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Coronary heart disease in moderately hypercholesterolemic, hypertensive black and non-black patients randomized to pravastatin vs. usual care: The Antihypertensive and Lipid Lowering to Prevent Heart Attack Trial (ALLHAT-LLT)

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Abstract

Background—In previous analyses in the Antihypertensive and Lipid-Lowering to Prevent Heart Attack Trial (ALLHAT), Blacks had a significantly lower risk of coronary heart disease (CHD) in the pravastatin compared to the usual care group, while non-Blacks had no benefit from pravastatin. No previous statin trial has enrolled enough minority participants to analyze the results separately in Blacks.

Objectives—To determine if apparent racial differences in CHD in ALLHAT are explained by differences in baseline characteristics, adherence during the trial, or achieved blood pressure and lipid lowering.

Methods—This was a pre-specified subgroup analysis of a randomized controlled trial. Hypertensive, moderately hypercholesterolemic participants were assigned to open-label pravastatin (40 mg/day) or usual care. The outcome was a composite of non-fatal myocardial infarction and fatal CHD. We performed intention-to-treat survival analyses using Cox proportional hazards models, adjusting for baseline covariates (age, sex, aspirin use, history of CHD and diabetes, and baseline hypertension treatment), and time-varying levels of blood pressure and total cholesterol.

Results—After adjustment for baseline characteristics, there remained a significant interaction between race and treatment group ($p=0.02$). In stratified models, Blacks in the pravastatin group had a 29% lower risk of CHD (HR 0.71, 95% CI 0.57 – 0.90, $p=0.005$) compared to usual care, while

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non-Blacks had no benefit (HR 1.00, 95% CI 0.85 – 1.19, $p=0.95$). With further adjustment for achieved blood pressure and total cholesterol, the HR in Blacks was 0.65 (95% CI 0.45 – 0.96, $p=0.03$) and in non-Blacks was 1.07 (95% CI 0.81 – 1.41, $p=0.65$).

Conclusions—Our results suggest that pravastatin is effective in preventing CHD in blacks.

Randomized trials of cholesterol-lowering treatment with statins have shown significant reductions in the risk of myocardial infarction, death, the need for coronary revascularization, stroke, coronary heart disease (CHD) mortality and all-cause mortality (1). The effect on major CHD events is proportional to the absolute reduction in LDL-cholesterol achieved, and does not vary by important participant characteristics such as sex, previous history of CHD, treatment for hypertension, blood pressure, history of diabetes, blood pressure or level of baseline lipids (1). However, the effects of cholesterol-lowering treatment by race/ethnicity have not been examined, either in single trials or in meta-analyses.

The Antihypertensive and Lipid Lowering to Prevent Heart Attack Trial (ALLHAT) included a Lipid Lowering Trial (LLT) designed to evaluate the impact of treatment with an HMG CoA-reductase inhibitor (pravastatin) on all-cause mortality (primary endpoint) in a hypertensive cohort with other CHD risk factors. CHD was a prespecified secondary endpoint. A substantial proportion of the participants was Black (38%), a group that has been underrepresented in previous studies. The intervention group received pravastatin and the comparison group received usual care from their personal physicians, rather than a placebo. We have previously reported (2) that ALLHAT-LLT did not show a significant reduction in either cardiovascular events or mortality, in contrast to other large statin trials. One potential explanation for these findings was diminished power and a smaller than expected reduction in cholesterol resulting from treatment crossovers. In particular, a large proportion of participants in the usual care group (nearly 20% at Year 4) began lipid lowering therapy.

However, these analyses suggested a significant ($p=0.03$) race-treatment group interaction for CHD in the ALLHAT-LLT (2). Blacks had a significant 27% lower risk of CHD events in the pravastatin group, while non-Black subjects had no benefit from pravastatin (Figure 1). Since previous analyses did not adjust for potential confounders of the relationship between race and treatment effects, in this paper, we explore whether the apparent racial differences in CHD incidence in ALLHAT are explained by differences in baseline risk factors, adherence during the trial, or achieved blood pressure and lipid lowering.

Methods

The ALLHAT-LLT was a randomized and non-blinded large simple trial with participants assigned to either open-label pravastatin (40 mg/day) or usual care (UC) (2,3). ALLHAT was funded by the National Heart, Lung, and Blood Institute, with study medications supplied by Pfizer, Inc. (amlodipine and doxazosin), AstraZeneca (atenolol and lisinopril) and Bristol-Myers Squibb (pravastatin) and additional financial support provided by Pfizer, Inc.. The authors are solely responsible for the design and conduct of this study, all study analyses, the drafting and editing of the paper and its final contents.

Total cholesterol (TC) was measured at baseline and at the 2, 4, and 6-year annual visits. A fasting lipid profile was obtained at baseline in all participants and in a randomly selected 5% sample of UC and in a 10% sample of pravastatin participants. The primary outcome for the LLT was all-cause mortality. CHD defined as a composite of fatal CHD or nonfatal MI was a pre-specified secondary outcome.

Baseline characteristics were compared using analysis of variance for continuous variables and contingency table analyses for categorical data. Data were analyzed according to participants'

randomized treatment assignments (i.e. intention-to-treat analysis). Six-year cumulative event rates were calculated using the Kaplan-Meier procedure (4). Cox proportional hazards models were used to obtain hazard ratios and 95% confidence intervals for time-to-event outcomes and included the participant's entire trial experience. The proportional hazards assumption was examined by using log-log plots and testing a treatment by time interaction term (4), and was not violated for the outcomes considered here. To adjust for BP and cholesterol differences over time between treatment groups, Cox proportional hazards models with systolic BP, diastolic BP and total cholesterol values as time-varying covariates were used (5). Stata version 10 (Stata Corp, College Station, Tex) was used for all analyses.

Results

Baseline Characteristics

The baseline characteristics of the 10,355 ALLHAT-LLT participants, by treatment group and race, are shown in Table I. Overall, the mean age was 66 years, nearly half of the participants were women, and 38% were Black. About 10% of the Black participants had Hispanic ethnicity, and about 31% of non-Blacks were Hispanic. In both Blacks and non-Blacks, baseline characteristics in the pravastatin and UC groups were similar. Comparisons across the four non-randomized groups formed by race and treatment were generally significant due to differences between Black and non-Black participants. The following are the only comparisons with $p > 0.05$: baseline antihypertensive drug use, smoking, systolic blood pressure, total cholesterol both for participants with and without CHD at baseline, and treatment assignment in the ALLHAT antihypertensive trial. Compared to non-Black participants, Black participants were more likely to be female, were slightly younger and had fewer years of education. They were less likely to be treated with estrogen or aspirin, less likely to have a previous history of CHD, more likely to have diabetes, and had higher BMI. Blacks also had higher fasting glucose, higher HDL and lower TG levels.

Visit and Medication Adherence

More than 85% of expected study visits were attended by Black and non-Black participants in both the pravastatin and UC groups at all follow-up time points. In the pravastatin group, similarly high proportions of Blacks and non-Blacks reported taking statins throughout the study period, falling from 88%–89% in year 2 to 82%–84% in follow-up year 6 (Figure 2). Use of non-study statins and other lipid lowering drugs was low. Both Black and non-Black participants in the UC group were increasingly likely to be treated with statins as follow-up progressed (at Years 2, 4 and 6, respectively, 6, 12, and 20% of Blacks versus 9, 20, and 31% of non-Blacks).

Lipid Levels

Changes in total and LDL cholesterol levels for Blacks and non-Blacks during the trial are shown in Figure 3. At baseline, the total cholesterol levels of Blacks and non-Blacks were similar (approximately 223–224 mg/dl), but the LDL level in Blacks was about 3 mg/dl higher than in non-Blacks (147 mg/dl vs. 144 mg/dl). After 2 years of follow-up, the total cholesterol level in Blacks in the pravastatin group had decreased by 34 mg/dl, while in non-Blacks it had decreased by 35 mg/dl. In the UC group, total cholesterol level had declined by about 9 mg/dl in Blacks and 10 mg/dl in non-Blacks. The resultant absolute difference in the percentage change from baseline in total cholesterol between the pravastatin and UC group was thus just over 11% for both Blacks and non-Blacks at year 2 (Figure 3a). At year 4, total cholesterol levels continued to decline in all groups, with the total cholesterol differences between the pravastatin and UC group narrowing slightly to about 10%. By year 6, the total cholesterol lowering in the pravastatin group was 44 mg/dl for Blacks and 47 mg/dl for non-Blacks, while in the UC group it was 22 mg/dl for Blacks and 29 mg/dl for non-Blacks. As a result of the

disproportionately greater cholesterol lowering in the non-Blacks in the UC group, at 6 years the total cholesterol difference between the pravastatin and UC groups was 10% for Blacks and 8% for non-Blacks (Figure 3a).

The absolute differences from baseline in LDL in the pravastatin group were 32 mg/dl at year 2 to 42 mg/dl at year 6 in Blacks and 36 mg/dl in year 2 to 49 mg/dl at year 6 in non-Blacks. By Year 6 Blacks in the UC group had dropped their LDL cholesterol by 20 mg/dl, compared to 28 mg/dl in non-Blacks. The difference in the percentage change from baseline in LDL cholesterol between the pravastatin and UC group was 15% for Blacks and 17% for non-Blacks at year 2 and 4, and 14% in both Blacks and non-Blacks at Year 6 (Figure 3b).

Mean HDL cholesterol levels at baseline were about 52 mg/dl among Blacks and about 45 mg/dl among non-Blacks. In both Blacks and non-Blacks HDL rose by about 1–2 mg/dl and the changes were similar in both the pravastatin and UC groups. TG at baseline were about 124 mg/dl among Blacks and about 167 mg/dl among non-Blacks. There was no clear pattern of change by race or treatment group (data not shown).

Blood Pressure Levels

Although systolic blood pressure (SBP) was the same (145 mm Hg) at baseline in Blacks and non-Blacks, diastolic blood pressure (DBP) was about 1 mm Hg higher in Blacks (85 mm Hg) compared to non-Blacks (84 mm Hg). As in the ALLHAT antihypertensive trial overall population (6), compared to non-Blacks, Blacks had consistently about 3 mm Hg higher SBP and 2 mm Hg higher DBP throughout the lipid-lowering trial. In non-Blacks, SBP declined equally in the pravastatin and UC groups to 133 mm Hg. DBP in non-Blacks was also similar at all points, with the exception of year 6, at which point the UC group DBP was about 1 mm Hg higher than in the pravastatin group (74 mm Hg vs. 73 mm Hg). In contrast, in Blacks SBP was 2–3 mm Hg higher in the pravastatin group compared to the UC group at year 2 and year 4, although by year 6 SBP was similar (137 mm Hg). In Blacks, DBP differences between the treatment groups were <1 mm Hg at all time points, (77 mm Hg at year 6).

Multivariable modeling of CHD incidence

We examined multivariable models for CHD incidence adjusting for age, race, sex, aspirin use, previous history of CHD, history of diabetes, treatment for hypertension at baseline, baseline systolic and diastolic blood pressure, baseline total cholesterol and HDL cholesterol, antihypertensive treatment group assignment and lipid treatment group assignment. All of these variables were significant predictors of CHD except race, aspirin use, lipid treatment group and antihypertensive treatment group (last two columns of Table II). We additionally examined all 2-way interactions and biologically plausible 3-way interactions; none was significant except for the interaction between race and intervention group ($p=0.02$). Therefore we examined models stratified by Black vs. non-Black race. In both Blacks and non-Blacks, age, male sex, a previous history of CHD, diabetes, and baseline blood pressure were predictors of CHD (Table II). However, only in Blacks was randomization to the pravastatin treatment arm associated with a lower risk of CHD (HR = 0.71, 95% CI 0.57 – 0.90, $p = 0.005$). Because there was substantial missing data on fasting TG, including it in the multivariable model would have excluded nearly 1500 participants. Therefore, we conducted analyses including in the model both fasting and non-fasting baseline TG measurements. TG level was not a significant predictor of CHD, and the results were otherwise nearly identical.

We next examined stratified models that adjusted for changes in total cholesterol, systolic blood pressure and diastolic blood pressure during follow-up. In Blacks randomization to the pravastatin treatment arm remained associated with a lower risk of CHD (HR 0.65, 95% CI 0.45 – 0.96, $p = 0.03$). In these models the other covariates had generally similar associations

with CHD as in the models not adjusted for on-trial blood pressure and cholesterol changes (data not shown).

Discussion

Our results show that Black ALLHAT-LLT participants randomized to a lipid-lowering intervention with pravastatin had a statistically significant 27% lower risk of incident CHD events compared to UC. These results differed from the results in non-Black participants. We have shown that these findings are not due to confounding from other measured CHD risk factors. Adjustments for cholesterol measurements and blood pressure during follow-up also did not affect our results, suggesting that they were not primarily caused by the small treatment-associated differences in cholesterol lowering and blood pressure between Black and non-Black sub-groups, or by fewer Black participants in the UC group starting open-label statins.

Unlike most other statin trials, ALLHAT-LLT did not show a significant lowering of CHD, stroke or total mortality. This has been attributed to the modest difference in cholesterol lowering between the intervention and UC groups (10%), which was less than half of the average for other long-term statin trials (1,2). In other primary and secondary prevention trials that used pravastatin, LDL-cholesterol was generally lowered by 20%–30% in the active treatment group compared to placebo (7–10). These trials each found a 20% to 30% relative reduction in the risk of the composite endpoint of fatal CHD and non-fatal MI, and some also found a reduction in CVD death (7) and total mortality (9). Thus ALLHAT-LLT lacked the power to demonstrate the expected reductions in CHD and mortality. We did not find any non-race subgroups that differed from the overall results, which is also consistent with the results of other trials (1). However, most other statin trials have enrolled few Blacks and did not have had sufficient power to examine treatment effects in race subgroups. In the Justification for the Use of Statins in Prevention: an Intervention Trial Evaluating Rosuvastatin (JUPITER) study, which had 2224 Black participants, there was no difference in the primary endpoint comparing non-Hispanic white to all other participants, but results specifically in the Black participants have not been published (11). Thus our findings cannot be corroborated by the large and otherwise diverse population of subjects in previous studies.

Previous studies have not shown differences in the pharmacokinetic and cholesterol lowering response to statins between Blacks and Whites (12–14). Recently, the genetic ancillary study to ALLHAT (GenHAT) investigated the interaction of pravastatin treatment with a polymorphism in genes regulating homocysteine metabolism, methylenetetrahydrofolate reductase (MTHFR) and cystathionine-beta-synthetase (CBS), on CHD outcomes (15). The CC variant for the MTHFR 677 C>T genotype was found in 77% of Black ALLHAT-LLT participants, but only in 43% of non-Black participants. Participants with the CC variant had a significant protective effect of pravastatin against CHD (HR 0.71, 95% CI 0.58–0.87). Participants with the CT variant (HR 1.25, 95% CI 0.97–1.61) and TT variant (HR 0.80, 95% CI 0.50–1.28) did not have statistically significant protective effects of pravastatin against CHD (interaction hazard ratio $p=0.004$). The CBS 844ins68 I+ variant, was found in 44% Black but only 16% non-Black participants. The II and ID genotypes were associated with significantly reduced risk of CHD in those treated with pravastatin (HR 0.58, 95% CI 0.44–0.78) whereas the DD genotype showed no effect of statin therapy (1.01; 0.84–1.20); p for gene-treatment interaction 0.002. A higher prevalence in Blacks of the CC variant of the MTHFR 667 C>T and CBS 844ins68 I+ genotypes was also seen in the CARDIA study (16). Although these genotypes have not been consistently associated with homocysteine levels and CHD risk in previous studies (17–21), and the mechanism of greater protection from CHD with pravastatin in ALLHAT participants with these genotypes remains to be investigated, these intriguing findings offer an avenue for further pharmacogenetic exploration of the race-treatment interaction we observed.

There are some limitations to the interpretation of these results that deserve mention. First, we examined a large number of interactions, and it is possible that chance could explain our findings. Furthermore, only a small subsample of ALLHAT-LLT participants had LDL-cholesterol measurements; therefore we were not able to do time-dependent analyses using LDL-cholesterol as a covariate.

In the context of the modest cholesterol differences between treatment groups observed in ALLHAT-LLT, the results are consistent with evidence from other large trials that statins prevent CHD. ALLHAT-LLT enrolled the largest number of Blacks in any lipid lowering trial. We conclude that statins are effective for prevention of CHD in Blacks. Although the proportion of Blacks who are being treated for hypercholesterolemia according to current guidelines is improving, racial disparities in treatment and cholesterol lowering remain (22–24). These findings from the ALLHAT-LLT and GenHAT lend further support for the need to intensify efforts to eliminate these disparities.

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Figure 1.

CHD Event Rate by Race and Lipid Treatment Group

Blacks in the pravastatin group (black line) had a significantly lower risk of CHD events compared to non-Black subjects in the pravastatin group (blue line) and both Blacks (green line) and non-Blacks (red line) in the usual care group.

Abbreviations: CHD = coronary heart disease

Figure 2.

Percent on Statin by Race and Lipid Treatment Group

In the pravastatin group, high proportions of Blacks and non-Blacks reported taking statins throughout the study period. In the usual care group, statin use increased progressively, but increased more in non-Blacks than in Blacks.

Figure 3.**Figure 3A. Total Cholesterol by Race and Lipid Treatment Group**

Total cholesterol declined about 11% more in the pravastatin group compared to the usual care group for both Blacks and non-Blacks at year 2. At year 4, total cholesterol levels continued to decline in all groups, with the total cholesterol differences between the pravastatin and usual care group narrowing slightly to about 10%. By year 6, as a result of greater cholesterol lowering in the non-Blacks in the usual care group, the total cholesterol difference between the pravastatin and usual care groups was 10% for Blacks and 8% for non-Blacks.

Figure 3B. LDL Cholesterol by Race and Lipid Treatment Group

The difference in the percentage change from baseline in LDL cholesterol between the pravastatin and usual care group was 15% for Blacks and 17% for non-Blacks at year 2 and 4, and 14% in both Blacks and non-Blacks at Year 6.

Figure 4.

Table I

Baseline Characteristics of ALLHAT-LLT Participants by Treatment Group *

Characteristic	Blacks		Non-Blacks	
	Pravastatin N = 1991	Usual Care N = 1920	Pravastatin N = 3179	Usual Care N = 3265
Demographics				
Age				
Mean (SD), y	66.0 (7.8)	65.8 (7.6)	66.7 (7.6)	66.7 (7.5)
N (%)				
55 – 64, y	948 (47.6)	933 (48.6)	1363 (42.9)	1404 (43.0)
≥ 65, y	1043 (52.4)	987 (51.4)	1816 (57.1)	1861 (57.0)
Women, N (%)	1102 (55.4)	1049 (54.6)	1409 (44.3)	1491 (45.7)
Race, N (%)				
White, non-Hispanic			2107 (66.3)	2129 (65.2)
Black, non-Hispanic	1769 (88.9)	1722 (89.7)		
White, Hispanic			759 (23.9)	803 (24.6)
Black, Hispanic	210 (10.6)	181 (9.4)		
Other	12 (0.6)	17 (0.9)	313 (9.9)	333 (10.2)
Years of education, Mean (SD) †	10.0 (3.8)	10.0 (3.9)	11.2 (4.2)	11.2 (4.1)
Medication use, N (%)				
Women on estrogen	108 (9.8)	110 (10.5)	282 (20.0)	289 (19.4)
Aspirin use	439 (22.1)	443 (23.1)	1127 (35.5)	1194 (36.6)
Antihypertensive medication	1803 (90.6)	1739 (90.6)	2838 (89.3)	2924 (89.6)
On 1–2 drugs for ≥ 2 months	1723 (86.6)	1668 (86.9)	2731 (85.9)	2809 (86.0)
On drugs < 2 months	80 (4.0)	71 (3.7)	107 (3.4)	115 (3.5)
Current cigarette smoking, N (%) †	409 (26.0)	383 (25.2)	652 (24.1)	694 (25.0)
History of CHD, N (%)	195 (9.8)	216 (11.3)	500 (15.7)	564 (17.3)
Type 2 diabetes present, N (%)	776 (39.0)	741 (38.6)	1079 (33.9)	1042 (31.9)
BMI, kg/m ² , Mean (SD)	30.6 (6.3)	30.7 (6.6)	29.4 (5.6)	29.5 (5.8)
BP, mm Hg, Mean (SD)				
Visit 1 SBP/DBP	145 (14.2)/85 (9.9)	145 (14.5)/84 (10.1)	145 (13.6)/84 (9.7)	145 (13.7)/84 (9.7)
Fasting glucose, mg/dL, Mean (SD) †	125.5 (60.8)	124.9 (59.8)	120.4 (52.5)	120.5 (54.2)
Lipid Values, Mean (SD) † ‡				
With CHD at baseline				
Total cholesterol, mg/dL	207.4 (27.6)	206.5 (27.3)	204.3 (27.7)	204.2 (26.6)
LDL-cholesterol, mg/dL	131.9 (23.4)	131.4 (22.6)	128.2 (20.5)	127.5 (20.6)
HDL-cholesterol, mg/dL	50.2 (13.6)	50.3 (13.8)	43.3 (13.3)	42.8 (11.6)
Fasting triglycerides, mg/dL	118.9 (55.1)	116.9 (51.3)	164.6 (77.2)	165.8 (72.7)
Lipid Values, Mean (SD) ‡				
Without CHD at baseline				
Total cholesterol, mg/dL	226.4 (25.6)	227.0 (25.2)	226.7 (25.7)	227.2 (25.3)
LDL-cholesterol, mg/dL	148.9 (20.2)	149.3 (20.1)	147.6 (20.2)	147.9 (19.7)
HDL-cholesterol, mg/dL	51.6 (14.1)	51.7 (14.8)	45.5 (12.2)	45.4 (12.3)

Characteristic	Blacks		Non-Blacks	
	Pravastatin N = 1991	Usual Care N = 1920	Pravastatin N = 3179	Usual Care N = 3265
Fasting triglycerides, mg/dL	123.6 (57.8)	125.8 (59.4)	166.3 (71.2)	167.6 (76.1)
Antihypertensive randomization [§]				
Chlorthalidone, N (%)	712 (35.8)	692 (36.0)	1160 (36.5)	1191 (36.5)
Amlodipine, N (%)	439 (22.1)	412 (21.5)	683 (21.5)	706 (21.6)
Lisinopril, N (%)	412 (20.7)	396 (20.6)	682 (21.5)	677 (20.7)
Doxazosin, N (%)	428 (21.5)	420 (21.9)	654 (20.6)	691 (21.2)

Abbreviations: ALLHAT-LLT = Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial, LLT = Lipid-Lowering Trial; BMI = body mass index, CHD = coronary heart disease, HDL = high density lipoproteins, LDL = low density lipoproteins, SBP and DBP = systolic and diastolic blood pressure respectively and SD = standard deviation.

* Most comparisons across the 4 groups formed by race and treatment are significant due to difference between Black and non-Black participants. The following are the only comparisons with $p > 0.05$: antihypertensive medicate use, smoking, baseline antihypertensive drug use, antihypertensive randomization, SBP, serum cholesterol with or without evidence of CHD and LDL < 130 with no evidence of CHD.

[†] There is incomplete data for years of education (data missing on 524), cigarette smoking (1783), fasting glucose (2284), lipids with history of CHD (13) and lipids without history of CHD (69).

[‡] For total cholesterol, LDL and HDL mg/dL $0.0259 = \text{mmol/L}$. For triglycerides mg/dL $\times 0.0113 = \text{mmol/L}$. The LDL-cholesterol values were calculated using the Friedewald formula.

[§] The antihypertensive trial randomization for chlorthalidone, amlodipine, lisinopril and doxazosin was in a ratio of 1.7:1:1:1.

Main effects models for CHD

Table II

	Blacks			Non-Blacks			Overall		
	Hazard Ratio	95% CI	p-value	Hazard Ratio	95% CI	p-value	Hazard Ratio	95% CI	p-value
Age, 10 years	1.39	1.19 – 1.63	<0.001	1.51	1.34 – 1.71	<0.001	1.46	1.33 – 1.61	<0.001
Sex (M/F) *	1.44	1.12 – 1.85	0.005	1.60	1.31 – 1.96	<0.001	1.54	1.31 – 1.80	<0.001
Aspirin use (Y/N) *	1.10	0.84 – 1.44	0.475	1.18	0.98 – 1.41	0.078	1.15	0.99 – 1.34	0.061
Previous CHD (Y/N) *	2.07	1.51 – 2.85	<0.001	1.49	1.19 – 1.85	<0.001	1.64	1.37 – 1.97	<0.001
History of diabetes (Y/N) *	1.39	1.10 – 1.77	0.006	1.25	1.04 – 1.49	0.018	1.30	1.13 – 1.50	<0.001
Baseline hypertension treatment (Y/N) *	1.32	0.81 – 2.15	0.266	1.41	1.02 – 1.97	0.041	1.37	1.04 – 1.80	0.024
Baseline SBP, 10 mm Hg	1.12	1.02 – 1.23	0.020	1.13	1.05 – 1.22	0.001	1.13	1.00 – 1.27	<0.001
Baseline DBP, 10 mm Hg	0.79	0.69 – 0.90	<0.001	0.91	0.82 – 1.01	0.066	0.86	0.80 – 0.94	<0.001
Baseline total cholesterol, 10 mg/dL	1.05	1.00 – 1.10	0.059	1.04	1.00 – 1.07	0.043	1.04	1.01 – 1.07	0.007
Baseline HDL, 10 mg/dL Antihypertensive treatment group *	0.91	0.82 – 1.00	0.044	0.93	0.86 – 1.01	0.086	0.92	0.87 – 0.98	0.012
Doxazosin (Y/N)	1.15	0.84 – 1.59	0.378	0.94	0.74 – 1.20	0.629	1.01	0.83 – 1.22	0.916
Amlodipine (Y/N)	1.19	0.87 – 1.65	0.279	1.11	0.88 – 1.39	0.381	1.13	0.94 – 1.36	0.195
Lisinopril (Y/N)	1.30	0.95 – 1.79	0.107	0.92	0.72 – 1.17	0.514	1.04	0.86 – 1.26	0.702
Lipid treatment group (P/UC) *	0.71	0.57 – 0.90	0.005	1.00	0.85 – 1.19	0.955	0.89	0.77 – 1.02	0.092
Race (Black/non-Black)							1.03	0.88 – 1.20	0.700

Abbreviations: CHD = coronary heart disease, CI = confidence interval, DBP = diastolic blood pressure, HDL = high density lipoproteins, SBP = systolic blood pressure

* Sex: Male(1)/Female(0); Yes/No: Yes(1)/No(0); Lipid treatment: Pravastatin(1)/Usual Care(0); Antihypertensive treatment: Chlorthalidone is the comparator group (i.e. treated with Chlorthalidone if not treated by any of the other 3 drugs)