



THE IMPACT OF SYSTOLIC BLOOD PRESSURE LOWERING ON DEATH & CARDIOVASCULAR DISEASE

Hypertension is strongly correlated to death and cardiovascular disease. Previous studies indicate that the systolic blood pressure (SBP) goal should be below 140 mmHg; however, additional data indicate that there may be beneficial effects of antihypertensive agents in people below the current SBP goals. Before the new hypertension guidelines were released late this past year, there was some controversy over the optimal cutoff for treatment and most beneficial blood pressure goal for patients diagnosed with hypertension. This issue of *CLIPs* briefly summarizes an article that compares different SBP levels and what, if any, mortality or cardiovascular (CVD) benefits were seen through a systematic review and meta-analysis. If you need further information, please contact the Center for Healthcare Innovation and Patient Outcomes Research (CHIPOR) at chipor@samford.edu.

Brunström M, Carlberg B. Association of blood pressure lowering with mortality and cardiovascular disease across blood pressure levels: A systematic review and meta-analysis. *JAMA Intern Med.* 2018; 178(1):28-36.

Introduction

- Previous guidelines uniformly recommended treating HTN to a goal of <140/90 mmHg.
- The SPRINT study and a meta-analysis by Ettehad et al argued that lower SBP goals may be more beneficial in high-risk patients.
- Other meta-analyses were conducted as well, but results from the SPRINT studies and other analyses may be prone to interpretation inconsistencies.
- This systematic review and meta-analysis was conducted to obtain a more comprehensive study inclusion than previous meta-analysis and this evaluation calculated risk ratios and SEs from the raw data.

Primary Preventive Trials

- A total of 51 out of 74 trials were categorized as primary preventive and included over 190,000 study participants.
- The demographic characteristics included approximately 46% women, mean age of 63 years, mean baseline SBP of 154 mmHg, and a mean follow-up of 4.0 years. The mean SBP difference between treatment and control was 6.6 mmHg.
- The effect of BP lowering on end-stage renal disease was nonsignificant at all BP levels and showed no clear pattern across the different levels. See table 1 for detailed information on primary preventive trials.

Table 1. Summary of Primary preventive trials

Preventive study	Outcomes (RR; 95% CI)	Results
All-cause mortality	SBP: <140 mmHg: 0.98 (0.90-1.06) 140-159 mmHg: 0.87 (0.75-1.00) ≥160 mmHg: 0.93 (0.87-1.00)	Treatment benefits were seen for patients with a SBP >140 mmHg in preventing mortality from any cause, but more so in the group with a baseline SBP from 140-159 mmHg.
Cardiovascular mortality	SBP: <140 mmHg 1.03 (0.87-1.20) 140-159 mmHg 0.86 (0.65-1.14) ≥160 mmHg 0.85 (0.77-0.95)	The group that benefitted the most from treatment were the patients with a baseline SBP ≥160 mmHg, with a relative risk reduction from CV mortality of 15%. However only some benefit was shown for patients with a baseline SBP from 140-159 mmHg.

Preventive study	Outcomes (RR; 95% CI)	Results
Major Cardiovascular events (MACE)	SBP: <140 mmHg 0.97 (0.90-1.04) 140-159 mmHg 0.88 (0.80-0.96) ≥160 mmHg 0.78 (0.70-0.87)	Risk reduction of MACE was greatest in patients with a baseline SBP of ≥160 mmHg at 22% and 12% for baseline SBP 140-159 mmHg. No significant reductions in outcomes were seen for MACE at a baseline SBP <140 mmHg.
Coronary heart disease (CHD)	SBP: <140 mmHg 0.98 (0.88-1.09) 140-159 mmHg 0.86 (0.76-0.96) ≥160 mmHg 0.86 (0.78-0.94)	Treatment benefits were seen in patients with a baseline SBP >140 mmHg and risk for CHD was reduced by about 14%.
Stroke	SBP: <140 mmHg 0.85 (0.68-1.06) 140-159 mmHg 0.86 (0.72-1.01) ≥160 mmHg 0.69 (0.60-0.80)	Patients with a baseline SBP of ≥160 mmHg saw the most benefits from treatment in primary prevention of stroke, with SBP <160 mmHg seeing neutral benefits.
Heart failure (HF)	SBP: <140 mmHg 0.88 (0.78-0.98) 140-159 mmHg 0.87 (0.73-1.04) ≥160 mmHg 0.53 (0.42-0.67)	Treatment reduced risk of HF in patients with a baseline SBP <140 mmHg, and a statistically significant difference was observed in patients with SBP ≥160 mmHg group. The group with baseline SBP between 140-159 mmHg showed neutral effects.

Secondary Preventive Trials

- A total of eighteen trials, including over 100,000 participants, were categorized as either Coronary Heart Disease (CHD) trials or post-stroke trials.
- A total of five trials were categorized as mixed CVD trials, however the meta-analyses were inconclusive for all outcomes and were therefore judged to be noninformative. See table 2 for detailed information on preventive trials.

Table 2. Summary of Secondary Preventive Trials

Preventive Trial	Outcomes (RR; 95% CI)	Results
CHD Trials	All-cause mortality: 0.98 (0.89-1.07) CV mortality: 0.95 (0.84-1.09) MACE: 0.90 (0.84-0.97) CHD: 0.88 (0.77-1.00) Stroke: 0.86 (0.73-0.96) HF: 0.83 (0.72-0.96)	Treatment benefits for secondary prevention were seen for MACE, as well as in stroke, and HF. However, treatment effects were neutral in secondary prevention of CV mortality and all-cause mortality.
Post-stroke Trials	All-cause mortality: 1.00 (0.91-1.10) CV mortality: 0.91 (0.78-1.05) MACE: 0.88 (0.76-1.01) CHD: 0.89 (0.72-1.11) Stroke: 0.86 (0.74-1.01) HF: 0.85 (0.32-2.29)	Nonsignificant treatment effects/benefits were seen for MACE and secondary prevention of stroke. All other analyses show to be inconclusive in whether there are any treatment benefits seen across different SBP levels.

Summary

- Primary preventive BP lowering is associated with reduced risk for death and CVD if baseline SBP is 140 mmHg or higher, possibly refuting the previous view that the relative benefit of treatment is the same across BP levels and that lower is always better.
- This study also showed that at lower BP levels, treatment is not associated with any benefit in primary prevention but might offer additional protection for secondary prevention in patients with CHD.
- Although the newly released HTN guidelines state to treat to a BP goal of <130/80 mmHg for the majority of patients, this meta-analysis provided a more comprehensive insight into how blood pressure lowering affected mortality and CVD across different blood pressure levels and how this may affect treatment goals for different patient populations.