

# Review: Low-dose diuretics, but not high-dose diuretics and $\beta$ -blockers, reduce coronary heart disease and total mortality

Psaty BM, Smith NL, Siscovick DS, et al. **Health outcomes associated with antihypertensive therapies used as first-line agents. A systematic review and meta-analysis.** JAMA. 1997 Mar 5;277:739-45.

## Objective

To determine the effectiveness of various antihypertensive therapies used as first-line agents to prevent major disease end points.

## Data sources

Randomized controlled trials were identified by searching the MEDLINE database (1980 to 1995) based on the terms (cerebrovascular diseases or heart diseases) and randomized controlled trial and (antihypertensive agents [therapeutic use] or hypertension [drug therapy]). Additional articles were identified by scanning bibliographies of relevant review articles.

## Study selection

Trials were selected if they were  $\geq 1$  year in duration; were placebo controlled; used diuretic therapy,  $\beta$ -blocker therapy, calcium channel blockers, or angiotensin-converting enzyme inhibitors as antihypertensive

agents; were unconfounded by other therapies; and assessed major disease end points. Trials were excluded if they were multiple risk factor intervention trials, used other antihypertensive therapies, or compared  $\beta$ -blocker therapy with diuretic therapy.

## Data extraction

Data were extracted on treatment strategy, patient numbers, duration of the trial, coronary heart disease, stroke, congestive heart failure, total mortality, and cardiovascular death.

## Main results

18 trials involving 48 220 patients met the selection criteria. All 18 trials were included in previous reviews and evaluated diuretic therapy or  $\beta$ -blocker therapy. No trials evaluating calcium channel blockers or angiotensin-converting enzyme inhibitors were found. Trials were classified according to 3 treatment strategies: high-dose diuretic therapy ( $\geq$  equivalent of 50 mg of chlorthalidone or hydrochlorothiazide), low-dose diuretic therapy (equivalent of 12.5 to 25 mg/d of chlorthalidone or hydrochlorothiazide), and  $\beta$ -blocker therapy. High-dose diuretic therapy reduced stroke ( $P < 0.001$ )\*, congestive heart failure

( $P < 0.001$ )\*, and cardiovascular death ( $P = 0.03$ ). Low-dose diuretic therapy reduced stroke ( $P < 0.001$ )\*, coronary heart disease ( $P < 0.001$ )\*, congestive heart failure ( $P < 0.001$ )\*, mortality ( $P = 0.04$ ), and cardiovascular death ( $P < 0.001$ ).  $\beta$ -blocker therapy reduced stroke ( $P < 0.05$ )\* and congestive heart failure ( $P < 0.005$ )\*. (However, the absolute risk reductions were small ( $\leq 2.5\%$ ), thereby indicating numbers needed to treat over 40.)\*

## Conclusions

Diuretics and  $\beta$ -blockers used as first-line agents for the treatment of hypertension reduce the risk for stroke and congestive heart failure. In addition, low-dose diuretics reduce the risk for coronary heart disease and total mortality.

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\*Numbers calculated from data in article.

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## Commentary

The results of the review by Psaty and colleagues represent part of a paper that aims to answer the following question: Regarding health outcomes, which antihypertensive therapies qualify to be used as first-line agents for the treatment of hypertension? These investigators have also reviewed clinical trials in hypertension that evaluate surrogate end points (the Treatment of Mild Hypertension Study, a Veterans Affairs trial, and the Multicenter Isradipine Diuretic Atherosclerosis Study), clinical trials of secondary prevention (calcium channel blockers for coronary heart disease and angiotensin-converting enzyme inhibitors for congestive heart failure), and observational studies. Psaty and colleagues conclude that diuretic therapy

and  $\beta$ -blocker therapy are the only proven first-line agents for hypertension.

On the basis of results from large clinical trials, the authors consider both  $\beta$ -blocker therapy and nondihydropyridine calcium channel blockers for patients with coronary heart disease and angiotensin-converting enzyme inhibitors for patients with congestive heart failure to be "special indications." It is also worth emphasizing that the effectiveness of a low-dose diuretic-based antihypertensive strategy in the elderly is indisputable: 40 to 50 patients would need to be treated with low-dose diuretics for 5 years to prevent 1 additional major cardiovascular event, and 71 patients would need to be treated for 5 years to prevent 1 additional death (95%

CI 37 to 717). Conclusions were independent of the Hypertension Detection and Follow-up Study results (1) and confirmed 2 other reviews not cited in this paper (2, 3).

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## References

1. Ramsay LE. The Hypertension Detection and Follow-up Program: 17 years on. JAMA. 1997;277:167-70.
2. Insua JT, Sacks HS, Lau TS, et al. Drug treatment of hypertension in the elderly: a meta-analysis. Ann Intern Med. 1994; 121:355-62.
3. Guyeffier F, Froment A, Gouton M. New meta-analysis of treatment trials of hypertension: improving the estimate of therapeutic benefit. J Hum Hypertens. 1996;10:1-8.