

## Major Hypertension Cardiovascular Prevention Trials: Event Reduction

Trial	Patient number	Percentage Change in Trial Endpoint of Treatment Groups. All events (fatal and non fatal)			Intervention vs placebo unless otherwise specified
		Hypertension Trials			
		CVA	Cardiac	All CV	
SHEP (1)	4736	-36	-2	-34	Chlorthalidone & Atenolol
MRC (2)	4396	-25	-19	-17	HCT, Amiloride & Atenolol
STOP-H (3)	1627	-47	-13 (MI)	-17	HCT, Amiloride Atenolol, Metoprolol, Pindolol
<a href="#">Syst-Eur</a> (4)	4695	-42	-26	-31	Nitrendipine, Enalapril & HCT
<a href="#">HOT Trial</a> (5)	18790	-30 in DM subset (Target DBP 90 vs 80 mmHg)	-28 (p=0.05)	-50 in DM subset (Target DBP 90 vs 80 mmHg)	Felodipine based Rx: At end of study Felodipine (78%) ± ACE-i (41%), β-blocker (28%), HCT (22%)
		<ul style="list-style-type: none"> <li>• 68% on combo therapy</li> <li>• Study compared BP targets (<math>\leq 90,85,80</math> mm Hg)</li> </ul>			
<a href="#">CAPPP</a> (6)	10985	+25	-23	NS	Captopril vs β-blocker or diuretic
<a href="#">STOP-2</a> (7)	6614	NS	NS	NS	β-blocker or HCT vs ACE-i vs DHP-CCB
<a href="#">NORDIL</a> (8)	≈11,000	-20	+16	NS	Diltiazem vs β-blocker ± HCT
<a href="#">INSIGHT</a> (9)	6321	NS	NS	NS	Nifedipine vs HCT/Amiloride
<a href="#">PROGRESS</a> (10)	6105	-28	NS	-26	Perindopril alone (42%) ± Indapamide (58%)
		Outcomes driven by combination therapy			
<a href="#">LIFE</a> (11)	9193	-25	NS	-13	Losartan vs Atenolol
<a href="#">SCOPE</a> (12,13)	4964	-24	NS	NS	Candesartan (± diuretic) vs placebo (± diuretic)
		Outcomes driven by non-fatal stroke			

<a href="#">ALLHAT</a> (14,15)	33357	<ul style="list-style-type: none"> <li>• Doxazosin arm dropped - 25% increase major secondary endpoint, combined CVD outcome driven by 50% increase in CHF</li> <li>• Significant increase in CHF: LDD vs ACEi 19% &amp; CCB 38% (p&lt;.001)</li> </ul>	Chlorthalidone (LDD) vs Lisinopril (ACE-i), Amlodipine (CCB)& Doxazosin
		<p>15%                      NS                      10%</p> <p>increase                      increase</p> <p>ACE/LDD                      ACE/LDD</p> <p>p=0.002                      P=0.001</p> <p>(blacks)                      (blacks)</p>	LDD vs ACE-i vs CCB
<a href="#">ANBP2</a> (16)	6083	<ul style="list-style-type: none"> <li>• 11% decrease in CV event or death overall (p=0.05)</li> <li>• 17% decrease in CV event or death overall in males (p=0.02)</li> <li>• 32% decrease in first MI (p=0.04)</li> </ul>	ACE-inhibitor (90% enalapril) vs diuretic
		<p>NS                      NS                      NS</p>	
<a href="#">VALUE</a> (17)	15245	Fatal and serious non-fatal CV events	Valsartan vs Amlodipine
<a href="#">ACTION</a> (18)	7665	Hi risk Patients with stable CAD	Nifedipine vs placebo
<a href="#">INVEST</a> (19)	22576	Patients with HTN and CAD	Verapamil+
		No difference in death (all cause), MI, CVA, CV death, angina, BP control	Trandolapril vs Atenolol + HCT

1. Prevention of stroke by antihypertensive drug treatment in older persons with isolated systolic hypertension. Final results of the Systolic Hypertension in the Elderly Program (SHEP). SHEP Cooperative Research Group. JAMA 1991; 265:3255.

2. MRC trial of treatment of mild hypertension: principal results. Medical Research Council Working Party. Br Med J (Clin Res Ed) 1985; 291:97.

3. Dahlöf, B, Lindholm, LH, Hansson, L, et al. Morbidity and mortality in the Swedish Trial in Old Patients with Hypertension (STOP-Hypertension). Lancet 1991; 338:1281.

4. Staessen JA; Fagard R; Thijs L; Celis H; Arabidze GG; Birkenhager WH; Bulpitt CJ; de Leeuw PW; Dollery CT; Fletcher AE; Forette F; Leonetti G; Nachev C; O'Brien ET; Rosenfeld J; Rodicio JL; Tuomilehto J; Zanchetti A. Randomised double-blind comparison of placebo and active treatment for older patients with isolated systolic hypertension. The Systolic Hypertension in Europe (Syst-Eur) Trial Investigators. Lancet 1997350(9080):757-64.

5. Hansson, L, Zanchetti, A, Carruthers, SG, et al. Effects of intensive blood-pressure lowering and low-dose aspirin in patients with hypertension: Principal results of the Hypertension Optimal Treatment (HOT) randomised trial. Lancet 1998; 351:1755.

6. Hansson, L, Lindholm, LH, Niskanen, L, et al, for the Captopril Prevention Project (CAPPP) study group. Effect of angiotensin-converting-enzyme inhibition compared with conventional therapy on cardiovascular morbidity and mortality in hypertension: the Captopril Prevention Project (CAPPP) randomised trial. Lancet 1999; 353:611.

7. Hansson, L, Lindholm, LH, Ekblom, T, et al. Randomised trial of old and new antihypertensive drugs in elderly patients: cardiovascular mortality and morbidity the Swedish Trial in Old Patients with Hypertension-2 study [see comments]. *Lancet* 1999; 354:1751.
8. Hansson, L, Hedner, T, Lung-Johansen, P, et al, for the NORDIL Study Group. Randomised trial of effects of calcium antagonists compared with diuretics and beta-blockers on cardiovascular morbidity and mortality in hypertension: the Nordic Diltiazem (NORDIL) study. *Lancet* 2000; 356:359.
9. Brown, MJ, Palmer, CR, Castaigne, A, et al. Morbidity and mortality in patients randomised to double-blind treatment with a long-acting calcium-channel blocker or diuretic in the International Nifedipine GITS study: Intervention as a Goal in Hypertension Treatment (INSIGHT). *Lancet* 2000; 356:366.
10. Randomised trial of a perindopril-based blood-pressure-lowering regimen among 6105 individuals with previous stroke or transient ischaemic attack. PROGRESS Collaborative Group. *Lancet* 2001; 358:1033.
11. Dahlof, B, Devereux, RB, Kjeldsen, SE, et al. Cardiovascular morbidity and mortality in the Losartan Intervention for Endpoint reduction in hypertension study (LIFE): a randomised trial against atenolol. *Lancet* 2002; 359:995.
12. Hansson L, Lithell H, Skoog I, Baro F, Bánki CM, Breteler M et al .Study on COgnition and Prognosis in the Eldery (SCOPE). *Blood Press* 1999;8:177-83.
13. Lithell H, Hansson L, Skoog I , Elmfeldt D, Hofman A, Olofsson B, Trenkwalder P, Zanchetti A, for the SCOPE Study Group. The Study on Cognition and Prognosis in the Elderly (SCOPE): principal results of a randomized double-blind intervention trial. *J.of Hypertension* 2003; 21(5):875-886.
14. Davis BR, Cutler JA, Gordon DJ, Furberg CD, Wright JT Jr, Cushman WC, Grimm RH, LaRosa J, Whelton PK, Perry HM, Alderman MH, Ford CE, Oparil S, Francis C, Proschan M, Pressel S, Black HR, Hawkins CM. Rationale and design for the Antihypertensive and Lipid Lowering treatment to prevent Heart Attack Trial (ALLHAT). *Am J Hypertens* 1996;9:342-60.
15. The ALLHAT Officers and Coordinators for the ALLHAT Collaborative Research Group. Angiotensin-Converting Enzyme Inhibitor or Calcium Channel Blocker vs Diuretic: The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT). *JAMA*. 2002;288:2981-2997.
16. Wing LMH, Reid CM, Ryan MB, Beilin LJ, Brown MA, Jennings GLR, Johnston CI, McNeil JJ, Macdonald GJ, Marley JE, Morgan TO, West MJ for the Second Australian National Blood Pressure Study Group. A Comparison of Outcomes with Angiotensin-Converting-Enzyme Inhibitors and Diuretics for Hypertension in the Elderly *NEJM* 2003; 348(7):583-592.
17. Julius S, Kjeldsen SE, Brunner HR, et al for the VALUE Trial Group: Outcomes in hypertensive patients at high cardiovascular risk treated with regimens based on valsartan or amlodipine: the VALUE randomized trial. [Lancet 2004; 363\(9426\):2022-31.](#)
18. Poole-Wilson PA, Lubsen J, Kirwan BA, et al for the A Coronary disease Trial Investigating Outcome with Nifedipine gastrointestinal therapeutic system investigators: Effect of long-acting nifedipine on mortality and cardiovascular morbidity in patients with stable angina requiring treatment (ACTION trial): Randomised controlled trial. [Lancet 2004; 364\(9437\):849-57.](#)
19. Pepine CJ, Handberg EM, Cooper-DeHoff RM, et al for the INVEST Investigators: A calcium antagonist vs. a non-calcium antagonist hypertension treatment strategy for patients with coronary artery disease. The International Verapamil-Trandolapril Study (INVEST): A randomized controlled trial. [JAMA 2003; 290\(21\):2805-16.](#)