Antihypertensive drugs in very old people: a subgroup meta-analysis of randomised controlled trials


Authors' objectives
To assess the effectiveness of anti-hypertensive drugs in patients over 80 years of age.

Searching
The authors performed a literature review (details not reported) and contacted principal investigators of published trials and the authors of meta-analyses and the results of a systematic review on this topic for the Cochrane Collaboration.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs). Follow-up ranged from 2.1 to 6.8 (mean 3.5) years in length and the percentage lost to follow-up ranged between 0% and 9% (mean 3%).

Specific interventions included in the review
Anti-hypertensive drugs (beta blockers, thiazide, calcium antagonist, or alpha2 antagonist) compared with placebo, no treatment, or lower dosage. Dosages were not reported.

Participants included in the review
Patients 80 years of age or older with hypertension.

Outcomes assessed in the review
Fatal and non-fatal stroke, excluding transient ischaemic attack as the primary outcome. Secondary outcomes were death from all causes, cardiovascular death, fatal and non-fatal major coronary and cardiovascular events and congestive heart failure. Angina pectoris or coronary revascularisation alone were not classified as major coronary events. Deaths from pulmonary thromboembolism were included with cardiovascular deaths.

How were decisions on the relevance of primary studies made?
The authors do not state how the papers were selected for the review, or how many of the authors performed the selection.

Assessment of study quality
No formal assessment of quality was undertaken.

Data extraction
The authors do not state who, or how many of the authors, performed the data extraction.

Data were extracted for the categories of trial characteristics (number of patients and % of the total number, first-line treatment, blood pressure inclusion criteria, follow-up, and loss to follow-up), baseline characteristics (mean (SD) age in years, maximum age in years, percentage male and female, mean (SD) systolic and diastolic blood pressure, mean (SD) serum cholesterol) and clinical history (percentages of smokers, and percentages of participants with diabetes, myocardial infarction or stroke).

The authors calculated the relative risk of each outcome between treatment groups for each trial.

Methods of synthesis
How were the studies combined?
Pooled relative risk (RR) was calculated with 95% confidence intervals (95% CIs).

How were differences between studies investigated?
The authors tested for heterogeneity but have not named the tests used in the assessment.

Subgroup analyses were performed but excluding the data from two trials with open-label design to assess the possible influence of these trials' on the overall results. The authors also tested the robustness of the results by estimation of the number of additional trials with no treatment effect that would be needed to give a non-significant overall result in an updated meta-analysis.

Results of the review
Seven RCTs were included in the review with 1,670 participants (874 active participants and 796 control participants).

There was no heterogeneity in terms of primary outcome between trials (p = 0.37) or between the subgroups of trials of difference designs (p = 0.59). There was also no heterogeneity in secondary outcomes between trials.

There were 57 strokes and 34 deaths among 874 actively treated patients compared with 77 strokes and 28 stroke deaths among 796 controls, representing 1 non-fatal stroke prevented for about 100 patients treated each year.

Treatment prevented 34% of strokes (95% CI: 8, 52).

Rates of major cardiovascular events and heart failure were significantly decreased, by 22% and 39% respectively. However, there was no treatment benefit for cardiovascular death, and a non-significant 6% (95% CI: -5, 18) relative excess of death from all causes (245 deaths in the intervention group versus 223 in the control group).

The authors found that the positive results from the meta-analysis were not robust and that only one additional trial with no treatment effect was needed to make their results statistically non-significant.

Authors' conclusions
The inconclusive findings for mortality contrast with the benefit of treatment for non-fatal events.

CRD commentary
The authors have clearly stated their research question and some inclusion and exclusion criteria. The literature search is poor because the details of the search and the search strategy are not reported. It is not possible to determine whether the authors may have missed relevant studies.

The quality of the included studies was not formally assessed and the authors have not reported on how the articles were selected, or how many of the reviewers were involved in the data selection and extraction.

The data extraction is reported in tables and text and the statistical pooling was appropriate. There were tests for heterogeneity (but the method was not stated) and the authors have discussed several methodological and data limitations in the review.

The authors conclusions appear to follow from the results but should be viewed with caution because of the stated methodological limitations of the review.

Implications of the review for practice and research
Practice: the authors state that an age threshold beyond which hypertension should not be treated cannot be justified.

Research: The authors state that results of a large-scale specific trial are needed for definite conclusion that anti-hypertensive treatment is beneficial in very elderly hypertensive patients.
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Other publications of related interest
These additional published commentaries may also be of interest. Gray J. Review: antihypertensive drugs reduce stroke in patients 80 years of age or older. ACP J Club 1999;131:29. Gray J, review: antihypertensive drugs reduce stroke in patients 80 years or older. Evid Based Med 1999;4:144.

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This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.