Clinical Outcomes by Race and Ethnicity in the Systolic Blood Pressure Intervention Trial (SPRINT): A Randomized Clinical Trial

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BACKGROUND
The Systolic Blood Pressure Intervention Trial (SPRINT) showed that targeting a systolic blood pressure (SBP) of ≤ 120 mm Hg (intensive treatment) reduced cardiovascular disease (CVD) events compared to SBP of ≤ 140 mm Hg (standard treatment); however, it is unclear if this effect is similar in all racial/ethnic groups.

METHODS
We analyzed SPRINT data within non-Hispanic White (NHW), non-Hispanic Black (NHB), and Hispanic subgroups to address this question. High-risk nondiabetic hypertensive patients (N = 9,361; 30% NHB; 11% Hispanic) 50 years and older were randomly assigned to intensive or standard treatment. Primary outcome was a composite of the first...
Racial and ethnic differences in cardiovascular disease (CVD) remain a major public health challenge in the United States. Hypertension is one of the most important, modifiable CVD risk factors leading to coronary heart disease, stroke, end-stage renal disease, and overall mortality. Non-Hispanic Black (NHB) and Hispanic adults (compared to non-Hispanic Whites [NHWs]) have higher rates of uncontrolled blood pressure (BP) (50%, 54%, and 46%, respectively), and NHBs are at greater risk of hypertension-related CVD morbidity and mortality. CVD age-adjusted death rates are 33% higher among NHBs when compared to the overall US population. Hypertension-related age-adjusted mortality rates of adults aged 25 years and older are 127.2 vs. 135.9 per 100,000 populations for Hispanics vs. NHWs, respectively, though considerable heterogeneity in CVD risk is seen in Hispanics based on country of origin. These disparities cost the US health care system an estimated $49 billion per year. Therefore, BP control interventions to reduce CVD morbidity and mortality in underrepresented racial and ethnic groups are important at both the individual and population levels.

Over the past 2 decades, studies have demonstrated that lowering BP with antihypertensive medications reduces the risk of CVD morbidity and mortality, including in NHB and Hispanic populations. Until recently, there was insufficient data to determine optimal BP targets for the treatment of hypertension in these populations. Lowering systolic BP (SBP) with antihypertensive medications significantly reduced CVD morbidity and mortality in the Systolic Hypertension in Europe (Syst-Eur) Trial, and the Hypertension in the Very Elderly Program (SHEP), which included a racially diverse population (24% NHBs and 7% Hispanics) of 4,733 high-risk hypertensives with type 2 diabetes mellitus treated to a SBP target <120 mm Hg (compared to SBP <140 mm Hg), identified no difference in the primary CVD composite outcome but a significant reduction in stroke risk in the <120 mm Hg group.

More recently, random assignment to a SBP target <120 mm Hg compared to <140 mm Hg among people at high CVD risk (without diabetes or history of stroke) resulted in a 25% reduction in the primary outcome (a CVD composite) and a 27% reduction in all-cause mortality in the National Institutes of Health (NIH) sponsored Systolic Blood Pressure Intervention Trial (SPRINT). Of the 9,361 SPRINT participants, 30% were NHBs and 11% were Hispanic. Exploration of the trial results in non-Black compared to Black participants was a prespecified analysis. Thus, SPRINT provides a large database for the study of BP treatment targets in these diverse populations. This report describes the major outcomes in SPRINT by race and Hispanic ethnicity.

**METHODS**

**Patient selection**

Details of the SPRINT study design and rationale have been previously reported and more extensive details of the study protocol and procedures are publicly available. All participants gave written informed consent and the trial protocol was approved by the institutional review board at each participating site. The SPRINT cohort consisted of men and women, aged 50 years or older with a SBP between 130–180 mmHg on 0–4 antihypertensive medications and at high CVD risk. High CVD risk was defined by the presence of one or more of the following at study entry: clinical or subclinical CVD (other than stroke); chronic kidney disease (CKD) defined as an estimated glomerular filtration rate calculated with the 4-variable Modification of Diet in Renal Disease (MDRD) equation of 20–59 ml/min/1.73 m2 using the most recent serum creatinine drawn within the preceding 6 months; a Framingham Risk Score for 10-year CVD risk ≥15%; or age ≥75 years. Individuals with history of diabetes, stroke, polycystic kidney disease, or heart failure were excluded.

Race was self-reported by participants as Black (or AA), White, Native American, Asian, Native Hawaiian or other Pacific Islander, and other; and ethnicity was based upon independent self-identification as Hispanic or non-Hispanic.
In this report, the 984 participants who self-identified as Hispanic were considered part of that group (regardless of self-identified race). Non-Hispanic participants who self-identified as AA alone were grouped as NHB (n = 2802). Non-Hispanic participants who self-identified as White alone were grouped as NHW (n = 5399). 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 (n = 176).

**Intervention**

SPRINT participants were randomly assigned to 1 of 2 SBP targets standard (SBP <140 mm Hg) or intensive (SBP <120 mm Hg) treatment. SPRINT investigators initiated and adjusted antihypertensive medications to achieve the assigned SBP targets according to the SPRINT step-care treatment algorithm using US Food and Drug Administration approved antihypertensive drugs provided by the study. At each visit, trained clinical staff measured BPs with an automated BP device (Omron-HEM-907 XL) using standardized procedures. BP measurement requirements included measuring BP early in the visit and not following stressful exam components such as blood draws, proper positioning of the participant in a chair with back support, and proper cuff size determination. The SPRINT Manual of Procedures (MOP) stated that participants should be resting, not completing questionnaires, and not speaking with study staff during the 5-minute rest period or while BP measurements were being taken. The MOP also stated that staff should leave the room during the 5-minute rest period, and provided a script that staff could use to explain that they would be absent during the 5-minute rest period and would then enter the room and obtain the measurements without speaking to the participant.

**Study measures and outcomes**

At baseline, information on sociodemographics, cardiovascular risk factors, concomitant medications, social and medical history, anthropometrics, dementia screening, and quality of life measurements were collected on all eligible patients. Routine follow-up visits were conducted at 1, 2, 3, and every 3 months thereafter during the trial. Specific laboratory data (e.g., serum creatinine, fasting serum glucose) were collected at baseline and every 3 months. Additional visits were scheduled as needed for management of adverse effects or SBP goal attainment.

The primary outcome was a composite of the first occurrence of a myocardial infarction, acute coronary syndrome not leading to a myocardial infarction, stroke, compensated heart failure, or cardiovascular death. Major secondary outcomes included CVD mortality, all-cause mortality, and a composite of total mortality and the primary outcome. Other prespecified secondary outcomes analyzed in this report included decline in renal function or development of end-stage renal disease. Definitions of these outcomes were prospectively defined in the SPRINT protocol. Self-reported study outcomes were ascertained quarterly by clinical site staff using structured interviews for both treatment groups. Medical records and other corroborating data were collected for each potential outcome; all study outcomes were reviewed and adjudicated by the trial’s outcome committee using a prespecified protocol and blinded to treatment assignment.

In contrast to study outcomes, adverse events, including serious adverse events (SAEs), could be reported at any visit. SAEs were defined as an adverse experience judged by an investigator to be life threatening and/or resulting in death, permanent disability, or hospitalization or prolongation of hospitalization, whether or not the event was thought to be related to study intervention. SPRINT considered any emergency visit for heart failure, bradycardia, stroke, transient ischemic attack, or electrolyte abnormalities, and any syncope or injurious falls as a reportable SAE. Clinical and laboratory variables (serum potassium, creatinine levels, and estimated glomerular filtration rate) were also examined as potential adverse effects. An independent Data and Safety Monitoring Board (DSMB) monitored unblinded study data and provided oversight of participant safety.

**Statistical analysis**

Descriptive statistics (means and SD for continuous variables; frequencies and percentages for categorical variables) of baseline characteristics were computed by race/ethnicity and by treatment group within each stratum of race/ethnicity. Pairwise comparisons (i.e., each race/ethnicity compared to the other) were made using 1-way analysis of variance with pairwise contrasts for continuous variables and separate chi-square tests for categorical variables. Mean and SE of follow-up SBP was estimated by race/ethnicity and treatment group using mixed linear models with unstructured variance-covariance to control for within-subject correlation. Effect of treatment arm assignment on time to the first event within race/ethnicity stratum (i.e., CVD outcomes, mortality, CKD outcomes, and SAEs) was analyzed based on the intention-to-treat approach using univariable Cox proportional-hazards regression models for treatment arm assignment with 2-sided tests at the 5% level of significance and stratification by clinical site. Two-way interactions between treatment effect and race/ethnicity group were assessed using likelihood-ratio tests and Hommel’s technique to adjust for multiple comparisons. Since the subgroup definitions in this report differ from the prespecified race subgroup of Blacks vs. non-Blacks (in the prespecified comparison, the Black group included both Hispanic and non-Hispanic ethnicities who self-identified as Black while the non-Black group included both Hispanics and non-Hispanics who self-identified as White), outcome data for the prespecified race subgroups are presented in the Appendix (Supplementary Table S2). All analyses were performed using SAS version 9.4 software (SAS Institute, Cary, NC). Following a recommendation by the trial’s independent DSMB, the SPRINT BP intervention was halted on 20 August 2015 by the National Heart, Lung, and Blood Institute (NHLBI) Director after a mean follow-up of 3.26 years. Follow-up was censored at the date of last assessment for
a study event in each participant prior to 21 August 2015. This publication is based on a database that was frozen on 16 September 2016 and includes outcome events from baseline until the termination of the trial intervention on 21 August 2015.

RESULTS

Study participants

Figure 1 displays the CONSORT diagram for SPRINT by race/ethnicity group. Baseline characteristics by race/ethnicity and treatment assignment are provided in Table 1 and by race/ethnicity, pooled across treatment (Supplementary Table S1). After stratifying by race/ethnicity, few significant differences in baseline characteristics and risk profile were noted between treatment groups. Significant differences in weight between randomized treatment groups were seen in the Hispanic subgroup, statin use in NHBs, and aspirin use in NHWs (Table 1).

Blood pressure

SBP levels were similar by race/ethnicity stratum and between treatment groups at baseline (Table 1). SBP over time is shown in Figure 2. Overall, SBP decreased substantially during the first year of the study in all race/ethnicity groups and showed only modest differences between racial/ethnic groups for both SBP. Average postbaseline mean ± SE follow-up SBP in the standard arm was 134.7 ± 0.1 mm Hg in NHW, 135.5 ± 0.2 mm Hg in NHB, and 134.8 ± 0.3 mm Hg in Hispanic participants; compared to intensive arm values of 121.8 ± 0.2, 122.6 ± 0.2, and 119.9 ± 0.4 in NHW, NHB, and Hispanic participants, respectively. The mean number of antihypertensive medications prescribed were significantly higher in NHB (mean ± SE intensive arm 3.01 ± 0.03, standard arm 1.99 ± 0.03) compared to in NHW (intensive arm 2.74 ± 0.02, standard arm 1.75 ± 0.02; P value <0.0001 vs. NHB, both arms), and in Hispanics (intensive arm 2.70 ± 0.05, standard arm 1.77 ± 0.05; P value <0.0001 vs. NHB, both arms) (Figure 2).

Figure 1. Consort diagram. Race/ethnicity was self-reported and participants were classified as: Hispanic regardless of self-identified race; non-Hispanic Black if self-identified as African American alone; and non-Hispanic White if self-identified as White alone.
Table 1. Baseline clinical characteristics of SPRINT participants stratified by race/ethnicity and randomized group

| Characteristics                        | Non-Hispanic White (n = 5,399)a | Non-Hispanic Black (n = 2,802)a | Hispanic (n = 984)a |
|----------------------------------------|----------------------------------|----------------------------------|---------------------|
|                                        | Intensive | Standard | Intensive | Standard | Intensive | Standard |
| No. randomized                         | 2,698     | 2,701     | 1,379     | 1,423     | 503       | 481       |
| Age                                    |           |           |           |           |           |           |
| 50–64                                  | 782 (29.0)| 813 (30.1)| 824 (59.8)| 831 (58.4)| 267 (53.1)| 247 (51.4)|
| 65–74                                  | 939 (34.8)| 901 (33.4)| 329 (23.9)| 366 (25.7)| 147 (29.2)| 149 (31.0)|
| ≥75                                    | 977 (36.2)| 987 (36.5)| 225 (16.3)| 226 (15.9)| 89 (17.7) | 85 (17.7) |
| Female gender                          |           |           |           |           |           |           |
|                                        | 795 (29.5)| 757 (28.0)| 630 (45.7)| 641 (45.1)| 225 (44.7)| 229 (47.6)|
| Chronic kidney diseaseb                | 885 (32.8)| 893 (33.1)| 325 (23.6)| 312 (21.9)| 94 (18.7) | 96 (20.0) |
| Cardiovascular disease                 |           |           |           |           |           |           |
| Clinical                               | 526 (19.5)| 507 (18.8)| 135 (9.8) | 144 (10.1)| 65 (12.9) | 63 (13.1) |
| Subclinical                            | 207 (7.7) | 222 (8.2) | 121 (8.8) | 120 (8.4) | 47 (9.3)  | 48 (10.0) |
| Framingham 10-year CVD risk score (%)  | 26.8 ± 12.8| 26.8 ± 12.6| 21.7 ± 11.7| 21.9 ± 11.8| 23.0 ± 12.3| 22.4 ± 11.8|
| Baseline blood pressure                |           |           |           |           |           |           |
| SBP, mm Hg                             | 139.6 ± 15.5| 139.2 ± 15.2| 139.5 ± 16.7| 140.0 ± 15.8| 140.2 ± 14.5| 141.2 ± 15.1|
| DBP, mm Hg                             | 76.8 ± 11.4| 76.5 ± 11.6| 81.2 ± 12.5| 81.3 ± 12.3| 77.6 ± 11.2| 77.3 ± 11.2|
| Pulse, bpm                             | 65.2 ± 11.3| 65.2 ± 11.5| 68.7 ± 11.9| 68.4 ± 11.9| 65.4 ± 10.3| 66.1 ± 10.7|
| # of BP Medications                    | 1.78 ± 1.03| 1.78 ± 1.05| 1.78 ± 1.05| 1.78 ± 1.06| 1.78 ± 1.03| 1.78 ± 1.06|
| Weight, lbs.                           | 238 (8.8) | 230 (8.5) | 324 (23.6) | 315 (22.2) | 68 (13.6) | 45 (9.4)  |
| Smoking status                         | 1,340 (49.8)| 1,340 (50.0)| 453 (33.0) | 484 (34.2) | 157 (31.3) | 146 (30.5) |
| Statin use                             | 1,311 (48.9)| 1,338 (50.0)| 430 (31.4) | 513 (36.3) | 193 (38.6) | 198 (41.3) |
| Aspirin use                            | 906 (33.8)†| 805 (30.1)†| 365 (26.7) | 364 (25.8) | 120 (24.0) | 117 (24.4) |
| Baseline laboratory values             |           |           |           |           |           |           |
| Fasting glucose (mg/dl)                | 99.3 ± 13.2| 99.5 ± 11.9| 98.0 ± 15.3| 97.6 ± 16.1| 98.3 ± 11.6| 98.5 ± 12.2|
| Cholesterol, total (mg/dl)             | 186.4 ± 40.9| 186.3 ± 41.1| 196.6 ± 42.2| 195.2 ± 39.7| 192.8 ± 40.3| 194.9 ± 40.3|
| Cholesterol, LDL (mg/dl)               | 108.8 ± 34.5| 108.2 ± 34.4| 119.7 ± 36.4| 118.5 ± 34.3| 114.1 ± 35.2| 115.0 ± 34.2|
| Cholesterol, HDL (mg/dl)               | 52.3 ± 14.1| 41.9 ± 14.3| 54.9 ± 15.2| 55.3 ± 14.9| 50.7 ± 12.3| 50.6 ± 14.1|
| Triglycerides (mg/dl)                  | 127.7 ± 79.3| 131.7 ± 83.1| 113.1 ± 102.1| 110.0 ± 110.3| 140.6 ± 68.6| 149.8 ± 97.9|
| Potassium (mmol/l)                     | 4.28 ± 0.43| 4.27 ± 0.42| 4.07 ± 0.41| 4.08 ± 0.49| 4.19 ± 0.43| 4.21 ± 0.40|
| Sodium (mmol/l)                        | 139.9 ± 2.6| 140.0 ± 2.5| 140.5 ± 2.3| 140.4 ± 2.2| 140.3 ± 2.2| 140.2 ± 2.3|
| eGFR (ml/min/1.73 m2)                  | 68.3 ± 18.1| 68.0 ± 18.3| 76.3 ± 23.4| 76.7 ± 22.3| 78.0 ± 22.3| 77.2 ± 22.3|
| Creatinine (mg/dl)                     | 1.06 ± 0.31| 1.07 ± 0.31| 1.14 ± 0.40| 1.13 ± 0.38| 0.96 ± 0.33| 0.96 ± 0.34|

Plus–minus values are means ± SD. *P < 0.05, †P < 0.01 Standard vs. intensive arms. SI conversion factors: to convert the values for creatinine to micromoles per liter, multiply by 88.4. To convert the values for cholesterol to millimoles per liter, multiply by 0.0259. To convert the values for triglycerides to millimoles per liter, multiply by 0.0113. To convert the values for glucose to millimoles per liter, multiply by 0.0555. Abbreviations: BMI, Body Mass Index; BP, blood pressure; CVD, cardiovascular disease primary outcome; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; HDL, high-density lipoprotein; LDL, low-density lipoprotein; SBP, systolic blood pressure; SPRINT, Systolic Blood Pressure Intervention Trial.

aRace/ethnicity was self-reported and participants were classified as: Hispanic regardless of self-identified race; non-Hispanic Black if self-identified as African American alone; and non-Hispanic White if self-identified as white alone.

bChronic kidney disease was defined as an eGFR of less than 60 ml/min/1.73 m².
CVD outcomes

The HRs (95% confidence interval) (intensive vs. standard treatment groups) for the primary composite outcome were 0.70 (0.57–0.86), 0.71 (0.51–0.98), 0.62 (0.33–1.15) in NHWs, NHBs, and Hispanics, respectively (Table 2). For CV mortality, HRs were 0.49 (0.29–0.81) in NHW, 0.77 (0.37–1.57) in NHB, and 0.17 (0.01–1.08) in Hispanics, though for all-cause mortality they were 0.61 (0.47–0.80) in NHW, 0.92 (0.63–1.35) in NHB, 1.58 (0.73–3.62) in Hispanics. The effect of treatment arm assignment was homogenous with all interaction \( P \) values >0.05 across racial/ethnic groups for the primary CVD outcome, as well as the secondary outcomes of myocardial infarction, acute coronary syndrome, stroke, heart failure, CVD death, and primary outcome.

There appeared to be heterogeneity of effect for all-cause mortality and for non-CVD death (interaction \( P \) value = 0.008 and 0.006, respectively) (Table 2). However, after adjusting for multiple comparisons, the treatment by race/ethnicity interaction approached significance only for all-cause death (Hommel-adjusted \( P \) value = 0.062). CVD mortality was similarly reduced in all race/ethnicity groups (treatment by race/ethnic interaction \( P \) value = 0.098), including in treatment comparisons by Blacks vs. non-Blacks (Supplementary Tables S2 and S3), or whether Hispanics resided in Puerto Rico (\( n = 437 \)) or the US mainland (\( n = 550 \)) (data not shown). Treatment by residence interaction \( P \) values were 0.40, 0.68, and 0.43 for primary outcome, CVD mortality, and all-cause mortality, respectively.

CKD outcomes

The effect of treatment arm assignment on CKD outcomes (stratified by baseline CKD vs. non-CKD subgroup) by race/ethnicity is shown in Table 3 and Supplementary Table S2. The numbers of events in the CKD subgroup were small, particularly for the primary composite renal outcome of \( \geq 50\% \) reduction in estimated glomerular filtration rate or end-stage renal disease; treatment effects were similar across race/ethnicity groups for all 4 outcomes.

Serious adverse events

Results for SAEs are displayed in Table 4. Between the 2 treatment groups, no heterogeneity of effect was noted between the 3 racial ethnic groups in terms of overall SAEs or the 6 select SAEs: hypotension, syncope, bradycardia, electrolyte abnormality, injurious falls, or acute kidney injury.

DISCUSSION

We found that targeting a SBP <120 mm Hg compared to the currently recommended <140 mm Hg led to similar reductions in the relative risk for the primary outcome across major racial/ethnic groups—NHB (29%), NHW (30%), and Hispanics (38%). We also found that although NHBs required slightly more antihypertensive therapy to achieve this lower target, there was no difference in achieved SBP by race in the intensive arm.

Moreover, while statistically significant differences in baseline characteristics including cardiovascular risk profile (e.g., age, gender, cigarette smoking, prevalent CKD/CVD) were seen between the race/ethnic subgroups (Tables 1 and Supplementary Table S1), these differences were small. This suggests the benefit was unaffected by these population differences (though we had limited statistical power to detect such an effect). The population impact of implementing SPRINT may be even greater among NHBs given the higher prevalence of hypertension in this population and the fact that hypertension accounts for a greater proportion of CVD events among NHB and Hispanics.9

These findings are consistent with those in previous SPRINT publications13,25 and extends the findings of previous studies.26,27 In the Hypertension Detection Follow-up trial (HDFP) trial, Blacks (Hispanic ethnicity
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Table 2. Primary and secondary outcomes stratified by treatment group and race/ethnicity

| Outcome                      | Race/ethnicity   | Intensive arm | Standard arm | Intensive vs. standard hazard ratio | Interaction P value |
|------------------------------|------------------|---------------|--------------|-----------------------------------|---------------------|
|                              | N    | Events | % per Year | N    | Events | % per Year | HR  | Lower 95% CI | Upper 95% CI |
| Primary outcome<sup>a</sup>  |      |        |            |      |        |            |     |             |              |
| (Non-Hispanic) White         | 2,698 | 167   | 1.9        | 2,701 | 229   | 2.7        | 0.70 | 0.57        | 0.86         | 0.85        |
| (Non-Hispanic) Black         | 1,379 | 64    | 1.5        | 1,423 | 93    | 2.1        | 0.71 | 0.51        | 0.98         |             |
| Hispanic                     | 503  | 20    | 1.2        | 481  | 26    | 1.7        | 0.62 | 0.33        | 1.15         |             |
| Myocardial infarction        |      |        |            |      |        |            |     |             |              |             |
| (Non-Hispanic) White         | 2,698 | 69    | 0.8        | 2,701 | 88    | 1.0        | 0.77 | 0.56        | 1.05         | 0.63        |
| (Non-Hispanic) Black         | 1,379 | 22    | 0.5        | 1,423 | 35    | 0.8        | 0.64 | 0.36        | 1.09         |             |
| Hispanic                     | 503  | 9     | 0.6        | 481  | 13    | 0.8        | 0.48 | 0.18        | 1.18         |             |
| Acute coronary syndrome      |      |        |            |      |        |            |     |             |              |             |
| (Non-Hispanic) White         | 2,698 | 30    | 0.3        | 2,701 | 26    | 0.3        | 1.15 | 0.68        | 1.95         | 0.35        |
| (Non-Hispanic) Black         | 1,379 | 7     | 0.2        | 1,423 | 9     | 0.2        | 0.86 | 0.30        | 2.33         |             |
| Hispanic                     | 503  | 3     | 0.2        | 481  | 5     | 0.3        | 0.57 | 0.11        | 2.34         |             |
| Stroke                       |      |        |            |      |        |            |     |             |              |             |
| (Non-Hispanic) White         | 2,698 | 44    | 0.5        | 2,701 | 49    | 0.6        | 0.87 | 0.58        | 1.32         | 0.38        |
| (Non-Hispanic) Black         | 1,379 | 14    | 0.3        | 1,423 | 22    | 0.5        | 0.66 | 0.33        | 1.28         |             |
| Hispanic                     | 503  | 6     | 0.4        | 481  | 5     | 0.3        | 1.05 | 0.31        | 3.69         |             |
| Heart failure                |      |        |            |      |        |            |     |             |              |             |
| (Non-Hispanic) White         | 2,698 | 40    | 0.5        | 2,701 | 70    | 0.8        | 0.55 | 0.37        | 0.81         | 0.27        |
| (Non-Hispanic) Black         | 1,379 | 22    | 0.5        | 1,423 | 29    | 0.6        | 0.80 | 0.45        | 1.40         |             |
| Hispanic                     | 503  | 4     | 0.2        | 481  | 5     | 0.3        | 0.61 | 0.15        | 2.35         |             |
| Cardiovascular death         |      |        |            |      |        |            |     |             |              |             |
| (Non-Hispanic) White         | 2,698 | 23    | 0.3        | 2,701 | 45    | 0.5        | 0.49 | 0.29        | 0.81         | 0.098       |
| (Non-Hispanic) Black         | 1,379 | 13    | 0.3        | 1,423 | 18    | 0.4        | 0.77 | 0.37        | 1.57         |             |
| Hispanic                     | 503  | 1     | 0.1        | 481  | 6     | 0.4        | 0.17 | 0.01        | 1.08         |             |
| Non-CVD death                |      |        |            |      |        |            |     |             |              |             |
| (Non-Hispanic) White         | 2,698 | 57    | 0.6        | 2,701 | 82    | 0.9        | 0.69 | 0.49        | 0.97         | 0.006       |
| (Non-Hispanic) Black         | 1,379 | 30    | 0.7        | 1,423 | 26    | 0.6        | 1.16 | 0.68        | 1.98         |             |
| Hispanic                     | 503  | 12    | 0.7        | 481  | 4     | 0.3        | 3.28 | 0.98        | 14.77        |             |
| All-cause mortality          |      |        |            |      |        |            |     |             |              |             |
| (Non-Hispanic) White         | 2,698 | 89    | 1.0        | 2,701 | 144   | 1.6        | 0.61 | 0.47        | 0.80         | 0.008       |
| (Non-Hispanic) Black         | 1,379 | 51    | 1.2        | 1,423 | 56    | 1.2        | 0.92 | 0.63        | 1.35         |             |
| Hispanic                     | 503  | 19    | 1.1        | 481  | 12    | 0.8        | 1.58 | 0.73        | 3.62         |             |
| Primary outcome or death     |      |        |            |      |        |            |     |             |              |             |
| (Non-Hispanic) White         | 2,698 | 222   | 2.6        | 2,701 | 310   | 3.6        | 0.70 | 0.59        | 0.83         | 0.082       |
| (Non-Hispanic) Black         | 1,379 | 94    | 2.2        | 1,423 | 122   | 2.7        | 0.78 | 0.59        | 1.030        |             |
| Hispanic                     | 503  | 35    | 2.1        | 481  | 31    | 2.0        | 1.00 | 0.60        | 1.67         |             |

Abbreviations: CI, confidence interval, CVD, cardiovascular disease primary outcome; HR, hazard ratio.
<sup>a</sup>The primary outcome includes the first occurrence of myocardial infarction, acute coronary syndrome, stroke, heart failure, or death from cardiovascular causes. Median follow-up of 3.26 years.
was not reported), who made up 44% of study participants, had a significant reduction in all-cause mortality with more intensive “stepped” care compared to less intensive “referred” care.

While the BP target in HDFP was based on a DBP goal of <90 mm Hg, SBP decreased from a baseline of 159 mm Hg to 130 mm Hg by years 4 and 5.

In the ACCORD trial, the mean on-treatment intensive arm SBPs were 119.2 ± 0.2, 122.7 ± 0.4, and 121.7 ± 0.7 in the NHW, NHB, and Hispanic groups, respectively (written communication from P Byrington, November 2016). However, no benefit on the composite CVD outcome was seen with the <120 mm Hg target, either overall or in subgroups defined by race.

No racial or ethnic differences by treatment assignment were seen in renal outcomes or in SAEs in SPRINT. The AASK trial is the only other renal outcome trial with significant numbers of AAs and showed no benefit of more intensive therapy in this population with hypertensive renal disease except in participants with proteinuria (protein-to-creatinine ratio of more than 0.22). The small number of renal events in SPRINT make it unable to evaluate this finding.

Literature assessing incident CVD mortality in Hispanics and NHW found a statistically significant association between Hispanic ethnicity and lower CV and all-cause mortality despite having a worse CV risk profile when compared to NHW. This has been referred to as the Hispanic paradox. However, the risk profile of Hispanics in SPRINT was not greater than that seen in the other subgroups and did not result in an all-cause and cardiovascular-specific mortality advantage among Hispanics in SPRINT. Instead, we note a similar effect size on CV protection across NHWs, NHBs, and Hispanics. Though the sample sizes were small, SPRINT outcomes also did not

Table 3. CKD outcomes in the CKD and non-CKD subgroups, stratified by treatment group and race/ethnicity

| Outcome                                           | Subgroup                  | Intensive arm N | Events | % per Year | Standard arm N | Events | % per Year | Intensive vs. standard hazard ratio | Interaction P value |
|---------------------------------------------------|---------------------------|-----------------|--------|------------|----------------|--------|------------|------------------------------------|---------------------|
| CKD subgroup: composite renal outcome a            | (Non-Hispanic) White      | 885             | 8      | 0.3        | 893            | 7      | 0.24       | 1.14                               | 0.38 3.41 0.76      |
|                                                   | (Non-Hispanic) Black      | 325             | 9      | 0.9        | 312            | 8      | 0.79       | 1.09                               | 0.40 3.14           |
|                                                   | Hispanic                  | 94              | 0      | 0.0        | 96             | 0      | 0.00       | –                                  | –                   |
| CKD subgroup: incident albuminuria b               | (Non-Hispanic) White      | 365             | 49     | 4.3        | 346            | 60     | 5.7        | 0.79                               | 0.53 1.18 0.17      |
|                                                   | (Non-Hispanic) Black      | 118             | 11     | 3.0        | 106            | 18     | 5.7        | 0.26                               | 0.08 0.69           |
|                                                   | Hispanic                  | 35              | 4      | 3.7        | 41             | 7      | 5.8        | 1.39                               | 0.28 7.17           |
| Non-CKD subgroup: ≥30% eGFR reduction to CKD c     | (Non-Hispanic) White      | 1,808           | 88     | 1.5        | 1,798          | 21     | 0.4        | 4.38                               | 2.77 7.24 0.22      |
|                                                   | (Non-Hispanic) Black      | 1,046           | 42     | 1.3        | 1,103          | 16     | 0.5        | 2.61                               | 1.47 4.83           |
|                                                   | Hispanic                  | 406             | 17     | 1.3        | 383            | 4      | 0.3        | 4.02                               | 1.44 14.3           |
| Non-CKD subgroup: incident albuminuria             | (Non-Hispanic) White      | 965             | 81     | 2.7        | 955            | 101    | 3.4        | 0.77                               | 0.57 1.03 0.51      |
|                                                   | (Non-Hispanic) Black      | 576             | 45     | 2.5        | 642            | 65     | 3.4        | 0.73                               | 0.49 1.08           |
|                                                   | Hispanic                  | 219             | 15     | 2.1        | 213            | 15     | 2.2        | 0.80                               | 0.36 1.75           |

**Abbreviations:** CI, confidence interval; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate.

a For participants with CKD at baseline, composite renal outcome was the first occurrence of a reduction in eGFR by 50% (measure twice at least 90 days apart) or long-term dialysis or kidney transplant.

b Incident albuminuria denotes a urinary albumin to creatinine ratio of less than 10 mg/g at baseline and doubled to a creatinine ratio from less than 10 mg/g to 10 mg/g or greater (measured twice at least 90 days apart).

c Includes a 30% reduction in eGFR (measured twice at least 90 days apart) to an eGFR of less than 60 ml/min/1.73 m², dialysis, or a kidney transplant in participants without CKD at baseline.
The strengths of SPRINT include its large sample size, a diverse patient population, and its success in both implementing the protocol and achieving the SBP targets and difference in SBP between the 2 interventional groups throughout the trial, including in NHBs and Hispanics. While by design SPRINT was not powered to specifically examine treatment effects of the lower SBP goal in these subgroups, this analysis supports the benefits of intensive BP lowering on the primary composite endpoint which was similar across these race/ethnicity groups. A somewhat surprising limitation was the baseline characteristics and CVD risk profile of the NHB and Hispanic populations in Table 4.

### Table 4. Selected serious adverse events stratified by treatment group and by race/ethnicity

| Outcome                  | Race/ethnicity          | Intensive arm | Standard arm | Intensive vs. standard hazard ratio |
|--------------------------|-------------------------|---------------|--------------|------------------------------------|
|                          |                         | N  | Events | % per Year | N  | Events | % per Year | HR | Lower 95% CI | Upper 95% CI | P value |
| Any SAE<sup>a</sup>      | (Non-Hispanic) White    | 2,698 | 430    | 5.5        | 2,701 | 5.9    | 17.0       | 0.93 | 0.82          | 1.06          | 0.24    |
|                          | (Non-Hispanic) Black    | 1,379 | 146    | 3.6        | 1,379 | 147    | 3.6        | 1.02 | 0.81          | 1.29          |        |
|                          | Hispanic                | 503  | 42     | 2.7        | 481   | 29     | 1.9        | 1.40 | 0.87          | 2.24          |        |
| Hypotension              | (Non-Hispanic) White    | 2,698 | 38     | 0.4        | 2,701 | 27     | 0.3        | 1.40 | 0.86          | 2.30          | 0.28    |
|                          | (Non-Hispanic) Black    | 1,379 | 11     | 0.3        | 1,379 | 11     | 0.3        | 1.03 | 0.45          | 2.38          |        |
|                          | Hispanic                | 503  | 2      | 0.1        | 481   | 0      | 0.0        | --   | --            | --            |        |
| Syncope                  | (Non-Hispanic) White    | 2,698 | 39     | 0.5        | 2,701 | 31     | 0.4        | 1.24 | 0.77          | 1.99          | 0.94    |
|                          | (Non-Hispanic) Black    | 1,379 | 9      | 0.2        | 1,379 | 7      | 0.2        | 1.32 | 0.49          | 3.56          |        |
|                          | Hispanic                | 503  | 5      | 0.3        | 481   | 3      | 0.2        | 1.59 | 0.38          | 6.66          |        |
| Bradycardia              | (Non-Hispanic) White    | 2,698 | 32     | 0.4        | 2,701 | 29     | 0.3        | 1.10 | 0.66          | 1.81          | 0.30    |
|                          | (Non-Hispanic) Black    | 1,379 | 4      | 0.1        | 1,379 | 8      | 0.2        | 0.51 | 0.15          | 1.70          |        |
|                          | Hispanic                | 503  | 1      | 0.1        | 481   | 3      | 0.2        | 0.32 | 0.03          | 3.05          |        |
| Electrolyte abnormality<sup>b</sup> | (Non-Hispanic) White | 2,698 | 48     | 0.6        | 2,701 | 37     | 0.4        | 1.29 | 0.84          | 1.98          | 0.11    |
|                          | (Non-Hispanic) Black    | 1,379 | 16     | 0.4        | 1,379 | 13     | 0.3        | 1.27 | 0.61          | 2.64          |        |
|                          | Hispanic                | 503  | 4      | 0.3        | 481   | 0      | 0.0        | --   | --            | --            |        |
| Injurious fall<sup>c</sup> | (Non-Hispanic) White | 2,698 | 93     | 1.1        | 2,701 | 115    | 1.4        | 0.80 | 0.61          | 1.05          | 0.11    |
|                          | (Non-Hispanic) Black    | 1,379 | 26     | 0.6        | 1,379 | 21     | 0.4        | 1.28 | 0.72          | 2.27          |        |
|                          | Hispanic                | 503  | 6      | 0.4        | 481   | 2      | 0.1        | 2.88 | 0.58          | 14.3          |        |
| Acute kidney injury<sup>d</sup> | (Non-Hispanic) White | 2,698 | 65     | 0.8        | 2,701 | 49     | 0.6        | 1.34 | 0.93          | 1.94          | 0.46    |
|                          | (Non-Hispanic) Black    | 1,379 | 43     | 1.0        | 1,379 | 23     | 0.5        | 1.95 | 1.17          | 3.23          |        |
|                          | Hispanic                | 503  | 6      | 0.4        | 481   | 5      | 0.3        | 1.15 | 0.35          | 3.78          |        |

**Abbreviation:** CI, confidence interval; SAE, serious adverse event.

<sup>a</sup>SAEs were defined as an adverse experience judged by an investigator to be life threatening and/or resulting in death, permanent disability, hospitalization, or prolongation of hospitalization, whether or not the event was thought to be related to the study intervention.

<sup>b</sup>Electrolyte abnormality were adverse laboratory measures detected on routine or unscheduled tests; routine laboratory tests were performed at 1 month, then quarterly during the first year, then every 6 months.

<sup>c</sup>An injurious fall was defined as a fall that resulted in evaluation in an emergency department or that resulted in hospitalization.

<sup>d</sup>Acute kidney injury or acute renal failure were based on a primary or secondary diagnosis listed in the hospital discharge summary and was believed by the safety officer to be 1 of the top 3 reasons for admission or continue.

differ between Hispanics residing on the US mainland vs. those in Puerto Rico.

The strengths of SPRINT include its large sample size, a diverse patient population, and its success in both implementing the protocol and achieving the SBP targets and difference in SBP between the 2 interventional groups throughout the trial, including in NHBs and Hispanics.
SPRINT was not significantly higher than that of NHWs in SPRINT, which is not a representation of that found in the overall community. However, SPRINT assessment of race and ethnicity was through self-designation which also has its limitations. NHBs and Hispanics are admixed populations, and the US concept of race being only White or Black is seen as confusing and may have caused significant misclassification when trying to dichotomize White Hispanics and Black Hispanics. Finally, the small sample size of Hispanics limited meaningful comparisons making the analysis of Hispanics underpowered and potentially unstable.

The clinical implications of the SPRINT results are substantial. Considering the high prevalence of hypertension and uncontrolled hypertension among NHBs and Hispanics, intensive SBP lowering is bound to have a greater public health impact among these populations. Importantly, achieving lower SBP targets in NHB will require more antihypertensive therapy to achieve this goal. Our results indicate that most individuals above age 50 years with higher than average cardiovascular risk profile and SBP ≥130 mm Hg, including many above age 75 years old regardless of racial/ethnic origin benefit from treating to a SBP target of <120 mm Hg.

Overall, SPRINT findings showed benefit of a <120 mm Hg target (compared to one <140 mm Hg) in the NHB, Hispanic, and NHW populations and provide no evidence for heterogeneity of effect by race or ethnicity.

SUPPLEMENTARY MATERIAL

Supplementary data are available at American Journal of Hypertension online.

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DISCLOSURE

The authors declared no conflict of interest.

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