SUPPLEMENTAL MATERIAL

Search strategy

(((((("Ischemic Attack, Transient"[Mesh]) OR "Stroke"[Mesh]) OR (TIA[Text Word] OR 'Transient Ischemic Attack'[Text Word] OR 'Brain TIA'[Text Word] OR Stroke*[Text Word] OR cerebrovascular Accident*[Text Word] OR CVA[Text Word] OR 'Cerebrovascular Apoplexy'[Text Word] OR 'Vascular Accident'[Text Word] OR 'Brain Vascular Accident'[Text Word] OR 'Cerebrovascular Stroke'[Text Word] OR Apoplexy[Text Word] OR 'Cerebral Stroke*'[Text Word] OR 'Acute Stroke*'[Text Word] OR 'cerebrovascular disorders'[Text Word] OR 'basal ganglia cerebrovascular disease'[Text Word] OR 'brain ischemia'[Text Word] OR 'carotid artery diseases'[Text Word] OR 'carotid artery thrombosis'[Text Word] OR 'intracranial arterial diseases'[Text Word] OR 'cerebral arterial diseases'[Text Word] OR 'intracranial embolism[Text Word] AND thrombosis'[Text Word])))

AND

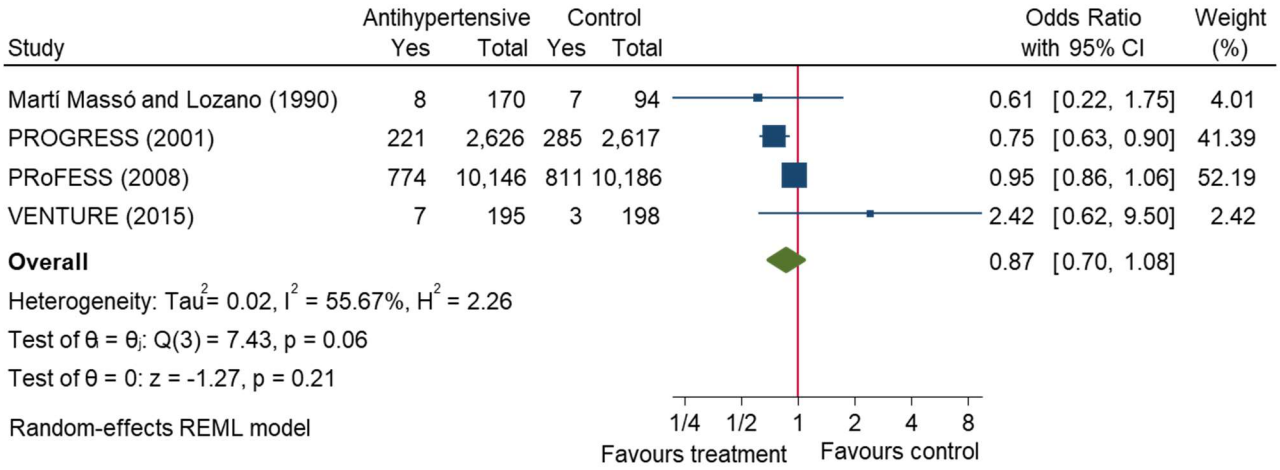
((((("Antihypertensive Agents"[Mesh]) OR ('Antihypertensive Agent*'[Text Word] OR Antihypertensives[Text Word] OR 'Anti-Hypertensive*'[Text Word] OR 'Anti Hypertensive*'[Text Word] OR 'Antihypertensive Drug*'[Text Word] OR 'Anti-Hypertensive Agent*'[Text Word] OR 'Anti Hypertensive Agent*'[Text Word] OR 'Anti-Hypertensive Drug*'[Text Word] OR 'Anti Hypertensive Drug*'[Text Word])))

OR ((((((((((((((((((((((((((((((((((("Doxazosin"[Mesh]) OR "Prazosin"[Mesh]) OR "Terazosin" [Supplementary Concept]) OR "Clonidine"[Mesh])) OR "Guanfacine"[Mesh]) OR "Guanabenz"[Mesh]) OR "Methyldopa"[Mesh]) OR "lofexidine" [Supplementary Concept]) OR "guanadrel" [Supplementary Concept]) OR "Guanethidine"[Mesh]) OR "Reserpine"[Mesh]) OR "azilsartan" [Supplementary Concept]) OR "candesartan" [Supplementary Concept]) OR "eprosartan" [Supplementary Concept]) OR "irbesartan" [Supplementary Concept]) OR "olmesartan" [Supplementary Concept]) OR "telmisartan" [Supplementary Concept]) OR "Valsartan"[Mesh]) OR "Losartan"[Mesh]) OR "benazepril" [Supplementary Concept]) OR "Captopril"[Mesh]) OR "Enalapril"[Mesh]) OR "Fosinopril"[Mesh]) OR "Lisinopril"[Mesh]) OR "moexipril" [Supplementary Concept]) OR "Perindopril"[Mesh]) OR "quinapril" [Supplementary Concept]) OR "trandolapril" [Supplementary Concept]) OR "carvedilol" [Supplementary Concept]) OR "Labetalol"[Mesh]) OR "Acebutolol"[Mesh]) OR "Pindolol"[Mesh]) OR "Penbutolol"[Mesh]) OR "Atenolol"[Mesh]) OR "Betaxolol"[Mesh]) OR "Bisoprolol"[Mesh]) OR "Celiprolol"[Mesh]) OR "Metoprolol"[Mesh]) OR "Nebivolol"[Mesh]) OR "Sotalol"[Mesh]) OR "Nadolol"[Mesh]) OR "Propranolol"[Mesh]) OR "Timolol"[Mesh:NoExp])) OR (("Doxazosin"[Title/Abstract] OR "Prazosin"[Title/Abstract] OR "Terazosin"[Title/Abstract] OR "Clonidine"[Title/Abstract] OR "Guanfacine"[Title/Abstract] OR "Guanabenz"[Title/Abstract] OR "Methyldopa"[Title/Abstract] OR "lofexidine"[Title/Abstract] OR "guanadrel" [Title/Abstract] OR "Guanethidine"[Title/Abstract] OR "Reserpine"[Title/Abstract] OR "azilsartan" [Title/Abstract] OR "candesartan"[Title/Abstract] OR "eprosartan"[Title/Abstract] OR "irbesartan"[Title/Abstract] OR "olmesartan"[Title/Abstract] OR "telmisartan"[Title/Abstract] OR "Valsartan"[Title/Abstract] OR "Losartan"[Title/Abstract] OR "benazepril"[Title/Abstract] OR "Captopril"[Title/Abstract] OR "Enalapril"[Title/Abstract] OR "Fosinopril"[Title/Abstract] OR "Lisinopril"[Title/Abstract] OR "moexipril"[Title/Abstract] OR "Perindopril"[Title/Abstract] OR "quinapril"[Title/Abstract] OR "trandolapril"[Title/Abstract] OR "carvedilol" [Title/Abstract] OR "Labetalol"[Title/Abstract] OR "Acebutolol"[Title/Abstract] OR "Pindolol"[Title/Abstract] OR "Penbutolol"[Title/Abstract] OR "Atenolol"[Title/Abstract] OR "Betaxolol"[Title/Abstract] OR "Bisoprolol"[Title/Abstract] OR "Celiprolol"[Title/Abstract] OR "Metoprolol"[Title/Abstract] OR "Nebivolol"[Title/Abstract] OR "Sotalol"[Title/Abstract] OR "Nadolol"[Title/Abstract] OR "Propranolol"[Title/Abstract] OR "Timolol"[Title/Abstract]))

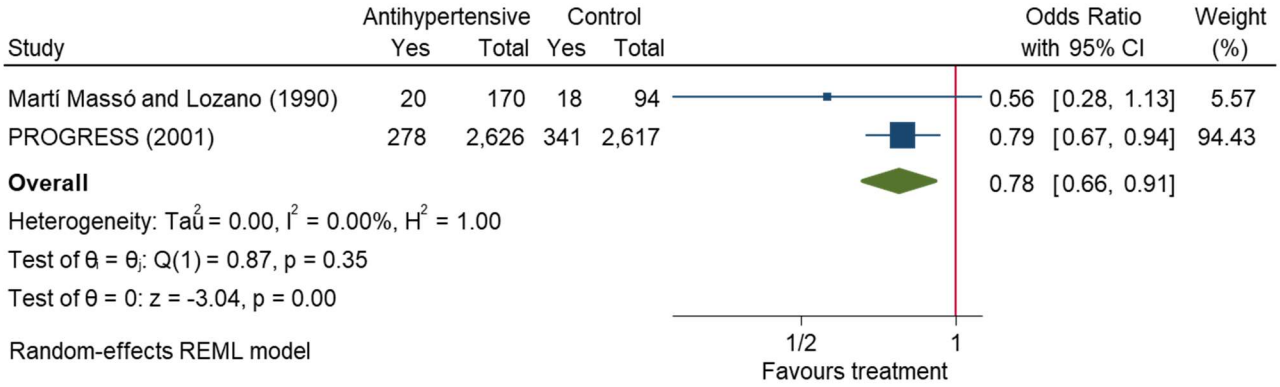
S Figure I. Forest plots of meta-analysis estimates of any BP-lowering drug against placebo/no treatment for secondary outcomes Ischemic stroke (A) and Ischemic stroke or TIA (B).

Legend: CI, confidence interval; θ, treatment effect

A. Ischemic stroke



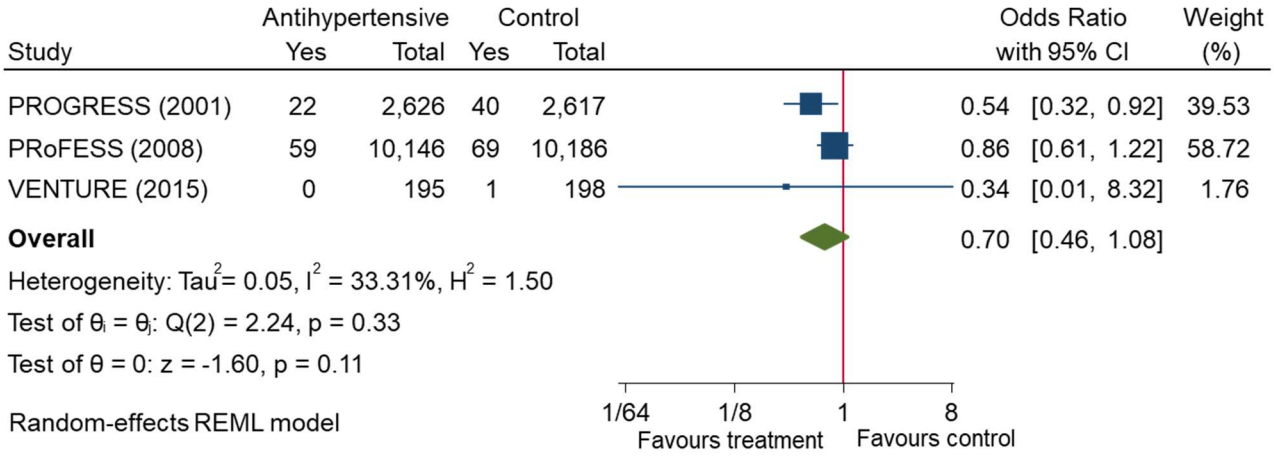
B. Ischemic stroke or TIA



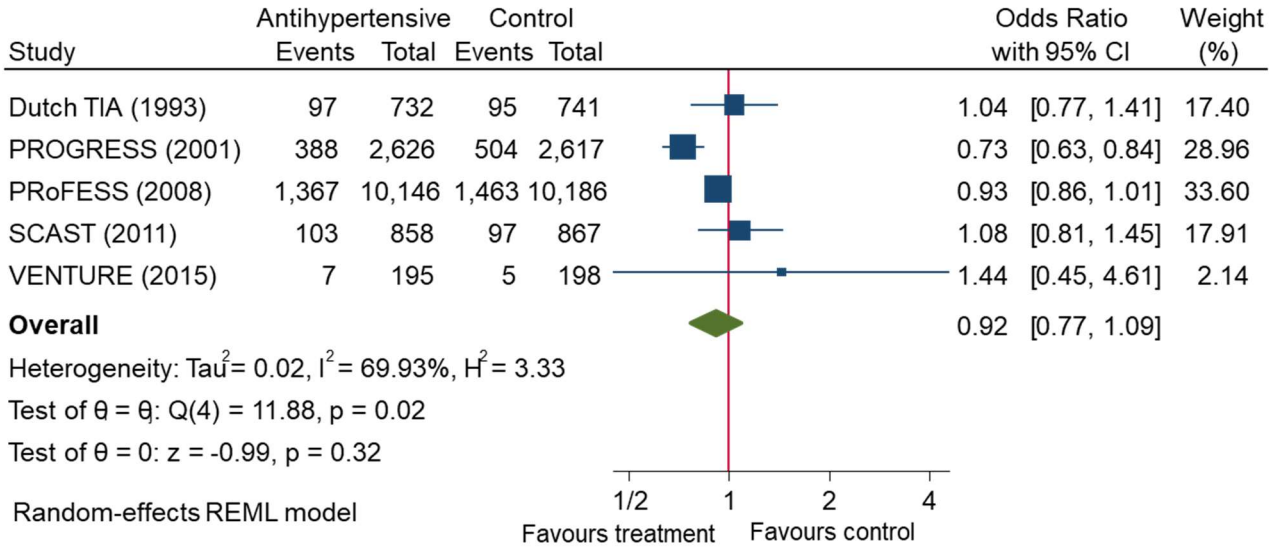
S Figure II. Forest plots of meta-analysis estimates of any BP-lowering drug against placebo/no treatment for secondary outcomes Hemorrhagic stroke (A), Cardiovascular event (B) and Fatal cardiovascular event (C).

Legend: CI, confidence interval; θ, treatment effect

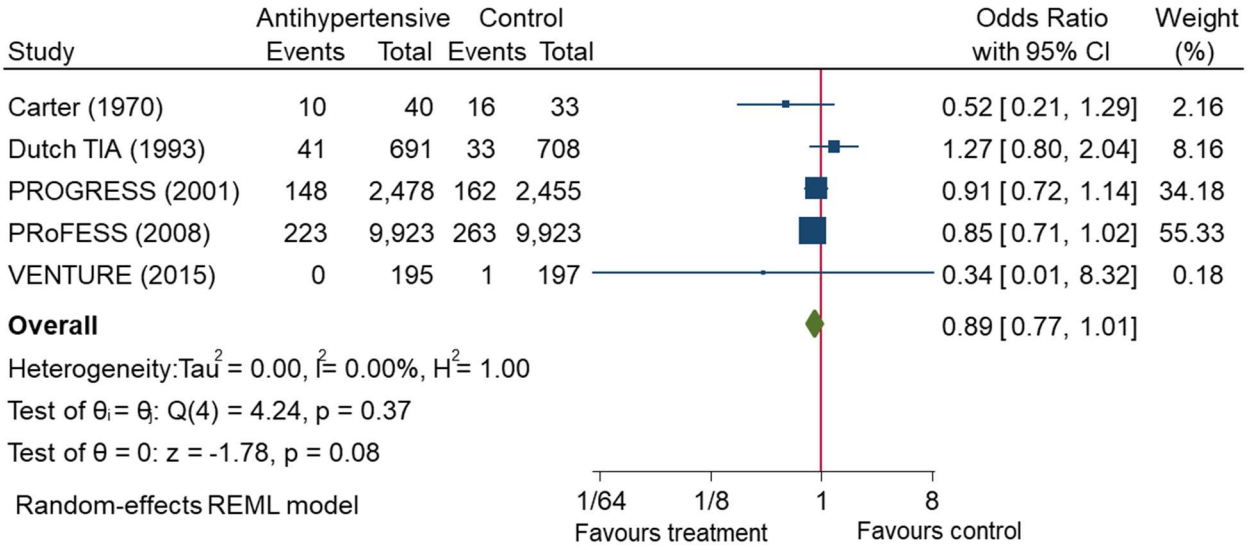
A. Hemorrhagic stroke



B. Cardiovascular event



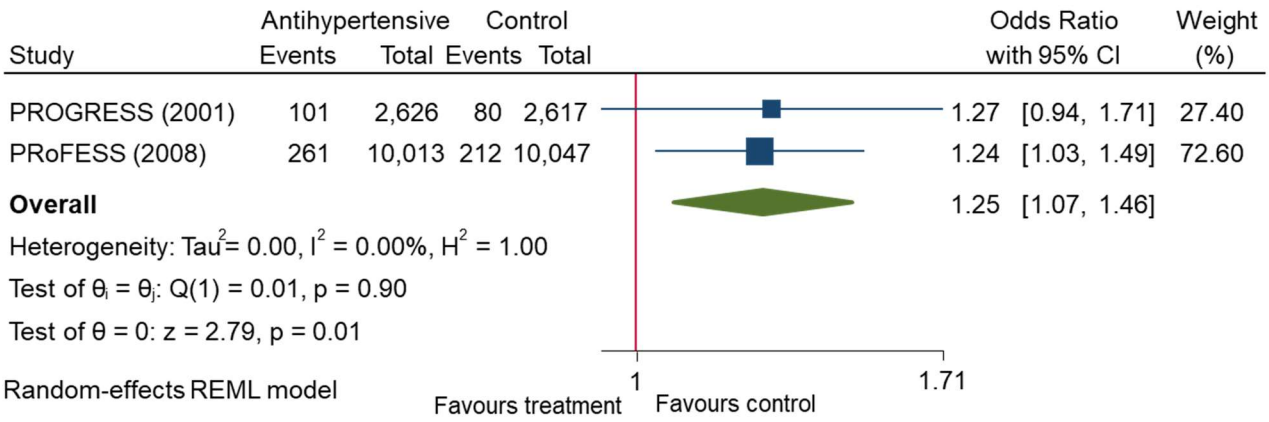
C. Fatal cardiovascular event



S Figure III. Forest plots of meta-analysis estimates of any BP-lowering drug against placebo/no treatment for secondary outcome Serious adverse events.

Legend: CI, confidence interval; θ, treatment effect

Serious adverse events



S Table I. Characteristics of the studies included in the qualitative synthesis only

Legend: HP, hypertensive patients; NA, not available

Study (year)	Index event (patients, n)	Intervention and control	Country	Time to randomization	Follow up, mean	HP only	Age, mean	Males, %
HSCSG (1974)[20]	Undetermined stroke, TIA (452)	Deserpidine/ methyclothiazide 0.5/5.0 mg/day for 6 weeks then, if well tolerated, 1/10 mg/day vs. Placebo	USA	< 1 year	3 years	Yes	59	60
TEST (1995)[21]	Ischaemic, haemorrhagic or undetermined stroke, TIA (720)	Atenolol 50 mg/day vs. Placebo	Sweeden	< 21 days	30 months	Yes	70	60
ALLHAT (2000)[22]	Undetermined stroke (NA)	Clorthalidone 12,5 to 25 mg/day vs. Doxasorzin 2 to 8 mg/day	USA and Canada	> 6 months	3 years	Yes	67	53
HOPE (2000)[23]	Undetermined stroke, TIA (1,013)	Ramipril 2,5 mg/day for one week, 5 mg/day for the next 3 weeks, and then 10 mg/day vs. Placebo	World	NA	5 years	No	66	73
SCOPE (2003)[24]	Undetermined stroke (194)	Candesartan 8 mg/day vs. Placebo	Europe	> 6 months	4 years	Yes	76	35
MOSES (2005)[25]	Ischaemic or haemorrhagic stroke, TIA (1,405)	Eprosartan 600 mg/day vs. Nitrendipine 10 mg/day for the first 3 weeks, then increased if required	Germany and Austria	< 2 years	30 months	Yes	68	54
FEVER (2005)[26]	Undetermined stroke, TIA (1,438)	Felodipine 5 mg/day vs. Placebo	China	> 6 months	40 months	Yes	61	61

S Table II. Pairwise meta-analysis estimates of any BP-lowering drug vs placebo from analysis of all studies, subgroup analyses and sensitivity analyses for each primary outcome.

Legend: OR, odds ratio; CI, confidence interval; NA, not applicable

	All-cause mortality		**All strokes**	
	OR (95% CI) [number of studies]	*I^2; Test for heterogeneity*	*OR (95% CI) [number of studies]*	*I^2; Test for heterogeneity*
Overall	1.01 (0.92-1.10) [n=6]	0%; p=0.42	0.79 (0.66-0.94) [n=6]	61%; p=0.01
Subgroup analyses				
Hypertension at inclusion		p=0.44*		p=0.92*
Hypertensive patients only	0.61 (0.17-2.19) [n=2]	30%; p=0.23	0.73 (0.14-3.82) [n=2]	79%; p=0.03
Hypertensive and normotensive patients	1.02 (0.93-1.11) [n=4]	0%; p=0.87	0.80 (0.68-0.95) [n=4]	68%; p=0.01
Time from ischemic stroke to randomization		p=0.57*		p=0.19*
Acute patients	2.04 (0.18-22.70) [n=1]	NA	1.81 (0.52-6.27) [n=1]	NA
Stabilized	1.01 (0.92-1.10) [n=5]	0%; p=0.33	0.77 (0.65-0.93) [n=5]	67%; p=0.00
Type of stroke				
Cardioembolic and non-cardioembolic	0.97 (0.81-1.16) [n=2]	0%; p=0.54	0.92 (0.42-2.01) [n=2]	50%; p=0.16
Non-cardioembolic	1.02 (0.92-1.13) [n=4]	0%; p=0.23	0.77 (0.60-0.99) [n=4]	69%; p=0.01
Sensitivity analyses				
Studies at low risk of bias	1.02 (0.93-1.11) [n=3]	0%; p=0.71	0.84 (0.70-1.01) [n=3]	66%; p=0.04

*Test of group differences