Review Article

More Versus Less Blood Pressure Lowering: An Update

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ABSTRACT

Purpose: This article summarizes the results of a recent systematic review and meta-analysis of the safety and efficacy of intensive blood pressure (BP) lowering, including an update with the SPRINT (Systolic Blood Pressure Intervention Trial) results. We discuss the consistency of results within this set of trials (eg, ACCORD [Action to Control Cardiovascular Risk in Diabetes] and SPRINT) and the results in the context of other BP-lowering trials, including the recently published HOPE3 (Heart Outcomes Prevention Evaluation–3) study.

Methods: This study was a narrative review with updated meta-analysis from systematic review of trials comparing more- versus less-intensive BP lowering.

Findings: With the addition of SPRINT, there are >20 trials comparing more- versus less-intensive treatment with 54,350 participants overall. Over an average of 3.9 years of follow-up, the average systolic BP was 133 mm Hg in the more-intensive treatment arms and 140 mm Hg in the less-intensive treatment arms. More-intensive BP lowering reduced the risk of major vascular events, with benefits seen across a range of groups defined according to baseline systolic BP (120–139 mm Hg, 140–159 mm Hg, or ≥160 mm Hg), age (<70 or >70 years), and main entry criterion (hypertension, diabetes, or renal disease).

Implications: The evidence accumulated thus far provides clear evidence of the benefits of BP lowering in the 120- to 140-mm Hg range for various high-risk patient groups. Although intensive BP lowering has side effects, these trials indicate that the benefits will predominate for those at high risk of major vascular events. (*Clin Ther*. 2016;38:2135–2141)

Key words: blood pressure, blood pressure targets, cardiovascular events, clinical practice, intensive blood pressure lowering, meta-analysis.

INTRODUCTION

The question of whether more blood pressure (BP) lowering will confer greater clinical benefits has been a topical one for at least 3 decades, ever since it became clear that BP was positively and continuously associated with cardiovascular disease.[1,2] This question is intrinsically linked with that of lower versus higher BP targets, and numerous trials sought to address this question by randomizing participants to more-intensive BP lowering to reach a lower target, versus less-intensive BP lowering to reach a standard target. The first 2 trials (HOT [Hypertension Optimal Treatment][3] and UKPDS [United Kingdom Prospective Diabetes Study][4]) were published in 1998; since then, 16 more trials have been published, most recently SPRINT (Systolic Blood Pressure Intervention Trial).[5] The challenge for an individual trial to reliably assess the effects of intensive BP lowering is to simultaneously achieve a large difference in BP reduction (eg, systolic blood pressure [SBP] >10 mm Hg or diastolic BP >5 mm Hg) and observe a large number of events (eg, many hundreds of cardiovascular events). Very few trials have achieved these 2 goals simultaneously. It is therefore particularly

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important to conduct meta-analyses to review all the evidence in context and overcome the problems of low power in individual trials.

The goal of the present review was to summarize the results of a recent systematic review and meta-analysis of the safety and efficacy of intensive BP lowering,[6] including an update with the SPRINT results.[7] We discuss the consistency of results within this set of trials (eg, ACCORD [Action to Control Cardiovascular Risk in Diabetes][8] and SPRINT[5]) and the results in the context of other BP-lowering trials, including the recently published HOPE3 (Heart Outcomes Prevention Evaluation–3) trial.[9]

RECENT EVIDENCE ASSESSING MORE- VERSUS LESS-INTENSIVE BP LOWERING

SPRINT randomized 9361 participants with systolic BP (SBP) between 130 and 180 mm Hg and increased risk of cardiovascular event (excluding those with stroke or diabetes) to a treatment target of SBP <140 mm Hg or <120 mm Hg. The treatment protocol for the intensive control group involved initial combination therapy, with monthly visits and treatment intensification, until the SBP target was reached or no further treatment was planned. If those in the control group had 1 measurement at <130 mm Hg or 2 measurements at <135 mm Hg, treatment was de-intensified. The trial was stopped early as a result of clear reductions in vascular and total mortality in the intensive treatment arm. The primary outcome (myocardial infarction [MI], acute coronary syndrome, stroke, heart failure, or death from cardiovascular causes) was reduced by 25% (95% CI, 11–34), and all-cause mortality was also significantly lower in the intensive treatment group.

Several aspects of SPRINT were intensely debated after its publication. Trials stopped early can exaggerate treatment effect estimates,[10] and some questioned how much this factor was relevant for SPRINT. However, the phenomenon is less important for trials such as SPRINT that observed large numbers of events. Importantly, SPRINT was stopped on the basis of 2 successive interim results. Second, some have noted that down-titration in usual care does not reflect normal practice. However, it was appropriate so that the trial could reliably address the hypothesis, and the SPRINT control group nonetheless had better control rates than usual care among many high-risk

Table I. Summary of more- versus less-intensive blood pressure (BP)-lowering trials.

Primary Inclusion Criteria	No. of Trials	Baseline BP, mm Hg	Mean BP in Active Group, mm Hg	Mean BP in Control Group, mm Hg	Difference in BP Reduction	Duration of Follow-up, y	No. of Participants	Mean Age, y	Female	No. of Major CV Events
Hypertension	6	168	137	142	4/3	3.6	31,821	65.0	51%	1114
Diabetes	5	143	125	138	12/6	5.3	6960	60.6	46%	866
Renal disease	6	138	128	137	10/4	6.0	2809	47.4	38%	234
Cerebrovascular disease	2	143	127	137	10/2	3.4	3399	64.1	37%	354
Multiple high-risk conditions	1	140	122	135	13/NR	3.3	9361	67.9	36%	319
All trials	20	156	133	140	7/4	3.9	54,350	64.0	46%	2887

CV = cardiovascular; NR = not reported.