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Influence of Metabolic Syndrome and Race on the Relationship between Intensive Blood Pressure Control and Cardiovascular Outcomes in the SPRINT Cohort

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Abstract

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Aims—To determine whether baseline metabolic syndrome (MetS) modifies the effect of intensive blood pressure control on cardiovascular (CV) outcomes, and whether effects varied by race/ethnicity.

Materials and Methods—We performed post-hoc analyses among Non-Hispanic Black (NHB), Non-Hispanic White (NHW), and Hispanic participants with and without MetS in the Systolic Blood Pressure Intervention Trial (SPRINT) randomized to a systolic blood pressure (SBP) target of less than 120 mm Hg (intensive group, N=4544) or one less than 140 mm Hg (standard group, N=4553). Median follow-up was 3.26 years. The primary outcome was the composite of the first occurrence of myocardial infarction (MI), stroke, heart failure, non-MI acute coronary syndrome, or (CV) death.

Results—Overall, 3521/9097 (38.7%) of subjects met criteria for MetS at baseline. Baseline characteristics were similar between SBP groups within each MetS subgroup except BMI was slightly higher in the Standard arm of the MetS subgroup (33.3+/-5.6 vs. 33.0+/-5.3, $p<0.01$) but similar across treatment arms in the non-MetS subgroup. The hazard ratio (HR) for the primary outcome was similarly reduced in subjects with or without baseline MetS (0.75 [95% CI 0.57, 0.96] and 0.71 [0.57, 0.87] respectively, adjusted p -value for treatment by subgroup interaction = 0.98). Similarly, there was no evidence of treatment by MetS subgroup interaction for all-cause mortality (adjusted interaction p value = 0.98). The findings were also similar across race/ethnic subgroups.

Conclusions—In this analysis the CV benefit of intensive SBP control did not differ among subjects by baseline MetS status, regardless of race/ethnicity.

Introduction

Hypertension is a well-established independent risk factor for cardiovascular disease (CVD). However, it is not clear how to individualize targets to maximize benefits among subgroups of patients with differing risk factors. It is well-recognized that the cluster of risk factors encompassing metabolic syndrome (MetS) is a strong early predictor of both type 2 diabetes^{1,2} and CVD²⁻⁶. In particular, racial differences in MetS components, including hypertension, obesity, dysglycemia, and dyslipidemia have been well documented,⁷⁻⁹ and contribute to disparities in CVD outcomes¹⁰⁻¹².

Recently, the Systolic Blood Pressure Intervention Trial (SPRINT) was conducted among a multiethnic/multiracial cohort of 9361 participants without diabetes randomized to Intensive (<120 mm Hg) or Standard (<140 mmHg) systolic blood pressure (SBP) control¹³. The study was terminated early after demonstrating a 25% reduction in the primary composite outcome (myocardial infarction, acute coronary syndrome, stroke, heart failure, or CV death) and a 27% reduction in all-cause mortality in the Intensive compared to the Standard group. The study population included 30% non-Hispanic Blacks and 11% Hispanics¹⁴⁻¹⁵. The initial analysis did not identify significant racial (Black vs. non-Black) differences in benefit of intensive SBP control on the primary CVD outcome in a pre-specified subgroup analysis. However, the influence of metabolic status on the CVD outcomes was not addressed.

The possibility that treatment heterogeneity may exist among patients with varying metabolic manifestations was suggested by findings from the Action to Control Cardiovascular Risk in Diabetes (ACCORD) study. Though only half the size of SPRINT, ACCORD reported no significant benefit in a similar SBP comparison in participants with well-established type 2 diabetes and a higher rate of serious adverse events attributed to the intervention¹⁶. A recent Cochrane meta-analysis concluded that there was insufficient evidence to recommend more intensive blood pressure management compared to standard control in patients with diabetes, although this was based heavily on the ACCORD study findings¹⁷. The objective of this analysis is to determine whether baseline MetS is associated with the response to intensive blood pressure control and to determine whether the response differs among the racial and ethnic populations in the SPRINT cohort.

Materials and Methods

Population

SPRINT enrolled 9,361 non-diabetic participants at high CVD risk, age ≥ 50 years, at 102 clinical centers. Extensive descriptions of the study rationale, design, procedures, and biochemical assays have been published previously^{13, 18-20}. The median follow-up period was 3.26 years.

Patients were randomly assigned to a SBP target <120 mmHg vs. SBP <140 mmHg. CVD risk was based upon a history of clinical or subclinical CVD, chronic kidney disease (4 variable MDRD eGFR 20-59 ml/min/1.73m²), 10 year Framingham risk score $\geq 15\%$ or age ≥ 75 years. Exclusion criteria included diabetes mellitus, history of stroke, symptomatic heart failure or reduced ejection fraction, dementia, expected survival less than 3 years, unintentional weight loss, evidence of orthostasis, or residing in a nursing facility. The trial protocol was approved by the institutional review board at each participating center and all participants provided written informed consent. Race was self-reported by participants as black (or African American), white, Native American, Asian, Native Hawaiian or other Pacific Islander, and other. Ethnicity was based upon independent self-identification as Hispanic or non-Hispanic. In this report, participants who self-identified as Hispanic were considered part of that group (regardless of self-identified race). Non-Hispanic participants who self-identified as African American alone were grouped as non-Hispanic Black (NHB). Non-Hispanic participants who self-identified as white alone were grouped as non-Hispanic White (NHW). Participants who self-identified as belonging to other race categories, selected more than one race category, or did not specify a race were excluded from this analysis.

Blood Pressure Measurement

At each visit, trained clinical staff measured blood pressures with an automated device (Omron-HEM-907 XL) using standardized procedures^{19,20}. Staff were instructed to program the device for the 5-minute rest period and three seated measurements were then to be taken at 1 minute intervals. The Manual of Operations specified that participants should be resting, not completing questionnaires, and not speaking with study staff during the 5-minute period, and that staff should not be present in the room for the rest period. A script was provided

that staff could use to explain that they would be absent during the 5-minute rest period and would then reenter the room and obtain the measurements without speaking to the participant^{13, 19-20}.

Study Measures

Demographic data were collected at baseline while clinical and laboratory data were collected at baseline and every 3 months.

MetS was defined using the National Cholesterol Education Program (NCEP) Adult Treatment Panel (ATP) III criteria²¹. The exception was that BMI was substituted for waist circumference, which was not measured in SPRINT. BMI is a component of MetS in other accepted classification systems^{22,23}. Thus the criteria include BMI ≥ 30 kg/m², HDL-C <50 mg/dl for women and <40 mg/dl for men, triglycerides ≥ 150 mg/dl, SBP ≥ 130 mm Hg or DBP ≥ 85 mm Hg, and fasting glucose ≥ 100 mg/dl. Since all participants met the BP criteria for MetS, subjects were considered to have MetS in the presence of 2 or more other components.

Body mass index (BMI) was calculated as body weight (kg) divided by height (m)². Glomerular Filtration Rate (GFR): race-adjusted eGFR was calculated using Modification of Diet in Renal Disease (MDRD) formula^{24,25}. The eGFR was categorized as ≥ 60 ml/min/(1.73m²).

Statistical Analyses

Descriptive statistics (means and standard deviations [SD] for continuous variables; frequencies and percentages for categorical variables) of baseline characteristics were computed by treatment arm within baseline MetS status (Table 1), and by treatment arm within race/ethnicity (Table 2). Statistical differences between MetS groups were compared using t-tests and chi-square tests. Differences between subgroups were assessed using one-way ANOVA and chi-square tests. Post-treatment SBP was estimated across the entire follow-up period from 6 through 48 months using a general linear model with random effects to account for within-subject correlation.

Effect of treatment arm assignment on time to the first event within MetS stratum (i.e., primary CVD outcome, mortality, and primary outcome or death) was analyzed based on the intention-to-treat approach using Cox proportional-hazards regression models with two-sided tests at the 5% level of significance and stratification by clinical site. Two-way interactions between treatment effect and MetS group were assessed using likelihood-ratio tests and Hommel's technique to adjust for multiple comparisons (26). Analysis of time-to-event outcomes by race/ethnicity within baseline MetS groups was performed in an analogous manner. Additional Cox models were fitted including age, gender and baseline eGFR as covariates. Appropriateness of the proportional hazards assumption was evaluated graphically by examining martingale residuals and Kolmogorov-type supremum tests²⁷. If warranted, a Heaviside function was employed to adjust estimates for non-proportionality²⁸. Product-limit survival estimates were used to make cumulative hazards plots for the primary CVD outcome and all-cause mortality by MetS status. All analyses were performed using SAS[®] version 9.4 software (SAS Institute, Inc., Cary, NC).

Results

Baseline Characteristics by MetS Status

Our study population included 2802 Non-Hispanic Blacks (NHB, 30%), 984 Hispanics (11%), and 5399 Non-Hispanic Whites (NHW, 58%). One hundred seventy-six (2%) participants reported being of other races and were excluded from further analysis in this report. Additionally, 88 participants with incomplete covariates could not have baseline MetS status determined and were excluded, leaving 9097 total. Overall, 3521/9097 (38.7%) of subjects met criteria for MetS at baseline, with similar proportions in the Intensive (38.2%) and Standard (39.2%) groups. BMI was slightly higher in the standard SBP arm compared to the Intensive arm in the MetS subgroup (33.3 ± 5.6 vs. 33.0 ± 5.3 , $p < 0.01$) but not in the non-MetS subgroup (Table 1). Baseline characteristics otherwise were similar between Intensive and Standard SBP control groups within each MetS subgroup. Differences between subjects with or without MetS are shown in Supplemental Table S1. In both treatment groups, participants with MetS were significantly younger, more likely to self-identify as Hispanic, and less likely to self-identify as NHB. Although all SPRINT participants met the blood pressure criterion for MetS, by definition, baseline SBP was significantly lower and diastolic blood pressure (DBP) was significantly higher in the MetS groups of both study arms. Subjects with MetS in both study arms were also prescribed a greater number of antihypertensive agents at baseline compared to those without MetS. There were significant differences in all non-BP MetS components across MetS subgroups, (Supplemental Table S1).

Baseline Characteristics Among Subjects within MetS Subgroups, by Race/ethnicity

Participants with MetS were further stratified by treatment arm within each race/ethnicity group (Supplemental Table S2). The Intensive group consisted of 28.5% NHB, 58.3% NHW, and 13.2% Hispanic, compared to 26.7%, 61.5%, and 11.8% in the Standard group respectively. In the NHW subgroup, the SBP was slightly higher in the Intensive group compared to the Standard treatment group at baseline (139.2 ± 15.8 vs. 137 ± 14.9 mmHg, $p < 0.01$). In the Hispanic group, the number of subjects with subclinical CVD was smaller in the Intensive group compared to the Standard group (11 [4.8%] vs. 23 [11%] respectively, $p < 0.05$).

There were significant differences across racial/ethnic groups in subjects with MetS at baseline, as expected (Supplemental Table S3). Notably, NHW were older, less likely to be female, and had lower DBP, lower renal function, more baseline clinical CVD, fewer never smokers, lower total cholesterol, and more statin use than NHB or Hispanics in both treatment groups. Likewise, among patients without MetS, there were baseline differences among race/ethnicity subgroups, including older age, lower frequency of females, lower renal function, more baseline clinical CVD, lower total cholesterol, higher fasting glucose, and more statin use in NHW compared to NHB or Hispanics in both treatment groups (Supplemental Table S4).

CV Events and Mortality

In subjects with MetS at baseline, the estimated mean SBP post 6 months of treatment was 121.7 (95% CI 121.4-122.1) mmHg in the Intensive group vs. 135.9 (95% CI 135.5-136.21) mmHg in the Standard group ($p<0.0001$). Similarly, in the non-MetS group, the estimated mean SBP post 6 months intervention was 119.7 (95% CI 119.3-120.1) mmHg in the Intensive group vs. 135.0 (95% CI 134.6-135.4) mmHg in the Standard group ($p<0.0001$). Table 2 shows univariable effects of Intensive versus Standard SBP treatment arm assignment and Cox proportional hazards models fitted to time to first CV event and mortality outcomes. Results are shown stratified by baseline MetS status. There were similar reductions in the hazard of the primary composite CV outcome in the Intensive compared to Standard arms in those with and without baseline MetS (0.75 [95% CI 0.57, 0.96] and 0.71 [0.57, 0.87], respectively; and for all-cause mortality (HR 0.74 [95%CI 0.53, 1.04] and 0.76 [95% CI 0.58, 0.99], in those with and without MetS, respectively; adjusted p-value for interaction 0.98 for both outcomes). In addition, the hazard for CV mortality as well as the primary CV outcome or death was reduced similarly in both MetS groups

In NHB, the estimated mean SBP post 6 months intervention was 121.3 (95% CI 120.9-121.8) mmHg in the Intensive group, and 135.9 (95% CI 135.5-136.4) in the Standard group ($p<0.001$). In NHW, the corresponding values were 121.1 (95% CI 120.8-121.4) mmHg and 135.4 (95% CI 135.0-135.7) ($p<0.001$), and in the Hispanic group, the corresponding values were 118.9 (95% CI 118.2-119.6) mmHg and 135.3 (95% CI 134.6-136.0) respectively ($p<0.001$). There were no significant differences in the response to intensive blood pressure treatment for the primary outcome according to MetS or racial/ethnic groups (Figure 1A). The nominal P-values for differences in the HR across racial/ethnic groups for all-cause mortality were marginally significant (Figure 1B). However, they did not remain significant after adjustment for multiple comparisons (Hommel adjusted P-value 0.47 in the MetS group and 0.36 in the no MetS group, respectively). Similar results were observed after adjusting models for baseline gender, eGFR, and age, as well as models adjusting for baseline differences in BMI, SBP, subclinical CVD, and smoking status (data not shown).

Figure 2 shows cumulative hazard plots for the primary CV outcome in participants with (2A) and without (2B) MetS at baseline. The figure for the group without MetS (2B) is indicative of a hazard ratio that changes after 2 years of follow-up (i.e., non-proportional hazards), which was confirmed by examining martingale residuals (p-value from supremum test for non-proportionality <0.0001). Similar patterns were observed for all-cause mortality, with separation of curves appearing to occur early in the MetS arm but not the non-MetS arm (Figure 2A-B). To account for non-proportionality in the group without MetS, models were refitted using a Heaviside function parameterization with distinct hazards up to and including two years versus after two years follow-up. For the primary composite CV outcome, the Intensive versus Standard arm hazard ratio was 0.99 (95% CI 0.75, 1.30) through two years and 0.41 (95% CI 0.29, 0.59) after two years. Similar results were observed in the group without MetS for all-cause mortality (HR and 95% CI 1.18 [0.80, 1.75] through two years; 0.52 [0.36, 0.76] after two years), and for primary CV outcome or death (HR and 95% CI 1.06 [0.83, 1.35] through two years; 0.48 [0.36, 0.64] after two

years). Adjustment for baseline covariates age, gender and eGFR did not materially alter these results.

Discussion

MetS is common among patients with hypertension and is a significant predictor of CV events as well as mortality. In this analysis, the beneficial effect of intensive SBP treatment on the primary CV outcomes, including mortality was similar in those with and without MetS, and did not differ between race/ethnicity subgroups. This finding extends the observations from the main SPRINT study, in which no significant treatment heterogeneity was observed among pre-specified baseline subgroups, including chronic kidney disease, age, gender, race, previous CV disease, or SBP¹³. A summary of key findings is presented in Table 3. In the subgroup without MetS at baseline there appears to be late separation (after two years follow-up) between Intensive and Standard SBP arms for both primary CV event and all-cause mortality. However, the treatment-specific event rates in the two MetS subgroups were similar over the entire course of follow-up.

The results provide insight regarding the efficacy of intensive blood pressure lowering efforts across the spectrum of metabolic disorders. In this case, intensive SBP intervention was associated with improved outcomes irrespective of the presence of baseline MetS, which is one of the earliest manifestations of future type 2 diabetes^{1,2}. By comparison, post-hoc analyses of UKPDS, which enrolled newly diagnosed patients with type 2 diabetes, suggested that more intensive blood pressure control was associated with reduced CV events (29) and indicated an additive effect of more intense (<130 mm Hg) vs. less intense SBP and glucose control³⁰. However, the target blood pressure was <150/80 mmHg in UKPDS and only 56% of subjects actually reached this target in the more intensive group. Nevertheless, the totality of evidence does not support the need for different blood pressure targets among patients with MetS or early type 2 diabetes. The later separation of cumulative hazards curves in subjects without MetS suggests that participants with MetS may benefit earlier from intensive SBP intervention than those without. However, this finding needs to be confirmed in other studies.

Finally, the ACCORD study, which was conducted among subjects with established diabetes, demonstrated nonsignificant reductions (other than a significant reduction in stroke risk) in CV outcomes with intensive BP control⁴. However, conclusions from the ACCORD trial are limited by a much lower event rate than expected and other design issues that could have missed a significant treatment effect. Thus, it has been argued that the results between SPRINT and ACCORD may be more similar than contradictory³¹, and this is demonstrated in post-hoc analyses³². Further study is needed to inform evidence-based comprehensive care practices as well as provide tailored future intervention strategies for the full spectrum of hypertensive patients.

Independent of treatment assignment, participants with MetS were younger, required more antihypertensive therapies at baseline, and had greater overall CV risk, in addition to known differences in actual MetS components. Marked racial/ethnic differences were observed in the distribution of components of MetS in this population, including a higher frequency of

obesity among NHB participants, and more frequent dyslipidemia and less frequent impaired fasting glucose among Hispanic participants, compared to other racial/ethnic groups respectively. This is in agreement with prior literature⁷⁻⁹. However, we also found that the effect of baseline MetS on the efficacy of intensive SBP control did not differ across categories of self-reported race/ethnicity. The findings are important in light of the differential clustering of CV risk factors among racial/ethnic subgroups in that studies which manipulate a single MetS component provide a unique opportunity for also understanding racial disparities in CVD outcomes³³. These findings are consistent with those from the Antihypertensive and Lipid Lowering Treatment to Prevent Heart Attack Trial (ALLHAT trial), in which MetS status did not significantly influence the response of various classes of antihypertensive agents on CV outcomes despite differing effects on metabolic parameters³⁴. Additional analyses of the effect of baseline race/ethnicity on the potential benefits of intensive blood pressure control are planned. Overall, the data do not support differential SBP targets based upon MetS status.

Notable strengths of SPRINT include a large sample size with diverse racial/ethnic backgrounds and geographic distribution. In addition, patients were selected for higher CV risk in order to ensure adequate power, and outcomes were prospectively adjudicated. There are a number of limitations that must also be considered. First, the diagnosis of diabetes for eligibility purposes was based upon clinical history and fasting glucose, not by more sensitive measures such as the oral glucose tolerance test. Moreover, we did not have formal measures of insulin sensitivity, or waist circumference which could have further elucidated the extent of metabolic derangements and underlying racial/ethnic differences. Regardless, it is possible that follow-up was too short for metabolic effect to manifest. In addition, there was comparatively less representation of Hispanic ethnicity compared to NHB or NHW and negligible representation from other backgrounds. Importantly, the results may not be generalizable to younger patients, patients with relatively low CV risk, and patients with extensive comorbidities. Thus additional study is needed in these groups. Finally, there are concerns that the blood pressure measurement technique used in SPRINT would result in systematically lower blood pressures than that obtained with typical clinical practice^{35, 36}. While this would potentially result in overtreatment if similar SBP targets are pursued in clinical practice, it is unlikely to obscure differences between those with and without MetS in their response to more intensive blood pressure lowering.

In conclusion, the effect of Intensive SBP control was associated with lower CVD rates compared to the Standard SBP control, and the results were consistent in non-diabetic individuals with and without MetS and regardless of race (Black vs. non-Black) or Hispanic ethnicity. Thus, the findings support intensive blood pressure control for patients with metabolic status intermediate between normoglycemia and diabetes, regardless of race or ethnicity.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1. Outcomes by race/ethnicity within MetS subgroups
 (A) Primary Outcome. (B) All-cause Mortality. *Nominal p-value for interaction

Figure 2. Outcomes by Metabolic Syndrome at Baseline

Cumulative hazards for the primary outcome (a composite of myocardial infarction, acute coronary syndrome, stroke, heart failure, or death from cardiovascular causes) in participants with MetS (A) and without MetS (B) at baseline. Cumulative hazards for death from any cause in participants with MetS (C) and without MetS (D) at baseline.

Table 1
Baseline Characteristics by Treatment Arm Within MetS Status

Characteristic	MetS (N=3521)		No MetS (5576)	
	Intensive (N=1737)	Standard (N=1784)	Intensive (N=2807)	Standard (N=2769)
Female, No. (%)	635 (36.6)	601 (33.7)	991 (35.3)	1003 (36.2)
Age, mean±SD, y	66±9	66±9	69±10	69±10
Senior subgroup (age ≥75), No. (%)	317 (18.3)	356 (20.0)	966 (34.4)	923 (33.3)
Race/Ethnicity [*] , No. (%)				
Non-Hispanic black	495 (28.5)	476 (26.7)	869 (31.0)	934 (33.7)
Non-Hispanic white	1013 (58.3)	1098 (61.6)	1667 (59.4)	1568 (56.6)
Hispanic	229 (13.2)	210 (11.8)	271 (10.0)	267 (9.6)
Blood pressure, mean±SD, mm Hg				
Systolic	139±15.8	138±15	140±16	141±16
Diastolic	80±11.7	79±12	77±12	78±12
Creatinine, mean±SD, mg/dL	1.07±0.33	1.08±0.33	1.08±0.35	1.08±0.34
eGFR, mean±SD, mL/min/1.73m ²	72±21	72±21	72±21	72±21
CKD subgroup (eGFR <60 mL/min/1.73 m ²), No. (%)	491 (28.3)	502 (28.1)	810 (28.9)	786 (28.4)
Clinical cardiovascular disease, No. (%)	268 (15.4)	299 (16.8)	457 (16.3)	408 (14.7)
Subclinical cardiovascular disease, No. (%)	135 (7.8)	138 (7.7)	240 (8.6)	246 (8.9)
Smoking history				
Current	236 (13.6)	222 (12.5)	391 (14.0)	367 (13.3)
Former	748 (43.1)	766 (43.0)	1189 (42.4)	1186 (42.9)
Never	753 (43.4)	793 (44.5)	1223 (43.6)	1214 (43.9)
Body mass index, mean±SD	33.3±5.6 [‡]	33.0±5.3	27.9±4.9	27.8±5.0
Total cholesterol, mean±SD, mg/dL	191±44	191±43	190±40	189±39
HDL cholesterol, mean±SD, mg/dL	45±11.7	44±11	58.7±14	58±14
Triglyceride, mean±SD, mg/dL	170±11.7	173±12.9	97±4.0	98±4.3
Fasting glucose, mean±SD, mg/dL	106±1.5	106±1.5	94±1.1	95±1.0
Number of antihypertensive agents (per patient), mean±SD	1.93±1.07	1.96±1.04	1.79±1.02	1.75±1.04
Statin use, No. (%)	752 (43.6)	816 (46.1)	1174 (42.0)	1213 (44.1)
Framingham 10-yr cardiovascular disease risk score, %, mean±SD	25.4±13.5	25.6±13.0	24.5±12.1	24.3±12.2
Metabolic Syndrome Components				
BMI ≥30 kg/m ²	1319 (76.2)	1323 (74.3)	640 (22.8)	617 (22.3)
HDL-c < 50 mg/dL (women) or < 40 mg/dL (men)	905 (52.1)	937 (52.5)	141 (5.0)	155 (5.6)
Triglycerides ≥150 mg/dL	931 (53.6)	963 (54.0)	183 (6.5)	203 (7.3)
Fasting glucose >100 mg/dL	1192 (68.6)	1227 (68.8)	551 (19.6)	559 (20.2)

^{*} 176 participants of other race/ethnicity excluded from analysis.

Test for difference between Intensive and Standard treatment groups (within MetS subgroups):

[†]P<0.05;

[‡]P<0.01.

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Table 2
Primary composite CV outcome and mortality by MetS status. Hazard ratios and tests of treatment×subgroup interaction from univariable proportional hazards models

Outcome	Subgroup	Intensive Arm			Standard Arm			Intensive vs. Standard Hazard Ratio				Trt × Subgroup Interaction	
		N	Num Events	% per Year	N	Num Events	% per Year	HR	Lower 95% CL	Upper 95% CL	P-value	Nominal P-value	Adjusted P-value *
Metabolic Syndrome (all PPTs)													
Primary Outcome	MetS at B/L	1737	105	1.86	1784	141	2.50	0.75	0.57	0.96	0.025	0.759	0.979
	NO MetS at B/L	2807	146	1.65	2769	205	2.34	0.71	0.57	0.87	0.001		
All Cause Mortality	MetS at B/L	1737	60	1.04	1784	80	1.37	0.74	0.53	1.04	0.087	0.910	0.979
	NO MetS at B/L	2807	98	1.07	2769	129	1.43	0.76	0.58	0.99	0.039		
CV Mortality	MetS at B/L	1737	18	0.31	1784	28	0.48	0.58	0.31	1.06	0.075	0.592	0.979
	NO MetS at B/L	2807	19	0.21	2769	39	0.43	0.49	0.28	0.84	0.009		
Primary Outcome or Death	MetS at B/L	1737	140	2.48	1784	184	3.25	0.77	0.61	0.96	0.021	0.979	0.979
	NO MetS at B/L	2807	210	2.36	2769	276	3.15	0.76	0.63	0.91	0.002		

* p-value adjusted for multiple comparisons

Table 3
Summary of Key Findings

- MetS was highly prevalent in the SPRINT study cohort (39% of the study population).
- The cardiovascular benefit of intensive blood pressure control was similar between patients with and without MetS.
- The CV mortality and all-cause mortality benefit of intensive blood pressure control was similar between patients with and without MetS.
- The effect of baseline MetS on the efficacy of intensive SBP control did not differ across categories of self-reported race/ethnicity.