Stratified effects of blood pressure-lowering treatment on long-term blood pressure: an individual patient-level meta-analysis involving 50 randomised trials and 334,219 participants

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Background: Meta-analyses of randomised controlled trials (RCT) have shown the efficacy of pharmacologic lowering of blood pressure (BP) in reducing cardiovascular disease (CVD) risk. While efficacy has been shown across important patient characteristics, meta-analysis based on aggregate data could not fully account for potential sources of variation due to individual-level characteristics. Moreover, it is unclear if any variation in treatment effects due to patient characteristics are reflected in differential effects of BP-lowering treatment on long-term BP according to these characteristics.

Purpose: We determined the effects of BP-lowering treatment on repeated measures of blood pressure, identified trial- and participant-level sources of heterogeneity, and examined consistency of these BP-lowering effects across different patient characteristics.

Methods: We conducted an individual patient-level data meta-analysis (N=50 trials) using one-stage approach. We classified trials according to trial design: drug comparison (N=28), placebo-controlled (N=21) and BP-lowering intensity (N=8) trials. We fitted mixed models with fixed treatment effects and fixed time effect, random intercepts at trial and participant level, and a random slope for time at participant level. We adjusted for age, sex and baseline BP (except when used as stratification factor). We used likelihood ratio test and Akaike information criterion to compare models.

Results: This meta-analysis included 334,219 (42% women) participants. At baseline, mean age=65 (SD=9) years, among whom 18% were current smokers, 47% had cardiovascular disease, 29% had diabetes, and 73% were previously on BP-lowering medication. Participants had an average of 8 BP measurements over 4 years of mean follow-up. For drug comparison trials, mean differences (95% confidence interval) in systolic BP (SBP) and diastolic BP (DBP) between comparison arms were 1.3 (1.2 to 1.3) mmHg and 0.5 (0.5 to 0.5) mmHg, respectively; for placebo-controlled trials, the SBP and DBP differences were 4.2 (4.0 to 4.3) mmHg and 1.9 (1.9 to 2.0) mmHg, respectively; and for BP-lowering intensity trials, the SBP and DBP differences were 8.2 (8.0 to 8.4) mmHg and 3.7 (3.6 to 3.9) mmHg, respectively. However, BP reduction differed by duration of follow-up, type of trial. In particular, for placebo-controlled and BP-intensity trials, heterogeneity in BP reductions according to patient characteristics such as baseline BP, age, sex, prior CVD, diabetes and non-randomised anti-hypertensive use were observed.

Conclusion: This study shows the role of pharmacologic agents in effectively reducing long-term BP across individuals with a wide range of characteristics. The magnitude of BP reduction varied by several patient characteristics. This might have implications for investigation and explanation of any differential effects of BP treatment on major clinical outcomes.

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