

EDITORIAL COMMENT

Achieving Intensive Systolic Blood Pressure Control

No Reason to Delay

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Randomized trials from multiple world regions have demonstrated a reduction in cardiovascular disease (CVD) risk with intensive systolic blood pressure (SBP) lowering.¹ In SPRINT (Systolic Blood Pressure Intervention Trial; [NCT01206062](#)), there was a 25% reduction (HR: 0.75; 95% CI: 0.64-0.89) in the primary outcome of a composite CVD event, and 27% reduction (HR: 0.73; 95% CI: 0.60-0.90) in all-cause mortality over a median of 3.3 years of follow-up with intensive treatment with an SBP goal of 120 mm Hg vs a standard SBP goal of 140 mm Hg.² In the STEP (Strategy of Blood Pressure Intervention in the Elderly Hypertensive Patients; [NCT03015311](#)) trial, the primary composite outcome of CVD was reduced by 26% (HR: 0.74; 95% CI: 0.60-0.92) among older adults randomized to an SBP goal of 110 to <130 mm Hg vs their counterparts randomized to an SBP goal of 130 to <150 mm Hg.³ Similarly to SPRINT, the median follow-up time in the STEP trial was 3.3 years. The relatively short duration of these trials has left doubts about the long-term benefit of intensive SBP lowering.

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In this issue of *JACC*, Song et al⁴ report on extended follow-up of the STEP trial. After the STEP trial intervention ended, all participants in the intensive and standard treatment groups were

offered intensive treatment (ie, treatment to an SBP goal of 110 to <130 mm Hg). This approach allowed the investigators to evaluate the CVD risk reduction with sustained intensive SBP lowering vs an approach of delayed intensive SBP lowering. Throughout follow-up of the original trial, the mean SBP was 126.7 mm Hg in the intensive-treatment group and 135.9 mm Hg in the standard-treatment group. However, at the end of the extended follow-up period, a median of 6.1 years after baseline, the mean SBP was 127.9 mm Hg in the sustained-intervention group and 129.5 mm Hg in the delayed-intervention group. The investigators report that sustained intensive SBP lowering reduced CVD risk by 18% (HR: 0.82; 95% CI: 0.71-0.96) compared with a delayed SBP-lowering intervention.

In addition to evaluating the long-term effect of intensive SBP lowering, the authors conducted a target trial emulation to estimate CVD risk reduction with treatment to an intensive SBP goal initiated from randomization vs being initiated at annual increments after randomization. Target trial emulation uses observational data to increase causal inferences that can be made by modeling a data structure that matches the principles of a randomized trial. In the target trial emulation, Song et al found a larger CVD risk reduction with earlier intensive treatment initiation. CVD risk was reduced by 17% with no delay in intensive SBP lowering, vs 12%, 8%, and 6% if intensive SBP lowering treatment was started, respectively, 1, 2, and 3 years later. These findings suggest that early initiation of intensive treatment produces a larger CVD risk reduction, and they are consistent with a secondary analysis of SPRINT that reported larger residual life expectancy with initiating antihypertensive treatment at younger ages.⁵

The study by Song et al⁴ adds to what is known about intensive BP control by providing new data on

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the reduction of CVD risk with sustained BP lowering over a relatively long period and by demonstrating the benefit of early initiation of intensive BP lowering with a diminishing CVD reduction if treatment is delayed. Multiple analyses have reported that intensive vs standard SBP goals produce costs per quality-adjusted life years gained that are below accepted willingness-to-pay levels.⁶ A time-to-benefit analysis found that 9, 19, and 34 months of intensive SBP lowering was needed to prevent 1 major adverse cardiovascular event per 500, 200, and 100 patients, respectively.⁵ The authors concluded that an intensive SBP goal may be appropriate for adults with a life expectancy of 3 or more years, which can be assessed with the use of a validated life expectancy calculator.

“Efforts aimed at achieving SBP goals of 110 to 130 mm Hg have the potential to substantially reduce CVD risk.”

As the study by Song et al⁴ suggests, delaying implementation by as little as 1 year misses the opportunity to reduce CVD risk. Possible barriers to adopting intensive BP control include the underrepresentation of complex, older adults in randomized trials, the time and effort needed to achieve lower SBP targets in busy clinics, and concerns about harms, such as falls, among older adults. Despite these implementation barriers, previous studies indicate that trials of intensive SBP lowering are generalizable to large portions of the population with hypertension. In addition, as demonstrated in multiple trials, intensive SBP goals can be achieved by following a standardized antihypertensive titration protocol. However, more potent antihypertensive medication regimens will need to be used. A meta-analysis published in 2025 provides a calculator to estimate the efficacy of different blood pressure lowering regimens.⁷ Finally, while concerns about side-effects should not be ignored, data from multiple randomized trials, including the STEP trial, indicate that most side-effects occur at similar rates in participants randomized to intensive and standard SBP goals. Implementation strategies including patient education on the benefits of intensive SBP

lowering, clinician feedback on the proportion of their patients with controlled BP, and health system-level treatment protocols have the potential to facilitate intensive SBP lowering.

Trial target emulation may be useful when randomized trials are not available to evaluate the comparative effectiveness or safety of interventions.⁸ A framework for using target trial emulation includes specifying the protocol of the hypothetical randomized pragmatic trial that would answer a causal question of interest (ie, the target trial) and using observational data to attempt to emulate that trial. Similarly to randomized trials, target trial emulations have protocols that specify eligibility criteria, treatment strategies, assignment procedures, follow-up period, outcomes, causal contrasts of interest (eg, intention to treat or on-treatment effects), and an analysis plan. The validity of results from a target trial emulation relies on a rigorous study design and transparency. Constructs to ensure rigor and transparency of target trial emulation have been proposed.⁹ This includes developing and registering a protocol before data are accessed and analyses are initiated, staging the analyses, and using a “clean room.” Staging is a process of reviewing results in steps and evaluating potential bias before proceeding to conducting comparative analyses. The clean room involves restricting access to the data used for the analysis, implementing policies for conducting exploratory analyses and protocol deviations, and maintaining audit logs. Even with a rigorous study design and transparency, the interpretation of a target trial emulation should consider threats to validity, which are study specific but include residual confounding and exposure and outcome misclassification dependent on the data used. A recent editorial by the commissioner of the U.S. Food and Drug Administration noted that target trial emulation has the potential to provide causal conclusions.¹⁰ It is likely that this approach for causal inference will become more common.

In summary, the study by Song et al⁴ provides important new data supporting intensive SBP lowering in older adults. Dissemination and implementation efforts aimed at achieving SBP goals of 110 to <130 mm Hg have the potential to substantially reduce CVD risk. Given the large evidence body supporting intensive SBP lowering, we think that it is time for health systems, clinicians, and patients to adopt this evidence-based SBP goal.

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Dr Muntner is founder and owner of Perisphere Real World Evidence; and has contracts with Amgen, Merck, and Novartis unrelated to the topic of this comment. Dr Bowling has reported that he has no relationships relevant to the contents of this paper to disclose.

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REFERENCES

1. Chen T, Shao F, Chen K, et al. Time to clinical benefit of intensive blood pressure lowering in patients 60 years and older with hypertension: a secondary analysis of randomized clinical trials. *JAMA Intern Med*. 2022;182(6):660–667. <https://doi.org/10.1001/jamainternmed.2022.1657>
2. SPRINT Research Group, Wright JT, Williamson JD, et al. A randomized trial of intensive versus standard blood-pressure control. *N Engl J Med*. 2015;373(22):2103–2116. <https://doi.org/10.1056/nejmoa1511939>
3. Zhang W, Zhang S, Deng Y, et al. Trial of intensive blood-pressure control in older patients with hypertension. *N Engl J Med*. 2021;385(14):1268–1279. <https://doi.org/10.1056/nejmoa2111437>
4. Song Q, Peng X, Bai J, et al. Intensive blood pressure control in older patients with hypertension: 6-year results of the STEP trial. *J Am Coll Cardiol*. 2025;86(17):1421–1433.
5. Vaduganathan M, Claggett BL, Juraschek SP, Solomon SD. Assessment of long-term benefit of intensive blood pressure control on residual life span: secondary analysis of the Systolic Blood Pressure Intervention Trial (SPRINT). *JAMA Cardiol*. 2020;5(5):576–581. <https://doi.org/10.1001/jamacardio.2019.6192>
6. King JB, Sakhuja S, Derington CG, et al. Annual cost of implementing intensive systolic blood pressure goals in the United States. *J Am Heart Assoc*. 2024;13(18):e034515. <https://doi.org/10.1161/jaha.124.034515>
7. Blood pressure treatment efficacy calculator. Accessed July 2, 2025. <https://www.bpmodel.org/>
8. Hernán MA, Dahabreh IJ, Dickerman BA, Swanson SA. The target trial framework for causal inference from observational data: why and when is it helpful? *Ann Intern Med*. 2025;178(3):402–407. <https://doi.org/10.7326/annals-24-01871>
9. Muntner P, Hernandez RK, Kent ST, et al. Staging and clean room: constructs designed to facilitate transparency and reduce bias in comparative analyses of real-world data. *Pharmacoepidemiol Drug Saf*. 2024;33(3):e5770. <https://doi.org/10.1002/pds.5770>
10. Makary MA, Prasad V. Priorities for a new FDA. *JAMA*. 2025;334(7):565–566. <https://doi.org/10.1001/jama.2025.10116>

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