

# Antihypertensive therapy with indapamide and perindopril reduced mortality in patients $\geq 80$ years

## STUDY DESIGN

**Design:** randomised placebo controlled trial (Hypertension in the Very Elderly Trial [HYVET]).

**Allocation concealment:** {concealed}\*.<sup>†</sup>

**Blinding:** blinded (patients, clinicians, and outcome adjudication committee).<sup>†</sup>

## STUDY QUESTION

**Setting:** 195 centres in Europe, China, Australasia, and Tunisia.

**Patients:** 3845 patients  $\geq 80$  years of age (mean age 84 y, 60% women) with persistent hypertension (mean sitting blood pressure [BP] 173/91 mm Hg). Exclusion criteria included accelerated or secondary hypertension, haemorrhagic stroke in the past 6 months, heart failure, gout, and dementia.

**Intervention:** sustained-release indapamide, 1.5 mg/day, with perindopril, 2 or 4 mg/day, added if needed to reach targets of systolic BP  $< 150$  mm Hg and diastolic BP  $< 80$  mm Hg (n = 1933) or placebo (n = 1912).

**Outcomes:** stroke, heart failure, any cardiovascular event, and death from any cause, cardiovascular cause, cardiac cause, or stroke.

**Follow-up period:** median 1.8 years.

**Patient follow-up:** 99.6% (intention-to-treat analysis).

## MAIN RESULTS

Antihypertensive treatment reduced risks of heart failure, any cardiovascular event, and death from stroke or any cause (table). At 2 years, target BP was achieved by 48% of the antihypertensive treatment group and 20% of the placebo group.

## CONCLUSION

In patients  $\geq 80$  years of age with persistent hypertension, antihypertensive therapy with indapamide and perindopril reduced all-cause mortality.

\*Bulpitt C, Fletcher A, Beckett N, et al. *Drugs Aging* 2001;**18**:151–64.

<sup>†</sup>See glossary.

Abstract and commentary also appear in "ACP Journal Club: The Best Evidence for Patient Care" in *Annals of Internal Medicine*.

## ABSTRACTED FROM

Beckett NS, Peters R, Fletcher AE, et al. Treatment of hypertension in patients 80 years of age or older. *N Engl J Med* 2008;**358**:1887–98.

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► **Clinical Impact Ratings:** Cardiology 7/7; GP/FP/Primary care 6/7; IM/Ambulatory care 6/7; Geriatrics 6/7

## Antihypertensive therapy v placebo in patients $\geq 80$ years of age with persistent hypertension\*

Outcomes at median 1.8 years	Rate per 1000 person-years			
	Antihypertensive	Placebo	RRR (95% CI)	NNT (CI)
Stroke	12	18	30% (–1 to 51)	Not significant
Heart failure	5.3	15	64% (42 to 78)	106 (87 to 162)
Cardiovascular event <sup>†</sup>	34	51	33% (18 to 46)	60 (43 to 113)
Death from all causes	47	60	20% (5 to 34)	82 (49 to 346)
Death from stroke	6.5	11	39% (1 to 62)	241 (151 to 9396)
Death from cardiovascular cause	24	31	23% (–1 to 40)	Not significant
Death from cardiac cause	6.0	8.4	29% (–19 to 58)	Not significant

\*Abbreviations defined in glossary. RRR, NNT, and CI calculated from data in article.

<sup>†</sup>Stroke, myocardial infarction, heart failure, or death from cardiovascular cause.

**H**YVET found that antihypertensive treatment in the very old decreased mortality and the incidence of heart failure, with benefits seen within the first year. Although the reduction in some outcomes did not reach statistical significance, perhaps because the trial was stopped early, the results are impressive.

An earlier meta-analysis of randomised trials on the same topic found a decrease in stroke but not mortality.<sup>1</sup> The HYVET authors speculated that the discrepancy in mortality results may be related to differences in treatment regimens, particularly the use of an angiotensin-converting enzyme inhibitor rather than a  $\beta$ -blocker. The finding of a mortality benefit needs to be replicated.

Of note, the target BP in HYVET and the trials included in the INDANA meta-analysis<sup>1</sup> was higher

than that recommended by current treatment guidelines.<sup>2</sup> This disparity raises the question of whether additional value would be provided in this age group by further lowering BP beyond the target pressure of 150/80 mm Hg, especially considering that this approach may increase adverse effects.

An important question about HYVET is whether the results are generalisable to most elderly people. The study sample was a relatively healthy group with low prevalence of diabetes mellitus and coronary artery disease. Patients with heart failure or dementia and those requiring nursing care were excluded. The relative benefits and risks of treating frail elderly people with multiple comorbid conditions were not addressed by this trial and may never be known. However, because heart failure is the most common reason for hospital admission in this population and

strokes can be life-altering events even to the very frail, antihypertensive treatment in moderation may be the best way to prevent these outcomes. Being 80 years of age or older should not preclude antihypertensive treatment.

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1. Gueyffier F, Bulpitt C, Boissel JP, et al. Antihypertensive drugs in very old people: a subgroup meta-analysis of randomised controlled trials. *INDANA Group. Lancet* 1999;**353**:793–6.
2. Chobanian AV, Bakris GL, Black HR, et al. Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. *Hypertension* 2003;**42**:1206–52.