

Xie X, Atkins E, Lv J, et al. **Effects of intensive blood pressure lowering on cardiovascular and renal outcomes: updated systematic review and meta-analysis.** *Lancet.* 2015 Nov 7. pii: S0140-6736(15)00805-3. doi: 10.1016/S0140-6736(15)00805-3. (Review) PMID: 26559744

BACKGROUND: Recent hypertension guidelines have reversed previous recommendations for lower blood pressure targets in high-risk patients, such as those with cardiovascular disease, renal disease, or diabetes. This change represents uncertainty about whether more intensive blood pressure-lowering strategies are associated with greater reductions in risk of major cardiovascular and renal events. We aimed to assess the efficacy and safety of intensive blood pressure-lowering strategies.

METHODS: For this updated systematic review and meta-analysis, we systematically searched MEDLINE, Embase, and the Cochrane Library for trials published between Jan 1, 1950, and Nov 3, 2015. We included randomised controlled trials with at least 6 months` follow-up that randomly assigned participants to more intensive versus less intensive blood pressure-lowering treatment, with different blood pressure targets or different blood pressure changes from baseline. We did not use any age or language restrictions. We did a meta-analysis of blood pressure reductions on relative risk (RR) of major cardiovascular events (myocardial infarction, stroke, heart failure, or cardiovascular death, separately and combined), and non-vascular and all-cause mortality, end-stage kidney disease, and adverse events, as well as albuminuria and progression of retinopathy in trials done in patients with diabetes.

FINDINGS: We identified 19 trials including 44 989 participants, in whom 2496 major cardiovascular events

were recorded during a mean 3.8 years of follow-up (range 1.0-8.4 years). Our meta-analysis showed that after randomisation, patients in the more intensive blood pressure-lowering treatment group had mean blood pressure levels of 133/76 mm Hg, compared with 140/81 mm Hg in the less intensive treatment group. Intensive blood pressure-lowering treatment achieved RR reductions for major cardiovascular events (14% [95% CI 4-22]), myocardial infarction (13% [0-24]), stroke (22% [10-32]), albuminuria (10% [3-16]), and retinopathy progression (19% [0-34]). However, more intensive treatment had no clear effects on heart failure (15% [95% CI -11 to 34]), cardiovascular death (9% [-11 to 26]), total mortality (9% [-3 to 19]), or end-stage kidney disease (10% [-6 to 23]). The reduction in major cardiovascular events was consistent across patient groups, and additional blood pressure lowering had a clear benefit even in patients with systolic blood pressure lower than 140 mm Hg. The absolute benefits were greatest in trials in which all enrolled patients had vascular disease, renal disease, or diabetes. Serious adverse events associated with blood pressure lowering were only reported by six trials and had an event rate of 1.2% per year in intensive blood pressure-lowering group participants, compared with 0.9% in the less intensive treatment group (RR 1.35 [95% CI 0.93-1.97]). Severe hypotension was more frequent in the more intensive treatment regimen (RR 2.68 [1.21-5.89], $p=0.015$), but the absolute excess was small (0.3% vs 0.1% per person-year for the duration of follow-up). INTERPRETATION: Intensive blood pressure lowering provided greater vascular protection than standard

regimens. In high-risk patients, there are additional benefits from more intensive blood pressure lowering, including for those with systolic blood pressure below 140 mmHg. The net absolute benefits of intensive blood pressure lowering in high-risk individuals are large.

FUNDING: National Health and Medical Research Council of Australia.