD. Among participants in the South, the risks of adverse cardiovascular outcomes followed similar trends as the overall study population, but none were significant (Table S16). In sensitivity analyses adjusting for visit adherence, all-cause mortality and heart failure treatment/hospitalizations were no longer significantly greater among quintile 1 participants (Table S17). Other outcomes (CHD, stroke, heart failure, combined cardiovascular disease, coronary revascularization, angina, PAD, and ESRD) were unchanged from the main findings.

Discussion

In a large, nationally dispersed RCT of antihypertensive therapy, we observed significant variation in blood pressure control and some cardiovascular outcomes, according to the socioeconomic context in which clinical care was provided. Participants receiving antihypertensive medication in the lowest-income sites compared with the highest-income sites had significantly worse blood pressure control and higher rates of heart failure hospitalizations, ESRD, and mortality, even after adjusting for demographic and clinical characteristics. However, certain outcomes were attenuated by visit adherence. Disparities in blood pressure control and all-cause mortality persisted in the subgroup of black participants, as did blood pressure control in the subgroup of those living in the South. Among these subgroups, we also observed similar trends for other cardiovascular outcomes (heart failure hospitalization/mortality, ESRD, angina, and coronary revascularization), although they were not statistically significant

Table 1. Baseline Characteristics of Study Population Across Socioeconomic Strata

	County Income Level					
Characteristic	Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5	
Demographics						
Total participants	2169 (100.0)	3562 (100.0)	4916 (100.0)	6721 (100.0)	10 458 (100.0)	
Age, y	66.1±8.4	66.4±7.4	67.1±7.7	67.1±7.4	67.0±7.5	
Women	1285 (59.2)	1645 (46.2)	2242 (45.6)	2899 (43.1)	4570 (43.7)	
Race						
White	242 (11.2)	1353 (38.0)	3208 (65.3)	4121 (61.3)	6830 (65.3)	
Black	1524 (70.3)	2189 (61.5)	1477 (30.0)	2432 (36.2)	2910 (27.8)	
American Indian	1 (0.1)	6 (0.2)	20 (0.4)	9 (0.1)	31 (0.3)	
Asian/Pacific Islander	1 (0.1)	2 (0.1)	15 (0.3)	26 (0.4)	322 (3.1)	
Other	401 (18.5)	12 (0.3)	196 (4.0)	133 (2.0)	365 (3.5)	
Hispanic	433 (20.0)	54 (1.5)	332 (6.8)	276 (4.1)	592 (5.7)	
Education						
High school or less	1855 (85.5)	2807 (78.8)	3383 (68.8)	4221 (62.8)	6090 (58.2)	
College	163 (7.5)	499 (14.0)	978 (19.9)	1630 (24.3)	2924 (28.0)	
Postgraduate school	46 (2.1)	111 (3.1)	209 (4.3)	373 (5.6)	774 (7.4)	
County characteristics						
COLA median income, \$, ×1000	21.8±2.4	29.2±1.1	33.0±1.3	38.2±1.6	49.6±8.7	
Income range (lower limit), \$, ×1000	15.6	26.9	30.8	35.2	41.0	
Income range (upper limit), \$, $\times 1000$	26.5	30.7	35.2	40.9	89.7	
No. of counties	35	45	62	75	155	
Geographic region						
East	2 (0.1)	12 (0.3)	748 (15.2)	1687 (25.1)	2545 (24.3)	
South	2134 (98.4)	3216 (90.3)	3399 (69.1)	2919 (43.4)	1941 (18.6)	
Midwest	2 (0.1)	322 (9.0)	510 (10.4)	1892 (28.2)	3299 (31.6)	
West	31 (1.4)	12 (0.3)	259 (5.3)	223 (3.3)	2673 (25.6)	
Baseline clinical characteristics						
Systolic blood pressure, mm Hg	145.0±16.8	145.3±15.8	145.7±15.9	147.5±15.6	145.7±15.5	
Diastolic blood pressure, mm Hg	83.7±10.7	82.9±10.0	82.3±10.2	84.1±9.9	83.7±10.0	
GFR (mL/min/1.73 m ²)	80.4±21.8	79.7±21.3	76.5±19.2	77.0±19.6	76.8±18.9	
Creatinine (mg/dL)	1.0±0.3	1.1±0.3	1.0±0.3	1.0±0.3	1.0±0.3	
Potassium (mEq/L)	4.3±0.7	4.3±0.7	4.3±0.7	4.3±0.7	4.4±0.6	
Fasting glucose (mg/dL)	127.2±61.7	128.4±63.0	121.5±55.3	123.0±58.7	120.9±53.1	
Receiving antihypertensive treatment						
On 1–2 medications for \geq 2 mo	1831 (84.4)	3086 (86.6)	4270 (86.9)	5809 (86.4)	9080 (86.8)	
On medications for <2 mo	58 (2.7)	126 (3.5)	137 (2.8)	273 (4.1)	365 (3.5)	
Untreated at baseline	280 (12.9)	350 (9.8)	509 (10.4)	639 (9.5)	1012 (9.7)	
Qualifying risk factors for ALLHAT						
History of atherosclerotic CVD^\dagger	904 (41.7)	1706 (47.9)	2556 (52.0)	3786 (56.3)	5721 (54.7)	
History of MI or stroke	309 (14.3)	876 (24.6)	1202 (24.5)	1731 (25.8)	2585 (24.7)	
History of coronary revascularization	102 (4.7)	391 (11.0)	780 (15.9)	986 (14.7)	1693 (16.2)	

Continued

Table 1. Continued

	County Income Level					
Characteristic	Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5	
Other atherosclerotic CVD	398 (18.4)	563 (15.8)	1117 (22.7)	1792 (26.7)	2720 (26.0)	
History of ST-segment depression/T-wave inversion	286 (13.2)	448 (12.6)	472 (9.6)	768 (11.4)	1003 (9.6)	
Type 2 diabetes mellitus	770 (35.5)	1450 (40.7)	1773 (36.1)	2333 (34.7)	3624 (34.7)	
HDL-C <35 mg/dL twice in past 5 y	72 (3.3)	270 (7.6)	606 (12.3)	913 (13.6)	1491 (14.3)	
LVH by ECG in past 2 y	640 (29.5)	674 (18.9)	692 (14.1)	977 (14.5)	1547 (14.8)	
LVH by echocardiogram in past 2 y	86 (4.0)	117 (3.3)	231 (4.7)	231 (3.4)	568 (5.4)	
History of CHD at baseline	14 (0.7)	41 (1.2)	71 (1.4)	81 (1.2)	132 (1.3)	
BMI, kg/m ²	30.4±6.4	29.9±6.2	29.5±5.8	30.0±6.0	29.7±6.1	
Current aspirin use	568 (26.2)	1186 (33.3)	1916 (39.0)	2705 (40.3)	4089 (39.1)	
Current estrogen supplementation [‡]	146 (6.7)	240 (6.7)	471 (9.6)	518 (7.7)	1059 (10.1)	
Lipid trial participants	720 (33.2)	922 (25.9)	1264 (25.7)	1362 (20.3)	2303 (22.0)	
Cigarette smoker						
Current	485 (22.4)	907 (25.5)	1114 (22.7)	1531 (22.8)	2173 (20.8)	
Past	678 (31.3)	1338 (37.6)	2046 (41.6)	2963 (44.1)	4616 (44.1)	
Never	1006 (46.4)	1317 (37.0)	1755 (35.7)	2227 (33.1)	3668 (35.1)	
Treatment group (antihypertensive randomization group)						
Chlorthalidone	994 (45.8)	1625 (45.6)	2254 (45.9)	3077 (45.8)	4774 (45.7)	
Amlodipine	587 (27.1)	967 (27.2)	1333 (27.1)	1807 (26.9)	2851 (27.3)	
Lisinopril	588 (27.1)	970 (27.2)	1329 (27.0)	1837 (27.3)	2833 (27.1)	

Data are given as number (percentage) or mean±SD. Quintile 1 is the lowest-income quintile, and quintile 5 is the highest-income quintile. ALLHAT indicates Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial; BMI, body mass index; CHD, coronary heart disease; COLA, cost-of-living adjusted median income; CVD, cardiovascular disease; GFR, glomerular filtration rate; HDL-C, high-density lipoprotein cholesterol; LVH, left ventricular hypertrophy; MI, myocardial infarction.

¹History of atherosclerotic CVD contains the following categories: history of MI or stroke, history of coronary revascularization, history of major ST-segment depression or T-wave inversion on any ECG in the past 2 years, and other atherosclerotic CVD.

[‡]Applies to female participants only.

(perhaps because of the smaller sample size). These data suggest that socioeconomic context is not a substitute for disparities in race or geography and confers independent risk for the outcomes of blood pressure control and all-cause mortality.

Although the association of socioeconomic context with hypertension outcomes is well described,^{24,25} the differences in certain clinical outcomes in this study are notable because they occurred in the context of a large RCT, which typically affords participants equal access to resources for hypertension care by doing the following: (1) assigning them to standardized protocols in which study medications are provided free of charge and (2) providing specific guidelines for the intensification of medication and provision of follow-up visits. Existing studies of hypertension-related RCTs have examined the effects of nonpharmacologic interventions on blood pressure response among populations of varying individual and neighborhood socioeconomic status, with mixed results.^{26–30} RCTs of pharmacologic interventions for

hypertension have examined the effect of other person-level demographic factors, such as race or sex, on cardiovascular outcomes, although not of community-level factors.^{19,21,31} To date, no studies have examined the association of socioeconomic context with blood pressure control or cardiovascular outcomes resulting from antihypertensive treatment in an RCT, which can be important for the interpretation and application of RCT findings to diverse populations. Still, other characteristics of low-income communities or of clinical care in low-income communities may explain the observed differences in blood pressure control and cardiovascular outcomes, even in the context of an RCT, including opportunities for healthy lifestyle behaviors (eg, healthy foods and exercise), clinical factors (eg, access to care, quality of care for hypertension, and other cardiovascular risk factors), and other aspects of the physical and social environment that can lead to increased stress or allostatic load and impact use and adherence. Moreover, educational level (and by extension, health literacy) is another marker of socioeconomic

 Table 2.
 Association Between Income and BP Control Across

 Socioeconomic Strata
 Socioeconomic Strata

	% With BP <140/90 mm Hg by County Income Level		Low-Income Effect*	
Outcome	Quintile 1	Quintile 5	Unadjusted OR (95% CI)	Risk-Adjusted OR (95% Cl)
Year 1	44.8	57.3	0.60 (0.55–0.67)‡	0.63 (0.56–0.70)‡
Year 2	45.2	59.6	0.56 (0.50–0.63)‡	0.58 (0.52–0.66)‡
Year 3	48.1	63.6	0.53 (0.47–0.59)‡	0.55 (0.49–0.62)‡
Year 4	50.2	67.1	0.49 (0.43–0.56)‡	0.53 (0.46–0.60)‡
Year 5	51.2	68.0	0.49 (0.42–0.58)‡	0.51 (0.43–0.61) [‡]
Year 6	50.0	69.3	0.44 (0.34–0.57)‡	0.48 (0.37–0.63) [‡]

Quintile 1 is the lowest-income quintile, and quintile 5 is the highest-income quintile. BP indicates blood pressure; OR, odds ratio.

*Unadjusted OR represents odds of achieving blood pressure control (<140/90 mm Hg) with the highest-income quintile, quintile 5, serving as the reference group, adjusting only for treatment group. Risk-adjusted OR represents odds of achieving blood pressure control (<140/90 mm Hg) with the highest-income quintile, quintile 5, serving as the reference group. Model adjusts for treatment group, age, sex, baseline systolic blood pressure and diastolic blood pressure, and qualifying risk factors for ALLHAT (Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial; body mass index [BMI], history of myocardial infarction or stroke, history of coronary revascularization, history of coronary heart disease at baseline, other atherosclerotic cardiovascular disease, participation in lipid-lowering trial, type 2 diabetes mellitus, history of major ST-segment depression or T-wave inversion, aspirin use, high-density lipoprotein cholesterol <35 mg/dL, left ventricular hypertrophy [LVH] by ECG, LVH by echocardiogram, cigarette smoking, and estrogen supplementation [a minority of study participants have missing values for the risk factors of BMI, history of major ST-segment depression or T-wave inversion, LVH by echocardiogram, cigarette smoking, and estrogen supplementation; the missing values for these participants were imputed]). [‡]P<0.001.

deprivation at the individual and community level that may impact cardiovascular outcomes; this marker was not the focus of our study.

Notably, participants in the lowest-income sites had lower visit adherence than those in the highest-income sites. Factors associated with visit adherence (eg, access to transportation, social support, and health behaviors) may indirectly impact some outcomes. Alternatively, visit adherence may have a direct effect on some outcomes, wherein attending more visits provides greater opportunities to improve certain outcomes. In a sensitivity analysis adjusting for visit adherence, certain cardiovascular outcomes were attenuated, although blood pressure reduction was similar. These findings suggest that factors associated with visit attendance may have an effect independent of medication adherence. Ultimately, however, more work is needed to understand the impact of visit attendance in clinical trials as well as in population-based efforts to improve blood pressure control.

Moreover, participants in the lowest-income sites were significantly less likely to receive coronary revascularization or be hospitalized or treated for angina; these disparities likely affected the composite CHD outcome, which contains coronary revascularization and hospitalized/treated angina as subcomponent outcomes. Although these findings were contrary to our hypothesis that socioeconomic context could lead to greater cardiovascular morbidity and related procedural interventions, it is plausible that differences in use patterns are related to variation in clinical presentation³² and cultural norms for seeking care, access to care, or other unmeasured factors. Numerous studies have previously shown that patients who are black or of lower socioeconomic status are less likely to receive procedures such as coronary revascularization.³³⁻³⁵ Likewise, given the disparities noted above, it may perhaps seem surprising that there was no statistically significant difference in the primary outcome (CHD) between participants in low- and high-income areas. However, this outcome may also have been affected by differences in use patterns and variation in clinical presentation. In this study design, we were unable to discern whether these outcomes are measuring the effect of true adverse cardiovascular events attributed to differences in hypertensive management or differences in access to or quality of care beyond the standard protocol of the trial.

We attempted to separate the effects of race from socioeconomic context by assessing socioeconomic groups within racial strata and found that the results of subgroup analyses did not differ from the overall findings. Previous studies have shown that black participants are less likely to achieve blood pressure control,³⁶ even in the context of RCTs (including in ALLHAT), possibly because of differences in medication and visit adherence.^{21,23,31,37} A range of economic and social factors may affect blood pressure control in black patients, including individual and neighborhood socioeconomic disparities, social isolation, risk of drug and alcohol use disorder lack of access to hypertension care, unemployment, lack of health insurance, and structural racism.^{11,38–40} It may be the case that in low-income areas, these factors are more potent, potentially explaining why comparisons by economic strata among black adults were consistent with findings from the total study population. Nevertheless, given the long history of socioeconomic and racial inequality in the United States, there may be shared or unique structural disparities leading to differences in RCT outcomes that we are unable to capture.

Limitations

There are several limitations to this study. First, it is possible that the county in which a clinical site is located may differ from a participant's county of residence. Although distance from residence to medical care varies by rurality, in an RCT, we assumed that people who participated in the study would

Table	3.	Association	Between	Income	and	Time	to	Cardiovascular	Event	Outcomes	Across	Economic	Strata
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	Incidence, %, by County I	ncome Level	Low-Income Effect*	
Outcome	Quintile 1	Quintile 5	Unadjusted HR (95% CI)	Risk-Adjusted HR (95% Cl)
Primary outcome				
CHD [†]	6.9	9.6	0.76 (0.64–0.90)‡	0.93 (0.78–1.11)
Secondary outcomes				
All-cause mortality	15.8	15.0	1.12 (1.00–1.26)	1.25 (1.10–1.41) [§]
Combined CHD	12.2	17.9	0.70 (0.61–0.79) [§]	0.89 (0.78–1.01)
Stroke	4.9	4.7	1.12 (0.91–1.38)	1.16 (0.93–1.45)
Combined CVD [¶]	21.9	29.4	0.74 (0.67–0.82) [§]	0.89 (0.81–0.99)‡
Components of secondary outcomes	-	-		
Heart failure	6.5	7.1	0.97 (0.81–1.17)	1.07 (0.88–1.29)
Hospitalized/fatal heart failure	5.8	5.5	1.13 (0.94–1.38)	1.26 (1.03–1.55) [‡]
Angina [#]	6.7	12.4	0.54 (0.46–0.65) [§]	0.70 (0.59–0.83) [§]
Coronary revascularization	4.2	8.7	0.50 (0.40–0.62) [§]	0.71 (0.57–0.89)‡
Peripheral arterial disease**	2.2	3.8	0.61 (0.45–0.82)‡	0.87 (0.64–1.18)
ESRD ^{††‡‡}	1.8	1.1	1.66 (1.15–2.39) [‡]	1.86 (1.26–2.73) [‡]

Quintile 1 is the lowest-income quintile, and quintile 5 is the highest-income quintile. CHD indicates coronary heart disease; CVD, cardiovascular disease; ESRD, end-stage renal disease; HR, hazard ratio.

*Unadjusted HR represents likelihood of having an adverse cardiovascular outcome with the highest-income quintile, quintile 5, serving as the reference group, adjusting only for treatment group. Risk-adjusted HR represents likelihood of having an adverse cardiovascular event with the highest-income quintile, quintile 5, serving as the reference group. Model adjusts for treatment group, age, sex, baseline systolic blood pressure and diastolic blood pressure, and qualifying risk factors for ALLHAT (Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial; body mass index [BMI], history of myocardial infarction or stroke, history of coronary revascularization, history of CHD at baseline, other atherosclerotic CVD, participation in lipid-lowering trial, type 2 diabetes mellitus, history of major ST-segment depression or T-wave inversion, aspirin use, high-density lipoprotein cholesterol <35 mg/dL, left ventricular hypertrophy [LVH] by ECG, LVH by echocardiogram, cigarette smoking, and estrogen supplementation [a minority of study participants have missing values for these participants were imputed]).

[†]CHD: fatal CHD or nonfatal myocardial infarction combined.

[‡]Р<0.05.

[§]*P*<0.001.

^{II}Combined CHD: fatal CHD and nonfatal myocardial infarction combined, coronary revascularization, and hospitalized angina.

[¶]Combined CVD: combined CHD, stroke, other treated angina, heart failure, and peripheral artery disease.

[#]Angina includes both hospitalized and treated angina.

**Peripheral arterial disease includes both hospitalized and treated PAD.

^{††}The following secondary outcomes from ALLHAT are not included: cancer and hospitalization for gastrointestinal tract bleeding.

^{‡‡}The following component of secondary outcomes was not included in this table: angina (hospitalized).

live reasonably close to their site. In addition, counties differ in size and may comprise several socioeconomic contexts; although we did not have data to study the effect of socioeconomic context at a more granular level (such as census tract), our use of county-level measures would tend to bias our findings toward the null, as it dilutes the true income status of a community. Furthermore, our analysis did not adjust for facility because we did not have data linking individual participants to individual facilities; it is likely that there were multiple participating facilities in certain counties. Third, area income may not be a perfect indicator of social risk factors, such as neighborhood violence or access to healthy foods, which can impact health outcomes. However, county-level analyses can serve as a reasonable proxy for social and economic stressors or the amount of resources available in a community and can be important for directing policy interventions. Fourth, although it is the largest completed randomized hypertension trial, the data from ALLHAT are nearly 20 years old and progress may have been made in the interim in addressing disparities in hypertension outcomes. Fifth, given that clinical sites in the South were more likely to be low income and enroll black participants, it may not be possible to disentangle the effects of race and geography from socioeconomic context; still, our subgroup analyses suggest that socioeconomic context is an independent factor for blood pressure control and some cardiovascular outcomes. Sixth, because we did not have access to unique location or clinic identifiers for each patient, we were unable to account for correlation of outcomes within an area. Although this may have resulted in overnarrow Cls, none of our key findings was marginal and, thus, it is reasonable to expect that they would have been unchanged even if we had accounted for such correlation. Seventh, data on medication adherence were insufficient to include in our secondary analyses, making them more difficult to delineate the extent to which medication adherence may have attenuated some outcomes. In addition, adherence to the standardized trial protocol was not measured in ALLHAT. It is possible that investigators in some areas were less adherent to the trial protocol or that there was variation in clinician practice for participants that required second- and third-line blood pressure medications, which could result in differences in how trial participants in different clinical sites were treated. These factors may have contributed to the observed differences in some outcomes, although they are difficult to measure. Moreover, although RCTs theoretically may ensure that participants have equal access to health care, this is not necessarily the case, as suggested by the differences in coronary revascularization that we noted. ALLHAT participants may have had equal access to hypertension care, but participants in different areas may not have had equal access to care not pertaining directly to hypertension treatment. Nevertheless, compared with other study formats, we expect that an RCT might create an environment that more closely approximates equity in healthcare access. Last, some may wonder whether these findings can be generalized to other populations; although this is an important question, the role of the distinctive US healthcare system likely serves as a confounder that may not allow study findings to be generalized to other countries.

Despite these limitations, there are also several advantages to using data from a nationwide RCT, such as ALLHAT. First, ALLHAT enrolled a diverse, representative North American population that may be more reflective of the diverse populations that many clinicians encounter in everyday practice. Second, ALLHAT is the largest-ever RCT of antihypertensive treatment, creating a larger and more diverse sample size for this study; it is possible that an antihypertensive RCT of this magnitude may not be conducted in the near future (if ever). Third, ALLHAT followed a large number of participants for an average of 5 years, allowing for measurement of numerous subsequent cardiovascular outcomes that would not be possible using data from, for example, an observational study.

Conclusions

In the largest RCT of antihypertensive medication therapy, in which participants had equal access to antihypertensive resources afforded by such a trial, we observed disparities in blood pressure control, heart failure morbidity, ESRD, allcause mortality, and coronary revascularization across socioeconomic strata, even after controlling for medication treatment arm, demographics, and clinical characteristics. These findings underscore the importance of measuring socioeconomic context in RCTs and suggest the need to invest in strategies to mitigate socioeconomic disparities and achieve more equitable outcomes in the care of hypertension.

Acknowledgments

We would like to thank Tara Liptak, for providing administrative support; Sara L. Pressel, for aiding in the acquisition of geographic ALLHAT (Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial) data; Minas Giannekas (mapchart.net), for aiding in the design of the Figure; and Anja Shahu, for aiding in the design of Figure S2.

Sources of Funding

Dr Shahu's work was supported by the National Institutes of Health–National Heart, Lung, and Blood Institute under award T35HL007649 and the Richard K. Gershon, MD, Student Research Fellowship at Yale University School of Medicine. The content is solely the responsibility of the authors and does not represent the official views of the National Institutes of Health. At the time of this study, Dr Spatz was supported by the Agency for Healthcare Research and Quality Patient-Centered Outcomes Research Institutional Mentored Career Development Program (K12HS023000). Dr Dhruva is supported by the Department of Veterans Affairs.

Disclosures

At the time of this study, Dr Shahu was affiliated with the Yale School of Medicine. Dr Krumholz is a recipient of research grants, through Yale, from Medtronic and Johnson & Johnson (Janssen) to develop methods of clinical trial data sharing and from Medtronic to develop methods for postmarket surveillance of medical devices; chairs a cardiac scientific advisory board for UnitedHealth; is a participant/participant representative of the IBM Watson Health Life Sciences Board; is a member of the Advisory Board for Element Science and the Physician Advisory Board for Aetna; and is the founder of Hugo, a personal health information platform. Drs Herrin, Desai, Krumholz, and Spatz work under contract with the Centers for Medicare and Medicaid Services to develop and maintain performance measures that are publicly reported.

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SUPPLEMENTAL MATERIAL

	County income level							
Characteristic	Q1	Q2	Q3	Q4	Q5			
	N (%)	N (%)	N (%)	N (%)	N (%)			
Total participants	2169 (100.0)	3562 (100.0)	4916 (100.0)	6721 (100.0)	10458 (100.0)			
Visit adherence*								
< 80%	1498 (69.1)	1946 (54.6)	2812 (57.2)	4099 (61.0)	6085 (58.2)			
$\geq 80\%$	644 (29.7)	1588 (44.6)	2044 (41.6)	2524 (37.6)	4264 (40.8)			
Missing	27 (1.2)	28 (0.8)	60 (1.2)	98 (1.5)	109 (1.0)			
Medication adherence [†]								
Ever < 80%	557 (25.7)	610 (17.1)	930 (18.9)	1300 (19.3)	2289 (21.9)			
Always $\geq 80\%$	788 (36.3)	2176 (61.1)	2766 (56.3)	3668 (54.6)	5810 (55.6)			
Missing	824 (38.0)	776 (21.8)	1220 (24.8)	1753 (26.1)	2359 (22.6)			

Table S1. Visit and medication adherence of study population across socioeconomic strata.

*Visit adherence was defined as the number of visits at six years divided by the number of expected visits. Adequate visit adherence was defined as attending \geq 80% of expected visits.

 \dagger Adequate medication adherence was defined as always taking \geq 80% of medications (self-reported by participants).

	County Income Level						
Outcome	Q1	Q2	Q3	Q4	Q5		
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)		
Systolic blood pressu	re						
Year 1	140.5 (18.6)	139.5 (16.9)	138.4 (17.3)	138.9 (16.2)	137.7 (16.0)		
Year 2	140.8 (19.1)	138.2 (16.3)	137.0 (17.2)	137.6 (16.2)	136.7 (15.9)		
Year 3	139.8 (18.4)	136.5 (16.6)	135.7 (16.6)	136.2 (16.2)	135.4 (15.5)		
Year 4	138.5 (18.4)	136.3 (17.0)	134.9 (16.5)	135.1 (16.3)	134.1 (15.3)		
Year 5	138.3 (19.0)	135.9 (16.7)	134.7 (16.7)	134.4 (15.6)	134.0 (14.9)		
Year 6	139.9 (21.3)	135.2 (17.6)	134.6 (16.1)	133.4 (15.9)	133.2 (15.9)		
Diastolic blood press	ure						
Year 1	80.8 (11.1)	79.3 (9.9)	78.1 (10.1)	79.6 (9.8)	79.2 (9.8)		
Year 2	80.0 (10.8)	78.4 (9.9)	77.3 (10.5)	78.2 (9.9)	78.1 (9.7)		
Year 3	78.8 (10.5)	77.1 (10.0)	76.3 (10.3)	76.7 (10.3)	76.8 (9.6)		
Year 4	78.7 (10.9)	76.6 (9.9)	75.5 (10.2)	75.9 (10.0)	76.0 (9.8)		
Year 5	78.5 (11.1)	75.6 (10.0)	74.4 (10.6)	74.3 (10.0)	75.1 (9.8)		
Year 6	78.2 (11.5)	73.8 (10.6)	73.6 (10.2)	73.4 (9.8)	74.0 (10.0)		

 Table S2. Mean blood pressure at years 1-6, stratified by income level.

Q1 indicates lowest income quintile; Q5, highest income quintile; SD, standard deviation.

Table S3. Mean change in blood pressure from baseline at years 1-6, stratified by income level.

	County Income Level							
Outcome	Q1	Q2	Q3	Q4	Q5			
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)			
Change in systolic	blood pressure com	pared with basel	ine					
Year 1	-4.0 (21.5)	-5.7 (19.2)	-7.1 (20.1)	-8.4 (19.3)	-7.8 (19.0)			
Year 2	-3.2 (22.5)	-6.9 (19.6)	-8.5 (21.1)	-9.6 (19.2)	-8.7 (19.1)			
Year 3	-4.3 (21.8)	-8.5 (20.5)	-9.8 (20.4)	-11.0 (20.0)	-9.9 (19.1)			
Year 4	-5.3 (21.7)	-8.5 (20.9)	-10.5 (20.6)	-11.9 (20.0)	-11.1 (19.3)			
Year 5	-4.6 (21.8)	-9.2 (20.7)	-11.1 (21.2)	-12.4 (19.9)	-11.3 (19.5)			
Year 6	-2.6 (24.5)	-9.8 (21.6)	-10.9 (20.5)	-13.1 (20.1)	-12.1 (20.3)			
Change in diastolic	blood pressure con	npared with base	eline					
Year 1	-2.7 (12.1)	-3.5 (10.6)	-4.2 (11.3)	-4.4 (10.9)	-4.4 (10.7)			
Year 2	-3.4 (12.2)	-4.3 (11.2)	-5.0 (11.8)	-5.9 (11.1)	-5.5 (11.0)			
Year 3	-4.7 (12.1)	-5.5 (11.8)	-6.0 (12.1)	-7.4 (11.6)	-6.8 (11.0)			
Year 4	-4.9 (12.3)	-6.0 (11.7)	-6.7 (12.2)	-8.1 (11.4)	-7.5 (11.3)			
Year 5	-5.2 (12.3)	-7.1 (11.6)	-7.8 (12.8)	-9.2 (11.3)	-8.6 (11.4)			
Year 6	-5.8 (12.8)	-8.7 (12.0)	-8.4 (12.5)	-10.4 (11.4)	-9.9 (11.6)			

Q1 indicates lowest income quintile; Q5, highest income quintile; SD, standard deviation.

Table S4. Blood pressure control* for all treatment groups combined, stratified by income level.

	County Income Level								
Outcome	Q1	Q2	Q3	Q4	Q5				
	N (%)	N (%)	N (%)	N (%)	N (%)				
Year 1	786 (44.8)	1625 (51.2)	2299 (54.9)	3037 (53.2)	5284 (57.3)				
Year 2	695 (45.2)	1578 (54.7)	2170 (57.6)	2916 (57.1)	5073 (59.6)				
Year 3	657 (48.1)	1580 (59.8)	2099 (61.0)	2867 (61.3)	4950 (63.6)				
Year 4	561 (50.2)	1489 (62.0)	1950 (63.4)	2734 (64.8)	4715 (67.1)				
Year 5	344 (51.2)	1055 (63.9)	1224 (65.0)	1635 (67.5)	2874 (68.0)				
Year 6	140 (50.0)	575 (64.3)	677 (64.7)	956 (71.6)	1499 (69.3)				

	County Income Level								
Outcome	Q1	Q2	Q3	Q4	Q5				
	N (%)	N (%)	N (%)	N (%)	N (%)				
Year 1	394 (48.9)	787 (53.5)	1103 (57.1)	1490 (56.7)	2522 (59.7)				
Year 2	356 (50.7)	783 (57.9)	1049 (60.0)	1432 (60.2)	2437 (62.1)				
Year 3	325 (51.8)	780 (63.2)	997 (62.7)	1360 (62.8)	2317 (64.6)				
Year 4	274 (53.4)	736 (65.8)	911 (63.5)	1299 (67.0)	2196 (67.9)				
Year 5	153 (50.2)	510 (67.3)	577 (65.9)	779 (69.8)	1392 (71.1)				
Year 6	63 (50.0)	278(69.7)	310 (64.0)	454 (72.2)	694 (70.2)				

 Table S5. Blood pressure control* for chlorthalidone treatment arm.

Table S6. Blood pressure control*	for amlodipine treatment arm.
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	County Income Level								
Outcome	Q1	Q2	Q3	Q4	Q5				
	N (%)	N (%)	N (%)	N (%)	N (%)				
Year 1	197 (41.8)	455 (52.7)	610 (53.6)	799 (52.5)	1472 (58.3)				
Year 2	171 (41.0)	427 (54.9)	580 (56.3)	788 (57.6)	1368 (58.7)				
Year 3	179 (47.7)	437 (60.0)	574 (60.5)	782 (61.8)	1411 (65.7)				
Year 4	148 (47.4)	395 (59.8)	553 (64.8)	740 (64.2)	1336 (68.4)				
Year 5	100 (54.1)	308 (65.1)	349 (65.1)	444 (67.1)	800 (68.3)				
Year 6	37 (46.3)	162 (60.9)	203 (67.4)	254 (71.3)	405 (68.3)				

Table S7. Blood pressure control* for li	isinopril treatment arm.
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		Cou	nty Income Level		
Outcome	Q1	Q2	Q3	Q4	Q5
	N (%) g	N (%)	N (%)	N (%)	N (%)
Year 1	195 (40.8)	383 (45.7)	586 (52.5)	748 (48.1)	1290 (52.3)
Year 2	168 (40.2)	368 (48.6)	541 (54.8)	696 (51.2)	1268 (56.1)
Year 3	153 (42.1)	363 (53.5)	528 (58.5)	725 (58.4)	1222 (59.7)
Year 4	139 (47.4)	358 (57.5)	486 (61.5)	695 (61.6)	1183 (64.3)
Year 5	91 (50.0)	237 (56.4)	298 (63.1)	412 (63.8)	682 (62.2)
Year 6	40 (54.1)	135 (59.0)	164 (62.8)	248 (70.7)	400 (68.8)

Table S8. Association between income and	blood pressure con	ntrol among black	ALLHAT
participants across socioeconomic strata.			

		County Income Level	Low Income Effect	Low Income Effect
Outcome	Q1	Q5	Unadjusted OR*	Risk-Adjusted OR*
	% with BP <140/90 mmHg	% with BP <140/90 mmHg	OR (95% CI)	OR (95% CI)
Year 1	43.5	51.7	0.72 (0.63-0.83)	0.70 (0.61-0.81)
Year 2	44.8	52.8	0.73 (0.63-0.85)	0.73 (0.62-0.85)
Year 3	46.4	57.6	0.64 (0.55-0.75)	0.65 (0.55-0.76)
Year 4	50.8	61.3	0.66 (0.55-0.78)	0.69 (0.58-0.82)
Year 5	49.1	63.7	0.55 (0.44-0.68)	0.55 (0.44-0.69)
Year 6	46.5	63.2	0.50 (0.37-0.68)	0.53 (0.38-0.74)

Q1 indicates lowest income quintile; Q5, highest income quintile; OR, odds ratio; BP, blood pressure; CI, confidence interval.

*Unadjusted OR represents odds of achieving blood pressure control (<140/90 mmHg) with the highest income quintile, Q5, serving as the reference group, adjusting only for treatment group. Risk-adjusted OR represents odds of achieving blood pressure control (< 140/90 mmHg), with the highest income quintile, Q5, serving as the reference group. Model adjusts for treatment group, age, sex, baseline SBP and DBP, and qualifying risk factors for ALLHAT (BMI†, history of MI or stroke, history of coronary revascularization, history of CHD at baseline, other ASCVD, participation in lipid-lowering trial, type II diabetes, history of major ST depression or T-wave inversion†, aspirin use, HDL-C < 35 mg/dL, LVH by ECG, LVH by echocardiogram†, cigarette smoking† and estrogen supplementation†).

[†]A minority of study participants have missing values for these risk factors. The missing values for these participants were imputed.

Fable S9. Association between income and blood pressure control among ALL	ЛАТ
participants living in the South across socioeconomic strata.	

		County Income Level	Low Income Effect	Low Income Effect
Outcome	Q1	Q5	Unadjusted OR*	Risk-Adjusted OR*
	% with BP <140/90 mmHg	% with BP <140/90 mmHg	OR (95% CI)	OR (95% CI)
Year 1	44.5	57.6	0.59 (0.52-0.68)	0.66 (0.56-0.77)
Year 2	44.9	57.0	0.61 (0.53-0.71)	0.72 (0.61-0.85)
Year 3	47.5	60.4	0.59 (0.51-0.69)	0.63 (0.53-0.75)
Year 4	49.9	63.7	0.57 (0.48-0.67)	0.61 (0.51-0.74)
Year 5	50.9	62.3	0.63 (0.51-0.78)	0.67 (0.52-0.86)
Year 6	50.0	69.7	0.44 (0.31-0.61)	0.51 (0.34-0.76)

Q1 indicates lowest income quintile; Q5, highest income quintile; OR, odds ratio; BP, blood pressure; CI, confidence interval.

*Unadjusted OR represents odds of achieving blood pressure control (<140/90 mmHg) with the highest income quintile, Q5, serving as the reference group, adjusting only for treatment group. Risk-adjusted OR represents odds of achieving blood pressure control (< 140/90 mmHg), with the highest income quintile, Q5, serving as the reference group. Model adjusts for treatment group, age, sex, baseline SBP and DBP, and qualifying risk factors for ALLHAT (BMI†, history of MI or stroke, history of coronary revascularization, history of CHD at baseline, other ASCVD, participation in lipid-lowering trial, type II diabetes, history of major ST depression or T-wave inversion†, aspirin use, HDL-C < 35 mg/dL, LVH by ECG, LVH by echocardiogram†, cigarette smoking† and estrogen supplementation†).

[†]A minority of study participants have missing values for these risk factors. The missing values for these participants were imputed.

Table S10.	Association between	income and bloo	d pressure con	ntrol across s	ocioeconomic
strata, adju	usted for visit adhere	ence.			

		County Income Level	Low Income Effect	Low Income Effect
Outcome	Q1	Q5	Unadjusted OR*	Risk-Adjusted OR*
	% with BP <140/90 mmHg	% with BP <140/90 mmHg	OR (95% CI)	OR (95% CI)
Year 1	44.8	57.3	0.61 (0.55-0.67)	0.63 (0.57, 0.70)
Year 2	45.2	59.6	0.56 (0.50-0.63)	0.58 (0.52, 0.66)
Year 3	48.1	63.6	0.53 (0.47-0.60)	0.55 (0.49, 0.63)
Year 4	50.2	67.1	0.49 (0.43-0.56)	0.53 (0.46, 0.60)
Year 5	51.2	68.0	0.51 (0.43-0.60)	0.52 (0.44, 0.63)
Year 6	50.0	69.3	0.44 (0.34-0.57)	0.48 (0.36, 0.62)

Q1 indicates lowest income quintile; Q5, highest income quintile; OR, odds ratio; BP, blood pressure; CI, confidence interval.

*Unadjusted OR represents odds of achieving blood pressure control (<140/90 mmHg) with the highest income quintile, Q5, serving as the reference group, adjusting only for treatment group. Risk-adjusted OR represents odds of achieving blood pressure control (< 140/90 mmHg), with the highest income quintile, Q5, serving as the reference group. Model adjusts for treatment group, age, sex, baseline SBP and DBP, qualifying risk factors for ALLHAT (BMI†, history of MI or stroke, history of coronary revascularization, history of CHD at baseline, other ASCVD, participation in lipid-lowering trial, type II diabetes, history of major ST depression or T-wave inversion†, aspirin use, HDL-C < 35 mg/dL, LVH by ECG, LVH by echocardiogram†, cigarette smoking† and estrogen supplementation†), and six year visit adherence^b.

[†]A minority of study participants have missing values for these risk factors. The missing values for these participants were imputed.

Table S11. Unadjusted adverse time-to-event cardiovascular outcomes for all treatment groups combined, stratified by income level.

	County Income Level				
Outcome	Q1	Q2	Q3	Q4	Q5
	N (%)	N (%)	N (%)	N (%)	N (%)
Primary outcome					
CHD*	150 (6.9)	374 (10.5)	494 (10.0)	699 (10.4)	1000 (9.6)
Secondary Outcomes					
All-cause mortality	342 (15.8)	596 (16.7)	833 (16.9)	1066 (15.9)	1571 (15.0)
Combined CHD [†]	264 (12.2)	631 (17.7)	932 (19.0)	1269 (18.9)	1868 (17.9)
Stroke	107 (4.9)	220 (6.2)	247 (5.0)	332 (4.9)	492 (4.7)
Combined CVD [‡]	475 (21.9)	1065 (29.9)	1521 (30.9)	1987 (29.6)	3077 (29.4)
Components of secondary outcomes					
Heart Failure	140 (6.5)	290 (8.1)	358 (7.3)	522 (7.8)	739 (7.1)
Hospitalized/fatal heart failure	125 (5.8)	218 (6.1)	290 (5.9)	447 (6.7)	572 (5.5)
Angina§	146 (6.7)	379 (10.6)	632 (12.9)	825 (12.3)	1299 (12.4)
Coronary revascularization	91 (4.2)	275 (7.7)	469 (9.5)	625 (9.3)	909 (8.7)
Peripheral arterial disease	48 (2.2)	153 (4.3)	209 (4.3)	204 (3.0)	397 (3.8)
ESRD#**	38 (1.8)	62 (1.7)	62 (1.3)	130 (1.9)	120 (1.1)

Q1 indicates lowest income quintile; Q5, highest income quintile; N, number of participants; CHD, coronary heart disease; CVD, cardiovascular disease; ESRD, end-stage renal disease.

*CHD: fatal CHD or nonfatal MI combined.

[†]Combined CHD: Fatal CHD, coronary revascularization, hospitalized angina.

‡Combined CVD: Combined CHD, stroke, other treated angina, HF, and peripheral artery disease.

§Angina includes both hospitalized and treated angina.

|Peripheral arterial disease (PAD) includes both hospitalized and treated PAD.

#The following secondary outcomes are not included in this table: cancer, hospitalized for GI bleeding.

	County Income Level				
Outcome	Q1	Q2	Q3	Q4	Q5
	N (%)	N (%)	N (%)	N (%)	N (%)
Primary outcome					
CHD*	74 (7.4)	162 (10.0)	225 (10.0)	327 (10.6)	468 (9.8)
Secondary Outcomes					
All-cause mortality	171 (17.2)	270 (16.6)	378 (16.8)	498 (16.2)	734 (15.4)
Combined CHD [†]	125 (12.6)	275 (16.9)	428 (19.0)	567 (18.4)	860 (18.0)
Stroke	49 (4.9)	89 (5.5)	94 (4.2)	160 (5.2)	231 (4.8)
Combined CVD [‡]	214 (21.5)	451 (27.8)	694 (30.8)	883 (28.7)	1374 (28.8)
Components of secondary outcomes					
Heart Failure	54 (5.4)	112 (6.9)	162 (7.2)	216 (7.0)	276 (5.8)
Hospitalized/fatal heart failure	48 (4.8)	83 (5.1)	135 (6.0)	188 (6.1)	224 (4.7)
Angina§	64 (6.4)	172 (10.6)	287 (12.7)	358 (11.6)	578 (12.1)
Coronary revascularization	46 (4.6)	115 (7.1)	206 (9.1)	271 (8.8)	399 (8.4)
Peripheral arterial disease	19 (1.9)	73 (4.5)	105 (4.7)	96 (3.1)	183 (3.8)
ESRD#**	16 (1.6)	20 (1.2)	30 (1.3)	65 (2.1)	53 (0.9)

Table S12. Unadjusted adverse cardiovascular outcomes for chlorthalidone treatment arm.

Q1 indicates lowest income quintile; Q5, highest income quintile; N, number of participants; CHD, coronary heart disease; CVD, cardiovascular disease; ESRD, end-stage renal disease.

*CHD: fatal CHD or nonfatal MI combined.

†Combined CHD: Fatal CHD, coronary revascularization, hospitalized angina.

‡Combined CVD: Combined CHD, stroke, other treated angina, HF, and peripheral artery disease.

§Angina includes both hospitalized and treated angina.

|Peripheral arterial disease (PAD) includes both hospitalized and treated PAD.

#The following secondary outcomes are not included in this table: cancer, hospitalized for GI bleeding.

	County Income Level				
Outcome	Q1	Q2	Q3	Q4	Q5
	N (%)	N (%)	N (%)	N (%)	N (%)
Primary outcome					
CHD*	41 (7.0)	107 (11.1)	136 (10.2)	203 (11.2)	248 (8.7)
Secondary Outcomes					
All-cause mortality	85 (14.5)	159 (16.4)	221 (16.6)	284 (15.7)	417 (14.6)
Combined CHD [†]	68 (11.6)	173 (17.9)	256 (19.2)	363 (20.1)	483 (16.9)
Stroke	31 (5.3)	50 (5.2)	64 (4.8)	88 (4.9)	123 (4.3)
Combined CVD [‡]	128 (21.8)	292 (30.2)	412 (30.9)	558 (30.9)	833 (29.2)
Components of secondary outcomes					
Heart Failure	45 (7.7)	99 (10.2)	106 (8.0)	106 (9.0)	239 (8.4)
Hospitalized/fatal heart failure	41 (7.0)	78 (8.1)	85 (6.5)	142 (7.9)	184 (6.5)
Angina§	38 (6.5)	100 (10.3)	168 (12.6)	230 (12.7)	349 (12.2)
Coronary revascularization	27 (4.6)	77 (8.0)	136 (10.2)	179 (9.9)	251 (8.8)
Peripheral arterial disease	14 (2.4)	35 (3.6)	48 (3.6)	52 (2.9)	99 (3.5)
ESRD#**	12 (2.0)	26 (2.7)	15 (1.1)	31 (1.7)	36 (1.3)

Table S13. Unadjusted adverse cardiovascular outcomes for amlodipine treatment arm.

Q1 indicates lowest income quintile; Q5, highest income quintile; N, number of participants; CHD, coronary heart disease; CVD, cardiovascular disease; ESRD, end-stage renal disease.

*CHD: fatal CHD or nonfatal MI combined.

[†]Combined CHD: Fatal CHD, coronary revascularization, hospitalized angina.

‡Combined CVD: Combined CHD, stroke, other treated angina, HF, and peripheral artery disease.

§Angina includes both hospitalized and treated angina.

|Peripheral arterial disease (PAD) includes both hospitalized and treated PAD.

#The following secondary outcomes are not included in this table: cancer, hospitalized for GI bleeding.

	County Income Level				
Outcome	Q1	Q2	Q3	Q4	Q5
	N (%)	N (%)	N (%)	N (%)	N (%)
Primary outcome					
CHD*	35 (6.0)	105 (10.8)	133 (10.0)	169 (9.2)	284 (10.0)
Secondary Outcomes					
All-cause mortality	86 (14.6)	167 (17.2)	234 (17.6)	284 (15.5)	420 (14.8)
Combined CHD [†]	71 (12.1)	183 (18.9)	248 (18.7)	339 (18.5)	525 (18.5)
Stroke	27 (4.6)	81 (8.4)	89 (6.7)	84 (4.6)	138 (4.9)
Combined CVD [‡]	133 (22.6)	322 (33.2)	415 (31.2)	546 (29.7)	870 (30.7)
Components of secondary outcomes					
Heart Failure	41 (7.0)	79 (8.1)	90 (6.8)	143 (7.8)	224 (7.9)
Hospitalized/fatal heart failure	36 (6.1)	57 (5.9)	69 (5.2)	117 (6.4)	164 (5.8)
Angina§	44 (7.5)	107 (11)	177 (13.3)	237 (12.9)	372 (13.1)
Coronary revascularization	18 (3.1)	83 (8.6)	127 (9.6)	175 (9.5)	259 (9.1)
Peripheral arterial disease	15 (2.6)	45 (4.6)	56 (4.2)	56 (3.0)	115 (4.1)
ESRD#**	10 (1.7)	16 (1.6)	17 (1.3)	34 (1.9)	41 (1.4)

Table S14. Unadjusted adverse cardiovascular outcomes for lisinopril treatment arm.

Q1 indicates lowest income quintile; Q5, highest income quintile; N, number of participants; CHD, coronary heart disease; CVD, cardiovascular disease; ESRD, end-stage renal disease.

*CHD: fatal CHD or nonfatal MI combined.

[†]Combined CHD: Fatal CHD, coronary revascularization, hospitalized angina.

‡Combined CVD: Combined CHD, stroke, other treated angina, HF, and peripheral artery disease.

§Angina includes both hospitalized and treated angina.

||Peripheral arterial disease (PAD) includes both hospitalized and treated PAD.

#The following secondary outcomes are not included in this table: cancer, hospitalized for GI bleeding.

	County Income Level		Low Income Effect	Low Income Effect
Outcome	Q1	Q5	Unadjusted HR*	Risk-Adjusted HR*
	Incidence, %	Incidence, %	HR (95% CI)	HR (95% CI)
Primary outcome				
CHD†	7.0	8.5	0.86 (0.69-1.08)	0.90 (0.71-1.14)
Secondary outcomes				
All-cause mortality	17.8	15.9	1.19 (1.03-1.39)	1.24 (1.06-1.44)
Combined CHD [‡]	11.2	14.4	0.81 (0.68-0.97)	0.89 (0.74-1.07)
Stroke	5.2	5.5	0.99 (0.76-1.30)	1.07 (0.81-1.41)
Combined CVD§	22.1	26.8	0.83 (0.73-0.94)	0.90 (0.79-1.03)
Components of secondary outcomes				
Heart Failure	6.9	6.7	1.09 (0.86-1.38)	1.18 (0.92-1.50)
Hospitalized/fatal heart failure	6.0	5.3	1.20 (0.92-1.55)	1.29 (0.99-1.68)
Angina	6.3	10.3	0.61 (0.49-0.77)	0.69 (0.55-0.87)
Coronary revascularization	2.8	4.8	0.60 (0.43-0.85)	0.69 (0.48-0.99)
Peripheral arterial disease#	2.1	3.3	0.67 (0.45-1.00)	0.75 (0.49-1.13)
ESRD**††	2.0	1.6	1.32 (0.83-2.09)	1.47 (0.91-2.36)

 Table S15. Association between income and time to cardiovascular outcomes among black

 ALLHAT participants across socioeconomic strata.

Q1 indicates lowest income quintile; Q5, highest income quintile; HR, hazard ratio; CI, confidence interval; CHD, coronary heart disease; CVD, cardiovascular disease; ESRD, end-stage renal disease.

*Unadjusted HR represents likelihood of having an adverse cardiovascular outcome, with the highest income quintile, Q5, serving as the reference group, adjusting only for treatment group. Risk-adjusted HR represents likelihood of having an adverse cardiovascular event, with the highest income quintile, Q5, serving as the reference group. Model adjusts for treatment group, age, sex, baseline SBP and DBP, and qualifying risk factors for ALLHAT (BMI‡‡, history of MI or stroke, history of coronary revascularization, history of CHD at baseline, other ASCVD, participation in lipid-lowering trial, type II diabetes, history of major ST depression or T-wave inversion‡‡, aspirin use, HDL-C < 35 mg/dL, LVH by ECG, LVH by echocardiogram‡‡, cigarette smoking‡‡ and estrogen supplementation‡‡).

[†]CHD: fatal CHD or nonfatal MI combined.

‡Combined CHD: Fatal CHD and nonfatal MI combined, coronary revascularization, hospitalized angina. §Combined CVD: Combined CHD, stroke, other treated angina, HF, and peripheral artery disease.

 $\|\mbox{Angina}\xspace$ includes both hospitalized and treated angina.

#Peripheral arterial disease (PAD) includes both hospitalized and treated PAD.

**The following secondary outcomes from ALLHAT are not included: cancer, hospitalized for GI bleeding.

††The following component of secondary outcomes was not included in this table: angina (hospitalized).

‡‡A minority of study participants have missing values for these risk factors. The missing values for these participants were imputed.

, i i i i i i i i i i i i i i i i i i i	County Income Level		Low Income Effect	Low Income Effect
Outcome	Q1	Q5	Unadjusted HR*	Risk-Adjusted HR*
	Incidence, %	Incidence, %	HR (95% CI)	HR (95% CI)
Primary outcome				
CHD†	6.8	9.0	0.79 (0.63-0.98)	0.94 (0.73-1.19)
Secondary outcomes				
All-cause mortality	15.8	14.7	1.12 (0.96-1.31)	1.14 (0.96-1.36)
Combined CHD [‡]	12.1	16.4	0.75 (0.63-0.88)	0.94 (0.78-1.13)
Stroke	5.0	4.2	1.24 (0.93, 1.65)	1.22 (0.89-1.68)
Combined CVD§	21.8	26.7	0.82 (0.72-0.93)	0.92 (0.80-1.06)
Components of secondary outcomes				
Heart Failure	6.4	7.3	0.93 (0.73-1.17)	0.93 (0.71-1.20)
Hospitalized/fatal heart failure	5.8	5.7	1.06 (0.82-1.37)	1.09 (0.82-1.45)
Angina	6.7	10.5	0.64 (0.52-0.80)	0.81 (0.64-1.03)
Coronary revascularization	4.3	8.1	0.54 (0.42-0.70)	0.76 (0.57-1.01)
Peripheral arterial disease#	2.2	3.3	0.69 (0.47-1.01)	1.02 (0.68-1.55)
ESRD**††	1.7	1.1	1.69 (0.99-2.89)	1.57 (0.87-2.82)

Table S16. Association between income and time to cardiovascular event outcomes among participants in ALLHAT living in the South across socioeconomic strata.

Q1 indicates lowest income quintile; Q5, highest income quintile; HR, hazard ratio; CI, confidence interval; CHD, coronary heart disease; CVD, cardiovascular disease; ESRD, end-stage renal disease.

*Unadjusted HR represents likelihood of having an adverse cardiovascular outcome, with the highest income quintile, Q5, serving as the reference group, adjusting only for treatment group. Risk-adjusted HR represents likelihood of having an adverse cardiovascular event, with the highest income quintile, Q5, serving as the reference group. Model adjusts for treatment group, age, sex, baseline SBP and DBP, and qualifying risk factors for ALLHAT (BMI‡‡, history of MI or stroke, history of coronary revascularization, history of CHD at baseline, other ASCVD, participation in lipid-lowering trial, type II diabetes, history of major ST depression or T-wave inversion‡‡, aspirin use, HDL-C < 35 mg/dL, LVH by ECG, LVH by echocardiogram‡‡, cigarette smoking‡‡ and estrogen supplementation‡‡).

†CHD: fatal CHD or nonfatal MI combined.

‡Combined CHD: Fatal CHD and nonfatal MI combined, coronary revascularization, hospitalized angina. §Combined CVD: Combined CHD, stroke, other treated angina, HF, and peripheral artery disease.

 $\|\mbox{Angina}\xspace$ includes both hospitalized and treated angina.

#Peripheral arterial disease (PAD) includes both hospitalized and treated PAD.

**The following secondary outcomes from ALLHAT are not included: cancer, hospitalized for GI bleeding.

††The following component of secondary outcomes was not included in this table: angina (hospitalized).

‡‡A minority of study participants have missing values for these risk factors. The missing values for these participants were imputed.

	County Income Level		Low Income Effect	Low Income Effect
Outcome	Q1	Q5	Unadjusted HR*	Risk-Adjusted HR*
	Incidence, %	Incidence, %	HR (95% CI)	HR (95% CI)
Primary outcome				
CHD†	6.9	9.6	0.71 (0.59-0.84)	0.87 (0.72-1.04)
Secondary outcomes				
All-cause mortality	15.8	15.0	0.93 (0.82-1.04)	1.03 (0.91-1.16)
Combined CHD [‡]	12.2	17.9	0.67 (0.58-0.76)	0.85 (0.74-0.97)
Stroke	4.9	4.7	1.01 (0.82-1.25)	1.06 (0.85-1.32)
Combined CVD§	21.9	29.4	0.71 (0.64-0.78)	0.86 (0.78-0.95)
Components of secondary outcomes				
Heart Failure	6.5	7.1	0.92 (0.77-1.11)	1.01 (0.84-1.23)
Hospitalized/fatal heart failure	5.8	5.5	1.06 (0.87-1.29)	1.19 (0.97-1.46)
Angina	6.7	12.4	0.55 (0.46-0.65)	0.69 (0.58-0.83)
Coronary revascularization	4.2	8.7	0.49 (0.40-0.61)	0.70 (0.56-0.88)
Peripheral arterial disease#	2.2	3.8	0.60 (0.44-0.81)	0.86 (0.63-1.17)
ESRD**††	1.8	1.1	1.52 (1.05-2.19)	1.70 (1.16-2.51)

Table S17. Association between income and time to cardiovascular event outcomes across economic strata, adjusted for visit adherence.

Q1 indicates lowest income quintile; Q5, highest income quintile; HR, hazard ratio; CI, confidence interval; CHD, coronary heart disease; CVD, cardiovascular disease; ESRD, end-stage renal disease.

*Unadjusted HR represents likelihood of having an adverse cardiovascular outcome, with the highest income quintile, Q5, serving as the reference group, adjusting only for treatment group. Risk-adjusted HR represents likelihood of having an adverse cardiovascular event, with the highest income quintile, Q5, serving as the reference group. Model adjusts for treatment group, age, sex, baseline SBP and DBP, and qualifying risk factors for ALLHAT (BMI‡‡, history of MI or stroke, history of coronary revascularization, history of CHD at baseline, other ASCVD, participation in lipid-lowering trial, type II diabetes, history of major ST depression or T-wave inversion‡‡, aspirin use, HDL-C < 35 mg/dL, LVH by ECG, LVH by echocardiogram‡‡, cigarette smoking‡‡ and estrogen supplementation‡‡).

†CHD: fatal CHD or nonfatal MI combined.

‡Combined CHD: Fatal CHD and nonfatal MI combined, coronary revascularization, hospitalized angina. §Combined CVD: Combined CHD, stroke, other treated angina, HF, and peripheral artery disease.

 $\|\mbox{Angina}\xspace$ includes both hospitalized and treated angina.

#Peripheral arterial disease (PAD) includes both hospitalized and treated PAD.

**The following secondary outcomes from ALLHAT are not included: cancer, hospitalized for GI bleeding.

††The following component of secondary outcomes was not included in this table: angina (hospitalized).

‡‡A minority of study participants have missing values for these risk factors. The missing values for these participants were imputed.

Figure S1. Eligibility criteria for ALLHAT participants in original trial.



BMI indicates body mass index; MI, myocardial infarction; CHD, coronary heart disease; ASCVD, atherosclerotic cardiovascular disease; HDL-C, high-density lipoprotein-C; LVH, left ventricular hypertrophy; ECG, electrocardiogram.



Figure S2. Flowchart of study exclusion criteria.





Q1 indicates lowest income quintile; Q5, highest income quintile.