Which Patients Does the SPRINT Study *Not* Apply To and What Are the Appropriate Blood Pressure Goals in These Populations?

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The Systolic Blood Pressure Intervention Trial (SPRINT)[1] is a large National Institutes of Health–sponsored multicenter randomized controlled trial that enrolled 9361 patients with a systolic blood pressure (SBP) of at least 130 mm Hg. The primary goal of SPRINT was to test whether reducing SBP to a lower goal (<120 mm Hg) than currently recommended (<140 mm Hg) would reduce the occurrence of cardiovascular disease (CVD) and chronic kidney disease (CKD) events. Enrolled patients were 50 years or older with an SBP ≥130 mm Hg and at least one of the following: a history of CVD, stage 3 CKD (estimated glomerular filtration rate 20–59 mL/min/1.73 m^2), an intermediate to high risk for CVD other than stroke, or age 75 years or older. A patient was defined as having CVD if they had a prior myocardial infarction, percutaneous coronary intervention, coronary artery bypass grafting, carotid endarterectomy or carotid stenting, peripheral arterial disease with revascularization, acute coronary syndrome, abdominal aortic aneurysm ≥5 cm with or without repair, a coronary calcium score >400, or left ventricular hypertrophy. Patients were defined as at intermediate or high risk for CVD based on the following: Framingham Risk Score for 10-year CVD risk of 15% based on laboratory work performed for lipids within the past 12 months. The primary outcome was a composite of cardiovascular events.

The SPRINT study was terminated early after 3.26 years on advisory of the data safety monitoring board. The results of the SPRINT study showed a 25% reduction in the primary combined cardiovascular outcome and a 27% reduction in mortality in the group randomized to SBP <120 mm Hg.[1,2] This obviously has important implications for blood pressure (BP) guidelines in this population. The baseline mean systolic and diastolic BPs were 139.7 mm Hg and 78.1 mm Hg, respectively. At 1 year, the mean SBP was 121.4 mm Hg in the intensive treatment group and 136.2 mm Hg in the standard treatment group. The SPRINT study included 28% of patients with CKD, 28% of patients were older than 75 years, 36% were women, and 20% had prior CVD. The sample was diverse and included 29.9% black, 10.5% Hispanic, and 57.7% white patients.

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Importantly, SPRINT excluded many patients with hypertension. Who were these populations? The following groups of patients with hypertension were excluded: those with a history of prior stroke, diabetes, polycystic kidney disease, any secondary cause for hypertension, glomerular filtration rate (GFR) <20 cc/min, >1 g of proteinuria per 24 hours, glomerulonephritis treated with immunosuppressive therapy, symptomatic heart failure within the past 6 months or left ventricular ejection fraction <35%, expected survival less than 3 years, cancer diagnosed within the past 2 years, organ transplant, cardiovascular event, procedure or hospitalization for unstable angina within the past 3 months, and all patients younger than 50 years.

Why were these patients excluded? Patients with diabetes were excluded as it was felt that this population had already been studied in the Action to Control Cardiovascular Risk in Diabetes (ACCORD) BP trial,[3] which did not show a cardiovascular advantage of lower SBP (<120 mm Hg) vs standard BP (<140 mm Hg) although there was a decreased risk of stroke. Patients with polycystic kidney disease have also been studied separately in the HALT Progression of Polycystic Kidney Disease study,[4] which recently showed that rigorous BP control was associated with a slower increase in total kidney volume, no overall change in the estimated GFR, a greater decline in the left ventricular mass index, and greater reduction in urinary albumin excretion. Patients with excessive proteinuria >1 g per 24 hours were also excluded, but, based on data from the Modification of Diet in Renal Disease (MDRD),[5] the Blood Pressure Control for Renoprotection in Patients With Nondiabetic Chronic Renal Disease (REIN),[6] and the African American Study of Kidney Disease and Hypertension (AASK)[7] studies, lower BP goals (<130/80 mm Hg) have been suggested and recommended by some guidelines in this patient population.[8] Renal transplant recipients were excluded in this population. There are no randomized controlled trials examining optimal levels of BP and this is a population that needs to be studied. BP threshold for treatment of kidney transplant recipients remains at 130/80 mm Hg, regardless of proteinuria.[9] The Secondary Prevention of Small Subcortical Strokes (SPS3) trial, which compared an SBP treatment target of <130 mm Hg with a target of 130 mm Hg to 149 mm Hg in participants with a recent lacunar stroke, showed a nonsignificant reduction in recurrent stroke in the group randomized to the lower target.[10] There are no specific studies that have evaluated BP targets in patients without other comorbidities who are

younger than 50 years and who often have predominantly diastolic hypertension.

Although the SPRINT study provided important information on managing SBP in older nondiabetic patients with substantial CVD risk, it is important to remember that these results cannot be generalized to the other populations outlined above. In the coming weeks we will hear a great deal more about SBP targets as SPRINT, like many prior randomized trials in hypertension, raises just as many new significant questions while at the same time providing clinically important answers in people with high BP.

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Supporting Information

Additional Supporting Information may be found in the online version of this article:

Table S1. Changes in ambulatory SBP among the E-group subjects using or not using prescription diuretics.

Table S2. Changes in ambulatory SBP in the E-group among the subjects who reached or did not reach the goal of <6 g/day salt intake.

Table S3. Trials regarding the effect of salt reduction on blood pressure.

Table S4. Changes in the 24-hour blood pressure among the E- and C-group subjects with baseline BP ≤130/80 mm Hg.

Table S5. Clinic blood pressure at the end of the study and 6 months later in the E-group.