# A review of the SPRINT Systolic Blood Pressure Intervention Trial
## By Dr. Marc Ferrini

**SPRINT Official Title**: Systolic Blood Pressure Intervention Trial
**Status :** Ongoing
**Overview**
To test whether a treatment program aimed at reducing systolic blood pressure (SBP) to a lower goal (120mmHg) than currently recommended (140mmHg) will reduce cardiovascular disease (CVD) risk.
**Study Type** Interventional
**Study Design** Multicenter, Randomized Efficacy Study Parallel Assignment Open label-Single Blind (Outcomes Assessor)
**Primary Endpoint**
Co-Primary endpoints:
1) The composite of cardiovascular death, non-fatal myocardial infarction and non-fatal stroke.
2) The composite of cardiovascular death, resuscitated cardiac arrest, non-fatal myocardial infarction, non-fatal stroke, heart failure and arterial revascularizations.
**Secondary endpoints**
All-cause mortality and the components of the co-primary endpoints.
Decline in renal function, Development of end stage renal disease (ESRD), Dementia, Decline in cognitive function, Small vessel cerebral ischemic disease, and new diagnosis of diabetes.
**Pre specified subgroups**

- cardiovascular disease at baseline
- chronic kidney disease at baseline
- sex
- race (black vs. nonblack)
- age (<75 vs. ≥75 years)
- base- line systolic blood pressure in three levels (≤132 mm Hg, >132 to <145 mm Hg, and ≥145 mm Hg).

**Number of Patients** **9361**
**Number of Sites** **102**
**Number of Countries** **1 (USA)**
**Study Period** **November 2010 to August 2015.**
On August 20, 2015, the NHLBI director accepted a recommendation from the data and safety monitoring board of the trial to inform the investigators and participants of the cardio- vascular-outcome results after analyses of the primary outcome exceeded the

monitoring boundary at two consecutive time points, thus initiating the process to end the blood-pressure intervention early.

**Follow-up** (median as of August 2015): 3.26 years.

**Principal Investigators**

David M. Reboussin,

Jackson T Wright Alfred Cheung Suzanne Oparil Mike Rocco Bill Cushman

**Program Manager**

National Heart, Lung, and Blood Institute NHLBI

Co-sponsorship: The National Institute of Diabetes and Digestive and Kidney Diseases,
The National Institute of Neurological Disorders and Stroke
The National Institute on Ageing

**SPRINT**

Elevated blood pressure (BP) is an important public health concern. It is highly prevalent and a risk factor for several adverse health outcomes, especially coronary heart disease, stroke, heart failure, chronic kidney disease, and decline in cognitive function.

The Systolic Blood Pressure Intervention Trial (SPRINT) was designed to test whether a treatment program aimed at reducing systolic blood pressure (SBP) to a lower goal (120mmHg) than currently recommended (140mmHg) could reduce cardiovascular disease (CVD) risk.

The SPRINT study enrolled more than 9 000 people from USA. It included patients aged over 50, with SBP from 130 to 180 mmHg and at least one associated item: additional CVD risk, clinical or subclinical CVD , chronic kidney disease, Framingham Risk Score for 10-year CVD risk ≥ 15%, or age ≥ 75 years. Most of them where already being treated for Hypertension. History of Stroke, Diabetes mellitus or Congestive heart failure (symptoms or EF < 35%) were major exclusion criteria.

The included patients finally represented high to very high risk population: 20% on secondary prevention, 28% age>75.

Participants were randomized in 2 groups:

1. The Intensive arm had a goal of SBP <120 mm Hg. One or more medications from the following classes of agents were provided by the study: Angiotension converting enzyme (ACE)-inhibitors Angiotension receptor blockers (ARBs) Direct vasodilators Thiazide-type diuretics Loop diuretics Potassium-sparing diuretics Beta-blockers Sustained-release calcium channel blockers (CCBs) Alpha1-receptor blockers
2. The Standard arm had a goal of SBP <140 mm Hg. Therapy was intensified if SBP ≥160 mm Hg at 1 visit; ≥140 mm Hg at 2 consecutive visits; Down-titration was done if SBP <130 mm Hg at 1 visit; <135 mm Hg at 2 consecutive visits

Thus, one can consider that SPRINT is an open label study with a blind analysis of the final data.

On August 20, 2015, the NHLBI director accepted a recommendation of the safety monitoring board based on an interim analysis of the primary outcome which exceeded the monitoring boundary at two consecutive time points, and decided to stop the study; the median follow-up was then 3.26 years (instead of the initial planned average of 5 years).

## RESULTS

At the end of the trial, SBP was lower in the Intensive treated arm (121.5 vs 134.6 mm Hg p ) with a greater number of therapeutic classes needed (3 vs 2 in the control arm)
Cardio vascular events (primary endpoint) were significantly lower (243 vs 319 p<0.001) in the intensive arm (1.65% vs. 2.19% per year hazard ratio 0.75; 95% CI: 0.64 to 0.890) resulting from the reduction of Heart failure and Cardiovascular Death while (surprisingly) no reduction of Stroke was noted.
All-cause mortality was also significantly lower in the intensive - treatment group (hazard ratio, 0.73; 95% CI, 0.60 to 0.90; P=0.003).
The numbers needed to treat to prevent a primary outcome event, death from any cause, and death from cardiovascular causes during the median 3.26 years of the trial were 61, 90, and 172, respectively.
These results were consistent across the pre-specified subgroups. There were no significant interactions between treatment and subgroups with respect to the primary outcome or death from any cause.
A total of 220 participants in the intensive-treatment group (4.7%) and 118 in the standard-treatment group (2.5%) had serious adverse events (hypotension, syncope and acute kidney injury or failure) that were classified as related to the intervention (HR 1.88; P<0.001)

## CONCLUSIONS

Among patients at high risk for cardiovascular events but without diabetes nor history of stroke, targeting a systolic blood pressure of less than 120 mm Hg, as compared with less than 140 mm Hg, resulted in lower rates of fatal and nonfatal major cardiovascular events and death from any cause, although significantly higher rates of some serious adverse events were observed in the intensive-treatment group.

## BIBLIOGRAPHY

**A Randomized Trial of Intensive versus Standard Blood-Pressure Control.**
SPRINT Research Group, Wright JT Jr, Williamson JD, Whelton PK, Snyder JK, Sink KM, Rocco MV, Reboussin DM, Rahman M, Oparil S, Lewis CE, Kimmel PL, Johnson KC, Goff DC Jr, Fine LJ, Cutler JA, Cushman WC, Cheung AK, Ambrosius WT.
N Engl J Med. 2015 Nov 26;373(22):2103-16. doi: 10.1056/NEJMoa1511939. Epub 2015 Nov 9.