Key Hypertension Trials – Bullet Points

Trial Name	Year	Patients	Intervention	BP Achieved	Results	Comments
VA Cooperative I (Effects of Tx on Morbidity in HTN, Results in Patients w/DBP Average 115-129 mmHg)	1967	• 143 pts • 54% AA, 100% male • Baseline BP 186/121	• Combo: HCTZ 50 BID, reserpine 0.1 BID, hydralazine 50 TID vs. P	• BP changes ○ Tx – ↓ 43/30 ○ P – No changes	• ↓ death – Tx 0/73, P 4/70 • ↓ morbid – Tx 1/73, P 10/70	• No clear DBP goal used • Tx group – ½ dose ↓ 2/2 low BP or side effects
VA Cooperative II (Effects of Tx on Morbidity in HTN, Results in Patients w/DBP Averaging 90-114)	1970	• 388 pts • ~40% AA, 100% male • Baseline BP ~164/104	• Combo: HCTZ 50 BID, reserpine 0.1 BID, hydral 25-50 TID vs. P ○ 50 TID hydral if DBP > 90	• BP changes ○ Tx – ↓ 27/17 ○ P – ↑ 4/1	• ↓ death – Tx 8/186, P 19/194 • ↓ morbid – T 18%, P 55%	• DBP goal ↓ to < 90
SHEP (Prevention of Stroke by Antihypertensive Drug Tx in Older Persons with Isolated Systolic HTN)	1991	• 4736 pts • 85% C, 57% F, 10% DM • Baseline BP 170/76	• Step 1: CTD 12.5-25 vs. P • Step 2: Atenolol 25-50 vs. P	• Tx: SBP 143 • P: SBP 155	• CVA – RR 0.64 • MI/CHD Death – RR 0.73 • Death – RR 0.87 (NS)	• 35% P group on BP meds • 1st trial showing ↓ SBP in "elderly" ↓ CV mortality
DASH (A Clinical Trial of the Effects of Dietary Patterns on Blood Pressure)	1997	• 459 pts • ~60% AA, ~50% F • < ¼ w/baseline SBP > 140 • Sodium intake stable	• Control: US diet vs. • F&V rich diet vs. • Combo diet (F&V + low-fat dairy, ↓ sat/total fat)	• N/A	• BP Changes ○ F&V (vs. con) – ↓ 7/3 ○ Combo (vs. con) – ↓ 11/6	• Combo diet ↓ BP most • BP ↓ more in pts w/HTN • K intake ↑ (2.9 g/d) w/combo diet • BP ↓ w/o weight loss
Syst-Eur (Randomized double-blind comparison of placebo + active tx for older pts w/isolated sys HTN)	1997	• 4695 pts • 66% F • Baseline BP 174/86	• Step 1: Nitrendipine 10-40 vs. P • Step 2-3: Enalapril 5-20 and/or HCTZ 12.5-25	• BP at 2 yrs ○ Tx – ~150/80 ○ P – ~160/85	• CVA – RR 0.58 • MACCE – RR 0.69 • Death – RR 0.86 (NS)	• Stopped early due to ↓ stroke
HOT (Effects of Intensive Blood-Pressure Lowering and Low-Dose Aspirin in Patients with Hypertension: Principal Results of the Hypertension Optimal Treatment (HOT) Randomized Trial)	1998	• 18,790 pts • 47% F, 8% DM • Baseline BP 170/105 • Also tested ASA vs P	• Three target DBPs ○ ≤ 90 ○ ≤ 85 ○ ≤ 80 • Step 1: Felodipine 5-10 • Step 2-4: ACEi or BB (+ dose ↑) • Step 5: Diuretic	• ≤ 90 – 143.7/85.2 • ≤ 85 – 141.4/83.2 • ≤ 80 – 139.7/81.1	• All patients ○ Major CV events – no Δ ○ Mortality – no Δ • Diabetic patients (90 vs. 80) ○ Major CV events – RR 2x ○ CV mortality – RR 3x	• Small Δ in BP and low # events ↓ differences • DM subgroup helped drive rec for < 130/80 • 2° analysis – least events at 130-140/80-85 • ASA reduced CV risk
UKPDS (United Kingdom Prospective Diabetes Study)	1998	• 1,148 pts • 87% C, 45% F • Newly dx DM • Baseline BP – 159/94	• Intensive control – < 150/85 • Loose control – < 180/105 • Main tx captopril or atenolol	• Tight – 144/82 • Loose – 154/87	• Tight control – ○ 32% ↓ DM mortality ○ 44% ↓ stroke ○ 37% ↓ microvasc disease	• ↓ all-cause mortality NS • Newly dx diabetic pts (compare vs. Accord)
HOPE (Heart Outcomes Prevention Evaluation)	2000	• 9,297 • 27%F, 38% DM • Known CVD or DM + CVD RF • 80% Hx CAD • Baseline BP 139/79	• 2x2 design • Ramipril 10 vs. P • Vitamin E vs P	• At 2 years ○ Ram – 136/76 ○ P – 139/77	• 1° outcome (MI, CVA, CV death) • Ramipril – RRR 22% • Reduced CV and all-cause mortality	• ACEi ↓ CVD/stroke • BP ↓ 3/2 in ram group • Limited ABPM study w/ sig BP ↓in ram group – clouds benefit of ACEi • No benefit to vit E
RENAAL (Reduction of Endpoints in NIDDM with the Angiotensin II Antagonist Losartan Trial)	2001	• 1,513 • ~1/2 C, 1/3 F, 100% DM • Median ACR 1.2g • Baseline BP 152/82	• Losartan 50-100 vs. P	• At end of study ○ ARB – 140/74 ○ P – 142/74	• 1° – time to 2x Cr, ESRD, death ○ Losartan – 16% RRR • ESRD RRR 28%	• ARB reduces progression of T2DN • No mortality benefit.
IDNT (Irbesartan Diabetic Nephropathy Trial)	2001	• 1,715 • ~70% C, ~1/3 F, 100% DM • Median ACR 1.9g • Baseline BP ~159/87	• Irbesartan 300 vs. • Amlodipine 10 vs. • Placebo • Target BP 135/85	• ARB – 140/77 • Amlo – 141/77 • P – 144/80	• 1° – time to 2x Cr, ESRD, death ○ ARB vs. P – RRR 20% ○ ARB vs. Amlo – RRR 23% ○ Amlo vs. P – No RR • Irbesartan ESRD RRR 23%	• ARB reduces progression of T2DN more than amlodipine • No mortality benefit

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AASK (Effect of Blood Pressure Lowering and Antihypertensive Drug Class on Progression of Hypertensive Kidney Disease)	2002	• 1094 pts • 100% AA, ~40% F • HTN CKD, eGFR 20-65 • Baseline BP ~150/95 • UPC 1/3 > 0.2 g/d	• 3x2 trial • MAP 102-107 vs. ≤ 92 • Metoprolol 50-200 vs. Ramipril 2.5-10 vs. amlodipine 5-10 • Open label-meds to make goal	• Goal ≤ 92: 128/78 • Goal 102-107: 141/85	• 1° outcome (↓GFR/ESRD/D) ○ ↓ BP did not ↓ 1° ○ R vs. M – 22% RRR ○ R vs A – 38% RRR • 10yr f/u -- If > 0.3g UPC, ↓ BP ↓ 1° (HR 0.73, < 400 pts)	• BP 2 mmHg ↓ for amlo • ACEi more effective than amlo and metop • More proteinuria ↓ = ↓ risk of ESRD
ALLHAT (Major Outcomes in High-Risk Hypertensive Patients Randomized to Angiotensin-Converting Enzyme Inhibitor or Calcium Channel Blocker vs. Diuretic)	2002	• 33,357 pts • 32% AA, 47%F, 36% DM • Baseline BP 146/84	• CTD 12.5-25 vs. • Amlodipine 2.5-10 vs0 • Lisinopril 10-40	• SBP (5 yrs) ○ CTD – 133.9 ○ Amlo – 134.7 ○ LSN – 135.9 • < 140/90 (5 yrs) ○ CTD – 68% ○ Amlo – 66% ○ LSN – 61%	• 1° outcome (CHD) – no Δ • Most 2° outcomes – no Δ • Stroke/CVD – ↑ 15/10% w/LSN vs. CTD • CHF – ↑ 38% w/amlo vs. CTD, ↑ 19% LSN vs. CTD	• Doxazosin inferior to CTD (esp. CHF), stopped early • CTD ↓ CVA > LSN • CTD ↓ CHF > AMLO/LSN • LSN less effective in AAs than CTD
VALIANT (Valsartan, Captopril, or Both in MI c/b CHF, Left Ventricular Dysfunction, or Both)	2003	• 14,703 pts • 94% C, 31% F, 23% DM • ≤10d post-MI w/CHF (sx or ↓ EF)	• CV Events Trial – ACE vs. ARB ○ Valsartan (80 BID) ○ Captopril (50 TID) ○ Combo (Val 40 BID, Cap 50)	• BP at 1 year • Val – 127/75 • Cap – 127/76 • Val/Cap – 125/75	• No Δ 1° or 2° outcomes • Valsartan not inferior • ↑ AEs w/combo (hypotension, AKI)	• No advantage to combo ACEi/ARB w/harm
ONTARGET (Telmisartan, Ramipril, or Both in Patients at High Risk for Vascular Events)	2008	• 25,620 pts • 73% C, 27% F • 38% DM, 85% CVD • Baseline BP 141/82	• ACE vs. ARB ○ Telmisartan (80 BID) ○ Ramipril (10 mg) ○ Combo	• Avg BP (vs. Ram) ○ ARB–↓ 0.9/0.6 ○ C–↓ 2.4/1.4	• No Δ 1° or 2° outcomes • ↑ AEs w/combo (hypotension, AKI)	• No advantage to combo ACEi/ARB w/harm • TRANSCEND (parallel study)–trend ↓ 1° w/ARB
HYVET (Treatment of Hypertension in Patients 80 Years of Age or Older)	2008	• 3,845 pts • 60% F, 7% DM, 32% ISH • Baseline BP 173/91	• Step 1: Indapamide SR 1.5 vs. p • Step 2: Perindopril 2-4 mg vs. p • Target BP < 150/80	• BP at 2 years ○ Tx ~143/78 ○ P ~158/84	• Tx improved outcomes ○ ↓ Death 21% ○ ↓ CVA 30%/↓ CHF 64%	• Tx HTN in "elderly" good • 3/4 pts between 80-85 yo • ½ tx group met < 150/90
Accomplish (Benazepril plus Amlodipine or Hydrochlorothiazide for Hypertension in High-Risk Patients)	2008	• 11,506 pts • 84% C, 40% F, 60% DM	• Compared combo pills ○ Benazepril 20-40/amlo 5-10 ○ Ben 20-40/HCTZ 12.5-25 • Target BP < 140/90 ○ <130/80 for DM, CKD	• B/A:131.6/73.3 • B/H:132.5/74.4 • < 140/90 ○ B/A: 75.4% ○ B/H: 72.4%	• 1° outcome – MACCE ○ Ben/Amlo – 9.6% ○ Ben/HCTZ – 11.8% • RRR 20%	• ACE/CCB may be more effective than ACE/HCTZ • Controversy re diuretic results vs. ALLHAT given use of HCTZ vs. CTD
ACCORD (Effects of Intensive Blood-Pressure Control in Type 2 Diabetes Mellitus)	2010	• 4,733 pts • 24% AA, 48% F • 100% DM, A1c 7.5-11 • Med duration of DM 10 • Baseline BP 139/76	• Intensive vs. Standard tx ○ Intensive SBP goal < 120 ○ Standard SBP goal < 140 • No specific drug requirements aside from using EBM drugs	• BP at 1 year ○ Intensive – 119.3/64.4 ○ Standard – 133.5/70.5	• 1° outcome – MI, CVA, CVD ○ Intensive – 1.87%/yr ○ Standard – 2.09%/yr ○ HR 0.88 (NS) • CVA – HR 0.59 (0.39-0.89) ○ Int (0.32%/yr) Stan (0.53%) • Serious adverse events ○ Int (3.3%) vs. Stan (1.3%)	• No clear benefit from intensive treatment. • Possible benefit in ↓ CVA. • Sig less events than expected → ↓ power • Avg of 10 years DM already, not newly diagnosed.
SPRINT (A Randomized Trial of Intensive versus Standard Blood-Pressure Control)	2015	• 9,361 pts • 32% AA, 36% F • High CVD risk but no DM • ~1/4 > 75, ~1/4 CKD • Baseline BP 140/78	• Intensive vs. Standard Tx ○ Intensive SBP goal < 120 ○ Standard SBP goal < 140 • CTD/amlodipine encouraged	• BP at 1 year ○ Intensive – 121.4 ○ Standard – 136.2	• 1° outcome – MACCE ○ Intensive – 1.65%/yr ○ Standard – 2.19%/yr ○ HR 0.75 • Mortality – HR 0.73 ○ Int (1%/yr) Stan (1.4%/yr)	• Small but clear benefit from intensive treatment • ↑ syncope, electrolytes, AKI in intensive group • Unobserved BP check may ↓ BP vs. other trials

Rob Rope, MD 2017