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EDITORIAL

INCIDENT DEMENTIA IN TRIALS OF ANTIHYPERTENSIVE TREATMENTS

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The Systolic Blood Pressure Intervention Trial (SPRINT) Memory and Cognition in Decreased Hypertension (MIND) study (1), failed to show a significant effect on the primary endpoint (probable dementia, hazard ratio [HR] 0.83; 95% CI, 0.67-1.04). Because this may be due to limited power, the results of SPRINT MIND were put in the context of major randomised and controlled hypertension trials (RCT) in which incident dementia had been adjudicated.

The same search strategy as in an earlier meta-analysis (up to 2015) (2) was used to identify trials which fulfilled the following criteria: 1) RCT, 2) antihypertensive treatment for at least 2 years, 3) dementia (not only cognitive decline or clinical impression) as an adjudicated endpoint. Trials not fulfilling those criteria were excluded. Seven trials were identified, five trials were placebo-controlled, one compared intensive vs. usual treatment (1), and in one antihypertensives were part of multidomain prevention (3). HRs with 95% CI, and a meta-analysis of trials using random effects model and test for heterogeneity were performed with NCSS statistical software 8 (www.ncss.com).

Clinical data and HRs with 95% CI for individual trials are shown in Table 1. In addition to total in-trial results, some subgroup and extension data, and mild cognitive impairment (MCI) for SPRINT MIND are presented. Except in the Study on Cognition and Prognosis in the Elderly (SCOPE) (small inter-group blood pressure differences), point estimates of HRs for dementia were generally below unity suggesting benefit. However, the results were statistically significant only for the Systolic Hypertension in Europe (Syst-Eur) trial extension and in SPRINT MIND when incident MCI was combined with probable dementia (1). When results of the seven trials were combined in a meta-analysis (only adjudicated dementia, n=1,297), active or a more intensive antihypertensive treatment was associated with a significant reduction of dementia by 13% (95% CI -3% to -23%, P=0.011). Although heterogeneity test (Cochran's Q) was nonsignificant (P=0.60), the studies are admittedly very different, but this would rather give robustness to summary result. The result has also biological plausibility from observational studies (2).

To the best of our knowledge, no other intervention has similar record of dementia reduction in randomized trials as antihypertensive treatment. This message should be actively promoted in ageing societies as a feasible, usually safe, and with generic drugs also inexpensive way of dementia prevention in younger-old people. However, this may not apply to frailest and oldest patients (4).

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Table 1
Randomized controlled trials about antihypertensive treatment and clinical adjudicated dementia

Trial	No.	Age, y	Mean/median follow-up, y	BP difference, systolic/ diastolic, mm Hg	Mean in-trial BP, control, active, mm Hg	Compar-ison	Active (n/No.)	Control (n/No.)	HR (95% CI)	Remarks
SHEP [a]	4736	>60, mean 72	4.5	12/4	155/77, 143/68	Placebo	37/2365	44/2371	0.84 (0.55-1.30)	
PROGRESS [a]	6105	mean 64	3.9	9/4	143/85, 134/81	Placebo	193/3051	217/3054	0.89 (0.74-1.07)	Post-stroke patients
Syst-Eur	2418	>60, mean 70		10/5	160/84, 150/79	Placebo				
- in-trial [a]			2.0				11/1238	21/1180	0.50 (0.25-1.02)	
- extension			3.9				21/1238	43/1180	0.38 (0.23-0.64)	
SCOPE [a]	4937	70-89, mean 76	3.7	3/2	147/81, 144/79	Placebo	62/2477	57/2460	1.08 (0.75-1.54)	84% in the placebo group received antihypertensives
HYVET-COG [a]	3336	>80, mean 83	2.2	15/6	159/84, 144/78	Placebo	126/1687	137/1649	0.90 (0.71-1.13)	
preDIVA	1168	mean 74.5	6.7	NA	NA	Multi-domain inter-vention vs. usual care				
- subgroup with untreated blood pressure at baseline [a]							31/646	36/522	0.69 (0.43-1.11)	HR 0.54 (95% CI 0.32-0.92) among adherent participants
SPRINT MIND	8563	mean 68	5.1	13/NA	135/NA, 122/NA	Systolic BP goal < 140 mm Hg vs <120 mm Hg				Comparison of usual and tighter blood pressure control
-dementia [a]							149/4278	176/4285	0.83 (0.67-1.04)	
- MCI							287/4278	353/4285	0.81 (0.69-0.95)	
-combined							402/4278	469/4285	0.85 (0.74-0.97)	
All antihypertensive trials with adjudicated dementia [a]	31 263						609/15 742	688/15 521	0.87 (0.77-0.97)	Meta-analysis of proportions in trials with random effects model, P=.011 Test for heterogeneity: Cochran's Q 4.59; P=.60

Abbreviations: BP, blood pressure. CI, confidence interval. MCI, mild cognitive impairment. HR, hazard ratio. CI, confidence interval. SHEP, the Systolic Hypertension in the Elderly Program. PROGRESS, the Perindopril Protection Against Recurrent Stroke Study. Syst-Eur, Systolic Hypertension in Europe. SCOPE, the Study on Cognition and Prognosis in the Elderly. HYVET-COG, The Hypertension in the Very Elderly Trial cognitive function assessment. preDIVA, Prevention of Dementia by Intensive VAscular care. SPRINT MIND, the Systolic Blood Pressure Intervention Trial Memory and Cognition in Decreased Hypertension. n = number with dementia (or MCI in SPRINT MIND). No. = total population. NA, not available.
a. Trials included in meta-analysis.