

BLOOD PRESSURE-LOWERING TREATMENT

TRIALS

NUMBER OF PARTICIPANTS	NUMBER OF WOMEN	PERCENTAGE OF WOMEN	MEAN AGE	MEAN FOLLOW-UP (YEARS)	TRIALS WITH ANALYSIS BY GENDER N, (%)
69,473	28,008	40.3%	70.2	3.2	3/5 (60%)

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TRIAL	YEAR	POPULATION	AGE	N° OF SUBJECTS	FOLLOW UP	TREATMENT	DESCRIPTION OF END-POINT	PRIMARY END-POINT	PRIMARY END-POINT HR	NOTES
		(Country)	mean ± sd, range	TOTAL (WOMEN n,%)	DURATION			TOTAL (WOMEN n,%) (MEN n,%)	(CI) P (WOMEN (MEN)	
ONTARGET (Yusuf et al ⁵⁰)	APRIL 2008	In patients with coronary, peripheral, or cerebrovascular disease or diabetes with end-organ damage International trial with significant European component	66.4±7.2 RAMIPRIL; 66.4±7.1 TELMISARTAN; 66.5±7.3 COMBINATION THERAPY	TOTAL 25620 (WOMEN: 6831, 27%) (MEN 18789)	Median of 56 months	RAMIPRIL (10 mg per day) vs TELMISARTAN (80 mg per day) vs both drugs (COMBINATION THERAPY)	Death from cardiovascular causes, myocardial infarction, stroke, or hospitalization for heart failure.	1423 (16.7%) TELMISARTAN 1412 (16.5%) RAMIPRIL 1386 (16.3%) COMBINATION THERAPY PRIMARY OUTCOME IN THE RAMIPRIL GROUP WOMEN 15.8% MEN 16.7%	RELATIVE RISK (TELMISARTAN VS. RAMIPRIL) = 1.01 [95% CI: 0.94 - 1.09] RELATIVE RISK (COMBINATION THERAPY VS. RAMIPRIL) = 0.99 [95% CI: 0.92- 1.07] TELMISARTAN VS. RAMIPRIL: P INTERACTION = 0.68 COMBINATION-THERAPY VS. RAMIPRIL: P INTERACTION = 0.82	Non-inferiority of telmisartan vs ramipril has been demonstrated. No significant effect of combination vs telmisartan alone No gender difference in the outcome

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HYVET (Beckett et al ⁴⁹)	MAY 2008	Patients who were 80 years of age or older and had a sustained systolic blood pressure of 160 mm Hg or more International trial with significant European component	83.6 ± 3.2 ACTIVE TREATMENT vs. 83.5 ± 3.1 PLACEBO RANGE: 80 to 105 years	TOTAL 3845 (WOMEN 2326, 60.5%) (MEN 1519)	Median of 1.8 years (mean 2.1 range 0 to 6.5)	INDAPAMIDE (sustained release, 1.5 mg) with or without 2 to 4 mg of perindopril) (ACTIVE TREATMENT) vs MATCHING PLACEBO	Fatal or nonfatal stroke	PLACEBO: 69 ACTIVE TREATMENT : 51	HR _{Unadjusted} = 0.70 [95% CI: 0.49 -1.01] P = 0.06 Reduction in the rate of stroke of 30% [95% CI: -1 - 51] P = 0.06	Results by gender not reported
ONTARGET (Mann et al ⁵¹)	AUG 2008	Patients with established atherosclerotic vascular disease or with diabetes with end-organ damage. International trial with significant European component	66.4±7.2 RAMIPRIL; 66.4±7.1 TELMISARTAN; 66.5±7.3 COMBINATION THERAPY	TOTAL 25620	Median of 56 months	Ramipril 10 mg a day, vs telmisartan 80 mg a day, vs a combination of both drugs	Dialysis or doubling of serum creatinine or death.	1147 (13.4%) TELMISARTAN, 1150 (13.5%) RAMIPRIL 1233 (14.5%) COMBINATION THERAPY	HR (TELMISARTAN VS. RAMIPRIL) = 1.00 [95% CI: 0.92–1.09] HR (COMBINATION-THERAPY VS. RAMIPRIL) = 1.09 [95% CI: 1.01 – 1.18] P=0.037	Percentage of women enrolled not reported in this publication (reported in the primary publication) Results by gender not reported.
TRANSCEND (Yusuf et al ⁵²)	SEPT 2008	Patients intolerant to ACE inhibitors with cardiovascular disease or diabetes with end-organ (European 61.1%, Asian (21.3%))	PLACEBO 66.9 ±7.4 TELMISARTAN 66.9±7.3	TOTAL 5926 (WOMEN: 2547, 43%) MEN: 3379	Median duration of follow-up was 56months (IQR 51 –64)	After a 3-week run-in period, randomisation to telmisartan 80 mg/day or placebo	Cardiovascular death or myocardial infarction or stroke, or hospitalization for heart failure	504 (17.0%) PLACEBO GROUP 465 (15.7%) TELMISARTAN GROUP PLACEBO GROUP: WOMEN 14.4% MEN 18.9%	HR = 0.92 [95% CI: 0.81 – 1.05] P=0.216; P_{INTERACTION} = 0.0842	The difference between telmisartan and placebo was not significant. No gender difference in the outcome.

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ACCOMP LISH (Jamerson et al ⁵³)	DEC 2008	Patients with hypertension at high risk for cardiovascular events (International with significant European component)	68.4±6.86 Benazepril + Amlodipine Group; 68.3±6.86 Benazepril + Hydrochlorothiazide Group:	11,506 (WOMEN 4542, 39.5%) (MEN 6964)	Mean of 36 months	Benazepril 20 mg and amlodipine 5 mg versus benazepril 20 mg and Hydrochlorothiazide 12.5 mg, once daily 1 month after randomization Benazepril increased to 40 mg daily in both groups.	Death from cardiovascular causes or nonfatal myocardial Infarction or nonfatal stroke or hospitalization for angina or resuscitation after sudden cardiac arrest or coronary revascularization.	552 (9.6%) Benazepril–amlodipine group, 679 (11.8%) benazepril–hydrochlorothiazide group WOMEN 187 (8.1%) Benazepril–amlodipine group, 218 (9.7%) benazepril–hydrochlorothiazide MEN 365 (10.6%) Benazepril–amlodipine group 461 (13.1%) benazepril–hydrochlorothiazide	HR = 0.80 [95% CI: 0.72 - 0.90] P<0.001 HR_{WOMEN} = 0.83 [95% CI: 0.68–1.01] P=0.06 HR _{MEN} = 0.80 [95% CI: 0.69–0.91] P=0.001	Trial terminated early after a mean follow-up of 36 months, when the boundary of the prespecified stopping rule was exceeded. No significant gender differences in the outcome

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INVEST analysis (Bangalore et al ⁵⁴)	JUNE 2009	Coronary artery disease (CAD) patients with hypertension	Mean of 66 ± 9.7 years age ≥ 50	22 576 (Women 11762, 52.1%) (Men 10814)	2 years	Verapamil-SR vs atenolol based strategies	Predictive value of Pulse Pressure (PP) Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), Median Arterial Pressure (MAP) for time to first occurrence of death (all-cause), non-fatal myocardial infarction (MI), or non-fatal stroke.	PP predictive value weaker than that of SBP, DBP and MAP	PP vs SBP PP vs DBP PP vs MAP P<0.0001	Results by gender not reported

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META-ANALYSIS

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		(Country)	mean ± sd, range	TOTAL (WOMEN n,%)	DURATION			TOTAL (WOMEN n,%) (MEN n,%)	(CI) P (WOMEN (MEN)	
BPLTTC meta-analysis of 31 trials (Turnbull et al ⁴⁶)	MAY 2008	Patients randomized to a blood pressure-lowering agent and control or patients randomized to regimens based on different classes of drug to lower blood pressure	Two age groups: <65 mean age 57, ≥65 years mean age 72	190606 <65 WOMEN 42% MEN 58% ≥65 years WOMEN 49% MEN 51%,	NA	Blood pressure-lowering treatment: a) angiotensin converting enzyme inhibitor (ACE-I) vs placebo, b) calcium antagonist vs placebo, (c) more intensive vs less intensive regimens, (d) angiotensin receptor blocker vs control regimen, (e) ACE-I vs diuretics/β blockers, (f) calcium antagonist vs diuretics/β blockers, (g) ACE-I vs calcium antagonists.	Major cardiovascular events	<i>Angiotensin converting enzyme inhibitor vs placebo</i> Age <65 813/9514 ACTIVE 1087/9640 CONTROL Age ≥65 1251/8005 ACTIVE 1490/7918CONTROL <i>Calcium antagonist vs placebo</i> Age <65 43/1310 ACTIVE 49/1287 CONTROL Age ≥65 130/2220 ACTIVE 170/2134 CONTROL <i>More vs less intensive blood pressure lowering regimen</i> Age <65 212/5024 ACTIVE 365/9360 CONTROL Age ≥65 156/2251 ACTIVE 260/4198 CONTROL	RR= 0.76 [95% CI 0.66 to 0.88] RR= 0.83 [95% CI 0.74 to 0.94] P _{HOMOGENEITY} 0.37 RR= 0.84 [95% CI 0.54 to 1.31] RR= 0.74 [95% CI 0.59 to 0.92] P _{HOMOGENEITY} 0.59 RR= 0.88 [95% CI 0.75 to 1.04] RR= 1.03 [95% CI 0.85 to 1.24] P _{HOMOGENEITY} 0.24	No differences between classes of drugs Results by gender not reported

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BPLTTC analysis (Turnbull et al ⁵⁵)	NOV 2008	Patients randomized to a blood pressure-lowering agent and control or patients randomized to regimens based on different classes of drug to lower blood pressure	WOME N 63.0 MEN 61.7 age≥18 for some trials age<84	TOTAL 190617 (WOMEN: 87349, 45.8%) (MEN: 103268)	2.0 to 8.4	Blood pressure-lowering treatment: a) angiotensin converting enzyme inhibitor (ACE-I) vs placebo, b) calcium antagonist vs placebo, (c) more intensive vs less intensive regimens, (d) angiotensin receptor blocker vs control regimen, (e) ACE-I vs diuretics/β blockers, (f) calcium antagonist vs diuretics/β blockers, (g) ACE-I vs calcium antagonists.	Major cardiovascular events	<i>Angiotensin converting enzyme inhibitor vs placebo</i> WOMEN 450/4200 ACTIVE 557/4153 CONTROL MEN 1614/13319 ACTIVE 2020/13405 CONTROL <i>Calcium antagonist vs placebo</i> WOMEN 86/1929 ACTIVE 104/1836 CONTROL MEN 87/1601 ACTIVE 115/1585 CONTROL <i>More vs less intensive blood pressure lowering regimen</i> WOMEN 178/3709 ACTIVE 251/6481 CONTROL MEN 331/4325 ACTIVE 479/7467 CONTROL	RR= 0.79 [95% CI 0.66 to 0.94] RR= 0.81 [95% CI 0.75 to 0.88] P _{HOMOGENEITY} 0.80 RR= 0.78 [95% CI 0.59 to 1.03] RR= 0.75 [95% CI 0.57 to 0.98] P _{HOMOGENEITY} 0.84 RR= 0.88 [95% CI 0.73 to 1.07] RR= 0.87 [95% CI 0.74 to 1.02] P _{HOMOGENEITY} 0.93	No difference between classes of drugs No gender differences in the outcomes

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BP reduction - Congestive heart failure meta-analysis of 31 trials (Verdecchia et al ⁴⁷)	MAR 2009	Hypertensive or high-risk subjects without CHF at entry	NA	225764	2 to 8.4 years	Angiotensin-converting enzyme inhibitors (ACEIs) vs. placebo, ACEIs vs. old drugs, angiotensinreceptor blockers (ARBs) vs. placebo, ARBs vs. old drugs, calcium-channel blockers CCBs vs. placebo, and CCBs vs. old drugs	Risk of congestive heart failure (CHF)	Total 6469	Risk reduction 21% (P = 0.007) (ACEIs vs. placebo) OR = 1.02 [95% CI: 0.84–1.24] ACEIs and comparators vs. diuretics/β-blockers OR = 1.18 [95% CI: 1.00–1.39] P= 0.048 (CCBs) OR = 0.76 [95% CI : 0.69–0.85] P<0.001 for each 5 mmHg reduction in systolic BP OR = 0.81 [95% CI: 0.72–0.92] P<,0.001 ACEIs or ARBs OR= 0.84 [95% CI: 0.74–0.96)] P=0.009 Studies without multiple risk factors required for entry	Percentage of women enrolled not reported Results by gender not reported

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Analysis from ADVANCE EUROPA, PROGRESS (Brugts et al ⁴⁸)	JUNE 2009	Patients with vascular disease or at a high risk of vascular disease.	63 ± 9 age ≥ 18	29 463 WOMEN : 8367, 28.4% MEN 21096	Mean of 4 years	Perindopril-based treatment regimen vs placebo.	Cardiovascular mortality, MI, and stroke.	<i>Major cardiovascular events:</i> Placebo 1788 Perindopril 1490 <i>All cause mortality:</i> Placebo 1210 Perindopril 1089	HR = 0.82 [95% CI: 0.76–0.87] P<0.001 HR = 0.89 [95% CI: 0.82–0.96] P=0.006 Subgroup analysis by gender P_{INTERACTION}=0.66 <i>Cardiovascular mortality</i> HR = 0.85 [95% CI: 0.76–0.95] P = 0.004 <i>Non-fatal myocardial infarction</i> HR = 0.80 [95% CI: 0.71–0.90] P<0.001 <i>Stroke</i> HR = 0.82 [95% CI: 0.74– 0.92] P =0.002 <i>Heart failure</i> HR = 0.84 [95% CI: 0.72–0.96] P = 0.015	Benefit of perindopril in all subgroup analysis, including gender