### Abstract

The Systolic Blood Pressure (SBP) Intervention Trial (SPRINT) showed that targeting SBP <120 mm Hg (intensive treatment, mean SBP: 121.5 mm Hg) versus <140 (standard treatment, mean SBP: 134.6 mm Hg) reduced cardiovascular events 25%. SPRINT has 2 implicit assumptions that could impact future US hypertension guidelines: (1) standard therapy controlled SBP similarly to that in adults with treated hypertension and (2) intensive therapy produced a lower mean SBP than in adults with treated hypertension and SBP <140 mm Hg. To examine these assumptions, US National Health and Nutrition Examination Survey 2009 to 2012 data were analyzed on 3 groups of adults with treated hypertension: (1) the SPRINT-like group had higher mean SBP than comparison groups, yet lower than SPRINT standard treatment group and (2) among groups 1 to 3 with SBP <140, SBP values were within <3 mm Hg of SPRINT intensive treatment. SPRINT results suggest that treatment should be continued and not reduced when treated SBP is <130, especially for the SPRINT-like subset. Furthermore, increasing the percentage of treated adults with SBP <140 could approximate SPRINT intensive treatment SBP without lowering treatment goals. (Hypertension. 2016;68:318-323. DOI: 10.1161/HYPERTENSIONAHA.116.07575.)

### Key Words:
- adult
- blood pressure
- cardiovascular disease
- diabetes mellitus
- hypertension
criteria for the SPRINT-like sample included one or more of the following:1-5: (1) history of myocardial infarction or angina, (2) chronic kidney disease with estimated glomerular filtration rate (mL/1.73 m²/min) of 20 to 59 or urine albumin/creatinine >600 mg/g creatinine, (3) 10-year Framingham cardiovascular disease risk ≥15%, or (4) age ≥75 years. Exclusion criteria were (1) age <50 years; (2) diagnosed and undiagnosed diabetes mellitus; (3) history of stroke; (4) history of heart failure; (5) SBP ≥180 mm Hg, ≥170 on >2 blood pressure (BP) meds; ≥160 on >3 BP meds; ≥150 on >4 BP meds; or (6) 0 to 1 health-care visits/yr (proxy for nonadherence).

Analyses were also conducted on 2 additional groups. One group included all adults ≥18 years with treated hypertension. The second group included adults ≥18 years with hypertension who were excluded from SPRINT. Additional SPRINT-like exclusion criteria for this group included diagnosed and undiagnosed diabetes mellitus, estimated glomerular filtration rate <20, and items in (5) and (6) above, that is, factors associated with uncontrolled and treatment-resistant hypertension.1,6,7

All adults included in the analysis had at least one valid BP measured. BP (mm Hg) was measured by trained professionals using sphygmomanometry and appropriately sized arm cuffs in volunteers after 5 minutes of seated rest. The first BP was excluded in estimating mean systolic and diastolic values for individuals with more than one value as recommended in NHANES procedure manuals.4,7

Hypertension was defined as systolic BP≥140 or diastolic BP ≥90 or both as a positive response to “Are you currently taking prescribed medication to lower your BP?” Treatment of hypertension was defined as the percentage of adults with prevalent hypertension reporting that they were taking prescription medication to lower BP.

Hypertension control was defined as SBP<140 for all adults.4 Percentage of treated hypertension controlled was calculated as the number of adults on antihypertensive medications and with SBP<140 divided by the number with treated hypertension.

Diabetes mellitus, which included individuals with diagnosed and undiagnosed disease, was defined as described.8 Cardiovascular disease included coronary heart disease as described.9 Stroke was defined by affirmative response to “Has a doctor ever told you that you had a stroke?”10 Congestive heart failure was defined by affirmative response to “Has a doctor ever told you that you had congestive heart failure?”10

Estimated glomerular filtration rate (mL/1.73 m²/min) was estimated using the Modification of Diet in Renal Disease equation11 used in SPRINT.3

Data Analysis

SAS Enterprise Guide 7.1 (Cary, NC) survey procedures were used for within-survey analyses and appropriate weights accounting for unequal probabilities of selection, oversampling, and nonresponse. The population weight attributed to each individual in NHANES was used to extrapolate to the number of US adults in the various groups reported. Data are reported as mean plus 1 SEM.

The SD (σ) of SBP for the 3 groups of adults with treated hypertension was calculated as described12; σ was used to estimate mean SBP values required to attain 88.1% control at SBP<140, which is the implied hypertension control rate in Healthy People 2020.13 Using a Z table,14 the 88.1 percentile corresponds to a Z score of 1.18, that is, 1.18 σ above the mean. Assuming σ=16 mm Hg, the mean SBP corresponding to 88.1% percentile=140-(1.18×16)=121.1. Z scores were then calculated for mean SBP<115<135 in 5-mm Hg increments using the equation Z=(X−μ)/σ, where X=SBP mm Hg, the upper boundary for hypertension control; and μ=135 mm Hg, X=130, μ=125 mm Hg, etc. Z scores were converted to percentiles (percent control) using the Z table.

Results

The process for selecting the 3 groups of adults in NHANES 2009 to 2012 with treated hypertension is provided in Figures 1 and 2 including (1) SPRINT-like group with participants ≥50 years, (2) all adults ≥18 years, and (3) adults ≥18 years excluding the SPRINT-like group and others with SPRINT-like exclusions.

Descriptive data for the three groups of adults with treated hypertension are provided in Table 1. The mean age of the participants in SPRINT-like subset was greater than that of participants in other 2 subsets; the subset excluding SPRINT participants was the youngest. The SPRINT-like subset had the lowest proportions of women, black, and Hispanic adults. SBP was highest in SPRINT-like adults and lowest in the subset excluding the SPRINT-like group. SBP control to <140 was highest in the subset excluding SPRINT-like participants (81.9%) and lowest in SPRINT-like participants (66.2%) and was intermediate in all treated adults (72.2%). The SD of SBP was highest in all adults and lowest in those ≥18 years with exclusions listed.

Descriptive data for the 3 groups of adults with treated hypertension and SBP<140 are shown in Table 2. The SPRINT-like group was the oldest and had the lowest proportions of women, black, and Hispanic adults. This group also had the highest mean SBP (123.3 mm Hg) and the lowest percentages controlled at each 5-mm Hg target below <140. Yet, even in the SPRINT-like group, 68.3% of those with SBP<140 also had SBP<130. The group with adults ≥18 years with exclusions were the youngest and had the highest proportion of women. The group also had the lowest mean SBP (118.9 mm Hg) and the largest percentages controlled at each of the 5-mm Hg targets below <140. In fact, 83.4% of this group had SBP<130 mm Hg.

The mean SBP at which 88.1% of adults are controlled to <140 was estimated. Mean SBP values required to reach 88.1% control to <140 fall as the SD (σ) of SBP rises from 14 to 18 mm Hg, whereas percentages controlled to SBP targets below <140 increase.

Discussion

SPRINT is a landmark study,1 which could support hypertension guideline changes including an SBP target well below <140 mm Hg, for example, <130 or <120. In fact, study investigators stated that “SPRINT provides evidence of benefits for an even lower SBP target than that currently recommended in most patients with hypertension.” Because SPRINT-like participants comprise roughly one fourth of all US adults with treated hypertension (Table 1), it seems the investigators assumed that benefits of target SBP<120 extend to patients excluded from SPRINT. Our study was designed to evaluate 2 implicit assumptions in SPRINT that could lead to a lower SBP target and more intensive treatment for millions of adults with hypertension.

The first assumption is that SPRINT standard treatment produced SBP values at least as low as the SBP of adults in the United States with treated hypertension. In 2009 to 2012, SPRINT-like adults in the United States attained a mean SBP of 133.0 (Table 1), which was lower than SPRINT standard therapy mean of 136.2 in the first year and 134.6 during the 3.26-year trial. Among all treated adults ≥18 years in the United States during this time period, mean SBP was lower at 130.1. In adults ≥18 years excluding the SPRINT-like subset and others with SPRINT-like exclusions, mean SBP was even lower at 124.6. SPRINT-like adults in the United States have mean SBP ≥3 mm Hg higher than all treated adults and ≥8 mm Hg above SBP values in adults ≥18 years excluding SPRINT-like adults and other SPRINT-like exclusion criteria. Yet, SPRINT-like adults in
the United States attained SBP values 3.2 mm Hg below SPRINT standard therapy participants at 1 year and 1.6 mm Hg lower than the 3.26-year mean. Thus, SPRINT standard therapy could lead to an overestimation of the benefits of SPRINT intensive therapy in the US population of adults with treated hypertension.

SPRINT participants rested 5 minutes alone in a room before BP was measured in triplicate with an automated device and averaged, a process termed “automated office” BP.14 The automated office BP protocol with 5 minutes of rest leads to SBP 6.9 mm Hg lower than daytime ambulatory values,15,16 which matches the difference between automated office SBP and daytime ambulatory SBP with SPRINT intensive treatment.14 SPRINT standard treatment led to automated office SBP values 3 mm Hg lower than daytime

**Figure 1.** The process is shown for selecting Systolic Blood Pressure Intervention Trial (SPRINT)-like adults ≥50 y old. Both the National Health and Nutrition Examination Survey (NHANES) sample size (N) and the number of subjects represented in the US population (Pop n) based on sample weight assigned to each subject are shown. BP indicates blood pressure; HTN, hypertension; and SBP, systolic blood pressure.

**Figure 2.** Left, The diagram depicts the process for selecting adults ≥18 y with treated hypertension (HTN) and the subset with exclusions. National Health and Nutrition Examination Survey (NHANES) sample sizes and the US population numbers represented are provided. Right, The process is shown for selecting adults ≥18 y with treated HTN excluding the Systolic Blood Pressure Intervention Trial (SPRINT)-like group and others with SPRINT-like exclusions. BP indicates blood pressure; and SBP, systolic blood pressure.
ambulatory SBP. In contrast, automated office BP without 5 minutes of rest produces values comparable to daytime ambulatory BP values. Thus, SBP 1.6 to 3.2 mm Hg lower in NHANES SPRINT-like adults than in SPRINT standard treatment participants would likely have been larger if comparable measurement methods were used.

The SPRINT standard treatment protocol contributed to higher values than in US adults with treated hypertension. The SBP goal for SPRINT standard treatment was 135 to 139 mm Hg. The SPRINT protocol specified reducing antihypertensive medication on any single visit when SBP was <130 and when SBP was <135 on 2 consecutive visits. The majority of US adults with treated hypertension controlled to <140 also had SBP <130 (Table 1) and would have had their antihypertensive therapy reduced with SPRINT standard treatment.

The second implicit assumption in SPRINT is that intensive treatment with target SBP <120 leads to lower SBP than in treated hypertensives with SBP <140. If this assumption is not correct, then the rationale for lowering the SBP target to <120 or <130 for adults with treated hypertension is less compelling, and the rationale for raising the percentage of adults with hypertension controlled to <140 is strengthened. In NHANES, 66.2% of all SPRINT-like adults with treated hypertension were controlled to an SBP <140. Their mean SBP was 123.3, which is 1.8 mm Hg higher than the SPRINT intensive treatment mean, and 68.3% of them had SBP <130. Given BP measurement differences between NHANES and SPRINT, SBP was probably lower in the NHANES’ SPRINT-like group with SBP <140 than in SPRINT intensively treated subjects.

Among all treated adults with hypertension, 72.2% had SBP <140, their mean SBP was 120.9, and 74.8% of the controlled group had SBP <130. Among treated adults ≥18 years excluding the SPRINT-like group and others with SPRINT-like exclusions, 81.9% had SBP <140, their mean SBP was 118.9, which is 2.6 mm Hg below the SPRINT intensive-treatment mean, and 83.4% of the controlled subset also had SBP <130. Thus, US adults with treated hypertension and SBP <140 have mean SBP values similar to that in SPRINT intensive treatment.

Of importance, SPRINT results suggest that the mean SBP values among US adults with treated hypertension and SBP <140 are not too low, especially for the SPRINT-like subset. SPRINT results further suggest that the large proportion of adults treated for hypertension who have SBP <130 are at lower risk for cardiovascular events and that their antihypertensive medications should not be reduced to raise SBP to 135 to 139. SPRINT provides important new data to a previous evidentiary review indicating that the SBP target of <140 reflects expert opinion.
Although control rates to SBP <140 in our report may seem high, hypertension control to <140/<90 among all US adults improved from 23.9% in 1988 to 1994 to 53.8% in 2009–2010. During this time, the proportion of adults treated for hypertension who were controlled to <140/<90 rose from 50.6% to 70.4%. Thus, the comparatively high rates of control to SBP <140 among adults with treated hypertension in this study are consistent with previous reports.

These observations suggest that increasing the percentage of US adults with treated hypertension controlled to SBP <140 could approximate values observed with SPRINT intensive treatment without lowering target SBP. In this regard, Healthy People 2020 aims to control hypertension in 61.2% of all adults with hypertension by treating 69.5% of them. The implied control rate among treated adults is 88.1%, that is, 0.695 treated×0.881 controlled/treated=0.612 or 61.2% controlled. This estimate excludes untreated adults with nonhypertensive BP. When the update to Healthy People 2020 was published, the SBP target was <140 mm Hg, which included adults with diabetes mellitus and chronic kidney disease.

Mean SBP values in all treated US adults were estimated assuming that 88.1% were controlled to <140. The estimates included a credible range of interindividual SDs for SBP (Table 1) recognizing the SD of SBP typically declines as mean SBP falls. The results suggest that mean SBP values similar to that in SPRINT intensive treatment would be attained if 88.1% of adults were controlled to SBP <140. Of note, because SBP values in treated adults are skewed toward higher values, median SBP is less than mean. In other words, >50% of patients have BP values below the mean. Thus, actual control rates to <140 and the other targets shown would be higher than estimates provided.

There are potential risks of lowering target SBP. The Hypertension Optimal Treatment (HOT) Study experience would be higher than estimates provided.

The potential benefits and risks of lowering the potential benefit is that an analogous sequence of events occur with SBP goals <120 or <130 and lead to mean SBP values in treated hypertension patients below the mean associated with benefit with SPRINT intensive treatment. This is not a declaration that mean DBP <80 in adults with diabetes mellitus and hypertension or mean SBP <120 in nondiabetic adults with high-risk hypertension lack benefit or are harmful. Rather, evidence-based medicine as translated in clinical guidelines, health-care quality metrics, and performance incentives can get ahead of the evidence with potential downside risk. In fact, lower SBP targets in SPRINT (hypotension, acute kidney injury) and ACCORD (Action to Control Cardiovascular Risk in Diabetes) were associated with more adverse events.

Several limitations of our report are noteworthy. First, NHANES is an observational, cross-sectional assessment at one time point, whereas SPRINT intervened on a cohort of patients with repeated assessments over time. Yet, NHANES is used as a proxy for hypertension treatment and control in the United States. Second, BP values in SPRINT and NHANES are not directly comparable given major methodological differences in measurement as discussed. In fact, BP values in NHANES participants likely would have been significantly lower if measured using SPRINT methods. Third, unlike SPRINT, our NHANES analysis did not include individuals with untreated SBP 130 to 139, because the Seventh Joint National Committee defined hypertension in untreated adults as an SBP ≥140 during 2003–2013, which includes the time period of our NHANES analysis. Adults with diabetes mellitus comprised the largest group of patients with an SBP <140 (goal <130), and they were excluded from SPRINT. Fourth, we included only adults with treated hypertension, because SPRINT participants were treated for hypertension. Fifth, 10% of participants in the SPRINT intensive treatment group had automated office SBP ≥140, whereas our comparison group of treated and controlled hypertensive adults excluded individuals with SBP ≥140 mm Hg. We addressed this limitation by estimating mean SBP values in all treated adults if Healthy People 2020 control targets were attained. Finally, we attempted to select a SPRINT-like sample from NHANES participants, but precise matching was impossible. For example, heart failure in NHANES was defined by self-report. SPRINT excluded adults with heart failure in the previous 6 months or ejection fraction <55%.

In summary, SPRINT standard treatment led to higher mean SBP than in US adults with treated hypertension. SPRINT intensive treatment led to mean SBP comparable to that in adults with treated hypertension controlled to <140. SPRINT results indicate that the large proportion of adults with SBP <140 who also achieve SBP <130 are benefiting and should not have treatment withdrawn. SPRINT fills a gap in prior guidance for goal SBP <140 based on expert opinion.

**Perspectives**

US adults with treated hypertension and SBP <140 attain mean SBP similar to that in SPRINT intensive treatment and most of them have SBP <130. Estimates suggest that mean SBP values similar to the values in SPRINT intensive treatment would also occur in all treated adults if the implied Healthy People 2020 goal of controlling 88.1% of them to SBP <140 mm Hg is attained. The potential benefits and risks of lowering the SBP target should be considered in future hypertension guidelines. Future guidelines should also recognize that SPRINT measured automated office BP after 5 minutes of rest, which leads to BP values below daytime ambulatory readings.

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References

Novelty and Significance

What Is New?

- Adults with treated hypertension in the United States are achieving lower systolic blood pressure (SBP) than Systolic Blood Pressure Intervention Trial (SPRINT) standard treatment participants, and the subset with SBP <140 is attaining mean SBP comparable to SPRINT intensive therapy.
- Estimates suggest that raising the percentage of treated adults with SBP <140 to 88.1%, a Healthy People 2020 goal, would also lead to mean SBP in all treated adults comparable to SPRINT intensive treatment.

What Is Relevant?

- The majority of US adults with treated hypertension controlled to <140 also have SBP <130. SPRINT suggests these individuals are deriving cardiovascular benefit from lower SBP and should not have treatment reduced to raise their SBP to 135 to 139 mm Hg.

Summary

SPRINT results support the Healthy People 2020 goal of increasing hypertension control to SBP <140 from current levels of >72.2% to 88.1% of treated adults. Recommendations to lower target SBP to values <140 should consider benefits and risks.
Systolic Blood Pressure Intervention Trial (SPRINT) and Target Systolic Blood Pressure in Future Hypertension Guidelines
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