Stroke prevention (updated)

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In people with previous stroke or TIA: non-surgical prevention

Blood pressure reduction

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In this section:

Summary

Cardiovascular events

Compared with placebo/no treatment Blood pressure-lowering treatments (beta-receptor antagonists, diuretics, ACE inhibitors) are more effective at 3 years at reducing stroke, MI, and total vascular events in people with a prior stroke or TIA (high-quality evidence).

ACE inhibitors compared with placebo ACE inhibitors are more effective at reducing MI in people with a prior stroke or TIA, but no more effective at reducing stroke or vascular events (moderate-quality evidence).

Diuretics compared with placebo/no treatment Diuretics are more effective at reducing stroke and vascular events in people with a prior stroke or TIA, but no more effective at reducing MI (moderate-quality evidence).

Diuretic plus ACE inhibitor compared with placebo/no treatment The combination of a diuretic plus an ACE inhibitor is more effective at reducing stroke, MI, and vascular events in people with a prior stroke or TIA (moderate-quality evidence).

Beta-blockers compared with placebo/no treatment Beta-blockers are no more effective at reducing stroke, MI, or vascular events in people with a prior stroke or TIA (moderate-quality evidence).

Mortality

Compared with placebo/no treatment Blood pressure-lowering treatments (beta-receptor antagonists, diuretics, ACE inhibitors) are no more effective at reducing vascular death or all-cause mortality in people with a prior stroke or TIA (moderate-quality evidence).

For GRADE evaluation of interventions for stroke prevention, see table.

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Benefits

We found two systematic reviews comparing blood pressure-lowering treatment (beta-receptor antagonists, diuretics, ACE inhibitors, or calcium channel blockers) versus placebo or no treatment. [13] [14]

Blood pressure-lowering treatment versus placebo or no treatment:

The first review (search date not reported, 7 RCTs, 15,527 people with a prior stroke or TIA, followed up for 2–5 years), [13] found that antihypertensive treatment (beta-receptor antagonists, diuretics, ACE inhibitors) reduced blood pressure by a mean of 8 mm Hg systolic/4 mm Hg diastolic, and significantly reduced stroke, MI, and total vascular events after a mean of 3 years of treatment compared with placebo or no treatment (stroke: 689/7779 [9%] with treatment *v* 888/7748 [11%] with control; OR 0.76, 95% CI 0.63 to 0.92; MI: 244/7729 [3%] with treatment *v* 311/7699 [4%] with control; OR 0.79, 95% CI 0.63 to 0.98; total vascular events [stroke, MI, or vascular death]: 993/7729 [13%] with treatment *v* 1232/7699 [16%] with control; OR 0.79, 95% CI 0.66 to 0.95). However, blood pressure-lowering treatments did not significantly reduce vascular death or all-cause mortality compared with placebo or no treatment (vascular death: OR 0.86, 95% CI 0.70 to 1.06; all-cause mortality: OR 0.91, 95% CI 0.79 to 1.05). [13] The second systematic review (search date 2003) examined the effects of blood pressure lowering generally in all population groups, not just in those with previous stroke or TIA (absolute numbers of those people with previous stroke or TIA not reported). [14] In subgroup analysis, it found that, in those people with stroke or previous TIA, blood pressure lowering-treatment significantly reduced the risk of stroke compared with placebo (RCTs in whom 'most' or 'all' had a history of stroke or TIA: RRR 22%, 95% CI 12% to 31%; RCTs and absolute numbers in analysis not reported; results presented graphically). [14]

ACE inhibitors versus placebo:

The first review found that, compared with placebo, ACE inhibitors significantly reduced MI, but did not significantly reduce stroke or vascular events (2 RCTs; 3574 people; OR for MI: 0.74, 95% CI 0.56 to 0.98; OR for stroke: 0.92, 95% CI 0.75 to 1.13; OR for vascular events: 0.83, 95% CI 0.61 to 1.12). [13]

Diuretics versus placebo or no treatment:

The first review found that, compared with placebo or no treatment, diuretics significantly reduced stroke and vascular events, but did not significantly reduce MI (3 RCTs; 6216 people; stroke: OR 0.68, 95% CI 0.50 to 0.92; vascular events: OR 0.75, 95% CI 0.63 to 0.90; MI: OR 1.06, 95% CI 0.63 to 1.78). [13]

Diuretic plus ACE inhibitor versus placebo or no treatment:

The first review found that a diuretic plus an ACE inhibitor significantly reduced stroke, MI, and vascular events compared with placebo or no treatment (1 RCT; 3544 people; stroke: OR 0.55, 95% CI 0.45 to 0.68; vascular events: OR 0.58, 95% CI 0.48 to 0.69; MI: OR 0.55, 95% CI 0.38 to 0.79). [13]

Beta-blockers versus placebo or no treatment:

The first review found that beta-blockers did not significantly reduce stroke, MI, or vascular events compared with placebo (2 RCTs; 2193 people; stroke: OR 0.93, 95% CI 0.72 to 1.20; MI: OR 0.94, 95% CI 0.60 to 1.45; all vascular events: OR 1.01, 95% CI 0.81 to 1.27). [13]

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Harms

The systematic reviews gave no information on adverse effects. [13] [14] Two RCTs identified by the first systematic review found that atenolol increased the risk of adverse effects leading to discontinuation of treatment (most commonly fatigue, cold extremities, bradycardia, dizziness, or subjective discomfort) compared with placebo (first RCT: 108/732 [15%] with atenolol *v* 56/741 [8%] with placebo; significance data not reported; second RCT: 63/372 [17%] with atenolol *v* 35/348 [10%] with placebo; significance data not reported). [15] [16] The largest RCT identified by the first review found that perindopril with or without added indapamide slightly but significantly increased the risk of people discontinuing treatment compared with placebo (714/3051 [23%] with treatment *v* 636/3054 [21%] with placebo; P = 0.02). [17] Another RCT identified by the first review found that ramipril slightly increased the risk of people discontinuing treatment compared with placebo (1343/4645 [29%] *v* 1268/4652 [27%]; significance data not reported). These adverse-event data were based on analyses of people with and without prior cerebrovascular events. [18]

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Comment

The first systematic review found that a larger reduction in blood pressure was associated with a greater relative reduction in stroke and in vascular events. [13] The review also found that the effects of blood pressure lowering-treatments on stroke and on all vascular events varied according to the antihypertensive regimen used; those drug regimens which reduced blood pressure the most also achieved the greatest reduction in stroke or vascular events. [13] The second review, which included RCTs in all population groups (not just people with previous stroke or TIA), performed a meta-regression analysis to assess the relationship between net reduction in systolic blood pressure and the risk of stroke. [14] The review found that that a dose–response relationship existed between blood pressure and stroke risk, and that a 10 mm Hg reduction in systolic blood pressure was associated with a relative reduction in the risk of stroke of 31% (further details not reported). [14] The first review found that, across all control groups, the average risk of stroke 11.5%, and the average risk of vascular events 16% (ARR for stroke and for vascular events with treatment compared with control: 3%, about 1% a year). [13] The largest RCT included in the review compared 4 years of the ACE inhibitor perindopril plus the diuretic indapamide (added at the discretion of the treating physician) versus placebo. The relative risk reduction of stroke and vascular events remained similar, regardless of baseline blood pressure and the type of qualifying cerebrovascular event (ischaemic or haemorrhagic). [17] It found that, compared with placebo, perindopril plus the diuretic indapamide reduced blood pressure by 9/4 mm Hg, and reduced stroke and major vascular events (stroke: RR 0.72, 95% CI 0.62 to 0.83; major vascular events: RR 0.74, 95% CI 0.66 to 0.84). [17]

Clinical guide:

Overviews of observational studies in healthy middle-aged and elderly people, as well as in those with a history of cerebrovascular events, found no evidence of a threshold below which treatment was ineffective for reducing stroke, at least down as far as about 115/75 mm Hg. [3] [19] [20] [21] However, it seems appropriate to be particularly cautious about lowering blood pressure in people with known severe stenosis of the carotid or vertebral arteries, because of the possibility of precipitating a stroke. [22] Observational studies in people with severe bilateral stenosis found that lower blood pressure was associated with an increased risk of stroke, suggesting that aggressive blood pressure lowering may not be advisable in this group. [23]

References

3. Eastern Stroke and Coronary Heart Disease Collaborative Research Group. Blood pressure, cholesterol, and stroke in eastern Asia. *Lancet* 1998;352:1801–1807. [PubMed]

13. Rashid P, Leonardi-Bee J, Bath P. Blood pressure reduction and secondary prevention of stroke and other vascular events. A systematic review. *Stroke* 2003;34:2741–2749. [PubMed]

14. Lawes C, Bennett DA, Feigin VL, et al. Blood pressure and stroke. An overview of published reviews. *Stroke* 2004;35:1024–1033. [PubMed]

15. Eriksson S, Olofsson BO, Wester PO for the TEST study group. Atenolol in secondary prevention after stroke. *Cerebrovasc Dis* 1995;5:21–25.

16. Dutch TIA Trial Study Group. Trial of secondary prevention with atenolol after transient ischaemic attack or non-disabling ischaemic stroke. *Stroke* 1993,24:543–548.

17. PROGRESS Collaborative Group. Randomised trial of a perindopril-based blood-pressure-lowering regimen among 6105 individuals with previous stroke or transient ischaemic attack. *Lancet* 2001;358:1033–1041. [PubMed]

18. The Heart Outcomes Prevention Evaluation Study Investigators. Effects of an angiotensin-converting-enzyme inhibitor, ramipril, on cardiovascular events in high-risk patients. *New Engl J Med* 2000;342:145–153. [PubMed]

19. Prospective Studies Collaboration. Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. *Lancet* 2002;360:1903–1913. Search date not reported; primary sources Medline, Embase, abstracts of meetings, and contact with investigators. [PubMed]

20. Rodgers A, MacMahon S, Gamble G, et al, for the United Kingdom Transient Ischaemic Attack Collaborative Group. Blood pressure and risk of stroke in patients with cerebrovascular disease. *BMJ* 1996;313:147. [PubMed]

21. Neal B, Clark T, MacMahon S, et al, on behalf of the Antithrombotic Trialists' Collaboration. Blood pressure and the risk of recurrent vascular disease. *Am J Hypertension* 1998;11:25A–26A.

22. Staessan JA, Wang J. Blood-pressure lowering for the secondary prevention of stroke. *Lancet* 2001;358:1026–1027. [PubMed]

23. Rothwell PM, Howard SC, Spence JD, for the Carotid Endarterectomy Trialists' Collaboration. Relationship between blood pressure and stroke risk in patients with symptomatic carotid occlusive disease. *Stroke* 2003;34:2583–2592. [PubMed]