Major Hypertension Cardiovascular Prevention Trials: Event Reduction

<table>
<thead>
<tr>
<th>Trial</th>
<th>Patient number</th>
<th>Percentage Change in Trial Endpoint of Treatment Groups. All events (fatal and non fatal) Hypertension Trials</th>
<th>Intervention vs placebo unless otherwise specified</th>
</tr>
</thead>
<tbody>
<tr>
<td>SHEP (1)</td>
<td>4736</td>
<td>CVA -36 Cardiac -2 All CV -34</td>
<td>Chlorthalidone &amp; Atenolol HCT, Amiloride &amp; Atenolol HCT, Amiloride Atenolol, Metoprolol, Pindolol Nitrendipine, Enalapril &amp; HCT Felodipine based Rx: At end of study Felodipine (78%) ± ACE-i (41%), β-blocker (28%), HCT (22%)</td>
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<tr>
<td>MRC (2)</td>
<td>4396</td>
<td>-25 -19 -17</td>
<td></td>
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<tr>
<td>STOP-H (3)</td>
<td>1627</td>
<td>-47 -13 (MI) -17</td>
<td></td>
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<tr>
<td>Syst-Eur (4)</td>
<td>4695</td>
<td>-42 -26 -31</td>
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<tr>
<td>HOT Trial (5)</td>
<td>18790</td>
<td>-30 in DM subset (Target DBP 90 vs 80 mmHg) -28 (p=0.05) -50 in DM subset (Target DBP 90 vs 80 mmHg)</td>
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<tr>
<td></td>
<td></td>
<td>• 68% on combo therapy</td>
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<td>• Study compared BP targets (≤ 90,85,80 mm Hg)</td>
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<tr>
<td>CAPPPP (6)</td>
<td>10985</td>
<td>+25 -23 NS</td>
<td>Captopril vs β-blocker or diuretic β-blocker or HCT vs ACE-i vs DHP-CCB Diltiazem vs β-blocker ± HCT Nifedipine vs HCT/Amiloride Perindopril alone (42%) ± Indapamide (58%)</td>
</tr>
<tr>
<td>STOP-2 (7)</td>
<td>6614</td>
<td>NS NS NS</td>
<td></td>
</tr>
<tr>
<td>NORDIL (8)</td>
<td>≈11,000</td>
<td>-20 +16 NS</td>
<td></td>
</tr>
<tr>
<td>INSIGHT (9)</td>
<td>6321</td>
<td>NS NS NS</td>
<td></td>
</tr>
<tr>
<td>PROGRESS (10)</td>
<td>6105</td>
<td>-28 NS -26 Outcomes driven by combination therapy</td>
<td></td>
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<tr>
<td>LIFE (11)</td>
<td>9193</td>
<td>-25 NS -13</td>
<td></td>
</tr>
<tr>
<td>SCOPE (12,13)</td>
<td>4964</td>
<td>-24 NS NS Outcomes driven by non-fatal stroke</td>
<td></td>
</tr>
</tbody>
</table>
ALLHAT (14,15) 33357  
- Doxazosin arm dropped - 25% increase major secondary endpoint, combined CVD outcome driven by 50% increase in CHF
- Significant increase in CHF: LDD vs ACEi 19% & CCB 38% (p<.001)
  \[\text{increase ACE/LDD} = 15\% \\
  \text{increase ACE/LDD} = 10\% \\
  p = 0.002 \\
  p = 0.001 \text{(blacks)} \]

Chlorthalidone (LDD) vs Lisinopril (ACE-i), Amlodipine (CCB) & Doxazosin LDD vs ACE-i vs CCB

ANBP2 (16) 6083  
- 11% decrease in CV event or death overall (p=0.05)
- 17% decrease in CV event or death overall in males (p=0.02)
- 32% decrease in first MI (p=0.04)
  \[\text{NS} \quad \text{NS} \quad \text{NS} \]

ACE-inhibitor (90% enalapril) vs diuretic

VALUE (17) 15245 Hi risk
- Fatal and serious non-fatal CV events
- 10.6% valsartan vs 10.4% amlodipine

Valsartan vs Amlodipine

ACTION (18) 7665 Patients with stable CAD
- Nifedipine had no effect on MI rate

Nifedipine vs placebo

INVEST (19) 22576 Patients with HTN and CAD
- No difference in death (all cause), MI, CVA, CV death, angina, BP control

Verapamil+ Trandolapril vs Atenolol + HCT


4. Staessen JA; Fagard R; Thijs L; Celis H; Arabidze GG; Birkenhager WH; Bulpitt CJ; de Leeuw PW; Dollery CT; Fletcher AE; Fovere 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.


