

Moderately Elevated Blood Pressure

A Systematic Literature Review

Volume 2 – Tables

November 2004



SBU • Statens beredning för medicinsk utvärdering

The Swedish Council on Technology Assessment in Health Care

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Volume 2 – Tables

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Contents

Abbreviations of studies	12
Appendix 1	16
Abbreviations for Appendix 1, Tables 1–9	16
Table 1 Design Characteristics (1)	18
Design, control, active treatment, follow-up, endpoints, study quality	
Pharmacological	
Comparing drug treatments	
Multifactorial and non-pharmacological	
Hypertension after a cerebrovascular event	
Hypertension and kidney	
Hypertension and diabetes mellitus	
Hypertension and cardiovascular risk	
Table 2 Design Characteristics (2)	36
Designed to show, statistical power	
Pharmacological	
Comparing drug treatments	
Multifactorial and non-pharmacological	
Hypertension after a cerebrovascular event	
Hypertension and kidney	
Hypertension and diabetes mellitus	
Hypertension and cardiovascular risk	

Table 3	Design Characteristics (3)	44
	Inclusion and exclusion criteria	
	Pharmacological	
	Comparing drug treatments	
	Multifactorial and non-pharmacological	
	Hypertension after a cerebrovascular event	
	Hypertension and kidney	
	Hypertension and diabetes mellitus	
	Hypertension and cardiovascular risk	
Table 4	Patient Characteristics	58
	Pharmacological	
	Comparing drug treatments	
	Multifactorial and non-pharmacological	
	Hypertension after a cerebrovascular event	
	Hypertension and kidney	
	Hypertension and diabetes mellitus	
	Hypertension and cardiovascular risk	
Table 5	Outcomes (1)	72
	Absolute numbers	
	Pharmacological	
	Comparing drug treatments	
	Multifactorial and non-pharmacological	
	Hypertension after a cerebrovascular event	
	Hypertension and kidney	
	Hypertension and diabetes mellitus	
	Hypertension and cardiovascular risk	

Table 6	Outcomes (2)	86
	Relative rate per 1,000 patient years, and relative change in risk by intervention (%)	
	Pharmacological	
	Comparing drug treatments	
	Multifactorial and non-pharmacological	
	Hypertension after a cerebrovascular event	
	Hypertension and kidney	
	Hypertension and diabetes mellitus	
	Hypertension and cardiovascular risk	
Table 7	Outcomes (3)	104
	Statistical evaluation of endpoints	
	Pharmacological	
	Comparing drug treatments	
	Multifactorial and non-pharmacological	
	Hypertension after a cerebrovascular event	
	Hypertension and kidney	
	Hypertension and diabetes mellitus	
	Hypertension and cardiovascular risk	
Table 8	Blood pressure control and medication in the control groups	116
Table 9	Subjective adverse effects	122
	Pharmacological	
	Comparing drug treatments	
	Multifactorial and non-pharmacological	
	Hypertension after a cerebrovascular event	
	Hypertension and kidney	
	Hypertension and diabetes mellitus	
	Hypertension and cardiovascular risk	
References		134

Appendix 2	142
Abbreviations for Appendix 2, Tables 1–4	142
Table 1 Meta-analyses of the relationship between trials that measured the effects of antihypertensive therapy on left ventricular mass	144
Table 2 Design and characteristics	148
Studies before 1993	
Studies 1993 to 2003	
Table 3 LVH outcomes in studies using echo- or electrocardiographic (ECG) methods	166
Studies before 1993	
Studies 1993 to 2003	
Table 4 Blood pressure changes in studies using echo- or electrocardiographic (ECG) methods	184
Studies before 1993	
Studies 1993 to 2003	
References	202
 Appendix 3	 209
Abbreviations for Appendix 3, Tables 1–13	209
Table 1 MRFIT	210
Mortality in coronary heart disease	
Morbidity in coronary heart disease	
Table 2 MRC-Older	214
Cardiovascular morbidity	
Table 3 MRC	216
Cardiovascular morbidity	
Morbidity in coronary heart disease	

Table 4	ANPBS	220
	All cause mortality and cardiovascular morbidity	
Table 5	EWPHE	224
	Cardiovascular morbidity	
	Cardiovascular mortality	
Table 6	HEP	228
	Stroke morbidity	
Table 7	HDFP	230
	Stroke morbidity	
	Total mortality	
Table 8	VA II	234
	Cardiovascular morbidity	
Table 9	SHEP	236
	Cardiovascular morbidity	
	Total mortality	
	Acute myocardial infarction	
	Stroke incidence	
Table 10	STOP	238
	Cardiovascular morbidity	
Table 11	Oslo Mild hypertension	240
	Cardiovascular morbidity	
Table 12	Syst-Eur	242
	Cardiovascular morbidity	
	Cardiovascular mortality	
	Total mortality	
	Stroke incidence	
Table 13	Syst-China	244
	Cardiovascular events	
	Stroke incidence	
	References	246

Abbreviations of studies

For a description of the studies, see Volume 1, Chapter 10 and Tables.

AASK	African American Study of Kidney Disease and Hypertension
ABCD	Appropriate Blood Pressure Control in Diabetes
ALLHAT	Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial
ANBPS	The Australian National Blood Pressure Study
ANBP2	Australian Comparative Outcome Trial of Angiotensin-Converting Enzyme Inhibitor- and Diuretic-Based Treatment of Hypertension in the Elderly
BBB	Behandla Blodtryck Bättre (Treat Blood Pressure Better)
CAPPP	Captopril Prevention Project
CONVINCE	Controlled Onset Verapamil Investigation of Cardiovascular Endpoints
DIABHYCAR	Non-Insulin-Dependent Diabetes, Hypertension, Microalbuminuria or Proteinuria, Cardiovascular Events and Ramipril
ELSA	European Lacidipine Study on Atherosclerosis

ESPIRAL	Efecto del Tratamiento Antihypertensivo Sobre la Progresión de la Insuficiencia Renal en Pacientes no Diabéticos (Effect of Antihypertensive Treatment on the Progression of Renal Failure in Non-Diabetic Patients)
EUROPA	European Trial on Reduction of Cardiac Events with Perindopril in Patients with Stable Coronary Artery Disease
EWPHE	The European Working Party on High Blood Pressure in the Elderly Trial
FACET	Fosinopril versus Amlodipine Cardiovascular Events Randomized Trial
GPPT	Gothenburg Primary Preventive Trial
HAPPHY	Heart Attack Primary Prevention in Hypertension
HDFP	Hypertension Detection and Follow-up Program
HEP	Hypertension in Elderly Patients
HOPE	Heart Outcome Prevention Evaluation Study
HOT	Hypertension Optimal Treatment
HSCSG	Hypertension-Stroke Cooperative Study Group
HYVET pilot	Hypertension in Very Elderly Trial
IDNT	Irbesartan Diabetic Nephropathy Trial
INSIGHT	International Nifedipine GITS Study Intervention as a Goal in Hypertension Treatment

INVEST	International Verapamil-Trandolapril Study
IPPPSH	The International Prospective Primary Prevention Study in Hypertension
J-MIND	The Japan Multicenter Investigation of Antihypertensive Treatment for Nephropathy in Diabetes
LIFE	Losartan Intervention For Endpoint Reduction in Hypertension
MAPHY	Metoprolol Atherosclerosis Prevention in Hypertension, extension of the HAPPHY study
MIDAS	Multicenter Isradipine Diuretic Atherosclerosis Study
MONICA	Multinational Monitoring of Trends and Determinants in Cardiovascular Disease
MRC	A British study by the Medical Research Council
MRC Older	Medical Research Council Trial of Treatment of Hypertension in Older Adults
MRFIT	Multiple Risk Factor Intervention Trial
NICS-EH	National Intervention Cooperative Study in Elderly Hypertensive
NORDIL	Nordic Diltiazem Study
PATS	Post-Stroke Antihypertensive Treatment Study
PROGRESS	Perindopril Protection Against Recurrent Stroke Study

RENAAL	Reduction of Endpoints in NIDDM with Angiotensin II Antagonist Losartan Study
RIS	Risk Factor Intervention Trial
SCOPE	Study on Cognition and Prognosis in Elderly
SHEP	Systolic Hypertension in Elderly Program
STOP	The Swedish Trial in Old Patients with Hypertension. Also STOP 2 on more recently developed drugs
Syst-China	Systolic Hypertension in China
Syst-Eur	Systolic Hypertension in Europe
TEST	Tenormin after Stroke and TIA
TOMHS	Treatment of Mild Hypertension Study
STONE	Trial of Nonpharmacological Intervention in the Elderly
UKPDS	United Kingdom Prospective Diabetes Study
USPHS	US Public Health Service Study
VA II	Veterans Administration Study II
VALUE	Valsartan Antihypertensive Long-term Use Evaluation
VA-NHLBI	Veterans Administration – National Heart, Lung, and Blood Institute Feasibility Trial
VHAS	Verapamil in Hypertension and Atherosclerosis

Abbreviations for Appendix 1, Tables 1–9

Design characteristics

Design

DB	= Double-blind
O	= Open
PROBE	= Prospective randomised open study with blinded endpoint evaluation
S	= Stratified
SB	= Single-blind

Control

Edu	= Health education
N	= No care
UC	= Usual care or referred care
P	= Placebo

Active treatment(s)

alpha-md	= Alpha-methyldopa
ace	= Acebutolol
ami	= Amiloride
aml	= Amlodipine
ate	= Atenolol
cln	= Clonidine
ben	= Bendrofluthiazide
can	= Candesartan cilexetil
cap	= Captopril
ctn	= Chlorthalidone
des	= Deserpidine
dil	= Diltiazem
dox	= Doxazosin
ena	= Enalapril
fel	= Felodipine
fos	= Fosinopril
fur	= Furosemide
gua	= Guanethidine
ind	= Indelolol
irb	= Irbesartan
hctz	= Hydrochlorothiazide

hyd	= Hydralazine
isr	= Isradipine
lac	= Lacidipine
lis	= Lisinopril
los	= Losartan
met	= Metoprolol
mctz	= Methyclothiazide
nic	= Nicardipine
nif	= Nifedipine
nit	= Nitrendipine
oxp	= Oxprenolol
per	= Perindopril
pin	= Pindolol
pro	= Propranolol
ram	= Ramipril
res	= Reserpine
spi	= Spironolactone
tran	= Trandolapril
tri	= Triamterene
val	= Valsartan
ver	= Verapamil

ASA	= Acetylsalicylic acid
Nut	= Nutritional intervention: weight loss, Na ⁺ restriction, reduced alcohol intake, stop smoking, lipid lowering therapy
SC	= Stepped care
Str	= Stress management and relaxation programme

Quality

A maximum total sum was 16 (0–2 on each of 8 questions), overall evaluation was scored 1–5.

Patient characteristics

End of study mean BP and End of study mean group difference in BP by treatment may not be fully congruent due to rounding of numbers.

% Below goal BP: as defined in the individual papers.

Outcome: For all studies the total number of events represent all events that have been reported, since first events have not always been reported separately.

Stroke: includes all intracranial haemorrhage and definite cerebral infarction.

Coronary heart disease: includes sudden death.

Other vascular mortality: includes e.g. ruptured aneurysms, severe CHF, and pulmonary embolism.

Relative change in risk by intervention: calculated as $\text{Treat} - \text{Control} / \text{Control} \times 100$.

Further abbreviations

ACEi	= Angiotensin converting enzyme inhibitors	DBP	= Diastolic blood pressure
AE	= Subjective adverse effects, biochemical adverse effects not included	ECG	= Electrocardiography
Alpha-B	= Alpha1-receptor blockers	FH	= Fundus hypertonicus
AP	= Angina pectoris	HT	= Hypertension
ARB	= Angiotensin receptor blocker	LVH	= Left ventricular hypertrophy
BB	= Beta-adrenoceptor blocker based	MAP	= Mean arterial pressure
BMI	= Body mass index	MI	= Myocardial infarction
BP	= Blood pressure	Non-BB	= Non beta-adrenoceptor blocker based
CCB	= Calcium channel blockers	NYHA	= New York Heart Association
CHD	= Coronary heart disease	Rx	= Prescribed therapy
CHF	= Congestive heart failure	SC	= Stepped care
CV	= Cardiovascular	SR	= Slow release
D	= Diuretics	SBP	= Systolic blood pressure
		TIA	= Transitory ischemic attack
		UC	= Usual care or referred care

Missing figures indicate that data were not reported or are not applicable.

Appendix 1, Table 1 Design Characteristics (1).

Study, year Reference	Design	Control	Active treatment(s)	Follow-up min-max; mean (ys)
<i>Pharmacological</i>				
VA II, 1970 [12,13,80,89]	DB	P	hctz+res+hyd	1-5.5; 3.8 ¹
USPHS, 1977 [83]	DB, S (sex, age)	P	ctz+res	6.5-9; 7.0
VA-NHLBI, 1978 [15]	DB	P	1. ctn; 2. add res	1.5
HDFP, 1979 [7,9,10,17-19, 23,26,87]	O, S (BP, sex)	UC	1. ctn and/or tri and/or spi; 2. add res or alpha-md; 3. add hyd; 4. add gua; 5. other	5-5; 5.0
ANBPS, 1980 [1,29,35]	SB, S (age, sex)	P	1. hctz; 2. (add) alpha-md or pro or pin; 3. add hyd or cln	4.0 ¹
Oslo, 1980 [61]	O	N	1. hctz; 2. add alpha- md or pro; 3. other	5-6.5; 5.5
MRC, 1985 [5,24,75]	SB, S (age, sex)	P	1. ben or prop; 2. add alpha-md or gua	5.5

Primary endpoint(s)	Other major (ie hard) endpoints	Quality, total sum; overall evaluation (mean±SEM)	Study quality and relevance
CV mortality and morbidity related to HT and atherosclerosis		12.2±0.7; 3.6±0.3	High
Mortality, stroke, MI		8.7±1.2; 2.4±0.3	Medium
Mortality, stroke, MI		10.1±1.1; 2.2±0.3	High
Mortality	Mortality by cause, CV morbidity	11.5±1.4; 3.4±0.4	High
Mortality, CV morbidity		13.7±0.6; 3.9±0.3	High
CV morbidity		12.1±0.7; 3.0±0.2	High
Mortality, stroke, MI		12.2±0.5; 3.6±0.5	High

The table continues on the next page.

Appendix 1, Table 1 continued

Study, year Reference	Design	Control	Active treatment(s)	Follow-up min-max; mean (ys)
EWPPHE, 1985 [36–38]	DB, S (age, sex, cardiovascular complications)	P	1. hctz+tri; 2. add alpha-md	4.7
HEP, 1986 [45]	O	UC	1. ate; 2. add ben; 3. add alpha-md; 4. other	1–10; 4.4
SHEP, 1991 [28,46,53,55,65]	DB, S (previous antihyperten- sive medication, center)	P	1. ctn (+K ⁺); 2. add ate or res	–5.8; 4.5
STOP, 1991 [48]	DB	P	1. ate/pro/pin or hctz+ami; 2. ate/pro/pin and hctz+ami	0.5–5.5; 2.1 ¹
MRC older, 1992 [21]	SB, S (sex, center)	P	1. hctz+ami or ate; 2. hctz+ami and ate; 3. add nif	5.8
TOMHS, 1993 [33,76]	DB, S (previous antihypertensive medication)	P	1. ace or aml or ctn or dox or ena; 2. add ctn or ena. Nut to all drug and pla- cebo groups	4.0–5.2; 4.4

Primary endpoint(s)	Other major (ie hard) endpoints	Quality, total sum; overall evaluation (mean±SEM)	Study quality and relevance
Fatal and non-fatal stroke	Mortality by cause, cardiac and CV morbidity	11.1±0.7; 3.0±0.2	High
Mortality, stroke, MI		12.0±0.6; 3.0±0.2	High
Stroke	Mortality by cause, cardiac and CV morbidity	14.0±0.4; 3.9±0.1	High
CV mortality, stroke, MI	Mortality	15.2±0.3; 4.4±0.2	High
Mortality, stroke, coronary events (ie MI, sudden death)		12.8±0.7; 3.3±0.3	High
CV morbidity and mortality; influences on quality of life, side effects, biochemistry, BP, echocardiographic changes and ECG		11.4±1.2; 2.8±0.5	High

The table continues on the next page.

Appendix 1, Table 1 continued

Study, year Reference	Design	Control	Active treatment(s)	Follow-up min-max; mean (ys)
BBB, 1994 [56]	PROBE	UC	DBP ≤80 mm Hg vs UC (90–100 mm Hg)	5.9
Syst-Eur, 1997 [84–86,91]	DB	P	1. nit; 2. add ena; 3. add hctz	0.1–8.1; 2.0
HOT, 1998 [60,63,64]	PROBE (for BP)	UC with DBP ≤90 vs ≤85 vs ≤80 mm Hg	1. fel; 2. add ACEi or beta-blocker; 3. increase doses	3.3–4.9; 3.8
	DB (for ASA)		ASA vs placebo	
Syst-China, 2000 [70,92]	SB, S (sex, previ- ous CV complica- tion, center)	P	1. nit; 2. add cap or hctz; 3. add both	0.1–7.8; 3.0
SCOPE, 2003 [69]	DB	P	1. can; 2. add hctz; 3. add other	3–5; 3.7
HYVET Pilot, 2003 [44]	O	P	1. ben vs lis vs placebo; 2. add dil	1.1

Primary endpoint(s)	Other major (ie hard) endpoints	Quality, total sum; overall evaluation (mean±SEM)	Study quality and relevance
Can DBP ≤80 mm Hg be obtained in previously treated patients? Influence on side effects	CV morbidity and mortality	9.4±0.9; 2.1±0.3	Medium
Stroke	All cause mortality, MI, vascular death	15.2±0.4; 3.3±0.3	High
CV mortality, stroke, MI		13.4±0.7; 3.6±0.3	High
Stroke	All cause mortality, MI, vascular death	11.3±0.9; 2.8±0.3	High
CV mortality, stroke, MI	Mortality by cause	13.2±0.7; 3.3±0.2	High
Total mortality, CV mortality and total stroke morbidity		10.3±0.6; 2.3±0.3	High

The table continues on the next page.

Appendix 1, Table 1 continued

Study, year Reference	Design	Active treatments	Follow-up min-max; mean (ys)
Comparing drug treatments			
IPPPSH, 1985 [3]	DB, S (age, sex)	1. oxp vs placebo; 2. add diuretic; 3. add vasodilator; 4. sympatholytic	3–5; 4.0
HAPPHY, 1987 [95]	O, S (age, cholesterol, smoking, SBP)	1. ate/met vs ben/ hctz+optional K ⁺ / ami/tri; 2. add hyd; 3. add spi; 4. add other	3.8
MAPHY, 1988 [94]	O, S (age, cholesterol, smoking, SBP)	1. met vs ben/hctz; 2. add hyd or spi or other	2.3–10.8; 5.0
Yurenev, 1992 [99]	O	1. beta-blocker (mostly pro) vs other (mostly diuretics, vasodilators); 2. add other	4.0
MIDAS, 1996 [41]	D, S (center)	1. isr vs hctz; 2. add ena	3.0
VHAS, 1997 [81]	DB (initial 6 months) O (final 18 month)	1. ver vs ctn; 2. add cap	2.0
NICS-EH, 1999 [31]	DB	1. nic vs hctz	4.5
CAPPP, 1999 [59,77]	PROBE	1. cap vs beta- blocker/diuretics or both; 2. add other	6.1
STOP-2, 1999 [58,67]	DB	1. ate/met/pin or hctz+ami vs ena/lis or fel/isr; 2. add hctz+ami or beta-blocker	4.0–6.3; 5.0

Primary endpoint(s)	Other major (ie hard) endpoints	Quality, total sum; overall evaluation (mean±SEM)	Study quality and relevance
Fatal and non-fatal MI	Mortality by cause, stroke	12.2±0.8; 3.4±0.2	High
Mortality, fatal and non-fatal MI	Mortality by cause, stroke	13.9±0.5; 4.0±0.3	High
CV morbidity	Mortality by cause	10.3±0.7; 2.7±0.3	High
Myocardial morphology and function; development of hypertensive complications		7.7±1.2; 3.1±0.4	Medium
Rate of progression of carotid artery intima-media thickness	CV events	10.0±1.0; 2.0±0.4	Medium
Antihypertensive effect and safety	CV morbidity	10.3±0.5; 2.2±0.3	High
CV morbidity and mortality		11.3±0.8; 2.1±0.4	High
CV mortality, stroke and MI	All cause mortality	13.7±0.6; 3.9±0.3	High
CV mortality	All cause mortality	14.4±0.5; 4.4±0.3	High

The table continues on the next page.

Appendix 1, Table 1 continued

Study, year Reference	Design	Active treatments	Follow-up min-max; mean (ys)
NORDIL, 2000 [57]	PROBE	1. dil vs diuretics or beta-blocker or both; 2. add ACEi or alpha- blocker	4.5
INSIGHT, 2000 [43,71]	DB	1. nif vs hctz+ami; 2. add ate or ena; 3. add other	≥3; 3
LIFE, 2002 [47,68]	DB	1. los vs ate; 2. add hctz; 3. add CCB	>4; 4.8
ALLHAT, 2002 [6,20]	DB (for BP)	1. ctu vs aml vs lis vs dox; 2. add beta-blocker or central acting or vasodilator	4–8; 4.9
	O (for pravastatin)	pravastatin vs placebo	
ELSA, 2002 [101]	DB, S for (carotid artery intima media thickness)	1. lac vs ate; 2. add hctz	3.8
CONVINCE, 2003 [40]	DB	1. ver vs ate or hctz; 2. add ACEi	2.0–4.2; 3 ¹
ANBP2, 2003 [97]	PROBE	1. ena vs hctz; 2. add beta-blocker; 3. add CCB; 3. add alpha-blocker	4.1
INVEST, 2003 [79]	PROBE	1. ver SR vs ate; 2. add tran/hctz	0–5.4; 2.7
VALUE, 2004 [62]	DB	1. val vs aml; 2. add hctz; 3. add other	3.2–6.2; 4.2

Primary endpoint(s)	Other major (ie hard) endpoints	Quality, total sum; overall evaluation (mean±SEM)	Study quality and relevance
CV mortality, stroke and MI	Stroke, MI	13.9±0.4; 4.0±0.3	High
CV mortality, stroke, MI and CHF	Mortality by cause	14.7±0.3; 3.4±0.4	High
CV mortality, stroke and MI	All cause mortality	15.1±0.3; 4.5±0.2	High
Fatal CHD and non-fatal MI	All cause mortality, stroke	13.5±0.4; 3.9±0.2	High
Rate of progression of carotid artery intima media thickness	All cause mortality, CV morbidity	10.6±1.4; 2.8±0.4	High
CV mortality, stroke and MI	All cause mortality	11.9±0.9; 2.9±0.4	High
CV morbidity	Mortality by cause	13.0±0.5; 3.7±0.2	High
All cause mortality	CV mortality, angina pectoris, adverse events, hospitalizations, inadequate BP control	13.3±0.5; 3.7±0.2	High
Non-fatal MI and fatal cardiac events	Fatal and non-fatal MI, stroke, CHF	14±0.7; 3.5±0.3	High

The table continues on the next page.

Appendix 1, Table 1 continued

Study, year Reference	Design	Control	Active treatment(s)	Follow-up min-max; mean (ys)
<i>Multifactorial and non-pharmacological</i>				
GPPT, 1986 [96]	O	UC	Nut and 1. beta-blocker or thiazide; 2. beta-blocker and thiazide; 3. add hyd; 4. add other	10.3
MRFIT, 1990 [2,4,16,22, 25,32]	O	UC	Nut and 1. ctn/htcz or tri/spi; 2. add res or alpha-md or pro; 3. add hyd; 4. add gua	6-8; 6.9
Patel, 1985 [78]	O	Edu	Edu+Str	4.0
Stamler, 1987 [88]	O, S (anti- hypertensive medication, age, weight, Na ⁺ intake)	N or drugs cont'd	Nut	4.0
RIS, 1998 [52]	O	UC	Nut	6.0-7.8; 6.6
TONE, 1998 [93]	O	UC	Obese: weight reduction and/or salt reduction Non-obese: salt reduction	11.2-3.0; 2.4

Primary endpoint(s)	Other major (ie hard) endpoints	Quality, total sum; overall evaluation (mean±SEM)	Study quality and relevance
CV morbidity		12.6±0.8; 2.9±0.6	High
CHD mortality	Mortality by cause	10.4±1.4; 2.9±0.4	High
BP	Mortality, CV morbidity	9.3±0.9; 2.0±0.2	Medium
BP, need of medication	Mortality, CV morbidity	11.1±1.2; 2.2±0.4	High
CV events	MI, stroke, CV mortality	12.2±1.1; 3.4±0.5	High
High BP or CV events	MI, stroke	12.0±0.9; 2.7±0.3	High

The table continues on the next page.

Appendix 1, Table 1 continued

Study, year Reference	Study characteristics	Design	Control	Active treatment(s)
<i>Hypertension after a cerebrovascular event</i>				
HSCSG, 1974 [8]	Prior stroke or TIA, and hyper- tension	DB, S (age, race, DBP level, stroke category)	P	des+mctz
Dutch TIA, 1993 [34]	Prior minor stroke or TIA, no BP criteria	DB	P	ate
TEST, 1995 [49]	Prior stroke or TIA, and hyper- tension	DB	P	ate
PATS, 1995 [27]	Prior minor stroke or TIA, no BP criteria	DB	P	ind
PROGRESS, 2001 [30]	Prior minor stroke or TIA, no BP criteria	DB, S (age, sex, center, prior stroke or TIA, entry SBP, intention to use per or per+ind)	P	1. per; 2. add ind
<i>Hypertension and kidney</i>				
ESPIRAL, 2001 [72]	Primary renal disease and HT	O		1. fos vs nif; 2. add fur; 3. add ate; 4. add dox

	Follow-up min–max; mean (ys)	Primary endpoint(s)	Other major (ie hard) endpoints	Quality, total sum; overall evaluation (mean±SEM)	Study quality and relevance
	1–5.7; 2.3	Stroke recurrence	Mortality, cardiac and CV morbidity	10.9±1.3; 2.4±0.3	High
	2.6	CV mortality, stroke and MI	Mortality by cause, stroke	10.2±1.4; 2.4±0.3	High
	1.1–3.9; 2.6	All cause mortality, stroke and MI		9.2±1.8; 1.8±0.3	Medium
	2	Fatal and non- fatal stroke	CHD death, MI	12.0±0.7; 2.9±0.3	High
	3.9	Fatal and non- fatal stroke	Mortality by cause, MI, major CV events	15.2±0.2; 4.2±0.2	High
	3	ESRD and doubling of serum creatinin	CV mortality, MI, stroke	10.5±1.0; 2.1±0.3	High

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Appendix 1, Table 1 continued

Study, year Reference	Study characteristics	Design	Control	Active treatment(s)
AASK, 2002 [98]	Hypertensive non-diabetic renal disease	DB	UC	Intensive (MAP <92 mm Hg) vs moderate (MAP 102–107 mm Hg), <i>and</i> 1. ram vs met vs aml; 2. add fur, cln, dox, vasodilators
<i>Hypertension and diabetes mellitus</i>				
UKPDS, 1998 [14]	Diabetes mellitus type 2 and HT	O	UC	Intensive (<150/ 85 mm Hg) vs moderate (<180/ 105 mm Hg), <i>and</i> 1. cap vs ate; 2. add fur; 3. add nif; 4. add alpha-md; 5. add alpha- blocker
FACET, 1998 [90]	Diabetes mellitus type 2 and HT	O		1. fos vs aml; 2. add aml or fos
ABCD, 2000 [50,51,82]	Diabetes mellitus type 2 and HT	DB	UC	Intensive (DBP 70 mm Hg) vs moderate (DBP 80–90 mm Hg), <i>and</i> 1. nis vs ena; 2. add met; 3. add hctz

Follow-up min-max; mean (ys)	Primary endpoint(s)	Other major (ie hard) endpoints	Quality, total sum; overall evaluation (mean±SEM)	Study quality and relevance
3.8	Progression rate of renal dysfunction	ESRD and mortality	12.4±1.1; 3.3±0.4	High
8.4	Fatal and non- fatal event related to diabetes, and all cause mortality	MI, stroke, vascular mortality	12.7±0.9; 3.7±0.3	High
2.5-3.5; 2.8	Serum lipids	CV events	9.6±0.8; 2.3±0.3	Medium
5.3 ¹	Creatine clearance	CV mortality, stroke, MI	10.6±1.0; 2.5±0.2	High

The table continues on the next page.

Appendix 1, Table 1 continued

Study, year Reference	Study characteristics	Design	Control	Active treatment(s)
RENAAL, 2001 [42]	Diabetes mellitus type 2 and nephropathy; all were HT	DB	P	1. los vs placebo; 2. add diuretics, CCB, alpha- blocker, beta- blocker or central acting drugs
IDNT, 2001 [66]	Diabetes mellitus type 2 and nephropathy and HT	DB	P	1. irb vs aml vs placebo; 2. add other
J-MIND, 2001 [39]	Diabetes mellitus type 2 and HT	O		1. nif vs ena; 2. add fur or alpha-blocker
DIABHYCAR, 2004 [73]	Diabetes mellitus type 2 and microalbumin- uria, HT in 50%	DB	P	1. ram vs placebo
Hypertension and cardiovascular risk				
HOPE, 2000 [11,100]	High CV risk, HT in 47%	DB	P	ram vs placebo and vitamin E vs placebo
EUROPA, 2003 [54]	CHD, HT in 27%	DB	P	per vs placebo

¹ Stopped prematurely

Follow-up min-max; mean (ys)	Primary endpoint(s)	Other major (ie hard) endpoints	Quality, total sum; overall evaluation (mean±SEM)	Study quality and relevance
2.3–4.6; 3.4	Mortality, ESRD, and doubling of serum creatinine	CV morbidity and mortality	13.1±0.6; 3.1±0.3	High
2.6	Mortality, ESRD, and doubling of serum creatinine	CV mortality, MI	12.8±1.5; 3.7±0.4	High
2	Progression of nephropathy	CV events	9.5±0.9; 1.7±0.2	Medium
3.9	CV mortality, stroke, MI, HF, and ESRD		13.2±0.5; 2.8±0.3	High
4.5 ¹	CV mortality, stroke, and MI	All cause mortal- ity	13.9±0.5; 3.9±0.3	High
4.2	CV mortality, non-fatal CHD	All cause mortal- ity, stroke, MI	13.4±0.4; 3.2±0.4	High

Appendix 1, Table 2 Design Characteristics (2).

Study, year Reference	Designed to show	Alpha	Beta
Pharmacological			
VA II, 1970 [12,13,80,89]	Significant reduction in CV mortality and morbidity	Not available	
USPHS, 1977 [83]	A reduction of total mortality to the same level as the non-vascular mortality in the male American population	0.05	0.95
VA-NHLBI, 1978 [15]	Feasibility trial for identification and recruitment, and maintaining adequate compliance in mild hypertensive patients, and feasibility of protocol as written for future large scale study	Not available	
HDFP, 1979 [7,9,10,17–19, 23,26,87]	A 40% reduction in mortality	0.05	0.90
ANBPS, 1980 [1,29,35]	A 30% reduction in mortality and CV morbidity	0.05	0.90
Oslo, 1980 [61]	Significant reduction in CV complications	Not available	
MRC, 1985 [5,24,75]	A 40% reduction in mortality due to stroke and hypertension, and stroke morbidity	0.01	0.95
EWPHE, 1985 [36–38]	A 40% reduction in cerebrovascular mortality	0.05	0.90
HEP, 1986 [45]	A 33% reduction in events (stroke including TIA, MI)	0.05	0.90

The table continues on the next page.

Appendix 1, Table 2 continued

Study, year Reference	Designed to show	Alpha	Beta
SHEP, 1991 [28,46,53, 55,65]	A 32% reduction in total stroke	0.05	0.90
STOP, 1991 [48]	Significant reduction in CV mortality, stroke or MI, assuming a 1.75% risk reduction per 1 mm Hg SBP reduction	0.05	0.90
MRC older, 1992 [21]	A 30% reduction in total stroke	0.02	0.90
TOMHS, 1993 [33,76]	Clinically meaningful differences between any two groups on quality of life, side effects, biochemistry, echocardiography, ECG	0.01	0.90
BBB, 1994 [56]	No difference in CV morbidity related to a change in DBP of 10 mm Hg	0.05	0.80
Syst-Eur, 1997 [84–86,91]	A 40% reduction in total stroke incidence	0.01	0.90
HOT, 1998 [60,63,64]	A 25% reduction in CV mortality	0.05	0.90
Syst-China, 2000 [70,92]	A 40% reduction in total stroke	0.01	0.90
SCOPE, 2003 [69]	A 23% risk reduction in major CV events	0.05	0.87

The table continues on the next page.

Appendix 1, Table 2 continued

Study, year Reference	Designed to show	Alpha	Beta
HYVET Pilot, 2003 [44]	Pilot study, no power calculation was performed	Not available	
Comparing drug treatments			
IPPPSH, 1985 [3]	A 35–50% reduction in MI and sudden death	0.05	0.90
HAPPHY, 1987 [95]	A 30% reduction in CHD morbidity	0.05	0.90
MAPHY, 1988 [94]	A 30% reduction in CHD morbidity	0.05	0.90
Yurenev, 1992 [99]	Complications related to HT	Not available	
MIDAS, 1996 [41]	A 30–40% reduction of the carotid artery intima media thickness progression	0.05	0.90
VHAS, 1997 [81]	A 25% difference in BP reduction between treatments	0.05	0.90
NICS-EH, 1999 [31]	Prevention of cerebral or CV complications	Not available	
CAPPP, 1999 [59,77]	A 20% reduction in fatal and non-fatal stroke and MI, and other CV mortality	0.05	0.80
STOP-2, 1999 [58,67]	A 25% reduction in CV mortality	0.05	0.90

The table continues on the next page.

Appendix 1, Table 2 continued

Study, year Reference	Designed to show	Alpha	Beta
NORDIL, 2000 [57]	A 20% reduction in fatal and non-fatal stroke and MI, and other CV mortality	0.05	0.80
INSIGHT, 2000 [43,71]	A 25% reduction in morbidity and mortality in stroke, MI, CHF, sudden death	0.05	0.80
LIFE, 2002 [47,68]	A 15% reduction in combined incidence of CV morbidity and mortality	0.05	0.80
ALLHAT, 2002 [6,20]	A 16% reduction in fatal CHD and non-fatal MI	0.0178	0.83
ELSA, 2002 [101]	A difference in changes of carotid artery intima media thickness between groups of 0.04 mm	0.05	0.95
CONVINCE, 2003 [40]	14% reduction in stroke, non-fatal MI and CV mortality	0.05	0.84
ANBP2, 2003 [97]	A 25% CV morbidity	0.05	0.90
INVEST, 2003 [79]	A 20% reduction in all cause mortality, stroke reduction and MI	0.05	0.85
VALUE, 2004 [62]	A 15% reduction in cardiac mortality or morbidity	0.05	0.90

The table continues on the next page.

Appendix 1, Table 2 continued

Study, year Reference	Designed to show	Alpha	Beta
<i>Multifactorial and non-pharmacological</i>			
GPPT, 1986 [96]	The extent to which one can induce changes in risk factors by means of a population based intervention programme, and to measure the effects on mortality, stroke and MI	Not available	
MRFIT, 1990 [2,4,16,22, 25,32]	A 25% reduction in CHD mortality	0.05	0.90
Patel, 1985 [78]	Blood pressure reduction	Not available	
Stamler, 1987 [88]	A 25% points difference between the groups concerning how many were still not receiving anti-hypertensive drugs	0.05	0.90
RIS, 1998 [52]	A 30% reduction in stroke, MI and other fatal and non-fatal CV events	0.05	0.80
TONE, 1998 [93]	A 25% reduction in the occurrence of high BP following an attempt to withdraw the antihypertensive therapy	0.05	0.80
<i>Hypertension after a cerebrovascular event</i>			
HSCSG, 1974 [8]	A 50% change in an assumed 10% annual stroke recurrence rate	Not available	
Dutch TIA, 1993 [34]	A 20% reduction in vascular mortality or non-fatal stroke	0.05	0.80
TEST, 1995 [49]	A 20% reduction in mortality, non-fatal stroke or MI	0.05	0.80

The table continues on the next page.

Appendix 1, Table 2 continued

Study, year Reference	Designed to show	Alpha	Beta
PATS, 1995 [27]	A 25% reduction in fatal and non-fatal stroke	0.01	0.90
PROGRESS, 2001 [30]	A 30% reduction in stroke	0.05	0.90
Hypertension and kidney			
ESPIRAL, 2001 [72]	Reduction in the time to doubling of serum creatinine or to ESRD and need to enter dialysis program	0.05	Not available
AASK, 2002 [98]	Rate of change in the decline in glomerular filtration rate	0.05	≥0.88
Hypertension and diabetes mellitus			
UKPDS, 1998 [14]	A 25% reduction in all cause mortality and fatal and non-fatal events related to diabetes	0.05	0.71
FACET, 1998 [90]	A 10% reduction in total cholesterol	0.05	0.80
ABCD, 2000 [50,51,82]	Progression of type 2 diabetic complications	Not available	
RENAAL, 2001 [42]	A 20% reduction in the composite endpoint of all cause mortality, ESRD and doubling of serum creatinine	0.048	0.95
IDNT, 2001 [66]	A 26% difference in the composite endpoint of all cause mortality, ESRD and doubling of serum creatinine	0.05	0.90

The table continues on the next page.

Appendix 1, Table 2 continued

Study, year Reference	Designed to show	Alpha	Beta
J-MIND, 2001 [39]	Reduction in the onset and progression of diabetic nephropathy	Not available	
DIABHYCAR, 2004 [73]	A 20% reduction in CV mortality, stroke, non-fatal MI, HF and ESRD	0.05	0.90
<i>Hypertension and cardiovascular risk</i>			
HOPE, 2000 [11,100]	A 18% relative risk reduction in CV mortality, stroke and MI	0.05	0.90
EUROPA, 2003 [54]	A 16% relative reduction in all cause mortality, non-fatal MI, unstable AP and cardiac arrest with successful resuscitation	0.05	0.90

Appendix 1, Table 3 Design Characteristics (3).

Study, year Reference	Inclusion criteria
Pharmacological	
VA II, 1970 [12,13,80,89]	DBP 90–114 mm Hg (seated). Average of the 2 last of repeat clinic visits during a 2–4 month placebo pre-randomisation period.
USPHS, 1977 [83]	Average DBP of 90–114 mm Hg by repeat home blood pressure measurements at previous screening followed by DBP >89 mm Hg (seated, 20 min rest) on 2 of 3 clinic visits during a 3 month placebo pre-randomisation period.
VA-NHLBI, 1978 [15]	DBP 85–105 mm Hg (seated, 5 min rest, mean of 3 readings) on third clinic visit during a 2 month placebo pre-randomisation period (DBP 85–115 and 85–110 mm Hg on first and second visits, respectively). Previous screening (DBP 90–120 mm Hg) performed.
HDFP, 1979 [7,9,10,17–19,23,26,87]	Mean of second and third DBP >95 mm Hg at 1 home visit and, at a subsequent clinic visit, mean of second and fourth DBP 90–104, 105–114, and >114 mm Hg, in stratum I, II and III, respectively (seated, 5 min rest, V).
ANBPS, 1980 [1,29,35]	<200/95–109 mm Hg (seated, 5 min rest, mean of 2 readings). Average of 2 screening centre visits.
Oslo, 1980 [61]	SBP 150–179 and/or DBP 95–109 mm Hg (seated, 5 min rest, last of 2 readings). Average of the 2 highest values of 1 screening and 2 clinic visits.
MRC, 1985 [5,24,75]	<200/90–109 mm Hg (seated, 10 min rest, 2 readings). Average of 4 readings on 2 screening visits, which had to be confirmed on a subsequent clinic visit (mean of 2 readings).
EWPHE, 1985 [36–38]	160–239/90–119 mm Hg (seated, 5 min rest, 3 readings). Average of the last readings on 3 clinic visits during a placebo pre-randomisation period of at least 1 month.
HEP, 1986 [45]	SBP 170–280 and/or DBP 105–120 mm Hg (seated, short rest) on each of 3 screening visits.

Exclusion criteria

Secondary HT, renal failure, malignancy, FH III–IV, cerebral haemorrhage, dissecting aneurysm, uncontrolled CHF, suspected or demonstrated non-compliance (tested during pre-randomisation period).

Secondary HT, renal failure, FH III–IV, stroke, MI, AP, abnormal ECG, radiographic cardiomegaly, valvular heart disease, diabetes mellitus, marked hypercholesterolemia. Previous arterial thrombosis or vascular insufficiency, ongoing antihypertensive medication.

Evidence of target organ damage, insulin dependent diabetes mellitus, concomitant fatal disease, history of depression, gout or peptic ulcer within last 2 years, treatment with vasoactive drugs, signs of non-compliance.

Bedfast and institutionalised persons.

Secondary HT, renal failure, stroke or MI within last 3 months, AP or other signs of CHD, cerebrovascular disease, serious hypotensive complications, potentially fatal disease, asthma, diabetes mellitus, gout, taking combination of oestrogen and progesterone or tricyclic antidepressants, antihypertensive medication within last 3 months.

Secondary HT, renal failure, FH III–IV, CHD, CV disease, intermittent claudication, CHF, valvular heart disease, abnormal ECG, hepatic disease, malignancy and chronic disease such as rheumatoid arthritis, endocrine disorder, psychiatric disease, abuse, social misadjustment stroke or MI within last 3 months, AP or other signs of CHD, antihypertensive medication within last 1 year.

Secondary HT, stroke or MI within last 3 months, AP, intermittent claudication, diabetes mellitus, gout, non-compliance (tested during pre-randomisation period), ongoing antihypertensive medication.

Secondary HT, renal failure, FH III–IV, uncontrolled CHF, vascular aneurysms, history of stroke or hypertensive encephalopathy, orthostatic hypotension, hepatic disease, malignancy, insulin dependent diabetes mellitus, gout, asthma, serious concomitant disease, ongoing antihypertensive medication.

Atrial fibrillation, A–V heart block, CHF, diabetes mellitus needing drug treatment, gout, asthma, serious concomitant disease, ongoing antihypertensive medication.

The table continues on the next page.

Appendix 1, Table 3 continued

Study, year Reference	Inclusion criteria
SHEP, 1991 [28,46,53,55,65]	160–219/<90 mm Hg (seated, 2 readings). Average of the 4 readings, 2 at each of 2 clinic visits. Previous screening performed (160–219/<100 mm Hg).
STOP, 1991 [48]	<231/105–120 or 180–230/90–120 mm Hg (supine, 5 min rest, mean of 2 readings) on 3 clinic visits during a 1 month pre-randomisation period.
MRC older, 1992 [21]	160–209/<115 mm Hg (seated, mean of second and third reading). Average of 3 visits during a 2 month run-in period. To be confirmed at 2 clinic visits before randomisation.
TOMHS, 1993 [33,76]	DBP 90–99 mm Hg (seated, 5 min rest, 2 readings) on first and second visit, and on average from all 3 eligibility visits. If on antihypertensive treatment by only 1 agent and DBP <95 mm Hg, patients were included if DBP was 85–89 mm Hg on 3 visits following withdrawal.
BBB, 1994 [56]	DBP 90–100 mm Hg (supine, 5 min rest) on 3 consecutive visits with ongoing therapy.
Syst-Eur, 1997 [84–86,91]	SBP 160–219 and DBP <95 mm Hg (seated, average of 6 readings, 2 at 3 visits 1 month apart) and standing SBP ≥140 mm Hg, average of 6 measurements.
HOT, 1998 [60,63,64]	DBP 100–115 mm Hg (seated, 3 readings) at 2 qualifying visits 7 days apart.
Syst-China, 2000 [70,92]	SBP 160–219 and DBP <95 (seated, average of 6 readings, 2 at 3 visits 1 month apart) and standing SBP ≥140 mm Hg, average of 6 measurements.
SCOPE, 2003 [69]	160–179/90–99 mm Hg (seated, mean of 2 readings) on 2 consecutive visits and mini mental state examination score of 24 or more.
HYVET Pilot, 2003 [44]	SBP 160–219 and DBP 95–109 mm Hg (later changed to 90–109 mm Hg; seated, 2 readings on 2 occasions 1 month apart), standing SBP >140 mm Hg.

Exclusion criteria

Major CV diseases, renal failure, malignancy, alcoholic hepatic disease, medical management problems.

MI or stroke within last 1 year, AP requiring drugs other than glyceryl trinitrates, serious concomitant disease, >30 mm Hg fall in SBP on standing.

Secondary HT, renal failure, MI or stroke within last 3 months, CHF, AP, diabetes mellitus, asthma, serious intercurrent disease or malignancy, serum K⁺ <3.4 or >5.0 mmol/L, on antihypertensive drugs.

More than one type of antihypertensive medication, CV disease, serious concomitant disease, gross overweight, excess alcohol intake, ≥50% of meals eaten out of home, unwillingness to attempt nutritional changes, inability to make echocardiographic registrations.

CHD, somatic disorder that may cause deterioration with health within last 5 years, psychiatric disease, or alcoholism.

Secondary HT, retinal haemorrhage or papilloedema, stroke, MI within last 1 year prior to study, or dissecting aortic disease, CHF, serum creatinine ≥180 µmol/L, history of severe nose bleeding, dementia, abuse, concomitant severe CV or non-CV disease.

Malignant or secondary HT, stroke or MI within last 12 months, decompensated CHF, insulin treated diabetes mellitus, serious concomitant disorder that could affect survival during the next 2–3 years.

Serum creatinine >180 µmol/L, patients with severe concomitant CV or non-CV disease.

Secondary HT, orthostatic hypotension or SBP <140 mm Hg after 2 min standing upright, stroke or MI within last 6 months, CHF, abuse, concomitant serious diseases.

Accelerated HT, severe CHF, serum creatinine >150 µmol/L, cerebral haemorrhage within last 6 months, renal arterystenosis, gout, dementia, conditions expected to limit survival severely.

The table continues on the next page.

Appendix 1, Table 3 continued

Study, year Reference	Inclusion criteria
Comparing drug treatments	
IPPPSH, 1985 [3]	DBP 100–125 mm Hg (seated) on 2 out of 3 pre-randomisation clinic visits.
HAPPHY, 1987 [95]	DBP 100–130 mm Hg (seated, 5 min rest, 2 readings). Average of 4 readings on 2 clinic visits.
MAPHY, 1988 [94]	DBP 100–130 mm Hg (seated, 5 min rest, 2 readings). Average of 4 readings on 2 clinic visits.
Yurenev, 1992 [99]	>160/95 mm Hg (3 measurements). Echocardiographic evidence of LVH.
MIDAS, 1996 [41]	DBP $\geq$ 90 mm Hg on each of 3 weekly visits on placebo and $\geq$ 1 early atherosclerotic lesion(s) in extra-cranial carotid arteries (by ultrasonography).
VHAS, 1997 [81]	SBP $\geq$ 160 and DBP $\geq$ 95 mm Hg (seated) following 3 weeks of placebo.
NICS-EH, 1999 [31]	SBP 160–220 and DBP <115 mm Hg (seated) at 2 separate occasions, 2–4 weeks apart.
CAPP, 1999 [59,77]	DBP $\geq$ 100 mm Hg in untreated patients (supine, 2 readings) on 2 occasions 1 week apart; in treated patients DBP $\geq$ 100 mm Hg must be documented in previous medical records.
STOP-2, 1999 [58,67]	Supine DBP $\geq$ 180/105 mm Hg (supine, 5 min rest) on 3 occasions separated by at least 1 week.

Exclusion criteria

FH III–IV, stroke, MI, AP, relevant valvular heart disease, CHF, A–V heart block II–III, sick sinus syndrome or bradycardia <50/min, intermittent claudication, insulin dependent diabetes mellitus, asthma, renal, hepatic, gastrointestinal or other concomitant serious disease, pregnancy, suspected non-compliance.

Malignant or secondary HT, stroke, MI, AP, A–V heart block II–III, CHF, obstructive lung disease, diabetes mellitus, gout, hepatic disease, severe alcoholism, malignancy or other serious disease; conditions requiring treatment with diuretics or beta-blocker.

Malignant or secondary HT, stroke, MI, AP, A–V heart block II–III, CHF, obstructive lung disease, diabetes mellitus, gout, hepatic disease, severe alcoholism, malignancy or other serious disease; conditions requiring treatment with diuretics or beta-blocker.

Secondary HT, CHD, reasons that would limit participation.

Malignant or secondary HT. Insulin-dependent diabetes mellitus. Cerebrovascular disease, carotid endarterectomy, CHF, cardiac arrhythmias, coronary intervention, uncontrolled AP or recent MI. Elevated levels of lipids, blood glucose, serum creatinine, or liver enzymes.

Secondary HT, recent history (within last 6 months) of stroke, MI or unstable AP, severe peripheral artery disease, arrhythmias, CHF, serum creatinine >1.7 µg/dL, hepatic insufficiency, hyperuricemia (>7 mg/dL) hypercalemia (<3.8 mmol/L), diabetes mellitus type 1 or uncontrolled type 2, familial hyperlipidemia, serious concomitant disease.

CV disorder, arrhythmia, CHD, CHF, valvular heart disease, serum creatinine ≥2.0 mg/dL, marked hepatic dysfunction, retinal changes, diabetes mellitus requiring drug treatment.

Secondary HT, CHD requiring treatment with beta-blocker, serum creatinine >150 µmol/L, somatic disease with likelihood of deterioration of health within a few years.

Orthostatic hypertension with >30 mm Hg fall in SBP on standing, severe or incapacitating illness.

The table continues on the next page.

Appendix 1, Table 3 continued

Study, year Reference	Inclusion criteria
NORDIL, 2000 [57]	DBP ≥ 100 mm Hg (supine, resting) on ≥ 2 consecutive visits, at least 1 week apart, in previously untreated patients with risk factors such as diabetes mellitus, hypercholesterolemia, smoking or LVH; or DBP ≥ 110 mm Hg on ≥ 2 consecutive visits, at least 1 week apart, in previously untreated patients without risk factors; or DBP ≥ 100 mm Hg on ≥ 3 consecutive visits over 3 months in previously untreated patients without risk factors; or DBP ≥ 100 mm Hg on ≥ 2 consecutive visits, at least 1 week apart, in previously treated patients without risk factors.
INSIGHT, 2000 [43,71]	SBP ≥ 150 and DBP 95 or SBP ≥ 160 mm Hg (seated, 5 min rest, 3 readings) and ≥ 1 more of the following: current smoker, total cholesterol ≥ 6.43 mmol/L, diabetes mellitus, CHD, peripheral vascular disease, LVH, family history of CVD, proteinuria > 0.5 g/24h.
LIFE, 2002 [47,68]	160–200 and/or 95–115 mm Hg (seated) as a mean of recordings after 1 and 2 weeks on single-blind placebo, and LVH on ECG.
ALLHAT, 2002 [6,20]	Seated BP $> 140/90$ mm Hg if untreated or patients on anti-hypertensive drugs and $< 160/100$ mm Hg (seated), and one or more manifestation of atherosclerotic disease (MI or stroke > 6 months prior to study, revascularisation procedures, documented atherosclerotic disease) or diabetes mellitus type 2 or HDL < 35 mg/dL or LVH or ischemic ECG or current smoking.
ELSA, 2002 [101]	150–210/95–115 mm Hg (seated, 3 readings), total cholesterol ≤ 320 mg/dL, triglycerides ≤ 300 mg/dL, serum creatinine ≤ 1.7 mg/dL, and a readable ultrasound carotid artery scan with maximum intima media thickness ≤ 4.0 mm.
CONVINCE, 2003 [40]	140–190/90–110 mm Hg or ongoing antihypertensive medication and $< 175/100$ mm Hg, and 1 additional risk factor (MI > 12 months or stroke > 6 months prior to randomisation, current or recent smoker, diabetes mellitus type 2, LVH, HDL < 35 mg/dL, LDL > 1.59 mg/dL, total cholesterol > 250 mg/dL, TIA, body weight $\geq 25\%$ above ideal, or known atherosclerotic disease.

Exclusion criteria

Secondary HT, arrhythmias, stroke or MI within last 6 months, CHF.

Malignant HT, stroke or MI within last 12 months, previous coronary intervention, CHF, unstable insulin dependent diabetes mellitus, subarachnoidal haemorrhage.

Malignant or secondary HT, SBP >200 or DBP >115 mm Hg during placebo, stroke or MI within last 6 months, angina pectoris requiring treatment with a beta-blocker or a calcium channel blocker, CHF or an ejection fraction $\leq 40\%$, aortic stenosis, serum creatinine >160 $\mu\text{mol/L}$, a disease expected to cause a substantial deterioration of the patient's health during the next 4 to 6 years, abuse.

Symptomatic MI, AP or stroke within the last 6 months, CHF or an ejection fraction <35%, serum creatinine >2 mg/dL, requirement for more than 2 antihypertensive drugs to achieve satisfactory BP control, SBP >180 or DBP >110 mm Hg on 2 separate readings, concomitant disease with likelihood of non-CV death during the study.

Recent stroke or MI, insulin dependent diabetes mellitus.

Secondary HT, CHF NYHA II–IV, arrhythmias, renal impairment, abuse, working evening, night or shift, malignancy, other serious concomitant disease.

The table continues on the next page.

Appendix 1, Table 3 continued

Study, year Reference	Inclusion criteria
ANBP2, 2003 [97]	SBP >160 or DBP >90 mm Hg if SBP $\geq$ 140 mm Hg (seated) as an average of 2 visits.
INVEST, 2003 [79]	Essential hypertension requiring drug therapy and documented CHD.
VALUE, 2004 [62]	Untreated SBP 160–210 and/or DBP 95–115 mm Hg (seated) or ongoing treatment for hypertension, and $\geq$ 50 years, and risk factors (diabetes mellitus, smoking, hypercholesterolemia, LVH without strain on ECG, proteinuria, serum creatinine >1.7 mg/dL) and/or disease factors (MI, peripheral vascular disease, stroke or TIA, LVH with strain on ECG). Males 50–59 years needed 3 risk factors or 1 disease factor; females 2 risk factors and 1 disease factor; males and females 60–69 years needed 2 risk factors or 1 disease factor; males and females $\geq$ 70 years needed 1 risk factor or 1 disease factor.
Multifactorial and non-pharmacological	
GPPT, 1986 [96]	SBP >175 and/or DBP >115 mm Hg (seated, 5 min rest, 1 reading) on 2 screening visits, or ongoing antihypertensive medication.
MRFIT, 1990 [2,4,16,22,25,32]	DBP 90–115 mm Hg (1 reading) on screening visit, followed by DBP >89 mm Hg (seated, 5 min rest, mean of 2 readings), or ongoing antihypertensive medication, and CHD risk in the upper 15% according to Framingham data. Average of 2 pre-randomisation clinic visits.
Patel, 1985 [78]	Two of: >139/89 (seated, 5 min rest, mean of 2 readings at 1 screening visit) and not taking antihypertensive drugs, cholesterol >6.2 mmol/L, >9 cigarettes a day.
Stamler, 1987 [88]	Patients previously receiving antihypertensive drug therapy, mostly within the HDFP study. DBP <90 mm Hg (seated, 5 min rest, mean of 2 readings) on 2 pre-randomisation visits and 10–49% overweight and/or Na ⁺ intake >2.8 g/d. Randomisation into nutritional intervention and discontinuation of medication (group 1), no intervention and discontinuation (group 2), or no intervention and continued medication (group 3).

Exclusion criteria

Malignant HT, CV events within last 6 months, serum creatinine >2.5 mg/dL, dementia, life threatening illness.

Unstable AP, intervention for CAD or stroke within last month, treatment with beta-blocker within last 2 months, arrhythmia, HF, severe renal failure.

SBP >210 mm Hg, MI, stroke, CABG or PTCA within last 3 months CHF requiring ACE inhibitors, relevant valvular disease, renal artery stenosis, severe renal failure or hepatic disease.

MI within last 2 years.

CHD, stroke, diabetes mellitus requiring medication, severe hypercholesterolemia (>9 mmol/L), on lipid lowering drugs, body weight >50% over ideal weight, concomitant disease or other reasons that would limit participation.

Major CV complications or other major disease, history of problem drinking.

The table continues on the next page.

Appendix 1, Table 3 continued

Study, year Reference	Inclusion criteria
RIS, 1998 [52]	Treatment for hypertension and one or more of the following: total cholesterol >6.5 mmol/L, tobacco smoking, diabetes mellitus.
TONE, 1998 [93]	SBP <145 mm Hg and DBP <85 mm Hg (seated, mean of 3 readings), mean of 3 visits, while taking 1 antihypertensive drug.
Hypertension after a cerebrovascular event	
HSCSG, 1974 [8]	BP 140–220/90–115 mm Hg (supine, 15 min rest). Average of the second and third clinic visit during a 6 week placebo pre-randomisation period <i>and</i> a history of stroke and/or TIA during the previous year.
Dutch TIA, 1993 [34]	TIA or minor stroke within last 3 months prior to randomisation.
TEST, 1995 [49]	TIA or stroke within last 3 weeks prior to randomisation.
PATS, 1995 [27]	History of TIA or stroke, irrespective of BP level. Clinically stable for at least 4 weeks before inclusion.
PROGRESS, 2001 [30]	History of TIA or stroke within last 5 years, irrespective of BP level. Clinically stable for at least 2 weeks before inclusion.
Hypertension and kidney	
ESPIRAL, 2001 [72]	>140/90 mm Hg or ongoing antihypertensive medication, <i>and</i> serum creatinine (133–442 µmol/L).
AASK, 2002 [98]	Afro-Americans with DBP ≥95 mm Hg, <i>and</i> hypertensive renal disease (glomerular filtration rate 20–65 mL/min/1.73 m ²) and no other causes of renal insufficiency.
Hypertension and diabetes mellitus	
UKPDS, 1998 [14]	SBP ≥160 and/or DBP ≥90 mm Hg in untreated, or SBP ≥150 and/or DBP ≥85 mm Hg in treated hypertensive patients (3 readings) on 3 separate clinical visits, <i>and</i> diabetes mellitus type 2.

Exclusion criteria

Malignancy and other serious chronic disease.

Stroke or MI within last 6 months, CHD, CHF, arrhythmias, valvular heart disease, blood glucose >260 mg/dL or insulin dependent diabetes mellitus, obstructive lung disease, serum creatinine >2 mg/dL, psychiatric illness, cancer within last 5 years, body mass index <21 kg/m², >33 kg/m² (males) or >37 kg/m² (females); abuse.

Non-ambulatory patients, concomitant disease, which may be influenced adversely by study treatment.

Patients with cerebral ischemia of other origin than arterial thrombosis or embolism.

SBP ≤140 and DBP ≤80 mm Hg or heart rate ≤50 beats/min, CHF, subarachnoid haemorrhage.

Secondary HT, CHF, rheumatic valvular disease, atrial fibrillation, insulin-dependent diabetes mellitus, hyperthyroidism, severe hepatic or renal disease, haemorrhagic disease, malignancy.

No definite indication of ACE inhibition or definite contraindication to ACE-inhibitors.

Previous history of recent CV disease (stroke, MI, CHF), diabetes mellitus.

Accelerated or malignant HT within last 6 months, secondary HT, CHF, diabetes mellitus, urinary protein: creatinine ratio >2.5, serious systemic disease.

Malignant or uncontrolled HT, severe vascular episodes, ketonuria, serum creatinine >175 µmol/L, retinopathy, uncorrected endocrine abnormality, severe concurrent illness likely to limit life.

The table continues on the next page.

Appendix 1, Table 3 *continued*

Study, year Reference	Inclusion criteria
FACET, 1998 [90]	SBP >140 or DBP >90 mm Hg on ≥ 3 consecutive visits, or SBP >160 or DBP >95 mm Hg on ≥ 2 visits during at least 3 months. Duration of hypertension less than 1 year, <i>and</i> diabetes mellitus type 2.
ABCD, 2000 [50,51,82]	DBP ≥ 80 mm Hg, <i>and</i> diabetes mellitus type 2.
RENAAL, 2001 [42]	SBP 100–200 and DBP ≤ 110 mm Hg (seated), <i>and</i> diabetes mellitus type 2. Proteinuria (urinary albumin: creatinine ratio ≥ 300 mg/g) or 24h urinary protein excretion >500 mg and serum creatinine 1.5–3.0 mg/dL (≥ 1.3 mg/dL for females).
IDNT, 2001 [66]	SBP >135 and/or DBP >85 mm Hg (seated) or documented treatment for hypertension, <i>and</i> diabetes mellitus <i>and</i> proteinuria >900 mg/24h.
J-MIND, 2001 [39]	SBP ≥ 140 and/or DBP ≥ 90 mm Hg (supine), <i>and</i> diabetes mellitus type 2.
DIABHYCAR, 2004 [73]	Diabetes mellitus type 2, age >50 years, urinary albumin excretion ≥ 20 mg/L.
Hypertension and cardiovascular risk	
HOPE, 2000 [11,100]	CHD or peripheral vascular disease or stroke or diabetes mellitus plus at least 1 of: hypertension (>160/>90 mm Hg) or ongoing treatment, total cholesterol >5.2 mmol/L, HDL cholesterol <0.9 mmol/L, current smoker, microalbuminuria >300 mg/24h, or evidence of previous vascular disease.
EUROPA, 2003 [54]	110–180/ ≤ 100 mm Hg and documented CHD.

Exclusion criteria

History of CHD, stroke or any other morbid condition with poor prognosis, serum creatinine >1.5 mg/dL, microalbuminuria >40 µg/min, the use of lipid lowering drugs, aspirin or antihypertensive agents other than diuretics and beta-blockers.

Stroke, MI or unstable AP within 6 months, or coronary intervention within 3 months prior to study start, unstable AP within last 6 months, CHF NYHA III–IV, serum creatinine >265 µmol/L.

MI or CABG within last month, stroke, PTCA within last 6 months, TIA within last 12 months. CHF, history of non-diabetic renal disease or renal artery stenosis. Primary hyperaldosteronism, or phaeochromocytoma, HbA_{1c} >12%.

Stroke within last 3 months or TIA within last 6 months, an acute coronary syndrome within last 3 months, CHF NYHA III–IV,

Malignant hypertension, renal artery stenosis, overt proteinuria. HbA_{1c} >12% within 1 month prior to study start.

MI within last 3 months, HF, serum creatinine >150 µg/L, treatment with insulin ACEi or ARB, urinary tract infection.

Uncontrolled HT, complex congenital heart disease, valvular heart disease, cor pulmonale, ejection fraction <40%, malignant arrhythmias, planned coronary intervention or heart transplant, renal disease, any other major non-cardiac illness expected to reduce life expectancy or interfere with study participation.

Stroke or TIA within last 3 months prior to study, valvular heart disease, hypertrophic cardiomyopathy, CHF, serum creatinine >150 mmol/L, concomitant serious disease.

Appendix 1, Table 4 Patient Characteristics.

Study, year Reference	Interven- tion	No of patients screened	No of patients at entry	No of patients at follow-up	Age Range; mean
Pharmacological					
VA II, 1970 [12,13,80,89]	Treatment Control		186 194	157 167	24–75; 51
USPHS, 1977 [83]	Treatment Control	>1 600	193 196	142 146	21–55; 44
VA-NHLBI, 1978 [15]	Treatment Control	118 157	508 504	410 400	21–50; 38
HDFP, 1979 [7,9,10,17–19, 23,26,87]					
Strata I–III	Treatment Control	159 468	5 485 5 455	5 477 5 439	30–69; 51
Stratum I	Treatment Control		3 903 3 922	3 895 3 911	--; 51
ANBPS, 1980 [1,29,35]	Treatment Control	104 171	1 721 1 706	1 679 1 660	30–69; 50
Oslo, 1980 [61]	Treatment Control	16 200	406 379	406 379	40–49; 45
MRC, 1985 [5,24,75]	Treatment Control	515 000	8 700 8 654	≈7 000 ≈7 000 ⁵	35–64; 52
EWVPE, 1985 [36–38]	Treatment Control		416 424	404 412	≥60; 72
HEP, 1986 [45]	Treatment Control	10 718	419 468		60–79; 69
SHEP, 1991 [28,46,53, 55,65]	Treatment Control	447 921	2 365 2 371		>60; 72

	% Male	% White	Entry BP	End of study mean BP	End of study mean group difference in BP by treatment	% Below goal BP at end of study
	100	58	164/104	135/86 169/106	31/19 ¹	
	80	72	147/99	132/88 147/98	18/10 ²	
	81	74	--/93		--/7 ³	
	54	56	159/101	--/84 --/89	5/5	65 44
	55	61	152/96	--/83 --/88	--/4	64 43
	63	100	157/100	--/88 --/94 ⁴	--/6	
	100	100	156/97	128/84 148/93	17/10	
	52	99	161/98	138/86 149/92	11/6	75 46
	30	100	183/101	149/85 172/94 ⁶	22/7 ²	
	31		196/99	162/77 180/88	18/11	62 31
	43	86	170/77	144/68 155/71	12/4	72 40

The table continues on the next page.

Appendix 1, Table 4 continued

Study, year Reference	Interven- tion	No of patients screened	No of patients at entry	No of patients at follow-up	Age Range; mean
STOP, 1991 [48]	Treatment Control		812 815	812 815	70–84; 76
MRC older, 1992 [21]	Treatment Control	125 861	2 183 2 213	≈3 000 ⁸	65–74; 70
TOMHS, 1993 [33,76]	Treatment Control	11 914	668 234	898	45–69; 55
BBB, 1994 [56]	Tight Less tight		1 065 ¹⁰ 1 062 ¹⁰	1 985	46–71; 60
Syst-Eur, 1997 [84–86,91]	Treatment Control	8 926	2 398 2 297	705 682	>60; 70
HOT, 1998 [60,63,64]	DBP ≤90 DBP ≤85 DBP ≤80		6 264 6 264 6 264	5 907 5 913 5 890	50–80; 62
Syst-China, 2000 [70,92]	Treatment Control		1 253 1 141	1 138 1 019	>60; 67
SCOPE, 2003 [69]	Treatment Control		2 477 2 460	4 929	70–89; 76
HYVET Pilot, 2003 [44]	Diuretic ACEi Control		426 431 426	416 424 416	80–96; 84
Comparing drug treatments					
IPPPSH, 1985 [3]	BB Non-BB		3 185 3 172	3 165 3 165	40–64; 52
MRC, 1985 [5,24,75]	BB Non-BB	515 000	4 403 4 297	≈7 000 ≈7 000 ⁵	35–64; 52

	% Male	% White	Entry BP	End of study mean BP	End of study mean group difference in BP by treatment	% Below goal BP at end of study
	37	100	195/102	166/85 193/95	19/8	87/45 ⁷
	42		185/91	151/77 164/82 ⁹	14/6 ⁹	
	62	80	140/91	127/79 133/82	7/4	
	53		155/95 155/94	141/83 152/91	11/9	
	33		174/86	151/79 161/84	10/5	
	53		170/105 170/105 170/105	144/85 141/83 140/81	3/2 4/4 1/2	
	64		171/86	151/81 159/84	8/3	
	36		166/90 167/90	145/80 149/82	4/2	
	47		182/100 182/100 181/100	152/84 151/84 174/95	1/0 22/11 23/11	
	50		173/108	144/89 147/90	4/1	80 74
	52	99	161/98	139/86 135/86 ⁹	4/1	73 75

The table continues on the next page.

Appendix 1, Table 4 *continued*

Study, year Reference	Interven- tion	No of patients screened	No of patients at entry	No of patients at follow-up	Age Range; mean
HAPPHY, 1987 [95]	BB Non-BB		3 297 3 272	3 265 3 240	40–64; 52
MAPHY, 1988 [94]	BB Non-BB		1 609 1 625	1 609 1 624	40–64; 53
Yurenev, 1992 [99]	BB Non-BB		150 154		--; 45
MRC older, 1992 [21]	BB Non-BB	125 861	1 102 1 081	≈1 500 ⁸	65–74; 70
MIDAS, 1996 [41]	CCB D	18 800	442 441		40–≤70; 59
VHAS, 1997 [81]	CCB D	7 839	707 707	559 545	40–65; 54
NICS-EH, 1999 [31]	CCB D		215 214	204 210	≤60; 70
CAPPP, 1999 [59,77]	ACEi BB/D		5 492 5 493	5 294 5 290	25–66; 53
STOP-2, 1999 [58,67]	BB/D ACEi CCB		2 213 2 205 2 196	2 213 2 205 2 196	70–84; 76
NORDIL, 2000 [57]	CCB BB/D		5 410 5 471	5 386 5 443	50–69; 60
INSIGHT, 2000 [43,71]	CCB D		3 289 3 286	1 898 2 116	55–80; 65
LIFE, 2002 [47,68]	ARB BB		4 605 4 588	4 601 4 580	55–80; 67

	% Male	% White	Entry BP	End of study mean BP	End of study mean group difference in BP by treatment	% Below goal BP at end of study
	100	>99	166/107	140/89 140/88	0/1	75 79
	100		167/108	142/89 143/90	0/1	
	100		168/106		3/1 ¹¹	
	42		185/91	151/77 151/78 ⁹	0/1	
	78	72	150/97	134/84 130/84	4/0	
	49		169/102	140/86 141/85	-1/0	69 67
	33	Japanese	172/94	147/81 147/79	0/2	
	53		162/100 160/98	150/88 148/87	2/1	
	33		194/98	159/81 160/82 160/81	-1/1 -1/0 0/1	
	49		173/106	154/97 151/97	3/0	
	47		173/99	138/82 138/82	0	58 57
	46	93	174/98	144/81 145/81	1/0	49 46

The table continues on the next page.

Appendix 1, Table 4 *continued*

Study, year Reference	Interven- tion	No of patients screened	No of patients at entry	No of patients at follow-up	Age Range; mean
ALLHAT, 2002 [6,20]	D CCB ACEi Alpha-B		15 255 9 048 9 054 9 061	14 836 ¹² 8 790 ¹³ 8 778 ¹³ 8 723 ¹³	>55; 67
ELSA, 2002 [101]	CCB BB	3 407	1 177 1 157	755 764	45–75; 56
CONVINCE, 2003 [40]	CCB BB/D		8 241 8 361	8 179 8 297	≥55; 66
ANBP2, 2003 [97]	ACEi D	54 288	3 044 3 039	2 978 2 940	65–84; 72
INVEST, 2003 [79]	CCB BB		11 267 11 309	21 414	≥50; 66
VALUE, 2004 [62]	ARB CCB		7 649 7 596	7 529 7 462	≥50; 67
<i>Multifactorial and non-pharmacological</i>					
GPPT, 1986 [96]	Treatment Control	7 495	686	686	47–55; 50
MRFIT, 1990 [2,4,16,22, 25,32]	Treatment Control	361 662	4 019 3 993	4 005 3 980	35–57; 46
Patel, 1985 [78]	Treatment Control	1 132	99 93	91 84	35–64; --

% Male	% White	Entry BP	End of study mean BP	End of study mean group difference in BP by treatment	% Below goal BP at end of study
53	46	146/84	134/75 135/75 136/75 137/76 ¹⁴	1/0 2/0 1/0 3/1	68 66 61 58 ¹⁴
55	98	164/101 163/101	142/86 142/86	0	
44	84	150/87 150/87	137/79 137/80	0/1	
49		168/91	141/69 142/69	1/0	
48	48	150/86	131/76 131/76	0/0	
57	89	155/87 155/88	139/79 137/78	2/1	
100		169/106 ¹⁵			
100	93	141/96 ¹⁵	128/81 130/86	7/4	70 --
61		145/88 ¹⁶	139/85 146/92	6/7	

The table continues on the next page.

Appendix 1, Table 4 *continued*

Study, year Reference	Interven- tion	No of patients screened	No of patients at entry	No of patients at follow-up	Age Range; mean
Stamler, 1987 [88]	Treatment Control		97 ¹⁷ 44 ¹⁹ ; 48 ²⁰	177	≥35; 56
RIS, 1998 [52]	Treatment Control		253 255	253 255	50–72; 66
TONE, 1998 [93]	Treatment Na ⁺ reduction Weight reduction Their com- bination Control	8 787	340 147 147 341	332 145 141 331	60–80; 67
<i>Hypertension after a cerebrovascular event</i>					
HSCSG, 1974 [8]	Treatment Control	501	233 219	205 195	<75; 59
Dutch TIA, 1993 [34]	BB Placebo		732 741	732 741	54% were >65 50% were >65
TEST, 1995 [49]	BB Placebo		372 348		
PATS, 1995 [27]	D Placebo		2 841 2 824	2 679 2 674	--; 60

	% Male	% White	Entry BP	End of study mean BP	End of study mean group difference in BP by treatment	% Below goal BP at end of study
	64	86	120/78 ¹⁸	133/84 ¹⁷ 129/84 ¹⁹ ; 126/80 ¹⁶	1/2 vs group 2 ^{17,19} -8/-4 vs group 3 ^{17,20} -4/-1 vs group 2 and 3 ^{17,19,20}	
	100		156/88 154/87	153/83 157/85	4/2	
	53	77	128/71	124/69 124/70 122/68 127/71	3/2 3/1 5/3	63 73 65 71
	59	20	167/100		25/12	
	66		158/91 157/91			
	61		161/88 161/89	157/85 161/89	4/4	
	72	Chinese	154/93	143/86 149/89	6/3	

The table continues on the next page.

Appendix 1, Table 4 continued

Study, year Reference	Interven- tion	No of patients screened	No of patients at entry	No of patients at follow-up	Age Range; mean
PROGRESS, 2001 [30]	ACEi+D Placebo		3 051 3 054	3 049 3 053	30–90; 64
Hypertension and kidney					
ESPIRAL, 2001 [72]	ACEi CCB		129 112		24–74; 46
AASK, 2002 [98]	ACEi CCB ²¹ BB	2 802	436 217 441	309 145 300	18–70; 55
	Intensive Moderate		540 554	380 374	
Hypertension and diabetes mellitus					
UKPDS, 1998 [14]	ACEi BB		400 358		--; 56
	Intensive Moderate		758 390	1 101	
FACET, 1998 [90]	ACEi CCB	1 172	189 191	188 188	--; 63
ABCD, 2000 [50,51,82]	CCB ACEi		235 235		40–74; 58
	Intensive Moderate		237 233		

% Male	% White	Entry BP	End of study mean BP	End of study mean group difference in BP by treatment	% Below goal BP at end of study
70	61	147/86	134/79 143/83	9/4	
58		156/96	136/83 142/82	6/2	
61	0	151/96	135/82 133/81 135/81	2/1 0/1 2/0	
		152/96	128/78 141/85	13/7	
54	86	159/93	144/83 143/81	1/2	
		160/94	144/82 154/87	10/5	
60		171/95	157/88 153/86	4/2	ACEi: 59 for SBP, and 89 for DBP. CCB: 61 for SBP, and 90 for DBP
66	66	156/98	134/78 135/80	-1/2	
			132/78 138/86	6/8	

The table continues on the next page.

Appendix 1, Table 4 continued

Study, year Reference	Interven- tion	No of patients screened	No of patients at entry	No of patients at follow-up	Age Range; mean
RENAAL, 2001 [42]	ARB Placebo		751 762	748 762	31–70; 60
IDNT, 2001 [66]	ARB CCB Placebo		579 567 569	574 565 565	30–70; 59
J-MIND, 2001 [39]	CCB ACEi		228 208	156 137	--; 60
DIABHYCAR 2004 [73]	ACEi Placebo	25 468	2 443 2 469	2 037 2 037	>50; 65
Hypertension and cardiovascular risk					
HOPE, 2000 [11,100]	ACEi Placebo		4 645 4 652	9 288	>55; 66
EUROPA, 2003 [54]	ACEi Placebo		6 110 6 108	6 107 6 108	≥18; 60

¹ At 4 months.

² At 1 year.

³ At 8 months.

⁴ Mean DBP during the trial.

⁵ People lapsing from follow-up were about 19%.

⁶ At 3 years.

⁷ DBP <95 mm Hg; corresponding rates for complete BP goal (160/95 mm Hg) were 27 and 4%, respectively.

⁸ About 25% of the subjects were lost to follow-up.

⁹ Values derived from figures.

¹⁰ Total number of patients at entry were 2,127 but the numbers in each group are not reported. 1,065 and 1,062 are approximations.

¹¹ Higher on beta-adrenoceptor blockade based therapy.

¹² Completed visit at 1 year, 4 years of follow-up.

¹³ 5 years of follow-up.

% Male	% White	Entry BP	End of study mean BP	End of study mean group difference in BP by treatment	% Below goal BP at end of study
63	48	153/82	140/74 142/74	2/0	
67	73	159/87	138/73 137/76 138/74	1/3 0/1 1/-2	
50	Japanese	163/90	140/88 133/78	7/10	
69		145/82	143/81 145/82	2/0	
74		139/79	136/76 139/77	3/1	
85		137/82	128/78 133/80	5/2	

¹⁴ 4 years of follow-up.

¹⁵ In the hypertensive part of the study population.

¹⁶ Note that 49% of the patients had DBP <90 mm Hg; 37% had SBP <140 mm Hg.

¹⁷ Treatment group with nutritional intervention and discontinuation of medication (group 1). At end of study 50 patients received antihypertensive drugs. There were 5 major CV morbid events not further classified.

¹⁸ Patients were receiving antihypertensive drugs.

¹⁹ Control group with no nutritional intervention and discontinuation of medication (group 2). At end of study 40 patients received antihypertensive drugs. There was 1 major CV morbid event not further classified.

²⁰ Control group with no nutritional intervention and continuation of medication (group 3). At end of study 48 patients received antihypertensive drugs. There were 2 major CV morbid events not further classified.

²¹ Due to results on renal function patients were switched to open label medication for safely reasons 1 year ahead of termination of the study.

Appendix 1, Table 5 Outcomes (1), absolute numbers.

Study, year Reference	Interven- tion	Stroke			Coronary heart disease		
		fatal	non- fatal	all	fatal	non- fatal	all
Pharmacological							
VA II, 1970 [12,13,80,89]	Treatment	1	4	5	6	5	11
	Control	7	13	20	11	2	13
USPHS, 1977 [83]	Treatment	0	0	0	2	6	8
	Control	0	2	2	2	5	7
VA-NHLBI, 1978 [15]	Treatment	0	0	0	2	6	8
	Control	0	0	0	0	5	5
HDFP, 1979 [7,9,10,17–19, 23,26,87] Strata I–III	Treatment	29	73	102	131	144 ¹	274 ¹
	Control	52	106	158	148	195 ¹	343 ¹
Stratum I	Treatment	17	4 ²	21	86	105 ¹	191 ¹
	Control	31	19 ²	50	107	129 ¹	236 ¹
ANBPS, 1980 [1,29,35]	Treatment	3	10	13	5	28	33
	Control	6	16	22	11	22	33
On treatment	Treatment	2	7	9	2	18	20
	Control	4	13	17	8	17	25
Oslo, 1980 [61]	Treatment	0	0	0	6	8	14
	Control	2	3	5	2	8	10
MRC, 1985 [5,24,75]	Treatment	18	42	60	106	116	222
	Control	27	82	109	97	137	234
EWPHE, 1985 [36–38]	Treatment	21			29		
	Control	31			47		
On treatment	Treatment	12	11	21	17	12	29
	Control	19	17	36	29	19	48
HEP, 1986 [45]	Treatment	4	16	20	25	10	35
	Control	15	24	39	28	10	38

	Other vascular mortality	Total vascular mortality	Non- vascular mortality	Total mortality	Analysis by intention- to-treat	% on assigned regimen at end of study
	1 1	8 19	2 2	10 21	No	
	0 0	2 2	0 0	2 2	Yes	54 39
	0 0	2 0	0 0	2 0	Yes	
	35 40	195 240	154 179	349 419	No	78 58
	19 27	122 165	109 126	231 291	No	75 54
	0 1	8 18	17 17	25 35	Yes	66 63
	0 1	4 13	5 6	9 19	No	
	1 2	7 6	3 3	10 9	No	100 83
	10 15	134 139	114 114	248 253	Yes ³	63 65
	17 15	67 93	61 54	135 149	Yes	41 29
	13 13	42 61	31 28	73 89		
	8 7	37 50	23 19	60 69	Yes	95 91

The table continues on the next page.

Appendix 1, Table 5 continued

Study, year Reference	Interven- tion	Stroke			Coronary heart disease		
		fatal	non- fatal	all	fatal	non- fatal	all
SHEP, 1991 [28,46,53,55,65]	Treatment	10	96	106	59	50	109
	Control	14	149	163	73	74	147
STOP, 1991 [48]	Treatment	4	26	30	10	19	29
	Control	15	41	56	20	22	42
MRC older, 1992 [21]	Treatment	37	64	101	85	43	128
	Control	42	92	134	110	49	159
TOMHS, 1993 [33,76]	Treatment						26 ⁵
	Control						12 ⁵
BBB, 1994 [56]	Tight			8	8	12	20
	Less tight			11	3	15	18
Syst-Eur, 1997 [84–86,91]	Treatment	16	34	50	40 ⁶	50 ⁶	90 ⁶
	Control	21	57	78	52 ⁶	70 ⁶	122 ⁶
HOT, 1998 [60,63,64]	DBP £90			94			127
	DBP £85			111			107
	DBP £80			89			107
Syst-China, 2000 [70,92]	Treatment	10	35	45	19 ⁶	5 ⁶	24 ⁶
	Control	20	39	59	23 ⁶	8 ⁶	31 ⁶
SCOPE, 2003 [69]	Treatment	24	68	92	18	54	72
	Control	26	93	119	18	47	65
HYVET Pilot, 2003 [44]	D	6	0	6			
	ACEi	7	5	12			
	Control	11	7	18			
Comparing drug treatments							
IPPPSH, 1985 [3]	BB	5	40	45	40	49	89
	Non-BB	10	38	48	46	49	95
MRC, 1985 [5,24,75]	BB			42			103
	Non-BB			18			119

	Other vascular mortality	Total vascular mortality	Non- vascular mortality	Total mortality	Analysis by intention- to-treat	% on assigned regimen at end of study
	21	90	123	213	Yes	69
	25	112	130	242		56
	3	17	19	36	Yes	84
	6	41	22	63		77
	39	161 ⁴	140 ⁴	301	Yes ⁴	44
	28	180 ⁴	135 ⁴	315		47
					Yes	72
						59
					Yes	
	3	59	64	123	Yes	
	4	77	60	137		
		87	101	188	Yes	
		90	104	194		
		96	111	207		
	4 ⁷	33	28	61	Yes	
	1 ⁷	44	38	82		
	103	141	114	259	Yes	ARB: 26
	108	152	114	26		Placebo: 18
		23	7	30	Yes	
		22	5	27		
		19	3	22		
	0	45	63	108	Yes	76
	0	56	58	114		72
		65	55	120	Yes	37
		69	59	128		52

The table continues on the next page.

Appendix 1, Table 5 *continued*

Study, year Reference	Interven- tion	Stroke			Coronary heart disease		
		fatal	non- fatal	all	fatal	non- fatal	all
HAPPHY, 1987 [95]	BB	3	29	32	54	84	132
	Non-BB	10	32	42	50	75	115
MAPHY, 1988 [94]	BB	2	21	23	36	44	80
	Non-BB	9	18	27	43	54	97
Yurenev, 1992 [99]	BB	1	5	6	0	7	7
	Non-BB	4	7	11	3	3	6
MRC older, 1992 [21]	BB	21	35	56	52	28	80
	Non-BB	16	29	35	33	15	48
MIDAS, 1996 [41]	CCB			6			8
	D			3			7
VHAS, 1997 [81]	CCB	2	1	3	3	2	5
	D	0	4	4	4	1	5
NICS-EH, 1999 [31]	CCB	2	6	8			2
	D	0	8	8			2
CAPPP, 1999 [59,77]	ACEi	20	173	193	27	137	164
	BB/D	22	127	149	35	128	163
STOP-2, 1999 [58,67]	BB/D	51	186	237	108	46	154
	ACEi	50	165	215	107	32	139
	CCB	46	161	207	111	68	179
NORDIL, 2000 [57]	CCB	21	138	159	28	155	183
	BB/D	22	174	196	25	132	157
INSIGHT, 2000 [43,71]	CCB	12	55	67	33	61	94
	D	11	63	74	28	56	84
LIFE, 2002 [47,68]	ARB			232			198
	BB			309			188

	Other vascular mortality	Total vascular mortality	Non- vascular mortality	Total mortality	Analysis by intention- to-treat	% on assigned regimen at end of study
				96 101	Yes	86 83
	4 2	42 57	23 26	65 83	Yes	81 74
	0 0	1 7	0 0	1 7		
	22 17	95 66	72 68	167 134	Yes	37 52
	1 1		5 6	8 9		55 ⁸ 54 ⁸
	0 0	5 4	0 0	5 4	Yes	
			0 2			
	29 38	76 95		Same for ACEi and BB/D	Yes	
	62 69 55	221 226 212	148 154 150	369 380 362	Yes	
	131 115	180 162	51 66	231 228	Yes	
	15 13	60 52	93 100	153 152	Yes	
		204 234	179 197	383 431	Yes	84 80

The table continues on the next page.

Appendix 1, Table 5 continued

Study, year Reference	Interven- tion	Stroke			Coronary heart disease		
		fatal	non- fatal	all	fatal	non- fatal	all
ALLHAT, 2002 [6,20]	D	163	512	675	298	1 064	1 362
	CCB	91	286	377	168	630	798
	ACEi	116	341	457	157	639	796
	Alpha-B	76	325	401	105	394	499
	D	92	434	528	184	634	818
ELSA, 2002 [101]	CCB			9			18
	BB			14			17
CONVINCE, 2003 [40]	CCB			133			133
	BB/D			118			166
ANBP2, 2003 [97]	ACEi	29	91	120	40 ⁹	141	181
	D	15	94	109	52 ⁹	149	201
INVEST, 2003 [79]	CCB		131			151	
	BB		148			153	
VALUE, 2004 [62]	ARB			322			369
	CCB			281			313
Multifactorial and non-pharmacological							
GPPT, 1986 [96]	Treatment	64	147	211	462	375	837
	Control	77	131	208	462	387	849
MRFIT, 1990 [2,4,16,22,25,32]	Treatment				75		
	Control				77		
Patel, 1985 [78]	Treatment				0	2	
	Control				1	0	
Stamler, 1987 [88]	Treatment	1 ¹¹			1 ¹¹		
	Control	0 ¹² ; 0 ¹³			0 ¹² ; 2 ¹³		
RIS, 1998 [52]	Treatment	7	25	32	23	25	48
	Control	3	13	16	17	22	39

	Other vascular mortality	Total vascular mortality	Non- vascular mortality	Total mortality	Analysis by intention- to-treat	% on assigned regimen at end of study
	684	1 145	1 058	2 203	Yes	
	438	697	559	1 256		
	435	708	606	1 314		
			317	769		
			561	1 258		
		4		13	Yes	
		8		17		
		152		337		
		143		319		
	15	84	111	195	Yes	58
	15	82	128	210		62
		431		873	Yes	
		431		893		
				841	Yes	
				818		
				1 293	Yes	
				1 318		
		101	74	175	Yes	77
		94	77	171		65
		0	2	2	Yes	≈20?
		1	1	2		--
	0 ¹¹	2 ¹¹	1 ¹¹	3 ¹¹	Yes	44 ¹¹
	0 ¹² ; 0 ¹³	0 ¹² ; 2 ¹³	0 ¹² ; 0 ¹³	0 ¹² ; 2 ¹³		7 ¹² ; 100 ¹³
	12	42	22	64	Yes	
	4	24	17	41		

The table continues on the next page.

Appendix 1, Table 5 *continued*

Study, year Reference	Interven- tion	Stroke			Coronary heart disease		
		fatal	non- fatal	all	fatal	non- fatal	all
TONE, 1998 [93]	Treatment						
	Na ⁺ reduction			1			2
	Weight reduction			0			2
	Their combination			1			2
	Control			2			4
<i>Hypertension after a cerebrovascular event</i>							
HSCSG, 1974 [8]	Treatment	6	31	37	4	3	7
	Control	10	32	42	7	2	9
Dutch TIA, 1993 [34]	BB	11	41	52	28	17	45
	Placebo	8	54	62	24	16	40
TEST, 1995 [49]	BB		63			13	
	Placebo		58			14	
PATS, 1995 [27]	D	60	99	159	17		
	Placebo	77	140	217	13		
PROGRESS, 2001 [30]	ACEi + D	42	275	317	58	60	118
	Placebo	50	380	430	62	96	158
<i>Hypertension and kidney</i>							
ESPIRAL, 2001 [72]	ACEi	0	1	1	3		
	CCB	2	0	2	4		
AASK, 2002 [98]	Intensive						
	Moderate						
	ACEi						
	CCB						
	BB						

	Other vascular mortality	Total vascular mortality	Non- vascular mortality	Total mortality	Analysis by intention- to-treat	% on assigned regimen at end of study
					Yes	
	5	15	11	26	No	
	2	19	5	24		
	2	41	23	64	Yes	
	1	33	25	58		
				51		
				60		
	16	93	53	146	Yes	
	17	107	51	158		
	81	181	125	306	Yes	
	86	198	121	319		
					Yes	
		0.6 ¹⁴		1.6 ¹⁴		
		0.7 ¹⁴		1.9 ¹⁴		
		0.5 ¹⁴		1.5 ¹⁴		
		0.9 ¹⁴		1.7 ¹⁴		
		0.8 ¹⁴		2.0 ¹⁴		

The table continues on the next page.

Appendix 1, Table 5 *continued*

Study, year Reference	Interven- tion	Stroke			Coronary heart disease		
		fatal	non- fatal	all	fatal	non- fatal	all
<i>Hypertension and diabetes mellitus</i>							
UKPDS, 1998 [14]	Intensive	9	29	38	70	51	107
	Moderate	11	26	34	46	29	69
	BB			17			46
	ACEi			21			61
FACET, 1998 [90]	ACEi			4			10
	CCB			10			13
ABCD, 2000 [50,51,82]	Intensive			Not sign			15
	Moderate						14
	CCB				3	22	25 (27 ¹⁶)
	ACEi				0	5	5 (9 ¹⁶)
RENAAL, 2001 [42]	ARB						50
	Placebo						68
IDNT, 2001 [66]	ARB						
	CCB						
	Placebo						
J-MIND, 2001 [39]	CCB			2			1
	ACEi			5			1
DIABHYCAR 2004 [73]	ACEi	29	89	118	9	52	61
	Placebo	32	84	116	19	59	78

	Other vascular mortality	Total vascular mortality	Non- vascular mortality	Total mortality	Analysis by intention- to-treat	% on assigned regimen at end of study
	3 ¹⁵ 4 ¹⁵	82 61	52 22	134 83	Yes	
				59 75	Yes	
				4 5	Yes	
				Intensive sign less than moderate	Yes	<50 <50
		10 (11 ¹⁶) 5 (6 ¹⁶)	7 8	17 13		
				158 155	Yes	
				87 83 93	Yes	
					Yes	
				334 324	Yes	

The table continues on the next page.

Appendix 1, Table 5 continued

Study, year Reference	Interven- tion	Stroke			Coronary heart disease		
		fatal	non- fatal	all	fatal	non- fatal	all
<i>Hypertension and cardiovascular risk</i>							
HOPE, 2000 [11,100]	ACEi	17	139	156	65	394	459
	Placebo	44	182	226	141	429	570
EUROPA, 2003 [54]	ACEi			98	25	295	320
	Placebo			102	40	378	418

¹ Non-fatal MI ascertained from medical history (from Collins et al, Lancet 1990;335:827–38).

² From Collins et al, Lancet 1990;335:827–38.

³ Only minor differences between the results of the intention-to-treat and on treatment analyses (results not published).

⁴ Vascular mortality and deaths from cancer were 28 and 20 in the diuretic group, 40 and 48 in the atenolol group, and 87 and 51 in the placebo group by on treatment analyses; corresponding figures for cancer deaths by intention-to-treat were 49, 59 and 99.

⁵ Also includes CHF, surgery for aortic aneurysm, coronary by pass surgery, coronary artery angioplasty, thrombolytic therapy, hospitalisation for unstable angina pectoris.

⁶ Including fatal and non-fatal CHF.

⁷ Renal failure and pulmonary embolism.

⁸ On monotherapy.

⁹ CHD events including MI.

	Other vascular mortality	Total vascular mortality	Non- vascular mortality	Total mortality	Analysis by intention- to-treat	% on assigned regimen at end of study
	200 192	282 377	200 192	482 569	Yes	
		215 249	160 171	375 420	Yes	

¹⁰ Non-fatal CHD diagnosed as probable MI by ECG in addition 3 possible MI in the control group and 1 in the active group, respectively. ECG not available in all.

¹¹ Treatment group with nutritional intervention and discontinuation of medication (group 1). At end of study 50 patients received antihypertensive drugs. There were 5 major CV morbid events not further classified.

¹² Control group with no nutritional intervention and discontinuation of medication (group 2). At end of study 40 patients received antihypertensive drugs. There was 1 major CV morbid event not further classified.

¹³ Control group with no nutritional intervention and continuation of medication (group 3). At end of study 48 patients received antihypertensive drugs. There were 2 major CV morbid events not further classified.

¹⁴ Events reported as percent of study group.

¹⁵ Including renal disease.

¹⁶ As reported in an additional later publication [82].

Appendix 1, Table 6 Outcomes (2), relative rate per 1,000 patient years, and relative change in risk by intervention (%).

Study, year Reference	Intervention	Stroke		
		fatal	non-fatal	all
Pharmacological				
VA II, 1970 [12,13,80,89]	Treatment	1.4	5.7	7.1
	Control	9.5	17.6	27.1
	% Change	−85	−68	−74
USPHS, 1977 [83]	Treatment	0.0	0	0
	Control	0.0	1.5	1.5
	% Change		−100	−100
VA-NHLBI, 1978 [15]	Treatment	0.0	0.0	0.0
	Control	0.0	0.0	0.0
	% Change			
HDFP, 1979 [7,9,10,17−19,23,26,87] Strata I−III	Treatment	1.1	2.7	3.7
	Control	1.91	3.9	5.8
	% Change	−44	−32	−36
Stratum I	Treatment	0.9	0.2	1.1
	Control	1.6	1.0	2.6
	% Change	−45	−79	−58
ANBPS, 1980 [1,29,35]	Treatment	0.4	1.5	1.9
	Control	0.9	2.3	3.2
	% Change	−50	−38	−41
On treatment	Treatment	0.3	1.0	1.3
	Control	0.6	1.9	2.5
	% Change	−50	−46	−47
Oslo, 1980 [61]	Treatment	0.0	0.0	0.0
	Control	1.0	1.4	2.4
	% Change	−100	−100	−100
MRC, 1985 [5,24,75]	Treatment	0.4	1.0	1.4
	Control	0.6	1.9	2.6
	% Change	−34	−49	−45

Coronary heart disease			Other vascular mortality	Total vascular mortality	Non- vascular mortality	Total mortality
fatal	non-fatal	all				
8.5	7.1	15.6	2.8	11.3	2.8	14.2
14.9	2.7	17.6	10.9	25.8	2.7	28.5
-43	163	-11	-74	-56	4	-50
1.5	4.4	5.9	0.0	1.5	0.0	1.5
1.5	3.6	5.1	0.0	1.5	0.0	1.5
1	22	16		1		1
2.6	7.9	10.5	0.0	2.6	0.0	2.6
0.0	6.6	6.6	0.0	0.0	0.0	0.0
	19	59				
4.8	5.2 ¹	10.0 ¹	1.2	7.1	5.6	12.7
5.4	7.2 ¹	12.6 ¹	1.5	8.8	6.6	15.4
-12	-27	-21	-13	-19	-14	-17
4.4	5.4 ¹	9.8 ¹	1.0	0.2	5.6	11.8
5.5	6.6 ¹	12.0 ¹	1.4	8.4	6.4	14.8
-58	-18	-19	-28	-26	-13	-20
0.7	4.1	4.8	0.0	1.2	2.5	3.6
1.6	3.2	4.8	0.2	2.6	2.5	5.1
-55	26	-1	-100	-56	-1	-27
0.3	2.6	2.9	0.0	0.6	0.7	1.3
1.2	2.5	3.7	0.2	1.9	0.9	2.8
-75	5	-21	-100	-69	-17	-53
2.7	3.6	6.3	0.4	3.1	1.3	4.5
1.0	3.8	4.8	1.0	2.9	1.4	4.3
180	-7	31	-53	9	7	7
2.5	2.7	5.2	0.2	3.1	2.7	5.8
2.3	3.2	5.5	0.2	3.3	2.7	5.9
9	-16	-6		-4	0	-2

The table continues on the next page.

Appendix 1, Table 6 *continued*

Study, year Reference	Intervention	Stroke		
		fatal	non-fatal	all
EWPHE, 1985 [36–38]	Treatment	10.8		
	Control	15.8		
	% Change	–32		
On treatment	Treatment	9.0	9.0	18.0
	Control	15.0	14.0	29.0
	% Change	–43	–36	–38
HEP, 1986 [45]	Treatment	2.2	8.7	12.5
	Control	7.3	11.7	21.4
	% Change	–70	–26	–42
SHEP, 1991 [28,46,53,55,65]	Treatment	0.9	9.0	10.0
	Control	1.3	14.0	15.3
	% Change	–29	–37	–36
STOP, 1991 [48]	Treatment	2.4	15.4	17.8
	Control	8.8	24.2	33.0
	% Change	–73	–36	–46
MRC older, 1992 [21]	Treatment	2.9	5.2	8.1
	Control	3.3	7.4	10.8
	% Change	–12	–30	–25
TOMHS, 1993 [33,76]	Treatment			
	Control			
	% Change			
BBB, 1994 [56]	Tight ³			1.5
	Less tight ³			2.1
	% Change			–27
Syst-Eur, 1997 [84–86,91]	Treatment	3.3	7.1	10.4
	Control	4.0	12	17.0
	% Change	–17	–43	–39

Coronary heart disease			Other vascular mortality	Total vascular mortality	Non- vascular mortality	Total mortality
fatal	non-fatal	all				
14.9			8.7	34.4	31.3	69.2
23.9			7.6	42.4	27.5	75.9
-38			14	-27	14	-9
12.0	9.0	21.0	9.0	30.0	22.0	52.0
23.0	14.0	37.0	10.0	48.0	22.0	70.0
-47	-36	-43	-10	-38	0	-26
13.6	5.4	19.0	4.3	20.1	12.4	32.5
13.6	4.9	-18.5	3.4	24.3	9.3	33.6
0	11	3	26	-17	33	-3
5.5	4.7	10.2	2.0	8.5	11.6	20.0
6.8	6.9	13.8	2.3	10.5	12.2	22.7
-20	-33	-27	-13	-20	-5	-13
5.9	11.2	17.2	1.8	10.1	11.2	21.3
11.8	13.0	24.8	3.5	24.2	13.0	37.2
-50	-13	-31	-50	-58	-13	-43
6.7	3.4	10.3	3.1	12.8	11.1	23.9
8.6	3.9	12.7	2.2	14.1	10.6	24.7
-22	-13	-19	40	-9	5	-3
		3.9 ²				
		5.1 ²				
		-24				
1.5	2.3	3.9				
0.6	2.9	3.5				
166	-20	11				
8.3 ⁴	10.4 ⁴	18.8 ⁴	0.6	12.3	13.3	25.6
11.3 ⁴	15.2 ⁴	26.6 ⁴	0.9	16.8	13.1	29.8
-26	-32	-29	-28	-27	2	-14

The table continues on the next page.

Appendix 1, Table 6 *continued*

Study, year Reference	Intervention	Stroke		
		fatal	non-fatal	all
HOT, 1998 [60,63,64]	DBP <90			3.7
	DBP <80			3.9
	% Change			−5
	DBP <85			4.7
	DBP <80			3.9
	% Change			18
	DBP <90			3.7
	DBP <85			4.7
	% Change			−20
Syst-China, 2000 [70,92]	Treatment	2.8	9.7	12.5
	Control	6.5	10.9	16.4
	% Change	−50	−10	−24
SCOPE, 2003 [69]	Treatment	2.7	7.6	10.3
	Control	2.9	10.4	13.3
	% Change	−8	−27	−23
HYVET Pilot, 2003 [44]	Treatment	12.8	0	12.8
	Control	23.5	14.9	38.4
	% Change	−45	−100	−67
Comparing drug treatments				
IPPPSH, 1985 [3]	BB	0.4	3.1	3.5
	Non-BB	0.8	3.0	3.8
	% Change	−50	5	−7
MRC, 1985 [5,24,75]	BB			1.9
	Non-BB			0.8
	% Change			58
HAPPHY, 1987 [95]	BB	0.2	2.3	2.6
	Non-BB	0.8	2.6	3.4
	% Change	−71	−11	−25
MAPHY, 1988 [94]	BB	0.3	2.6	2.9
	Non-BB	1.1	2.2	3.3
	% Change	−77	18	−14

Coronary heart disease			Other vascular mortality	Total vascular mortality	Non- vascular mortality	Total mortality
fatal	non-fatal	all				
		4.5		4.0	4.7	8.7
		5.3		3.7	4.2	7.0
		-16		10	10	10
		4.5		3.8	4.4	8.2
		5.3		3.7	4.2	7.9
		-16		3	3	3
		4.5		4.0	4.7	8.7
		4.5		3.8	4.4	8.2
		0		7	7	7
5.3 ⁴	1.4	6.7	1.1 ⁵	9.2	7.8	17.0
6.4 ⁴	2.2	8.6	0.3 ⁵	12.3	10.6	22.8
-17	-38	-23	300	-25	-26	-26
2.0	6.1	8.1	11.6	16.3	12.8	29.0
2.0	5.2	7.3	12.1	17.1	12.8	29.8
0	15	11	-5	-5	0	-3
				49.0	14.9	64.0
				40.5	6.4	46.9
				21	133	36
3.1	3.8	7.0	0.0	3.5	5.0	8.5
3.6	3.9	7.5	0.0	4.4	4.6	9.0
-13	0	-7		-20	8	-6
		4.8		3.0	2.5	5.5
		5.6		3.2	2.8	6.0
		-14		-6	-12	-8
4.4	6.8	10.2				7.7
4.1	6.1	11.1				8.2
6	10	-8				-6
4.5	5.5	9.9	0.5	5.2	2.9	8.1
5.3	6.6	11.9	0.3	7.0	3.2	10.2
-16	-18	-17	51	-26	-11	-21

The table continues on the next page.

Appendix 1, Table 6 *continued*

Study, year Reference	Intervention	Stroke		
		fatal	non-fatal	all
Yurenev, 1992 [99]	BB	0.7	3.3	4.0
	Non-BB	2.7	4.5	7.1
	% Change	-74	-27	-44
MRC older, 1992 [21]	BB	3.3	5.6	9.0
	Non-BB	2.5	4.7	7.3
	% Change	32	19	23
MIDAS, 1996 [41]	CCB			4.5
	D			2.3
	% Change			100
VHAS, 1997 [81]	CCB	1.4	0.7	2.1
	D	0	2.8	2.8
	% Change		-75	-25
NICS-EH, 1999 [31]	CCB	2.1	6.2	8.3
	D	0	8.2	8.3
	% Change		-25	0
CAPPP, 1999 [59,77]	ACEi	0.6	5.2	5.8
	BB/D	0.7	3.8	4.4
	% Change	-9	36	30
STOP-2, 1999 [58,67]	BB/D	4.6	16.8	21.4
	ACEi	4.5	14.9	19.4
	% Change	2	13	10
	BB/D	4.6	16.8	21.4
	CCB	4.2	14.6	18.7
	% Change	11	16	14
NORDIL, 2000 [57]	CCB	0.9	5.7	6.5
	BB/D	0.9	7.1	8.1
	% Change	-5	-21	-19
INSIGHT, 2000 [43,71]	CCB	1.2	5.6	6.8
	D	1.1	6.4	7.5
	% Change	9	-13	-10

Coronary heart disease			Other vascular mortality	Total vascular mortality	Non- vascular mortality	Total mortality
fatal	non-fatal	all				
0.0	4.7	4.7	0.0	0.7	0	0.7
1.9	1.9	3.9	0.0	4.7	0	4.7
-100	147	20		-85		-85
8.2	4.5	12.8	3.5	15.0	11.4	26.4
5.2	2.4	7.7	2.6	10.5	10.8	21.3
58	88	66	35	43	-6	-24
		6.0	0.8		3.8	6.0
		5.3	0.8		4.5	6.8
		14	0		-17	-11
2.1	1.4	3.5	0	3.5	0	3.4
2.8	0.7	3.5	0	2.8	0	2.8
-25	100	0		25		25
		2.1			0	
		2.1			2.1	
		0			-100	
0.8	4.0	4.9	0.9	2.3		
1.0	3.8	4.9	1.1	2.8		
-23	7	1	-24	-20		
9.8	4.2	13.9	5.6	20.0	13.4	33.3
9.7	2.9	12.6	6.2	20.4	13.9	34.3
1	44	11	-10	-2	-4	-3
9.8	4.2	13.9	5.6	20.0	13.4	33.3
10.0	6.1	16.2	5.0	19.2	13.6	32.7
-3	-32	-14	13	4	-1	2
1.2	6.4	7.5	5.4	7.4	2.1	9.5
1.0	5.4	6.4	4.7	6.7	2.7	9.4
12	17	17	14	11	-23	1
3.3	6.2	9.5	1.5	6.1	9.4	15.5
2.8	5.7	8.5	1.3	5.3	10.1	15.4
18	9	12	15	15	-7	1

The table continues on the next page.

Appendix 1, Table 6 *continued*

Study, year Reference	Intervention	Stroke		
		fatal	non-fatal	all
LIFE, 2002 [47,68]	ARB			10.5
	BB			14.0
	% Change			-25
ALLHAT, 2002 [6,20]	D	2.2	6.8	9.0
	CCB	2.1	6.5	8.5
	% Change	6	6	6
	D	2.2	6.8	9.0
	ACEi	2.6	7.7	10.3
	% Change	-16	-11	-12
	D	1.9	7.0	8.9
	Alpha-B	2.6	8.6	11.2
	% Change	-28	-18	-21
ELSA, 2002 [101]	CCB			2.0
	BB			3.1
	% Change			-36
CONVINCE, 2003 [40]	CCB			5.4
	BB/D			4.8
	% Change			13
ANBP2, 2003 [97]	ACEi	2.3	7.3	9.6
	D	1.2	7.5	8.7
	% Change	93	-3	10
INVEST, 2003 [79]	CCB		4.3	
	BB		4.8	
	% Change		-11	
HYVET Pilot, 2003 [44]	D	12.8	0	12.8
	Placebo	23.5	14.9	38.4
	% Change	-45	-100	-67
	ACEi	14.8	10.5	25.3
	Placebo	23.5	14.9	38.4
	% Change	-37	-29	-34

Coronary heart disease			Other vascular mortality	Total vascular mortality	Non- vascular mortality	Total mortality
fatal	non-fatal	all				
		9.0		9.2	8.1	17.3
		8.5		10.6	8.9	19.6
		5		-13	-9	-11
4.0	14.2	18.2	9.2	15.3	14.2	29.5
3.8	14.2	18.0	9.9	15.7	12.6	28.3
5	0	1	7	3	12	4
4.0	14.2	18.2	9.2	15.3	14.2	29.5
3.5	14.4	17.9	9.8	16.0	13.7	29.6
13	-1	2	7	-4	4	0
6.2	27.4	33.6	3.2	11.3	11.5	25.8
6.4	29.4	35.9	3.9	13.0	10.9	26.5
-4	-7	-6	-19	-13	5	-3
		4.0		0.9		2.9
		3.8		1.8		3.8
		6		-50		-24
		5.4		6.1		13.6
		6.7		5.8		12.9
		-20		6		6
3.2 ⁶	11.3	14.5	1.2	6.7	8.9	15.6
4.1 ⁶	12.0	16.1	1.2	6.6	10.3	16.9
-23	-6	-10	0	2	-13	-7
	5.0			14.2		28.7
	5.0			14.1		29.2
	0			0		
				49.0	14.9	64.0
				40.5	6.4	46.9
				21	133	36
				46.4	10.5	57.0
				40.5	6.4	46.9
				14	65	21

The table continues on the next page.

Appendix 1, Table 6 *continued*

Study, year Reference	Intervention	Stroke		
		fatal	non-fatal	all
VALUE, 2004 [62]	ARB CCB % Change			10.3 8.8 17
Multifactorial and non-pharmacological				
GPPT, 1986 [96]	Treatment Control % Change	0.6 0.7 -17	1.4 1.3 13	2.0 2.0 2
MRFIT, 1990 [2,4,16,22,25,32]	Treatment Control % Change			
Patel, 1985 [78]	Treatment Control % Change			
Stamler, 1987 [88]	Treatment Control	2.5 ⁸ 0.0 ⁹ ; 0.0 ¹⁰		
RIS, 1998 [52]	Treatment Control % Change	1.8 4.2 -56	7.8 14.9 -48	9.6 19 -50
TONE, 1998 [93]	Na ⁺ reduction Control % Change			1.2 2.3 -50
	Weight reduction Control % Change			0 2.3 -100
	Their combination Control % Change			2.7 2.3 16

Coronary heart disease			Other vascular mortality	Total vascular mortality	Non- vascular mortality	Total mortality
fatal	non-fatal	all				
		11.5				26.2
		9.8				25.6
		17				2
4.5	3.6	8.1				12.5
4.5	3.7	8.2				12.8
0	3	-1				-2
2.7				3.7	2.7	6.4
2.8				3.5	2.8	6.3
-4				6	5	1
0.0	5.0			0.0	5.0	5.0
2.7	0.0 ⁷			2.7	13.6	5.4
-100				-100	-63	-6
2.5 ⁸ 0.0 ⁹ ; 10.4 ¹⁰			0.0 ⁸ 0.0 ⁹ ; 0.0 ¹⁰	5.0 ⁸ 0.0 ⁹ ; 10.4 ¹⁰	2.5 ⁸ 0.0 ⁹ ; 0.0 ¹⁰	7.6 ⁸ 0.0 ⁹ ; 10.4 ¹⁰
10.2	13.2	23.4	2.4	14.4	10.2	24.6
13.7	14.9	28.5	7.1	25.0	13.1	38.0
-26	-11	-18	-66	-42	-22	-35
		5.4				
		4.7				
		16				
		5.4				
		4.7				
		16				
		2.4				
		4.7				
		-49				

The table continues on the next page.

Appendix 1, Table 6 *continued*

Study, year Reference	Intervention	Stroke		
		fatal	non-fatal	all
<i>Hypertension after a cerebrovascular event</i>				
HSCSG, 1974 [8]	Treatment	11.2	57.8	69.0
	Control	19.9	63.5	83.4
	% Change	−44	−9	−17
Dutch TIA, 1993 [34]	BB	5.8	21.5	27.3
	Placebo	4.2	28.4	32.6
	% Change	38	−24	−16
TEST, 1995 [49]	BB		6.5	
	Placebo		60.0	
	% Change		9	
PATs, 1995 [27]	D	10.6	17.4	28.0
	Placebo	13.6	24.8	38.4
	% Change	−23	−30	−27
PROGRESS, 2001 [30]	ACEi+D	3.4	22.5	26.0
	Placebo	4.1	31.1	35.2
	% Change	−16	−28	−26
<i>Hypertension and kidney</i>				
ESPIRAL, 2001 [72]	ACEi	0	2.6	2.6
	CCB	6.0	0	6.0
	% Change	−100		−57
AASK, 2002 [98]	Intensive	See Table 5		
	Moderate			
	ACEi	See Table 5		
	CCB			
	BB			

Coronary heart disease			Other vascular mortality	Total vascular mortality	Non- vascular mortality	Total mortality
fatal	non-fatal	all				
7.5	5.6	13.1	9.3	28.0	20.5	48.5
13.9	4.0	17.9	4.0	37.7	9.9	42.6
-46	41	-27	135	-26	107	2
14.7	8.9	23.6	1.1	21.5	12.1	33.6
12.6	8.4	21.0	0.5	17.3	13.1	30.5
17	6	13	100	24	-8	10
	13.4					52.7
	14.5					62.0
	-7					-15
3.0			2.8	16.4	9.0	28.0
2.3			3.0	18.9	9.3	25.7
29			-6	-14	3	-8
4.8	4.9	9.7	6.6	14.8	10.2	25.1
5.1	7.9	12.9	7.0	16.2	9.9	26.1
-6	-37	-25	-6	-8	3	-4
7.8						
11.9						
-35						

The table continues on the next page.

Appendix 1, Table 6 *continued*

Study, year Reference	Intervention	Stroke		
		fatal	non-fatal	all
<i>Hypertension and diabetes mellitus</i>				
UKPDS, 1998 [14]	Intensive	1.4	4.6	6.0
	Moderate	3.4	7.9	10.4
	% Change	−58	−43	−42
	ACEi			5.7
	BB			6.3
	% Change			−10
FACET, 1998 [90]	ACEi			6.0
	CCB			15.0
	% Change			−60
ABCD, 2000 [50,51,82]	Treatment			
	Control			
	% Change			
	CCB			
	ACEi			
	% Change			
RENAAL, 2001 [42]	ARB			
	Placebo			
	% Change			
IDNT, 2001 [66]	ARB			
	Placebo			
	% Change			
	CCB			
	Placebo			
	% Change			
J-MIND, 2001 [39]	CCB			4.4
	ACEi			12.0
	% Change			−64
DIABHYCAR, 2004 [73]	ACEi	3.0	9.3	12.4
	Placebo	3.3	8.7	12.0
	% Change	−8	7	2

Coronary heart disease			Other vascular mortality	Total vascular mortality	Non- vascular mortality	Total mortality
fatal	non-fatal	all				
11.0	8.0	16.8	0.5 ¹¹	12.9	8.2	21.0
14.0	8.9	21.1	1.2 ¹¹	18.6	6.7	25.0
-22	-10	-20	-61	-31	22	-17
		15.3				19.6
		18.2				22.3
		-16				-12
		15.1				6.0
		19.4				7.5
		-22				-19
2.6	18.7	21.3 (23.0 ¹²)		8.5 (9.4 ¹²)	6.0	14.5
0	4.3	4.3 (7.7 ¹²)		4.3 (5.1 ¹²)	6.8	11.1
	340	400 (200 ¹²)		100 (81 ¹²)	-13	31
		19.6				61.9
		26.2				59.8
		-25				3
				57.8		
				62.9		
				-8		
				56.3		
				62.9		
				-10		
		2.2				
		2.4				
		-9				
0.9	5.5	6.4				35.1
2.0	6.1	8.1				33.6
-52	-11	-21				4

The table continues on the next page.

Appendix 1, Table 6 continued

Study, year Reference	Intervention	Stroke		
		fatal	non-fatal	all
<i>Hypertension and cardiovascular risk</i>				
HOPE, 2000 [11,100]	ACEi	0.7	6.0	6.7
	Placebo	1.9	7.8	9.7
	% Change	−61	−24	−31
EUROPA, 2003 [54]	ACEi			3.8
	Placebo			4.0
	% Change			−4

¹ Non-fatal MI ascertained from medical history (from Collins et al, Lancet 1990;335:827–38).

² Also includes CHF, surgery for aortic aneurysm, coronary by pass surgery, coronary artery angioplasty, thrombolytic therapy, hospitalisation for unstable angina pectoris.

³ Total number of patients at entry were 2,127 but the numbers in each group are not reported. 1,065 and 1,062 are approximations.

⁴ Including fatal and non-fatal CHF.

⁵ Renal failure and pulmonary embolism.

⁶ CHD events including MI.

⁷ Non-fatal CHD diagnosed as probable MI by ECG in addition 3 possible MI in the control group and 1 in the active group, respectively ECG not available in all.

Coronary heart disease			Other vascular mortality	Total vascular mortality	Non- vascular mortality	Total mortality
fatal	non-fatal	all				
2.8	17.0	19.8	8.6	12.1	8.6	20.8
6.1	18.4	24.5	8.3	16.2	8.3	24.5
-54	-8	-19	4	-25	4	-15
1.0	11.5	12.5		8.4	6.2	14.6
1.6	14.7	16.3		9.7	6.7	16.4
-38	-22	-23		-14	-6	-11

⁸ Treatment group with nutritional intervention and discontinuation of medication (group 1). At end of study 50 patients received antihypertensive drugs. There were 5 major CV morbid events not further classified.

⁹ Control group with no nutritional intervention and discontinuation of medication (group 2). At end of study 40 patients received antihypertensive drugs. There was 1 major CV morbid event not further classified.

¹⁰ Control group with no nutritional intervention and continuation of medication (group 3). At end of study 48 patients received antihypertensive drugs. There were 2 major CV morbid events not further classified.

¹¹ Including renal disease.

¹² As reported in an additional later publication [82].

Appendix 1, Table 7 Outcomes (3), statistical evaluation of endpoints.

Study, year Reference	Intervention	Stroke		
		fatal	non-fatal	all
Pharmacological				
VA II, 1970 [12,13,80,89]	Treatment Control	nc	nc	nc
USPHS, 1977 [83]	Treatment Control	nc	nc	ns
VA-NHLBI, 1978 [15]	Treatment Control	ns	ns	ns
HDFP 1979 [7,9,10,17–19,23,26,87] Strata I–III	Treatment Control			†
Stratum I	Treatment Control			
ANBPS, 1980 [1,29,35]	Treatment Control	ns	*	*
On treatment	Treatment Control	ns	*	*
Oslo, 1980 [61]	Treatment Control	ns	ns	*
MRC, 1985 [5,24,75]	Treatment Control	nc	nc	*
EWPHE, 1985 [36–38]	Treatment Control	ns	nc	nc
On treatment	Treatment Control			†
HEP, 1986 [45]	Treatment Control	*	ns	*

* = significant for primary endpoint

ns = not significant for primary endpoint

nc = not calculated or reported for primary endpoint

† = significant for other major (ie hard) endpoint

Coronary heart disease			Total vascular mortality	Total mortality	Comment
fatal	non-fatal	all			
nc	nc	nc	nc	nc	
ns	ns	ns		ns	
ns	ns	ns		ns	
	†	†		*	
				*	
ns	ns	ns	*	ns	Active therapy superior
ns	ns	ns	*	*	Active therapy superior
ns	ns	ns	ns	ns	Active therapy superior
ns	ns	ns	ns	ns	Active therapy superior
†			†		Active therapy superior
†		†	†		Active therapy superior
ns	ns	ns	ns	ns	Active therapy superior

The table continues on the next page.

Appendix 1, Table 7 *continued*

Study, year Reference	Intervention	Stroke		
		fatal	non-fatal	all
SHEP, 1991 [28,46,53,55,65]	Treatment Control	ns	*	*
STOP, 1991 [48]	Treatment Control	*		*
MRC older, 1992 [21]	Treatment Control	ns	nc	*
TOMHS, 1993 [33,76]	Treatment Control			ns
BBB, 1994 [56]	Tight Less tight			ns
Syst-Eur, 1997 [84–86,91]	Treatment Control	ns	*	*
HOT, 1998 [60,63,64]	DBP <90 vs <80 DBP <85 vs <80 DBP <90 vs <85			ns
Syst-China, 2000 [70,92]	Treatment Control	*	ns	*
SCOPE, 2003 [69]	Treatment Control	ns	†	ns
HYVET Pilot, 2003 [44]	Treatment Control			*
Comparing drug treatments				
IPPPSH, 1985 [3]	BB Non-BB			
MRC, 1985 [5,24,75]	BB D			†

* = significant for primary endpoint

ns = not significant for primary endpoint

nc = not calculated or reported for primary endpoint

† = significant for other major (ie hard) endpoint

Coronary heart disease			Total vascular mortality	Total mortality	Comment
fatal	non-fatal	all			
	†	†			Active therapy superior
ns		ns	*	†	Active therapy superior
ns	ns	ns		ns	Active therapy superior
		ns	nc	nc	
ns	ns	ns			
ns	†	† ¹	ns	ns	Active therapy superior
		* ²	ns	ns	<80 mm Hg superior to <90 mm Hg
		ns ¹	†	†	Active therapy superior
ns	ns	ns	ns	ns	Active therapy superior
			ns	ns	Active therapy superior
ns	ns	ns			
	ns		ns		D therapy superior

The table continues on the next page.

Appendix 1, Table 7 *continued*

Study, year Reference	Intervention	Stroke		
		fatal	non-fatal	all
HAPPHY, 1987 [95]	BB Non-BB			
MAPHY, 1988 [94]	BB Non-BB	†		
Yurenev, 1992 [99]	BB Non-BB			ns
MRC older, 1992 [21]	BB D			ns
MIDAS, 1996 [41]	CCB D			ns
VHAS, 1997 [81]	CCB D			
NICS-EH, 1999 [31]	CCB D			ns
CAPPP, 1999 [59,77]	ACEi BB/D	ns	*	*
STOP-2, 1999 [58,67]	BB/D ACEi BB/D CCB			ns
NORDIL, 2000 [57]	CCB BB/D	ns	nc	*
INSIGHT, 2000 [43,71]	CCB D	ns	ns	ns
LIFE, 2002 [47,68]	ARB BB			*

* = significant for primary endpoint

ns = not significant for primary endpoint

nc = not calculated or reported for primary endpoint

† = significant for other major (ie hard) endpoint

Coronary heart disease			Total vascular mortality	Total mortality	Comment
fatal	non-fatal	all			
ns	ns	ns		ns	
*	*	*	†	†	BB therapy superior
		ns	*	†	BB therapy superior
		†	†	ns	D therapy superior
		ns	ns	ns	
			ns	ns	
		ns	ns		
ns	ns	ns	ns	ns	BB/D therapy superior
		*	ns	ns	ACEi therapy superior
		ns			
ns	ns	ns	ns	ns	CCB therapy superior
*	ns	ns	ns	ns	D therapy superior
		ns	ns	ns	ARB therapy superior

The table continues on the next page.

Appendix 1, Table 7 *continued*

Study, year Reference	Intervention	Stroke		
		fatal	non-fatal	all
ALLHAT, 2002 [6,20]	D CCB			ns
	D ACEi			†
	D Alpha-B			†
ELSA, 2002 [101]	CCB BB			
CONVINCE, 2003 [40]	CCB BB/D			ns
ANBP2, 2003 [97]	ACEi D	† ³	ns	ns
INVEST, 2003 [79]	CCB BB		ns	
VALUE, 2004 [62]	ARB CCB			ns
Multifactorial and non-pharmacological				
GPPT, 1986 [96]	Treatment Control	ns	ns	ns
MRFIT, 1990 [2,4,16,22,25,32]	Treatment Control			
Patel, 1985 [78]	Treatment Control			

* = significant for primary endpoint

ns = not significant for primary endpoint

nc = not calculated or reported for primary endpoint

† = significant for other major (ie hard) endpoint

Coronary heart disease			Total vascular mortality	Total mortality	Comment
fatal	non-fatal	all			
ns	ns	ns		ns	
ns	ns	ns		ns	D therapy superior
ns	ns	ns		ns	D therapy superior
			ns	ns	
		ns	ns	ns	
ns	†	*	ns	ns	D therapy superior for non-fatal CHD, ACEi therapy superior for all CHD
	ns		ns	ns	
		*		ns	CCB therapy superior
ns	ns	ns		ns	
ns					
		†			Active therapy superior

The table continues on the next page.

Appendix 1, Table 7 *continued*

Study, year Reference	Intervention	Stroke		
		fatal	non-fatal	all
Stamler, 1987 [88]	Treatment Control			
RIS, 1998 [52]	Treatment Control	ns	*	*
TONE, 1998 [93]	Treatment Control			ns
<i>Hypertension after a cerebrovascular event</i>				
HSCSG, 1974 [8]	Treatment Control	ns	ns	ns
Dutch TIA, 1993 [34]	BB Placebo	ns	ns	ns
TEST, 1995 [49]	BB Placebo		ns	
PATS, 1995 [27]	D Placebo	ns	nc	*
PROGRESS, 2001 [30]	ACEi+D Placebo	ns	*	*
<i>Hypertension and kidney</i>				
ESPIRAL, 2001 [72]	ACEi CCB			ns
AASK, 2002 [98]	Intensive Moderate			
	ACEi CCB BB			

* = significant for primary endpoint

ns = not significant for primary endpoint

nc = not calculated or reported for primary endpoint

† = significant for other major (ie hard) endpoint

Coronary heart disease			Total vascular mortality	Total mortality	Comment
fatal	non-fatal	all			
ns	ns	ns	*		Active therapy superior
		ns	nc	nc	
ns	ns	ns	ns	ns	
	ns		ns	ns	
		ns	ns	ns	D therapy superior
ns	†	†	ns	ns	Active therapy superior
		ns	ns	ns	
			† ⁴	ns	Intensive thera- py superior
			† ⁴		ACEi therapy superior

The table continues on the next page.

Appendix 1, Table 7 *continued*

Study, year Reference	Intervention	Stroke		
		fatal	non-fatal	all
<i>Hypertension and diabetes mellitus</i>				
UKPDS, 1998 [14]	Intensive			*
	Moderate			
	BB; ACEi			ns
FACET, 1998 [90]	ACEi CCB			ns
ABCD, 2000 [50,51,82]	Intensive			ns
	Moderate			
	CCB ACEi	nc	nc	nc
RENAAL, 2001 [42]	ARB Placebo			ns
IDNT, 2001 [66]	ARB Placebo			
	CCB Placebo			
J-MIND, 2001 [39]	CCB ACEi			nc
DIABHYCAR, 2004 [73]	ACEi Placebo		ns	ns
<i>Hypertension and cardiovascular risk</i>				
HOPE, 2000 [11,100]	ACEi Placebo	*	*	*
EUROPA, 2003 [54]	ACEi Placebo			ns

* = significant for primary endpoint

ns = not significant for primary endpoint

nc = not calculated or reported for primary endpoint

† = significant for other major (ie hard) endpoint

Coronary heart disease			Total vascular mortality	Total mortality	Comment
fatal	non-fatal	all			
		ns	* ⁵	ns	Active therapy superior
		ns	ns	ns	
		nc	ns	nc	
		ns		†	Active therapy superior
	†	†	ns		ACEi therapy superior
		ns	ns	ns	
		ns		ns	
		nc	ns	nc	
	ns	ns	ns	ns	
		*	*	†	ACEi therapy superior
	*	*	ns	ns	ACEi therapy superior

¹ Including fatal and non fatal CHF.

² MI (with silent MI excluded); p=0.05 for trend.

³ First CV event.

⁴ Total vascular mortality includes ESRD and death.

⁵ Deaths related to diabetes in the study is approximated with total vascular mortality.

Appendix 1, Table 8 Blood pressure control and medication in the control groups.

Study, year Reference	Intervention	Part of screened population (%)	Need of additional or combined Rx (%)
VA II, 1970 [12,13,80,89]	Active Placebo		
USPHS, 1977 [83]	Active Placebo		
HDFP, 1979 Strata I–III [7,9,10, 17–19,23,26,87]	SC UC	} 7	
ANBPS, 1980 [1,29,35]	Active Placebo	} 3	70 45
Oslo, 1980 [61]	Active Placebo	} 5	63 17
MRC, 1985 [5,24,75]	BB Non-BB Placebo	} } 2 }	22 29
EWPHE, 1985 [36–38]	Active Placebo		37 63
HEP, 1986 [45]	Active Control	} 8	≈67 ⁵
SHEP, 1991 [28,46,53,55,65]	Active Placebo	} 1	44
STOP, 1991 [48]	Active Placebo		67 80
MRC older, 1992 [21]	BB Non-BB Placebo	} 3	52 38

Active Rx in control group (%)	Average DBP <90 mm Hg during follow-up in placebo group (%)	Normotensive¹ at all follow-up visits in placebo group (%)	Accelerated hypertension, above specified BP limits (%)
Patients withdrawn			10
Need of Rx recorded as an event			12
12	33	21 ²	12
17			17
≈12	30–50 ³	18 ⁴	12
10			10
9			
44			15
	45 ⁶		
11			11

The table continues on the next page.

Appendix 1, Table 8 *continued*

Study, year Reference	Intervention	Part of screened population (%)	Need of additional or combined Rx (%)
TOMHS, 1993 [33,76]	All active Rx ⁷		17
	BB		14
	CCB		11
	D		18
	Alpha-B		22
	ACEi		20
	Placebo ⁷		33
IPPPSH, 1985 [3]	BB		70
	Non-BB		85
HAPPY, 1987 [95]	BB		32
	Non-BB		38
MAPHY, 1988 [94]	BB		≈33
	Non-BB		≈33
MRFIT, 1990 [2,4,16,22,25,32]	SC	} 2	
	UC		
Materson, 1993 [74]	All active Rx		
	BB		
	CCB		
	D		
	Alpha-B		
	ACEi		
	Placebo		
BBB, 1994 [56]	Tight		
	Less tight		
Syst-Eur, 1997 [84–86,91]	CCB	} 52	41
	Placebo		60
Syst-China, 2000 [70,92]	CCB		41 increased the dose of CCB
	Placebo		
SCOPE, 2003 [69]	ARB		49
	Placebo		66

Active Rx in control group (%)	Average DBP <90 mm Hg during follow-up in placebo group (%)	Normotensive ¹ at all follow-up visits in placebo group (%)	Accelerated hypertension, above specified BP limits (%)
33			
6 ⁸ 12 ⁸			
	25 ⁶		
58 25			
			0.5 5.5
		36 19	
84			

The table continues on the next page.

Appendix 1, Table 8 *continued*

Study, year Reference	Intervention	Part of screened population (%)	Need of additional or combined Rx (%)
HYVET Pilot, 2003 [44]	D		16
	ACEi		13
	Placebo		

¹ As defined in each trial.

² <95 mm Hg DBP without placebo.

³ <90 mm Hg DBP at some visits.

⁴ During year 0–3.

⁵ At 4 years; data derived from figure.

⁶ <95 mm Hg DBP at 1 year.

⁷ All groups received non-pharmacological treatment.

⁸ Cross over of active Rx.

Active Rx in control group (%)	Average DBP <90 mm Hg during follow-up in placebo group (%)	Normotensive ¹ at all follow-up visits in placebo group (%)	Accelerated hypertension, above specified BP limits (%)
0.8			

Appendix 1, Table 9 Subjective adverse effects
(AE; biochemical adverse effects not included).

Study, year Reference	Intervention	Mean follow-up (ys)	Lost to follow-up	Dropout (%)
<i>Pharmacological</i>				
VA II, 1970 [12,13,80,89]	Active Placebo			15 15
USPHS, 1977 [83]	Active Placebo		33 35	33 35
HDFP, 1979 Strata I–III [7,9,10,17–19, 23,26,87]	SC UC		0.4 0.7	
ANBPS, 1980 [1,29,35]	Active Placebo		2.4 2.7	
Oslo, 1980 [61]	Active No care		0.7 2.6	
MRC, 1985 [5,24,75]	BB Non-BB Placebo		≈19 ¹ ≈19 ¹ ≈19 ¹	
EWPPHE, 1985 [36–38]	Active Placebo		17 14	
HEP, 1986 [45]	Active UC		0 0	
SHEP, 1991 [28,46,53,55,65]	Active Placebo			
STOP, 1991 [48]	Active Placebo		0 0	
MRC older, 1992 [21]	BB Non-BB Placebo	} } 5.8 }	≈25 ≈25 ≈25	

	Total withdrawn from randomized Rx (%)	Withdrawn from randomized Rx due to AE (%)	Total AE frequency (%)	Change in treat- ment Rx group due to AE
	12	12		12 (were withdrawn)
	15	5		5 (were withdrawn)
		10		10 (were withdrawn)
		2		2 (were withdrawn)
	34			
	37			
	0	0		10
	17	0		
	41 ^{1,2} (13 ³)	≈20 ¹ (12 ³)		
	38 ^{1,2} (11 ³)	≈18 ¹ (12 ³)		
	44 ^{1,2} (14 ³)	≈5 ¹ (2 ³)		
	37	5		
	35	4		
			} ≈25 intolerable	
		13	28 intolerable	
		7	21 intolerable	
	16 ⁴	7		
	23 ⁴	6		
	63 ¹	30 (14 ⁵)		
	48 ¹	14		
	53 ¹			

The table continues on the next page.

Appendix 1, Table 9 continued

Study, year Reference	Intervention	Mean follow-up (ys)	Lost to follow-up	Dropout (%)
TOMHS, 1993 [33,76]	All active Rx ⁶ BB CCB D Alpha-B ACEi Placebo ⁶	} 4.4	} 0.9 ^{1,2}	
BBB, 1994 [56]	Tight Less tight	} 4.9	} 0	} 6
Syst-Eur, 1997 [84–86,91]	CCB Placebo	2	5 5	
HOT, 1998 [60,63,64]	DBP ≤80 DBP ≤85 DBP ≤90	} 3.8	2 2 2	
Syst-China, 2000 [70,92]	CCB Placebo	} 3.0	9 11	
SCOPE, 2003 [69]	ARB Placebo	} 3.6	} 0.2	
HYVET Pilot, 2003 [44]	D ACEi Placebo	} 1.1	2 1.6 2	
Comparing drug treatments				
IPPPSH, 1985 [3]	BB Non-BB	} 4.0	0.6 0.5	
HAPPHY, 1987 [95]	BB Non-BB	} 3.8	} 1	
MAPHY, 1988 [94]	BB Non-BB	} 5.0	0 0.1	

	Total withdrawn from randomized Rx (%)	Withdrawn from randomized Rx due to AE (%)	Total AE frequency (%)	Change in treat- ment Rx group due to AE
	11	2		6
	8			
	6			
	15			
	12			
	12			
	9	4		
	7		7	
			78	
	24	9.9		
	31	10.9		
		22	3.9 ⁷	
			3.1 ⁷	
			3.1 ⁷	
		15	74	
84% in placebo group on active treatment		17	72	
	3			
	4			
	0			
	24	11		
	28	13		
	15 ¹ (9 ³)	≈ 4 ¹ (2 ³)	19 ⁸	
	15 ¹ (8 ³)	≈ 4 ¹ (2 ³)	16 ⁸	

The table continues on the next page.

Appendix 1, Table 9 *continued*

Study, year Reference	Intervention	Mean follow-up (ys)	Lost to follow-up	Dropout (%)
Materson, 1993 [74]	All active Rx BB CCB D Alpha-B ACEi Placebo	} 1.0 }		
MIDAS, 1996 [41]	CCB D	3		
VHAS, 1997 [81]	CCB D	2		22 23
NICS-EH, 1999 [31]	CCB D	4.5		
CAPPP, 1999 [59,77]	ACEi D/BB	6.1	0.25 0.25	
STOP-2, 1999 [58,67]	BB/D ACEi CCB	5.3	0 0 0	
NORDIL, 2000 [57]	CCB BB/D	4.5	0.5 0.5	
INSIGHT, 2000 [43,71]	CCB D	3	2.6 2.5	12.6 11.9
LIFE, 2002 [47,68]	ARB BB	4.8	0.08 0.1	2.1 1.9
ALLHAT, 2002 [6,20]	D CCB ACEi D Alpha-B	4.9 3.2	2 2 2.6 3.5 4.9	0.5 0.6 0.6
ELSA, 2002 [101]	CCB BB	3.8	3 3	

	Total withdrawn from randomized Rx (%)	Withdrawn from randomized Rx due to AE (%)	Total AE frequency (%)	Change in treat- ment Rx group due to AE
	59; 19 during mo 2-12	2 during mo 2-12 6 during mo 2-12 1 during mo 2-12 14 during mo 2-12 5 during mo 2-12 6 during mo 2-12		
	20	9.3		
	18	8.2		
		11.4	57	
		11.4	55	
	9.8	2.9	17.2	
	11.8	4.2	18.1	
	39	22.6	49	
	30	16	42	
	15	13		
	19	17		
	11			
	11			
	14			
		20		
		19		

The table continues on the next page.

Appendix 1, Table 9 *continued*

Study, year Reference	Intervention	Mean follow-up (ys)	Lost to follow-up	Dropout (%)
CONVINCE, 2003 [40]	CCB BB/D	3	6.6 6.6	
ANBP2, 2003 [97]	ACEi D	4.1	2 3	0 0.06
INVEST, 2003 [79]	CCB BB	2.7	2.6 2.3	2.1 6.6
Multifactorial and non-pharmacological				
MRFIT, 1990 [2,4,16,22,25,32]	SC UC	} 6.9		
RIS, 1998 [52]	Intervention UC	} 6.6	0 0	
TONE, 1998 [93]	Na ⁺ -reduction Weight- reduction Their combination UC	} } 2.5 }	} } }	3
Hypertension after a cerebrovascular event				
Dutch TIA, 1993 [34]	BB Placebo	2.6	0 0	
PATS, 1995 [27]	D Placebo	2		5.7 5.3
TEST, 1995 [49]	BB Placebo	2.6		
PROGRESS, 2001 [30]	ACEi + D Placebo	3.9	0.06 0.03	

	Total withdrawn from randomized Rx (%)	Withdrawn from randomized Rx due to AE (%)	Total AE frequency (%)	Change in treat- ment Rx group due to AE
	37	16.3		
	38	15.3		
	9.1	2.8		
	8.8	2.3		
	35	15	21	
	30	8	14	
			25.2 (3.4 ⁹)	
			28.5 (3.6 ⁹)	
		17		
		10		
	23			
	21			

The table continues on the next page.

Appendix 1, Table 9 *continued*

Study, year Reference	Intervention	Mean follow-up (ys)	Lost to follow-up	Dropout (%)
Hypertension and kidney				
AASK, 2002 [98]	Tight	3.8	7 ¹⁰	0
	Less tight		7 ¹⁰	0
	BB		7 ¹⁰	0
	ACEi		10 ¹⁰	0
	CCB		6 ¹⁰	0
Hypertension and diabetes mellitus				
UKPDS, 1998 [14]	Tight	} 8.4	} 3	} 1 ¹²
	Less tight			
	BB			
	ACEi			
FACET, 1998 [90]	ACEi	} 3.5	0.5	8.5
	CCB		1	10.4
ABCD, 2000 [50,51,82]	Tight	} 5	} Several patients, num- bers not reported	
	Less tight			
	ACEi			
	CCB			
RENAAL, 2001 [42]	ARB	3.4	0.4	7.5
	Placebo		0	7.8
IDNT, 2001 [66]	ARB	} 2.6		
	CCB			
	Placebo			
J-MIND, 2001 [39]	CCB	} 2	17.5	
	ACEi		12	
DIABHYCAR, 2004 [73]	ACEi	} 3.9	62	344
	Placebo		98	334

Total withdrawn from randomized Rx (%)	Withdrawn from randomized Rx due to AE (%)	Total AE frequency (%)	Change in treat- ment Rx group due to AE
		0–55.1 ¹¹ 0.7–54.2 ¹¹	
		0.2–51.0 ¹¹ 0.7–54.9 ¹¹ 0–59.8 ¹¹	
	35 22		
19 23			
34.8 39.7	17.4 22.9		
46.5 53.5	17.2 21.7		
23.7			
31 34	7.5 11		
50 50	25 22	50 48	

The table continues on the next page.

Appendix 1, Table 9 *continued*

Study, year Reference	Intervention	Mean follow-up (ys)	Lost to follow-up	Dropout (%)
<i>Hypertension and cardiovascular risk</i>				
HOPE, 2000 [11,100]	ACEi Placebo	4.5		
EUROPA, 2003 [54]	ACEi Placebo	4.2	0.02	

¹ Cumulative percentage.

² Overall percentage, ie given as the other studies have been presented.

³ Also includes lost to follow-up.

⁴ Withdrawal rates excluding predefined terminating events.

⁵ Excluding withdrawals due to low pulse rate; this was a predefined criterion based on the actual heart rate and not on the negative subjective experience of a low heart rate.

⁶ All groups received non-pharmacological therapy.

⁷ Reported at visit after two years of study participation.

⁸ At 1 year.

⁹ Refers to "limitation of daily living " AE reports within brackets.

¹⁰ No GFR measurement, during final year of follow-up.

¹¹ The frequency of different adverse symptoms during follow-up.

¹² Refused follow-up.

	Total withdrawn from randomized Rx (%)	Withdrawn from randomized Rx due to AE (%)	Total AE frequency (%)	Change in treat- ment Rx group due to AE
	28.9			
	27.3			
	22.8	5.1		
	20.7	1.8		

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Abbreviations for Appendix 2, Tables 1–4

Intervention groups

Angiotensin converting enzyme inhibitors (ACEi)

ALE	=	Alecepril
BENA	=	Benazipril
CAPT	=	Captopril
CILA	=	Cilazapril
DERA	=	Derapril
ENAL	=	Enalapril
FOSI	=	Fosinopril
LISI	=	Lisinopril
MIBE	=	Mibefradil
PERI	=	Perindopril
PINA	=	Pinacidil
QUIN	=	Quinalapril
RAMI	=	Ramipril
SPIR	=	Spirapril
TEMO	=	Temocapril
TRAN	=	Trandolapril
URA	=	Urapidil

Angiotensin-II receptor blockade (ARB)

CAND	=	Candesartan
EPRO	=	Eprosartan
IRBE	=	Irbesartan
LOS	=	Losartan
VALS	=	Valsartan

Beta-blockers (BB)

ACEB	=	Acebutol
ATEN	=	Atenolol
BISO	=	Bisoprolol
CARVE	=	Carvedilol
CELI	=	Celiprolol
INDE	=	Indelolol
LABE	=	Labetalol
METO	=	Metoprolol
NEBI	=	Nebivolol
PROP	=	Propanolol
TERT	=	Tertalol

Calcium channel blockers (CCB)

AMLO	=	Amlodipine
DIL	=	Diltiazem
FELO	=	Felodipine
ISRA	=	Isradipine
LACI	=	Lacidipine
MANI	=	Manidipine
NIC	=	Nicardipine
NIF	=	Nifedipine
NILV	=	Nilvaldipine
NITR	=	Nitrendipine
RILM	=	Rilmedipine
VERA	=	Verapamil

Diuretics

CHLT	=	Chlorthalidone
FURO	=	Furosemide
HCTZ	=	Hydrochlorthiazide
INDAP	=	Indapamide
TRI	=	Trichlormethiazide
XIP	=	Xipamide

Alpha₁-receptor blockers (Alpha-BL)

BUNA	=	Bunazosin
DOXA	=	Doxazosin
PRAZ	=	Prazosin

Other agents

Alpha-MET	=	Alpha-methyldopa
CADR	=	Cadralazine
CLON	=	Clonidine
DILE	=	Dilevalol (beta ₂ -adrenoreceptor agonist)
HYDR	=	Hydralazine
MINOX	=	Minoxidil
TRIA	=	Triamteren

Placebo (PLAC)

PLAC	=	Placebo
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Further abbreviations

BMI	=	Body mass index	LVWT	=	Left ventricular wall thickness (cm)
BP	=	Blood pressure	M	=	Male
CAD	=	Coronary artery disease	Mo	=	Month(s)
CVD	=	Cardiovascular disease	MRI	=	Magnetic resonance image
DBP	=	Diastolic blood pressure	No	=	Number
DM2	=	Diabetes mellitus type 2	Non-PH	=	Non-pharmacological
ECG	=	Electrocardiography	PROBE	=	Prospective randomized open blinded endpoint
F	=	Female	PWT	=	Posterior wall thickness (cm)
IST	=	Intraventricular septum thickness (cm)	SBP	=	Systolic blood pressure
LVH	=	Left ventricular hypertrophy			
LVM	=	Left ventricular mass (gram)			
LVMI	=	Left ventricular mass index (gram per body surface, g/m ²)			

Appendix 2, Table 1 Meta-analyses of the relationship between trials that measured the effects of antihypertensive therapy on left ventricular mass.

Author Year Reference	Data sources	Inclusion criteria	Time
Dahlöf 1992 [11]	– Comp. based databases – Textbooks – Peer review	– Previously treated or untreated essential HT – All pts pharmacologic treatment – Echocardiography – Drop out <30%	1977 to 1990
Cruickshank 1992 [7]	– Medline – Embase – Biosis	– Previously treated or untreated essential HT – All pts pharmacologic treatment – Echocardiography	?
Fagard 1995 [17]	– Medline – Textbooks – Peer review	– Previously treated or untreated essential HT – All pts pharmacologic treatment – Randomized trials – Comparative, ≥ 2 classes of drugs – BB/Diuretics/CCB/ACEi	1984 to 1992
Schmieder 1996 [65]	– Dimdi – Medline – Ringdoc – Ades – Embase – Textbooks – Peer review	– Previously untreated essential HT – All pts pharmacologic treatment – Randomized and DB trials – PLAC/BB/Alpha-BL/CCB/ACEi/Diuretics – >7 pts per treatment arm – >4 weeks treatment duration – Echocardiography	To 1995
Schmieder 1998 [66]	– Dimdi – Medline – Biosis Pre-views – Embase – Scisearch – Textbooks – Peer review	– Previously untreated essential HT – All pts pharmacologic treatment – Randomized and DB trials – PLAC/BB/CCB/ACEi/Diuretics – >7 pts per treatment arm – >4 weeks treatment duration – Echocardiography	To 1996

	No of reviewed studies	No of incl studies/ No of incl pts	% random-ized trials	% previously untreated HT	% duration of treatment >6 mo/ >12 mo
	?	109/2 357	17	28	56/38
	?	104/2 107	29	?	?
	?	15/1 568	100	?	?
	471	39/1 394	100	100	~50/?
	>500	50/1 715	100	100	~50/?

The table continues on the next page.

Appendix 2, Table 1 continued

Author Year Reference	Data sources	Inclusion criteria	Time
Jennings 1998 [34]	– Medline – Textbooks – Peer review	– Previously treated or untreated essential HT – All pts pharmacologic treatment – Echocardiography – Drop out <30%	1990 to 1995
Klingbeil 2003 [37]	– Dimdi – Medline – Biosis – Previews – Embase – Scisearch – Textbooks – Peer review	– Previously untreated essential HT – All pts pharmacologic treatment – Randomized and DB trials – PLAC/BB/Alpha-BL/CCB/ACEi/Diuretics – >7 pts per treatment arm – >4 weeks treatment duration – Echocardiography	To Sept 2002

	No of reviewed studies	No of incl studies/ No of incl pts	% random-ized trials	% previously untreated HT	% duration of treatment >6 mo/ >12 mo
	?	32/1 896	?	25	?/~50
	?	80/4 113	100	100	~75/?

Appendix 2, Table 2 Design and characteristics.

Author Year Reference	No of patients entered	No of patients follow-up (%)	Mean follow-up	Mean age in years (range)
Studies before 1993				
Steensgaard- Hansen 1988 [73]	22	22 (100)	6 mo	? (49–70)
Dahlöf 1992 [10]	28	28 (100)	6 mo	? (20–65)
Schulte 1992 [68]	40	30 (75)	6 mo	53±? (23–63)
Studies 1993 to 2003				
Salcedo 1993 [63]	60	60 (100)	6 mo	59±10 (30–75)
Gonzalez- Fernandez 1993 [23]	27	27 (100)	6 mo	50±7
Senior 1993 [71]	151	128 (85)	6 mo	(20–75)
Gonzales- Juanatey 1994 [24]	31	28 (90)	12 mo	54±6
Jula 1994 [35]	91	76 (84)	12 mo	44±5 (31–55)

% male	Inclusion criteria	LVH assessed by	Inter- vention	Comments
68	DBP ≥ 95 –115	Echo	PINA NIF	Double-blind All subjects treated with HCTZ
100	DBP ≥ 95	Echo	ENAL HCTZ	Double-blind
73	DBP ≥ 90	Echo	NIF PERI	Double-blind HCTZ added if BP not controlled
43	– DBP ≥ 90 –114 – SBP ≥ 160	Echo	VERA Alpha-MET ATEN ENAL	Unclear blinding
52	– DBP 95–114 – $\uparrow$ LVMI	Echo	CAPT PLAC	Double-blind
52	– DBP ≥ 95 –120 – $\uparrow$ LVMI (M > 130 ; F > 110)	Echo	HCTZ NIF ATEN ENAL INDAP	Double-blind
?	DBP ≥ 90 –114	Echo	VERA NITR	Double-blind
66	DBP ≥ 90 –114	Echo	Non-PH PLAC	Non-pharmacol intervention

The table continues on the next page.

Appendix 2, Table 2 *continued*

Author Year Reference	No of patients entered	No of patients follow-up (%)	Mean follow-up	Mean age in years (range)
Wambach 1994 [81]	16	16 (100)	6 mo	? (40–75)
Komsuoglu 1994 [39]	37	30 (81)	12 mo	76±4 (70–82)
Henderson 1994 [31]	26	26 (100)	6 mo	33±9 (18–64)
Diez 1994 [16]	87	87 (100)	6 mo	47±10
Machnig 1994 [48]	86	51 (59)	9 mo	51±10 (18–70)
Agabiti-Rosei 1994 [2]	24	23 (99)	6 mo	59±10 (27–63)
Lièvre 1995 [46]	115	103 (90)	6 mo	54±?
Liebson 1995 [45]	902	At 12 mo: 762 (84) 24 mo: 746 (83) 36 mo: 703 (78) 48 mo: 636 (71)	12–48 mo	55

% male	Inclusion criteria	LVH assessed by	Inter- vention	Comments
63	– DBP ≥ 95 –109 – $\uparrow$ LVMI (M >134; F >110)	Echo	CELI ATEN	Double-blind
70	– BP $\geq 170/95$ –120 – $\uparrow$ LVMI (M >134; F >110)	Echo	NITR VERA	Double-blind
100	BP ≥ 140 –160/ ≥ 90 –95	Echo	CAPT PLAC	Double-blind Prev untreated pts
57	BP $\geq 160/95$	Echo	CAPT LISI QUIN	Unclear blinding
59	– DBP ≥ 95 –115 – $\uparrow$ LVM (IST >12 or PWT >11)	Echo	NITR CAPT NITR + CAPT	Unclear blinding
50	DBP ≥ 90 –114	Echo	AMLO ENAL	Single-blind
62	– Prev treated: DBP <110 – Prev untreated: BP <160/ ≥ 95 –110 – $\uparrow$ LVMI (M >120; F >98)	Echo	RAMI (1.5 mg) RAMI (5 mg) PLAC	Double-blind All pts treated with furosemid
?	– Prev untreated pts: DBP ≥ 90 –99 – Prev treated pts: DBP ≥ 85 –99	Echo	CHLT ACEB DOXA AMLO ENAL PLAC	Double-blind Data reported on 12 mo follow-up

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Appendix 2, Table 2 *continued*

Author Year Reference	No of patients entered	No of patients follow-up (%)	Mean follow-up	Mean age in years (range)
Vyssoulis 1995 [83]	40	40 (100)	12 mo	54±7
Kirpizidis 1995 [36]	35	31 (89)	6 mo	60±4
Rosatti 1995 [61]	24	21 (88)	12 mo	58±? (46–68)
Kohno 1995 [38]	31	31 (100)	12 mo	53±3
Agabiti-Rosei 1995 [1]	193	111 (58)	6 mo	52±1 (27–69)
Van Leeuwen 1995 [82]	44	36 (82)	6 mo	50±? (27–70)
Fogari 1995 [19]	30	30 (100)	6 mo	54±2 (25–65)
Grandi 1995 [28]	36	36 (100)	6 mo	44±6
Schobel 1996 [67]	43	43 (100)	6 mo	52±9

% male	Inclusion criteria	LVH assessed by	Inter- vention	Comments
80	DBP ≥ 95 –100	Echo	CELI METO	Double-blind
26	– DBP ≥ 95 –110 – $\uparrow$ LVMI (M >130; F >110)	Echo	FOSI NIF	Double-blind
67	– DBP ≥ 95 –114 – $\uparrow$ LVM (PWT ≥ 10 or IST ≥ 11 mm)	Echo	ATEN RAMI	Unclear blinding
65	– BP $\geq 160/95$ – $\uparrow$ LVM (PWT ≥ 12)	Echo	ENAL LISI	Unclear blinding
59	– DBP ≥ 95 –115 – $\uparrow$ LVMI (M >120; F >98)	Echo	RAMI ATEN	PROBE design
?	DBP ≥ 95 –114	Echo	LISI DIL	Double-blind
100	– DBP ≥ 95 – $\uparrow$ LVMI (≥ 131)	Echo	LISI HYDR	Double-blind Atenolol/ Chlorthalidone added if BP not controlled
50	– Amb BP >140/>90 – $\uparrow$ LVMI (M >130; F >110)	Echo	ISRA PERI	Unclear blinding All pts BMI <26
67	DBP ≥ 95 –114	Echo	BUNA METO	Double-blind

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Appendix 2, Table 2 *continued*

Author Year Reference	No of patients entered	No of patients follow-up (%)	Mean follow-up	Mean age in years (range)
Gottdiener 1997 [27]	1 105	230 (21)	12 mo	57±10
Sumimoto 1997 [74]	20	?	21 mo	58±? (42–73)
Scognamiglio 1997 [70]	75	70 (93)	9 mo	58±? (40–70)
Lacourciere 1997 [42]	42	38 (90)	14 mo	73±2
Giugliano 1997 [22]	45	42 (93)	6 mo	58±7
Kribben 1997 [40]	708	285 (40)	12 mo	? (21–70)
Fagard 1997 [18]	27	24 (89)	6.5 mo	48±9
Lombardo 1997 [47]	24	24 (100)	12 mo	46±9 (26–62)
Leenen 1996 [44]	30	30 (100)	6 mo	54±3 (18–80)

% male	Inclusion criteria	LVH assessed by	Inter- vention	Comments
100	DBP ≥ 95 –109	Echo	ATEN CAPT CLON DIL HCTZ PRAZ	Double-blind
55	– BP $\geq 160/90$ – $\uparrow$ LVMI (M ≥ 119 ; F ≥ 110)	Echo	ALE NIC	Unclear blinding
75	– $\uparrow$ LVMI (≥ 75) – DM2 (HbA1c $< 8\%$)	Echo	NITR CAPT	BP not specified Unclear blinding All pts with DM2
63	– DBP ≥ 95 –114 – $\uparrow$ LVMI (M ≥ 140 ; F ≥ 120)	Echo	HCTZ AMLO HCTZ + AMLO	Single-blind
56	– DM2 – DBP ≥ 90 –105	Echo	CARVE ATEN	Double-blind All pts with DM2
?	DBP ≥ 95 –114	ECG	ATEN NITR ENAL HCTZ	Double-blind LVH assessed by ECG
68	BP $\geq 160/90/\geq 95$	Echo	HCTZ/ TRIA TRAN	Double-blind
96	DBP ≥ 90 –114	Echo	FOSI AMLO	Single-blind Prev untreated pts Doxazosin added if DBP ≥ 90
77	DBP ≥ 95 –114 and Amb BP ≥ 90	Echo	DIL AMLO	Single-blind

The table continues on the next page.

Appendix 2, Table 2 *continued*

Author Year Reference	No of patients entered	No of patients follow-up (%)	Mean follow-up	Mean age in years (range)
Schmieder 1997 [64]	43	36 (94)	6 mo	51±9
Papademetriou 1997 [58]	241	134 (55)	6 mo	57±10
Ueno 1997 [80]	43	36 (84)	12 mo	52±1 (23–71)
Ofili 1998 [56]	104	94 (90)	36 mo	71±6 (≥60)
Cuspidi 1998 [9]	17	17 (100)	6 mo	44±7
Laufer 1998 [43]	37	28 (76)	12 mo	49±? (18–65)
Roman 1998 [60]	60	50 (83)	6 mo	51±7 (38–69)
Höglund 1998 [33]	66	60 (91)	6 mo	53±9
Tedesco 1998 [75]	77	70 (91)	22 mo	55±8 (31–75)
Sadowski 1998 [62]	73	56 (77)	12 mo	53±10 (PP: 46±11)
Beltman 1998 [4]	71	57 (80)	12 mo	54±10 (25–75)

% male	Inclusion criteria	LVH assessed by	Inter- vention	Comments
67	– BP $\geq$ 160/95 or DBP $\geq$ 90–114	Echo	BUNA METO	Double-blind
81	– DBP $\geq$ 95–114 – $\uparrow$ LVMI (M $\geq$ 119; F $\geq$ 98)	Echo	HCTZ ISRA	Unclear blinding 2:1 randomization
44	BP $\geq$ 160/95	Echo	NILV TEMO CADR	Unclear blinding
51	BP $\geq$ 160/90	Echo	CHLT PLAC	Double-blind
82	DBP $\geq$ 95–115	Echo	LOS VERA	Double-blind
87	DBP $\geq$ 95 – $\uparrow$ LVM (LVWT $\geq$ 1.2 cm)	Echo	ATEN CAPT	PROBE design All pts HCTZ if DBP >90
74	DBP $\geq$ 95–114	Echo	HCTZ RAMI	Double-blind
79	DBP $\geq$ 95–114 – $\uparrow$ LVMI (M >102; F >88)	Echo	MIBE ATEN	Double-blind
53	– DBP $\geq$ 95–114 – $\uparrow$ LVMI (M $\geq$ 130; F $\geq$ 110)	Echo	LOS HCTZ	Double-blind
70 (PP: 66)	– DBP $\geq$ 95–114 – $\uparrow$ LVMI (M >134; F >110)	Echo	RILM NIF	Double-blind Per protocol (PP) analysis
62	DBP $\geq$ 95–114	Echo	AMLO LISI	Double-blind Previously untreated pts

The table continues on the next page.

Appendix 2, Table 2 *continued*

Author Year Reference	No of patients entered	No of patients follow-up (%)	Mean follow-up	Mean age in years (range)
Sihm 1998 [72]	50	50 (100)	9 mo	46±8
Heesen 1998 [29]	51	44 (86)	6 mo	67±5
Molinero 1998 [54]	26	26 (100)	6 mo	55±7 (22–72)
Thürmann 1998 [78]	69	58 (84)	8 mo	56±10
Manolis 1998 [51]	45	35 (78)	6 mo	?
Gaudio 1998 [20]	50	44 (88)	6 mo	54±10 (29–70)
Gerritsen 1998 [21]	121	109 (90)	12 mo	62±8
Gosse 1999 [25]	54	47 (87)	6 mo	54±10 (18–75)
Modena 1999 [53]	169	159 (94)	18 mo	56±5

% male	Inclusion criteria	LVH assessed by	Intervention	Comments
84	– Pts with no LVH: DBP ≥ 100 and Amb DBP ≥ 95 – Other pts: BP $\geq 165/100$	Echo	ISRA HCTZ + Amilorid	Unclear blinding Atenolol or hydralazine added if DBP > 90 Complicated design!
23	BP $\geq 160 / < 95$	Echo	QUIN HCTZ/ Triam	Double-blind All pts prev untreated
42	– BP $\geq 140/90$–114 – No LVH: LVMI (M < 130; F < 100) – BMI < 30	Echo	VERA HCTZ + Amilorid	Single-blind
65	– DBP ≥ 95–114 and SBP ≥ 150–180 – $\uparrow$ LVMI (M > 130; F > 110)	Echo	ATEN VALS	Double-blind Per protocol analysis HCTZ added if DBP ≥ 95
89	DBP ≥ 95 –114	Echo	ISRA SPIR ISRA + SPIR	Double-blind
64	– DBP ≥ 100 – $\uparrow$ LVMI (M > 134; F > 110)	Echo	BENA NITR	Unclear blinding LVM also by MRI
62	– HbA1c $< 11.5\%$ – SBP < 200 and DBP ≥ 95–114	Echo	NITR ENAL PLAC	Double-blind All pts NIDMM
68	– DBP ≥ 95 –114 and SBP ≥ 160 –200	Echo	BISO VERA	Double-blind Post-hoc analyses
0	DBP ≥ 95 –114 and after 3 mo BP $< 140/90$	Echo	17-beta-estradiol PLAC	Double-blind All pts received conventional BP medic to obtain normal BP

The table continues on the next page.

Appendix 2, Table 2 *continued*

Author Year Reference	No of patients entered	No of patients follow-up (%)	Mean follow-up	Mean age in years (range)
Diamond 1999 [15]	27	17 (63)	6 mo	?
Topouchian 1999 [79]	69	59 (85)	6 mo	53±? (29–76)
Avanza 2000 [3]	61	46 (75)	10 mo	54±4 (40–60)
Gosse 2000 [26]	505	411 (81)	11 mo	54±11
Kuperstein 2000 [41]	22	21 (95)	6 mo	55±12
Brilla 2000 [6]	35	25 (71)	6 mo	57±2 (18–70)
Terpstra 2001 [76]	166	120 (72)	24 mo	67±4 (60–75)
Malmqvist 2001 [50]	51	47 (92)	12 mo	50±7 (32–66)

% male	Inclusion criteria	LVH assessed by	Inter-vention	Comments
53	DBP ≥ 95 –114	Echo	ENAL EPRO	Double-blind
55	DBP ≥ 95 –114	Echo	VERA TRAN TRAN + VERA	Double-blind
59	– DBP ≥ 95 –114 – $\uparrow$ LVMI (M >130; F >110)	Echo	ENAL LOS ENAL + LOS	Unclear blinding
56	– SBP ≥ 160 –209 – $\uparrow$ LVMI (M >120; F >100)	Echo	INDAP ENAL	Double-blind Per protocol (PP) analyses
43	– Fasting-Glucose <7.8 – BMI >27–45 – BP $\geq 160/\geq 95$ –114 – $\uparrow$ LVMI (M >100; F >75)	Echo	ATEN PERI	Double-blind Indapamide or amlodipine added if BP not controlled
77	– DBP >100 – No CAD – $\uparrow$ LVMI (M >134; F >110) – E/A ratio <1	Echo	LISI HCTZ	Double-blind No placebo wash- out! Prazosin added if BP not <160/90
55	BP ≥ 160 –220/ ≥ 95 –114	Echo	AMLO LISI	Double-blind
57	DBP ≥ 100	Echo	CAPT METO	PROBE design All pts previously untreated Subgroup analysis of CAPPP

The table continues on the next page.

Appendix 2, Table 2 *continued*

Author Year Reference	No of patients entered	No of patients follow-up (%)	Mean follow-up	Mean age in years (range)
Malmqvist 2001 [49]	115	94 (82)	12 mo	54±9 (31–74)
Mathew 2001 [52]	3 829	? (87 for all pts)	54 mo	67±7 (≥55)
Black 2001 [5]	171	111 (65)	12 mo	66±7 (≥55)
Devereux 2001 [14]	303	235 (78)	48 mo	63±9 (>50)
Novo 2001 [55]	46	46 (100)	6 mo	55±21 (34–76)
Pontremoli 2001 [59]	31	31 (100)	24 mo	49±1 (29–62)
Heesen 2001 [30]	97	62 (64)	24 mo	68±4 (60–75)
Schussheim 2001 [69]	29	29 (100)	6 mo	48±6

% male	Inclusion criteria	LVH assessed by	Inter-vention	Comments
66	– DBP ≥ 95–115 – $\uparrow$ LVMI (M >131; F >100)	Echo	IRBE ATEN	Double-blind
74	– Hypertension diagnosed – CVD or DM + ≥ 1 risk factors	ECG (LVH: Sokolow-Lyon: >35 mm)	RAMI PLAC	Double-blind LVH assessed by ECG Subgroup analysis of HOPE: hypertension in 46% (n=3 829)
49	BP ≥ 130 –159/ <90	Echo	FELO PLAC	Double-blind
66	– Prev treated pts: BP $\geq 140/90$ – Prev untreated pts: BP $\geq 150/90$ – $\uparrow$ LVMI (M >116; F >116; if <65 yrs; >104 if ≥ 65 yrs)	Echo	NIF ENAL	Double-blind
54	– BP $\geq 140/90$ – $\uparrow$ LVMI (M >134; F >110)	Echo	ENAL HCTZ ATEN VERA	Unclear blinding
61	BP $\geq 140/90$	Echo	LISI NIF	Unclear blinding CHLT added if BP not controlled
48	BP ≥ 160 / <95	Echo	LISI PLAC	Double-blind Prev untreated pts Per protocol analysis
53	DBP ≥ 100 <130	Echo	VERA NIF	Double-blind

The table continues on the next page.

Appendix 2, Table 2 *continued*

Author Year Reference	No of patients entered	No of patients follow-up (%)	Mean follow-up	Mean age in years (range)
Hinderliter 2002 [32]	144	82 (57)	6 mo	47±9
De Rosa 2002 [13]	50	42 (84)	36 mo	55±7 (52–62)
Cuspidi 2002 [8]	239	196 (82)	11 mo	53±9 (25–70)
Dahlöf 2002 [12]	225	219 (97)	9 mo	57±11 (21–80)
Okin 2003 [57]	9 222	9 193 (99)	48 mo	67±7 (55–80)

% male	Inclusion criteria	LVH assessed by	Intervention	Comments
45	– BP ≥ 130–180/≥ 95–110 – BMI ≥ 25–37 – Sedentary physical activity	Echo	Exercise + weight control Exercise only Control group	Life style modifications
50	DBP ≥ 95 –114	Echo	LOS ENAL	Double-blind
62	– BP ≥ 140–200/≥ 95–115 – $\uparrow$ LVMI (M > 120; F > 100)	Echo	CAND ENAL	Double-blind HCTZ added if DBP $\geq 140/90$
63	– SBP ≥ 140–200/≥ 95–115 – $\uparrow$ LVMI (M > 120; F > 105)	Echo	LOS ATEN	Double-blind HCTZ added if BP $\geq 140/90$
46	– BP ≥ 160–200/≥ 95–114 – $\uparrow$ LVH ECG	ECG (Cornell: > 2.440 mm x ms/ Sokolow-Lyon: > 38 mm)	LOS ATEN	Double-blind LVH assessed by ECG

Appendix 2, Table 3 LVH outcomes in studies using echo- or electrocardiographic (ECG) methods.

Author Year Reference	Variable (unit)	Intervention group	No of subjects	Baseline level of LVH
Studies before 1993				
Steensgaard-Hansen 1988 [73]	LVM (g)	PINA	12	326.3±126.2
		NIF	10	293.6±35.7
Dahlöf 1992 [10]	LVMI (g/m)	ENAL	14	146.3±10.3
		HCTZ	14	137.5±11.2
Schulte 1992 [68]	LVMI (g/m ²)	NIF	14	141±6
		PERI	16	148±5
Studies 1993 to 2003				
Salcedo 1993 [63]	LVMI (g/m ²)	VERA	15	180±27
		Alpha-MET	15	176±30
		ATEN	15	170±23
		ENAL	15	178±28
Gonzalez-Fernandez 1993 [23]	LVMI (g/m ²)	CAPT	14	149±17
		PLAC	13	155±40
Senior 1993 [71]	LVMI (g/m ²)	HCTZ	20	141.3±6.6
		INDAP	20	151.4±6.3
		NIF	19	170.4±6.6
		INDAP	22	144.1±5.3
		ATE	12	156.7±8.4
		INDAP	17	146.2±5.1
		ENAL	9	142.0±6.7
		INDAP	9	155.1±6.3
Gonzales-Juanatey 1994 [24]	LVMI (g/m ²)	VERA	14	159±31
		NITR	14	167±26

	Follow-up LVH	Within- group change	Within- group change in %	p-value	Between- group change	Between- group change in %
	251±?	−75.1±47.3	−23	<0.001	−49	−14
	268±?	−26.3±34.7	−9	0.04	−Reference	
	125.1±7.5	−21.2	−14.4 (−8.2 to −20.9)	<0.001	−11	−7
	127.7±6.2	−9.8	−7.1 (+3.8 to −18.4)		Reference	
	118±8	−23	−16.9	<0.01	−2	−2
	127±6	−21	−14.3	<0.01	−Reference	
	159±22	−21	−12	<0.05	+2	−1
	142±22	−34	−19	<0.01	−15	−8
	154±19	−16	−9	<0.05	+3	+2
	159±29	−19	−11	<0.05	Reference	Reference
	96±23	−53	−36	<0.001	−80	−53
	182±51	+27	+17	<0.01	Reference	
	135.6±8.3	−5.7	−4.0	NS	+20.0	+12.9
	125.7±4.6	−25.7	−16.9	<0.001	Reference	Reference
	148.2±6.2	−22.2	−13.0	<0.001	−3.2	+0.1
	125.1±4.3	−19.0	−13.1	<0.001	Reference	Reference
	142.9±10.3	−13.8	−8.8	<0.01	+1.6	+1.7
	130.8±6.5	−15.4	−10.5	<0.001	Reference	Reference
	130.0±5.9	−12.0	−8.5	<0.001	−0.3	−1.0
	143.4±5.2	−11.7	−7.5	<0.001	Reference	Reference
	136±20	−23	−14	<0.05	−3	−2
	147±21	−20	−12	<0.05	Reference	

The table continues on the next page.

Appendix 2, Table 3 *continued*

Author Year Reference	Variable (unit)	Intervention group	No of subjects	Baseline level of LVH
Jula 1994 [35]	LVMI (g/m ²)	Non-PH PLAC	38	123±26
			38	115±23
Wambach 1994 [81]	LVMI (g/m ²)	CELI ATEN	8	186±43
			8	164±24
Komsuoglu 1994 [39]	LVMI (g/m ²)	NITR VERA	16	155±28
			14	160±32
Henderson 1994 [31]	LVM (g)	CAPT PLAC	12	205±12
			14	207±14
Diez 1994 [16]	LVMI (g/m ²)	CAPT	30	102±6
		LISI	37	92±6
		QUIN	20	103±6
Machnig 1994 [48]	LVMI (g/m ²)	NITR	18	134±15
		CAPT	15	148±23
		NITR + CAPT	18	185±57
Agabiti-Rosei 1994 [2]	LVMI (g/m ²)	AMLO	12	154±34
		ENAL	12	134±30
Lièvre 1995 [46]	LVMI (g/m ²)	RAMI (1.5 mg)	35	134±8
		RAMI (5 mg)	33	143±6
		PLAC	35	134±5
Liebson 1995 [45]	LVM (g)	<i>At 12 mo:</i>		
		CHLT	111	207.6
		ACEB	103	203.7
		DOXA	113	199.1
		AMLO	100	191.7
		ENAL	105	202.2
		PLAC	186	205.0

	Follow-up LVH	Within- group change	Within- group change in %	p-value	Between- group change	Between- group change in %
	117±22 116±22	-6 +1	-5 +1	<0.05	-6 Reference	-6
	157±34 151±27	-27 -13	-15 -8	<0.05 NS	-14 Reference	-7
	151±23 155±28	-4 -4	-3 -3	NS NS	0 Reference	0
	202±12 232±16	-3 +25	-3.5 +12	NS <0.05	-22 Reference	-13
	89±4 77±4 92±5	-13 -15 -11	-13 -16 -11	<0.05 <0.05 <0.05	-2 -4 Reference	-2 -5
	115±19 118±23 131±23	-19 -30 -54	-14 -20 -29	<0.001 <0.001 <0.001	Reference -6 -12	-6 -12
	132±29 117±21	-22 -17	-14 -13	<0.01 <0.05	-5 Reference	-1
	127±? 132±? 138±?	-7±4 -11±4 +4±4	-4 -8 +3	NS 0.004	-11 -15 Reference	-7 -11
At 12 mo:	172.8 187.0 177.1 165.1 184.9 186.8	-34.8±4.6 -16.7±4.5 -22.0±3.6 -26.6±3.6 -17.3±4.6 -18.2±3.1	-17 -8 -12 -14 -9 -9	<0.05 <0.05 <0.05 <0.05 <0.05 <0.05	-17 +2 -4 -8 +1 Reference	-8 +1 -3 -5 0 Reference

The table continues on the next page.

Appendix 2, Table 3 *continued*

Author Year Reference	Variable (unit)	Intervention group	No of subjects	Baseline level of LVH
Vyssoulis 1995 [83]	LVMI (g/m ²)	CELI METO	20	140±14
			20	144±19
Kirpizidis 1995 [36]	LVMI (g/m ²)	FOSI NIF	16	146±17
			15	146±14
Rosatti 1995 [61]	LVMI (g/m ²)	ATEN RAMI	10	145±2
			11	147±7
Kohno 1995 [38]	LVMI (g/m ²)	ENAL LISI	16	166±26
			15	167±28
Agabiti-Rosei 1995 [1]	LVMI (g/m ²)	RAMI ATEN	56	135±6
			55	132±4
Van Leeuwen 1995 [82]	LVMI (g/m ²)	LISI	20	92±?
		DIL	16	98±?
Fogari 1995 [19]	LVMI (g/m ²)	LISI HYDR	15	172±19
			15	171±15
Grandi 1995 [28]	LVMI (g/m ²)	ISRA PERI	18	139±15
			18	142±14
Schobel 1996 [67]	LVMI (g/m ²)	BUNA METO	23	284±80
			20	282±74

	Follow-up LVH	Within- group change	Within- group change in %	p-value	Between- group change	Between- group change in %
	124±14 135±22	-16 -9	-11.8±4.0 -5.7±7.0	<0.001 0.002	-7 Reference	-5
	124±9 133±13	-22 -13	-15 -9	<0.001 <0.001	-9 Reference	-6
	117±4 116±3	-28 -31	-19 -21	<0.01 <0.01	-3 Reference	-2
	128±? 130±?	-38 -37	-23 -22	<0.05 <0.05	-1 Reference	-1
	121±7 130±4	-14 -2	-10 -2	<0.001 NS	-12 Reference	-8
	82±? 96±?	-9 (-16 to -2) -2 (-14 to 10)	-11 -2	<0.01 NS	-8 Reference	-9
	147±17 163±20	-25 -8	-14 -5	0.005 NS	-17 Reference	-9
	119±18 112±19	-20 -30	-14.5±4.7 -21.1±4.3	<0.005 <0.005	-10 Reference	-7
	259±67 254±70	-25±42 -28±44	-9 -10	<0.05 <0.05	+3 Reference	-1

The table continues on the next page.

Appendix 2, Table 3 *continued*

Author Year Reference	Variable (unit)	Intervention group	No of subjects	Baseline level of LVH
Gottdiener 1997 [27]	LVM (g)	ATEN	36	325±98
		CAPT	40	302±62
		CLON	36	329±69
		DIL	52	314±94
		HCTZ	38	310±83
		PRAZ	28	348±86
Sumimoto 1997 [74]	LVMI (g/m ²)	ALE	10	136±15
		NIC	10	132±11
Scognamiglio 1997 [70]	LVMI (g/m ²)	NITR	37	87±2
		CAPT	36	89±2
Lacourciere 1997 [42]	LVMI (g/m ²)	HCTZ	7	149±7
		AMLO	18	150±4
		HCTZ + AMLO	13	155±5
Giugliano 1997 [22]	LVMI (g/m ²)	CARVE	22	110±15
		ATEN	20	107±14
Kribben 1997 [40]	ECG	HCTZ ATEN NITR ENAL	No individual data	No individual data
Fagard 1997 [18]	LVM (g)	HCTZ +	11	239±78
		TRIA	14	278±91
		TRAN		
Lombardo 1997 [47]	LVMI (g/m ²)	FOSI	12	125±32
		AMLO	12	106±18
Leenen 1996 [44]	LVMI (g/m ²)	DIL	13	108±8
		AMLO	17	107±5

	Follow-up LVH	Within- group change	Within- group change in %	p-value	Between- group change	Between- group change in %
	321±?	-4±77	-1	0.75	Reference	
	287±?	-15±47	-5	0.05	-11	-4
	328±?	-1±49	-0.3	0.95	+3	+1
	307±?	-7±53	-2	0.35	-3	-1
	296±?	-14±49	-5	0.08	-10	-4
	342±?	-6±48	-2	0.52	-2	-1
	99±16	-37	-27	<0.01	-19	-13
	114±16	-18	-14	<0.01	Reference	
	81±1	-6	-7	<0.001	-2	-3
	86±2	-4	-4	<0.001	Reference	
	102±8	-47	-31	<0.001	Reference	
	104±5	-46	-31	<0.001	+1	0
	100±5	-55	-35	<0.001	-8	-4
	100±?	-10.3±6.4	-9	<0.001	0	0
	97±?	-10.2±7.2	-9	<0.001	Reference	
	No individual data					
	211±76	-28	-12	<0.05	Reference	
	238±79	-40	-14	<0.05	-12	-2
	100±12	-25	-21	<0.02	-8	-5
	89±10	-17	-16	<0.02	Reference	
	102±?	-6±2	-6	<0.05	Reference	
	97±?	-10±2	-9	<0.05	-4	-3

The table continues on the next page.

Appendix 2, Table 3 *continued*

Author Year Reference	Variable (unit)	Intervention group	No of subjects	Baseline level of LVH
Schmieder 1997 [64]	LVMI (g/m ²)	BUNA	20	146±34
		METO	16	144±26
Papademetriou 1997 [58]	LVMI (g/m ²)	HCTZ	45	165±36
		ISRA	89	170±36
Ueno 1997 [80]	LVMI (g/m ²)	NIVA	12	129±48
		TEMO	12	117±39
		CADR	12	110±30
Ofili 1998 [56]	LVMI (g/m ²)	CHLT	47	109±33
		PLAC	47	102±24
Cuspidi 1998 [9]	LVMI (g/m ²)	LOS	8	124±21
		VERA	9	117±17
Laufer 1998 [43]	LVMI (g/m ²)	ATEN	13	127±22
		CAPT	15	126±21
Roman 1998 [60]	LVMI (g/m ²)	HCTZ	28	93±20
		RAMI	22	104±20
Höglund 1998 [33]	LVMI (g/m ²)	MIBE	31	117±12
		ATEN	29	123±18
Tedesco 1998 [75]	LVM (g/m ²)	HCTZ	28	140±23
		LOS	42	139±19

	Follow-up LVH	Within- group change	Within- group change in %	p-value	Between- group change	Between- group change in %
	132±25 129±26	-20±37 -32±42	-10 -10	<0.05 <0.05	+1 Reference	0
	145±? 164±?	-19.8±21.2 -5.8±24.7	-12 -4	<0.001 0.12	-14 Reference	-8
	115±39 88±20 138±27	-14 -29 +28	-8.5±12.3 -22.8±13.5 +31.8±33.1	<0.05 <0.01 <0.01	-42 -57 Reference	-36 -50
	93±28 110±26	-16 +8	-17 (-4 to -28) +4 (-5 to +14)	<0.001 <0.01	-24 Reference	-19
	103±16 107±20	-21 -10	-17 -9	<0.05 NS	-11 Reference	-8
	131±? 128±?	+4 +2	+3 +2	NS NS	+2 Reference	+1
	92±23 95±20	-1 -9	-1 -9	NS <0.001	Reference -8	-8
	103±15 111±17	-13.5±16.5 -11.7±14.6	-11 -9	<0.001 <0.001	-2 Reference	-2
	135±21 128±21	-5 -11	-4 -8	NS <0.02	Reference -6	-4

The table continues on the next page.

Appendix 2, Table 3 *continued*

Author Year Reference	Variable (unit)	Intervention group	No of subjects	Baseline level of LVH
Sadowski 1998 [62]	LVMI (g/m ²)	RILM NIF	24	177±41
			32	173±35
Beltman 1998 [4]	LVMI (g/m ²)	AMLO LISI	28	88±21
			31	91±16
Sihm 1998 [72]	LVM (g)	ISRA HCTZ + Amilorid	25	358±128
			25	311±80
Heesen 1998 [29]	LVMI (g/m ²)	QUIN HCTZ/Triam	21	88±9
			23	94±9
Molinero 1998 [54]	LVMI (g/m ²)	VERA HCTZ + Amilorid	11	110±33
			15	114±29
Thürmann 1998 [78]	LVMI (g/m ²)	ATEN VALS	29	127±25
			29	127±23
Manolis 1998 [51]	LVMI (g/m ²)	ISRA	10	140±15
		SPIR	11	139±15
		ISRA + SPIR	14	148±16
Gaudio 1998 [20]	LVMI (g/m ²)	BENA	22	143±12
		NITR	22	136±6
Gosse 1999 [25]	LVMI (g/m ²)	BISO	23	126±27
		VERA	24	115±22
Gerritsen 1998 [21]	LVMI (g/m ²)	NITR	37	146±35
		ENAL	38	141±29
		PLAC	34	140±32

	Follow-up LVH	Within- group change	Within- group change in %	p-value	Between- group change	Between- group change in %
	155±40 146±36	-22.1±23.3 -26.9±29.5	-12 -16	<0.001 <0.001	Reference -5	-4
	77±?	-11.0 (-6.0 to -16.1)	-13	<0.05	Reference	
	78±?	-12.6 (-8.2 to -16.1)	-14	<0.05	-2	-1
	227±84 241±55	-130±75 -70±53	-37 -23	<0.001 <0.001	-61 Reference	-14
	64±13 66±13	-24 -28	-27 -30	<0.001 <0.001	+4 Reference	+3
	115±21 127±22	+5 +13	+5 +11	NS NS	-8 Reference	-6
	117±27 106±25	-10 -21	-8 -17	<0.01 <0.001	Reference -11	-9
	128±13 125±14 132±15	-12 -14 -16	-9 -10 -11	0.002 <0.001 0.002	+2 Reference -2	+1 Reference -1
	123±11 127±8	-20 -9	-14 -7	<0.001 <0.01	-11 Reference	-7
	124±31 115±27	-2 0	-2 0	NS NS	-2 Reference	-2
	138±? 140±? 149±?	-12.0±5.4 -1.0±4.7 +9.3±3.4	-8 -0.1 +6	<0.01 NS <0.01	-23 -10 Reference	-14 -6

The table continues on the next page.

Appendix 2, Table 3 *continued*

Author Year Reference	Variable (unit)	Intervention group	No of subjects	Baseline level of LVH
Avanza 2000 [3]	LVMI (g/m ²)	ENAL	15	141±4
		LOS	15	147±4
		ENAL + LOS	16	146±3
Modena 1999 [53]	LVMI (g/m)	17-beta- estradiol	82	81±17
		PLAC	79	84±16
Diamond 1999 [15]	LVMI (g/m)	ENAL	9	118±42
		EPRO	8	111±37
Topouchian 1999 [79]	LVMI (g/cm)	VERA	21	51.7±11.3
		TRAN	18	51.9±11.2
		VERA + TRAN	20	51.4±17.6
Gosse 2000 [26]	LVMI (g/m ²)	ENAL	206	138±36
		INDAP	205	144±40
Kuperstein 2000 [41]	LVMI (g/m ²)	PERI	10	98±9
		ATEN	11	101±11
Brilla 2000 [6]	LVMI (g/m ²)	LISI	11	170±16
		HCTZ	14	160±14
Terpstra 2001 [76]	LVMI (g/m ²)	AMLO	61	109±20
		LISI	63	114±23
Malmqvist 2001 [50]	LVMI (g/m ²)	CAPT	22	113±23
		METO	25	116±19
Malmqvist 2001 [49]	LVMI (g/m ²)	IRBE	44	154.3±35.0
		ATEN	50	143.5±25.1

	Follow-up LVH	Within- group change	Within- group change in %	p-value	Between- group change	Between- group change in %
	123±4	-18	-12.4±3.2	<0.05	-4	-3
	133±3	-14	-9.1±2.1	<0.05	Reference	
	116±4	-30	-20.5±5.0	<0.05	-16	-11
	75±17	-6	-7	<0.01	-3	-3
	81±16	-3	-4	0.05	Reference	
	92±?	-26±16	-22	0.005	-16	-13
	101±?	-10±31	-9	NS	Reference	
	47.0±10.7	-4.1	-8	<0.01	+0.8	+1
	47.0±10.1	-4.9	-9	<0.01	Reference	Reference
	47.5±17.1	-3.9	-8	<0.01	+1.0	+1
	136±37	-1.9±28.3	-1	NS	Reference	
	136±35	-8.4±30.5	-5	<0.001	-6	-4
	91±14	-7	-7	0.04	-7	-7
	101±18	0	0	0.24	Reference	
	177±15	+7	+4	NS	Reference	
	145±11	-15	-9	NS	-22	-13
	85±17	-25.7±12.6	-22	<0.001	Reference	
	87±16	-27.0±17.0	-24	<0.001	-3	-2
	97±?	-16±12	-14	<0.001	-9	-8
	109±?	-7±14	-6	0.015	Reference	
	128.3±?	-26.0±4.2	-17	<0.001	-12	-7
	129.4±?	-14.1±2.9	-10	<0.001	Reference	

The table continues on the next page.

Appendix 2, Table 3 *continued*

Author Year Reference	Variable (unit)	Intervention group	No of subjects	Baseline level of LVH
Mathew 2001 [52]	ECG LVH (%) (Sokolow- Lyon)	RAMI PLAC	4 135 4 146	<i>No of subjects with LVH:</i> 321 (7.8%) 355 (8.6%)
Black 2001 [5]	LVMI (g/m ²)	FELO PLAC	54 57	96±18 100±30
Devereux 2001 [14]	LVMI (g/m ²)	NIF ENAL	122 113	133±25 130±23
Novo 2001 [55]	LVMI (g/m ²)	ENAL HCTZ ATEN VERA	10 10 13 13	140±11 143±15 142±10 136±10
Pontremoli 2001 [59]	LVMI (g/m ²)	LISI NIF	16 15	56±3 63±3
Heesen 2001 [30]	LVMI (g/m ²)	LISI PLAC	30 32	104±18 92±20
Schussheim 2001 [69]	LVM (g)	VERA NIF	14 15	190±13 200±15
Hinderliter 2002 [32]	LVMI (g/m)	Exercise + weight control Exercise only Control group	36 27 19	48±10 50±11 51±14
De Rosa 2002 [13]	LVMI (g/m ²)	LOS ENAL	22 20	176±24 170±19

	Follow-up LVH	Within- group change	Within- group change in %	p-value	Between- group change	Between- group change in %
<i>No of subjects with LVH:</i>						
	336 (8.1%)	+15	+0.3		–39	–0.9
	406 (9.8%)	+54	+1.2		Reference	
	96±?	1±16	–0.5±16.1	NS	–2	–2
	103±?	+3±15	+3.0±14.8	NS	Reference	
	116±23	–16.9±18.4	–13	<0.01	–2	–2
	115±24	–14.7±20.6	–11	<0.01	Reference	
	118±11	–22	–16	<0.01	–12	–9
	133±15	–10	–7	NS	Reference	
	115±10	–27	–19	<0.01	–17	–12
	118±10	–18	–13	<0.01	–8	–6
	52±2	–4	–7	<0.05	+2	+3
	57±4	–6	–10	NS	Reference	
	79±16	–25	–25	<0.01	–8	–7
	75±15	–17	–18	<0.01	Reference	
	163±8	–27	–14	<0.05	–10	–5
	183±13	–17	–9	<0.05	Reference	
	48±?	0	0	NS	0	0
	48±?	–2	–4	NS	–2	–4
	51±?	0	0	NS	Reference	
	124±?	–52 (–110 to +32)	–29	NS	–11	–5
	129±?	–41 (–90 to +22)	–24	NS	Reference	

The table continues on the next page.

Appendix 2, Table 3 *continued*

Author Year Reference	Variable (unit)	Intervention group	No of subjects	Baseline level of LVH
Cuspidi 2002 [8]	LVMI (g/m ²)	CAND ENAL	91 105	141±24 143±27
Dahlöf 2002 [12]	LVMI (g/m ²)	LOS ATEN	114 105	150±30 148±30
Okin 2003 [57]	ECG LVH (Cornell: mm x ms)	LOS ATEN	4 285 4 248	2 837±1 071 2 823±1 032

	Follow-up LVH	Within- group change	Within- group change in %	p-value	Between- group change	Between- group change in %
	126±? 130±?	-15.0±22.6 -13.2±23.4	-11 -9	<0.001 <0.001	-2 Reference	-2
	143±? 144±?	-6.6±20 -3.7±21	-4 -2	<0.001 NS	-3 Reference	-2
	2 547±1 077 2 700±1 147	-288 -125	-10.2 -4.4	<0.001 <0.001	-163 Reference	-6

Appendix 2, Table 4 Blood pressure changes in studies using echo- or electrocardiographic (ECG) methods.

Author Year Reference	Variable	Intervention group	No of subjects	Baseline level of SBP/DBP
Studies before 1993				
Steensgaard- Hansen 1988 [73]	Echo LVM	PINA NIF	12 10	DBP: 101±5 112±10
Dahlöf 1992 [10]	Echo LVMI	ENAL HCTZ	14 14	Mean BP: 112.7±3.5 110.1±2.5
Schulte 1992 [68]	Echo LVMI	NIF PERI	14 16	149±4/104±2 157±4/106±2
Studies 1993 to 2003				
Salcedo 1993 [63]	Echo LVMI	VERA Alpha-MET ATEN ENAL	15 15 15 15	184±16/97±9 177±11/103±6 172±21/102±8 184±25/104±14
Gonzalez- Fernandez 1993 [23]	Echo LVMI	CAPT PLAC	14 13	167±11/103±6 162±11/101±6
Senior 1993 [71]	Echo LVMI	HCTZ INDAP NIF INDAP ATE INDAP ENAL INDAP	20 20 19 22 12 17 9 9	DBP: 99.7±1.1 102.3±1.5 103.6±1.2 100.4±0.6 102.8±1.8 102.8±1.5 103.1±2.4 102.9±1.7
Gonzales- Juanatey 1994 [24]	Echo LVMI	VERA NITR	14 14	168±12/104±5 164±14/102±6

Follow-up SBP/DBP	Within- group change	Within- group change in %	p-value	Between- group change	Between- group change in %
<i>DBP:</i> 90±? 97±?	-11±15 -15±9	-11 -13	0.02 0.001	+4 Reference	+2
<i>Mean BP:</i> 96.9±2.8 101.5±2.0	-16 -8	-14 -7	<0.001 <0.006	-8 Reference	-7
140±4/92±3 136±3/93±2	-9/-12 -21/-13	-6/-12 -13/-13	<0.01 <0.01	+12/+1 Reference	+7/+1
154±8/87±11 156±25/88±13 149±18/88±7 158±23/87±9	-30/-10 -21/-15 -23/-14 -26/-17	-16/-10 -12/-15 -13/-14 -14/-16	<0.01 <0.01 <0.01 <0.01	- - - -	- - - -
136±10/85±5 160±8/100±16	-31/-18 -2/-1	-19/-18 -1/-1	<0.001 NS	-33/-17 Reference	-18/-17
<i>DBP:</i> 85.3±2.1 87.6±2.1 91.3±1.6 89.3±1.8 85.7±1.9 86.3±1.7 85.7±2.0 87.4±2.1	-14.4 -14.7 -12.3 -11.1 -17.1 -16.5 -17.4 -15.5	-14.4 -14.3 -11.9 -11.1 -16.6 -16.1 -16.9 -15.1	<0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001	+0.3 Reference -0.8 Reference -0.6 Reference -1.9 Reference	-0.1 Reference -0.8 Reference -0.5 Reference -1.8 Reference
134±8/84±4 133±8/88±5	-34/-10 -31/-14	-20/-10 -19/-14	<0.001 <0.001	-3/+4 Reference	-1/+4

The table continues on the next page.

Appendix 2, Table 4 continued

Author Year Reference	Variable	Intervention group	No of subjects	Baseline level of SBP/DBP
Jula 1994 [35]	Echo LVMI	Non-PH PLAC	38	149±15/98±6
			38	144±12/97±5
Wambach 1994 [81]	Echo LVMI	CELI ATEN	8	145±15/91±7
			8	150±16/95±10
Komsuoglu 1994 [39]	Echo LVMI	NITR VERA	16	180±6/111±4
			14	183±7/113±3
Henderson 1994 [31]	Echo LVM	CAPT PLAC	12	139±5/88±7
			14	137±9/92±7
Diez 1994 [16]	Echo LVMI	CAPT	30	126±1 (×BP)
		LISI	37	121±2 (×BP)
		QUIN	20	119±3 (×BP)
Machnig 1994 [48]	Echo LVMI	NITR	18	152±11/101±7
		CAPT	15	147±11/99±6
		NITR + CAPT	18	160±12/101±9
Agabiti-Rosei 1994 [2]	Echo LVMI	AMLO	12	170±21/104±6
		ENAL	12	162±18/105±16
Lièvre 1995 [46]	Echo LVMI	RAMI (1.5)	35	161±2/95±2
		RAMI (5)	33	161±2/95±2
		PLAC	35	166±3/95±2

	Follow-up SBP/DBP	Within- group change	Within- group change in %	p-value	Between- group change	Between- group change in %
	134±12/89±6 135±10/92±5	-15/-9 -9/-5	-10/-9 -6/-5	<0.001 <0.001	-6/-4 Reference	-4/-4
	136±12/86±5 132±15/83±7	-9/-5 -18/-12	-6/-5 -12/-13	NS <0.001	+9/+7 Reference	+6/+8
	156±6/91±1 152±5/93±2	-24/-20 -31/-20	-13/-18 -17/-18	<0.001 <0.001	+7/0 Reference	+4/0
	126±9/81±9 130±11/86±11	-13/-7 -7/-6	-9/-8 -5/-7	<0.01 <0.01	-6/-1 Reference	-4/-1
	112±1 (×BP) 103±1 (×BP) 105±3 (×BP)	-14 -18 -14	-11 -15 -12	<0.001 <0.001 <0.001	0 -4 Reference	+1 -3
	137±13/87±10 134±13/89±9 143±8/89±8	-15/-14 -13/-10 -17/-12	-10/-14 -9/-10 -11/-12	<0.05 <0.05 <0.05	Reference +2/+4 -2/+2	+1/+4 -1/+2
	137±9/85±3 142±12/86±8	-33/-19 -20/-19	-19/-18 -12/-18	<0.001 <0.01	-13/0 Reference	-7/0
	153±?/90±? 147±?/88±? 157±?/91±?	-8±2/-5±1 -12±2/-7±2 -9±2/-4±2	-5/-5 -8/-7 -5/-4	NS NS NS	+1/-1 -3/-3 Reference	0/-1 -3/-3

The table continues on the next page.

Appendix 2, Table 4 continued

Author Year Reference	Variable	Intervention group	No of subjects	Baseline level of SBP/DBP
Liebson 1995 [45]	Echo LVM (12 mo)	CHLT	111	??
		ACEB	103	??
		DOXA	113	??
		AMLO	100	??
		ENAL	105	??
		PLAC	186	??
Vyssoulis 1995 [83]	Echo LVMI	CELI	19	160±15/103±5
		METO	21	160±13/105±5
Kirpizidis 1995 [36]	Echo LVMI	FOSI	16	DBP: 103±7
		NIF	15	104±6
Rosatti 1995 [61]	Echo LVM	ATEN	10	172±6/96±4
		RAMI	11	175±5/100±6
Kohn 1995 [38]	Echo LVMI	ENAL	16	182±11/104±6
		LISI	15	182±12/103±5
Agabiti-Rosei 1995 [1]	Echo LVMI	RAMI	56	161±2/103±1
		ATEN	55	165±2/104±1
van Leeuwen 1995 [82]	Echo LVMI	LISI	20	161±?
				103±?
		DIL	16	155±? 102±?
Fogari 1995 [19]	Echo LVMI	LISI	15	157±7/97±5
		HYDR	15	157±7/97±4
Grandi 1995 [28]	Echo LVMI	ISRA	18	155±8/106±7
		PERI	18	156±7/105±6

Follow-up SBP/DBP	Within- group change	Within- group change in %	p-value	Between- group change	Between- group change in %
??	-11.7/-12.3	??	<0.001	-9/-3 (vs P)	??
??	-17.0/-13.1	??	<0.001	-8/-4 (vs P)	??
??	-14.2/-11.7	??	<0.001	-5/-3 (vs P)	??
??	-15.6/-12.9	??	<0.001	-7/-4 (vs P)	??
??	-14.7/-11.5	??	<0.001	-6/-3 (vs P)	??
??	-9.1/-8.6	??	<0.01	Reference	??
132±14/87±6	-18/-16	-17±9/	<0.001	-3/0	-1/+1
135±11/87±5	-15/-18	-16±9 -16±6/ -17±5	<0.001	Reference	
DBP:					
85±6	-18	-17	<0.001	-3	-3
89±5	-15	-14	<0.001	Reference	
145±4/81±3	-27/-15	-16/-14	<0.05	Reference	
146±4/87±3	-29/-13	-17/-13	<0.05	-2/+2	-1/+1
151±?/90±?	-31/-14	-17/-13	<0.05	+3/-1	+2/+2
148±?/88±?	-34/-15	-19/-15	<0.05	Reference	
140±2/86±1	-21/-17	-13/-17	<0.001	0/+1	0/0
144±1/86±1	-21/-18	-13/-17	<0.001	Reference	
137±?	-23 (-29 to -17)	-15	<0.001	-10	-6
89±?	-15 (-18 to -12)	-14		-2	-2
141±?	-14 (-21 to -7)	-9	<0.05	Reference	
90±?	-12 (-15 to -9)	-12			
141±6/88±6	-16/-9	-10/-9	<0.001	+3/+1	+2/+1
138±6/87±5	-19/-10	-12/-10	<0.001	Reference	
135±6/92±6	-20/-14	-13.1/-13.3	<0.001	Reference	
136±7/91±5	-20/-14	-12.8/-13.1	<0.001	0/0	0/0

The table continues on the next page.

Appendix 2, Table 4 continued

Author Year Reference	Variable	Intervention group	No of subjects	Baseline level of SBP/DBP
Leenen 1996 [44]	Echo LVMI	DIL AMLO	13	24-h BP: 157±4/103±2
			17	158±3/102±2
Schobel 1996 [67]	Echo LVMI	BUNA METO	23	144±12/92±9
			20	145±15/92±5
Gottdiener 1997 [27]	Echo LVM	ATEN	36	SBP: 147±11
		CAPT	40	148±14
		CLON	36	151±14
		DIL	52	152±12
		HCTZ	38	152±14
		PRAZ	28	153±14
Sumimoto 1997 [74]	Echo LVMI	ALA	10	168±22/99±6
		NIC	10	176±14/97±5
Scognamiglio 1997 [70]	Echo LVMI	NITR	37	167±18/101±5
		CAPT	36	165±13/100±5
Lacourciere 1997 [42]	Echo LVM	HCTZ	7	163±8/96±1
		AMLO	18	166±4/99±1
		HCTZ + AMLO	13	164±4/101±1
Giugliano 1997 [22]	Echo LVMI	CARVE	23	161±13/99±5
		ATEN	22	163±14/98±4
Kribben 1997 [40]	ECG LVH	HCTZ ATEN NITR ENAL	No ind data	No individual data
Fagard 1997 [18]	Echo LVM	HCTZ +	11	163±14/104±9
		TRIA TRAN	14	168±20/111±13

Follow-up SBP/DBP	Within- group change	Within- group change in %	p-value	Between- group change	Between- group change in %
24-h BP:					
143±?/93±?	-14±3/-10±2	-9/-10	<0.001	Reference	
137±?/89±?	-21±3/-13±2	-13/-13	<0.001	-7/-3	-4/-3
133±11/83±5	-11±11/-9±8	-8/-10	<0.05	0/-1	0/-1
134±17/84±8	-11±12/-8±9	-8/-9	<0.05	Reference	
SBP:					
137±?	-9.5±13.1	-7	<0.001	Reference	
141±?	-7.2±14.8	-5	0.004	+3	+2
138±?	-12.6±12.0	-9	<0.001	-3	-2
139±?	-13.2±9.3	-9	<0.001	-3	-2
136±?	-15.5±10.8	-11	<0.001	-6	-4
142±?	-11.3±9.5	-7	<0.001	-1	0
140±13/87±11	-28/-12	-17/-12	<0.01	+6/+7	+2/+7
142±13/78±7	-34/-19	-19/-19	<0.01	Reference	
143±9/87±5	-24/-14	-14/-14	<0.05	-6/-2	-3/-2
147±12/88±4	-18/-12	-11/-12	<0.05	Reference	
150±3/86±1	-13/-10	-8/-10	<0.01	Reference	
150±2/87±1	-16/-12	-10/-12	<0.01	-3/-2	-2/-2
140±2/88±1	-24/-13	-15/-13	<0.01	-9/-3	-7/-3
148±?/88±?	-13±4/-11±4	-8/-11	<0.001	-3/-1	-1/-1
151±?/88±?	-12±4/-10±3	-7/-10	<0.001	Reference	
No individual data					
136±?/90±?	-27±9/-14±7	-17/-13	<0.001	Reference	
141±?/91±?	-27±16/-20±11	-16/-18	<0.001	0/-6	+1/-5

The table continues on the next page.

Appendix 2, Table 4 continued

Author Year Reference	Variable	Intervention group	No of subjects	Baseline level of SBP/DBP
Lombardo 1997 [47]	Echo LVMI	FOSI AMLO	12	24-h BP: 141±13/95±7
			12	137±8/91±8
Schmieder 1997 [64]	Echo LVMI	BUNA METO	20	24-h BP: 144±12/92±9
			16	148±14/96±7
Papademetriou 1997 [58]	Echo LVMI	HCTZ ISRA	45	161±17/101±6
			89	158±16/101±7
Ueno 1997 [80]	Echo LVMI	NILV TEMO CADR	12	174±10/104±7
			12	173±18/103±8
			12	171±16/103±7
Ofili 1998 [56]	Echo LVMI	CHLT PLAC	47	169±11/79±8
			47	172±13/79±8
Cuspidi 1998 [9]	Echo LVMI	LOS VERA	8	149±11/99±4
			9	156±13/103±7
Laufer 1998 [43]	Echo LVM	ATEN CAPT	13	153±10/102±6
			15	154±13/101±5
Roman 1998 [60]	Echo LVMI	HCTZ RAMI	28	24-h BP: 146±?/93±?
			22	153±?/96±?
Höglund 1998 [33]	Echo LVMI	MIBE ATEN	31	163±14/103±6
			29	163±18/103±6
Tedesco 1998 [75]	Echo LVM	HCTZ LOS	28	24-h BP: 156±11/96±8
			42	155±9/95±7

Follow-up SBP/DBP	Within- group change	Within- group change in %	p-value	Between- group change	Between- group change in %
24-h BP: 123±9/81±4 121±6/81±4	-18/-14 -16/-10	-13/-15 -12/-11	<0.001 <0.001	-2/-4 Reference	-1/-4
24-h BP: 135±17/85±6 135±17/84±8	-9/-7 -13/-12	-6/-8 -9/-13	<0.01 <0.01	+4/+5 Reference	+3/+5
136±?/88±? 140±?/89±?	-25±17/-13±7 -18±16/-12±9	-15/-13 -11/-12	<0.001 <0.001	-7/-1 Reference	-4/-1
141±12/87±8 140±5/86±6 140±7/84±7	-33/-17 -33/-17 -31/-19	-19/-16 -19/-17 -18/-18	<0.01 <0.01 <0.01	-2/+2 -2/+2 Reference	-1/+2 -1/+1
144±14/62±8 163±21/75±9	-25/-17 -9/-4	-14/-18 -8/-5	<0.001 <0.05	-16/-13 Reference	-6/-17
132±13/89±5 141±14/90±6	-17/-10 -15/-13	-11/-10 -10/-13	<0.05 <0.05	-2/+3 Reference	-1/+3
132±?/85±? 140±?/88±?	-21/-17 -14/-13	-14/-17 -9/-13	<0.001 <0.001	-7/-4 Reference	-5/-4
24-h BP: 132±?/84±? 147±?/91±?	-14/-9 -6/-5	-10/-10 -4/-5	<0.001 <0.001	Reference +8/+4	+6/+5
145±15/89±7 152±23/93±9	-18±14/-14±7 -11±19/-11±9	-11/-14 -7/-10	<0.001 <0.001	-7/-4 Reference	-4/-4
24-h BP: 145±13/89±12 133±11/84±6	-11/-7 -22/-11	-7/-7 -14/-11	<0.01 <0.001	Reference -11/-4	-7/-4

The table continues on the next page.

Appendix 2, Table 4 continued

Author Year Reference	Variable	Intervention group	No of subjects	Baseline level of SBP/DBP
Sadowski 1998 [62]	Echo LVMI	RILM	24	164±20/103±5
		NIF	32	158±20/103±5
Beltman 1998 [4]	Echo LVMI	AMLO	28	158±16/102±5
		LISI	31	161±15/100±4
Sihm 1998 [72]	Echo LVM	ISRA	25	174±17/111±7
		HCTZ + Amilor	25	168±14/109±7
Heesen 1998 [29]	Echo LVMI	QUIN	21	179±5/90±2
		HCTZ/ TRIA	23	178±5/90±2
Molinero 1998 [54]	Echo LVMI	VERA	11	169±8/101±6
		HCTZ + Amilor	15	168±13/103±3
Manolis 1998 [51]	Echo LVMI	ISRA	10	157±14/103±6
		SPIR	11	153±13/100±4
		ISRA + SPIR	14	164±19/105±7
Gaudio 1998 [20]	Echo LVMI	BENA	22	155±11/102±3
		NITR	22	159±12/102±3
Gerritsen 1998 [21]	Echo LVMI	NITR	37	168±18/90±9
		ENAL	38	165±15/92±8
		PLAC	34	166±18/93±8
Thürmann 1999 [77]	Echo LVMI	ATEN	29	160±14/103±6
		VALS	29	163±12/101±6
Gosse 1999 [25]	Echo LVMI	BISO	23	174±10/99±6
		VERA	24	168±11/101±5

	Follow-up SBP/DBP	Within- group change	Within- group change in %	p-value	Between- group change	Between- group change in %
	149±15/89±7 136±13/86±8	-15/-14 -22/-17	-9/-14 -14/-17	<0.001 <0.001	Reference -7/-3	-5/-3
	143±?/90±? 146±?/91±?	-16±17/-13±8 -17±14/-9±6	-9/-12 -10/-9	<0.05 <0.05	Reference -1/+3	-1/+3
	133±13/85±9 128±12/85±6	-41/-26 -40/-24	-24/-23 -24/-22	<0.001 <0.001	-1/-2 Reference	0/-1
	156±7/87±4 153±6/86±4	-26/-3 -25/-4	-15/-3 -14/-4	<0.001 <0.001	-1/+1 Reference	-1/+1
	157±9/89±4 159±9/94±4	-12/-12 -9/-9	-7/-12 -5/-9	<0.001 <0.001	-3/-3 Reference	-2/-3
	137±13/89±8 138±16/87±8 134±17/81±8	-20/-14 -15/-13 -30/-24	-13/-13 -10/-13 -18/-23	<0.001 <0.001 <0.001	-5/-1 Reference -15/-10	-3/0 Reference -8/-10
	137±8/83±4 136±6/85±3	-18/-19 -23/-17	-12/-19 -14/-17	<0.001 <0.001	+5/-2 Reference	+2/-2
	153±?/81±? 154±2/84±? 163±?/89±?	-15 ±/-9±2 -11±2/-8±1 -3±2/-4±1	-9/-10 -7/-9 -2/-4	<0.01 <0.01 NS	-12/-5 -8/-4 Reference	-7/-6 -5/-5
	147±18/90±7 146±13/90±7	-13/-13 -17/-11	-8/-13 -10/-11	<0.001 <0.001	Reference -4/-2	-2/-2
	150±?/92±? 152±?/94±?	-24/-7 -16/-7	-14/-7 -10/-7	<0.001 <0.001	-8/0 Reference	-4/0

The table continues on the next page.

Appendix 2, Table 4 continued

Author Year Reference	Variable	Intervention group	No of subjects	Baseline level of SBP/DBP
Modena 1999 [53]	Echo LVMI	17-beta- Estradiol PLAC	82 79	157±13/94±7 156±13/93±5
Diamond 1999 [15]	Echo LVMI	ENAL EPRO	8 9	153±11/99±10 154±11/97±11
Topouchian 1999 [79]	Echo LVMI	VERA TRAN VERA + TRAN	21 18 20	156±12/96±7 160±15/101±7 163±16/100±6
Avanza 2000 [3]	Echo LVMI	ENAL LOS ENAL + LOS	15 15 16	173±3/104±2 170±2/103±2 173±3/104±2
Gosse 2000 [26]	Echo LVMI	ENAL INDAP	206 205	172±11/102±7 172±11/101±7
Kuperstein 2000 [41]	Echo LVMI	PERI ATEN	10 11	148±9/97±3 149±13/98±4
Brilla 2000 [6]	Echo LVMI	LISI HCTZ	11 14	24-h BP: 137±5/86±4 136±4/80±2
Terpstra 2001 [76]	Echo LVMI	AMLO LISI	61 63	175±15/92±8 175±14/93±9
Malmqvist 2001 [50]	Echo LVMI	CAPT METO	22 25	24-h BP: 150±10/96±7 150±13/96±7

Follow-up SBP/DBP	Within- group change	Within- group change in %	p-value	Between- group change	Between- group change in %
129±7/75±7	-28/-19	-18/-20	<0.001	-2/0	-3/0
130±7/74±7	-26/-19	-15/-20	<0.001	Reference	
133±11/89±14	-20/-10	-12/-10	<0.001	-3/-2	-2/-2
137±12/89±14	-17/-8	-11/-8	<0.001	Reference	
137±17/86±10	-19/-10	-12±9/	<0.01	0/+1	0/+1
141±15/90±11	-19/-11	-10±9	<0.01	Reference	Reference
137±19/84±9	-26/-16	-12±8/ -11±8 -16±9/ -15±10	<0.01	-7/-5	-4/-5
145±?/87±?	-28/-17	-16/-16	<0.05	-6/-5	-3/-4
148±?/91±?	-22/-12	-13/-12	<0.05	Reference	
144±?/87±?	-29/-17	-17/-16	<0.05	-7/-5	-4/-4
147±?/89±?	-25±17/-12±10	-15/-13	<0.001	Reference	
147±?/88±?	-25±16/-13±10	-15/-13	<0.001	0/0	0/0
129±10/81±5	-19/-16	-13/-16	0.002	+3/0	+2/0
127±8/82±6	-22/-16	-15/-16	0.002	Reference	
24-h BP: 136±6/84±4	-1/-2	-1/-2	NS	+4/-1	+3/-1
131±3/79±3	-5/-1	-4/-1	NS	Reference	
148±16/83±6	-27/-9	-15/-10	<0.001	Reference	
149±17/87±8	-26/-6	-15/-6	<0.001	+1/+3	0/-4
24-h BP: 133±?/86±?	-17±12 -10±8	-11/-10	<0.001	0 +1	0 +1
133±?/85±?	-17±13/-11±10	-11/-11	<0.001	Reference	

The table continues on the next page.

Appendix 2, Table 4 continued

Author Year Reference	Variable	Intervention group	No of subjects	Baseline level of SBP/DBP
Malmqvist 2001 [49]	Echo LVMI	IRBE ATEN	47 53	165±18/105±7 159±20/102±8
Mathew 2001 [52]	ECG LVH	RAMI PLAC	4 135 4 146	321 (7.8%) 355 (8.6%)
Black 2001 [5]	Echo LVMI	FELO PLAC	54 57	149±7/83±6 150±8/84±6
Devereux 2001 [14]	Echo LVMI	NIF ENAL	122 113	171±21/98±10 172±21/98±10
Novo 2001 [55]	Echo LVMI	ENAL HCTZ ATEN VERA	10 10 13 13	160±10/ 106±7 153±10/104±8 158±11/104±5 158±10/102±5
Pontremoli 2001 [59]	Echo LVMI	LISI NIF	16 15	161±4/105±2 161±4/102±2
Heesen 2001 [30]	Echo LVMI	LISI PLAC	30 32	175±15/87±8 174±16/87±9
Schussheim 2001 [69]	Echo LVM	VERA NIF	14 15	164±3/103±2 174±4/105±2
Hinderliter 2002 [32]	Echo LVMI	Exercise + weight control Exercise only Control group	36 27 19	142±11/93±5 137±7/94±4 143±11/94±5
De Rosa 2002 [13]	Echo LVMI	LOS ENAL	22 20	155±?/103±? 159±?/102±?

Follow-up SBP/DBP	Within- group change	Within- group change in %	p-value	Between- group change	Between- group change in %
137±?/86±? 138±?/86±?	-28±3/-19±1 -21±2/-16±1	-17 /-18 -13/-16	<0.001 <0.001	-7/-3 Reference	-4/-2
336 (8.1%) 406 (9.8%)	+15 +54	+0.3 +1.2		-39 Reference	-0.9
137±?/80±? 148±?/84±?	-12±12/-3±7 -2±14/0.1±9	-8/-4 -1/0	<0.01 NS	-14/-3 Reference	-7/-4
150±?/85±? 150±?/86±?	-21±23/-13±11 -22±24/-12±11	-12/-13 -13/-12	<0.001 <0.001	+1/-1 Reference	+1/-1
130±12/85±8 135±12/88±8 131±12/84±8 139±12/88±6	-30/-21 -18/-16 -27/-20 -19/-14	-19/-20 -12/-15 -17/-19 -12/-14	<0.001 <0.01 <0.001 <0.01	-12/-5 Reference -9/-4 -1/+2	-7/-5 -5/-4 0/+1
135±2/87±1 138±2/87±2	-26/-18 -23/-15	-16/-17 -14/-15	<0.001 <0.001	-3/-3 Reference	-2/-2
161±16/81±7 163±17/80±9	-16/-6 -11/-7	-9/-7 -6/-8	<0.001 <0.001	-5/+1 Reference	-3/+1
143±4/91±2 151±5/90±3	-21/-14 -23/-15	-13/-14 -13/-14	<0.01 <0.01	+2/+1 Reference	0/0
134/88 136/89 139/92	-8/-5 -1/-5 -4/-2	-6/-5 -1/-5 -3/-2	NS NS NS	-3/-3 +3/-3	-3/-3 +2/-3
140±?/92±? 144±?/91±?	-15 (-23 to -6) -11 (-14 to -8) -11 (-28 to -2) -15 (-14 to -8)	-10 -11 -10 -11	<0.001 <0.001	0 0 Reference	0 0

The table continues on the next page.

Appendix 2, Table 4 *continued*

Author Year Reference	Variable	Intervention group	No of subjects	Baseline level of SBP/DBP
Cuspidi 2002 [8]	Echo LVMI	CAND ENAL	91 105	163±10/102±4 162±9/101±4
Dahlöf 2002 [12]	Echo LVMI	LOS ATEN	114 105	149±30/98±9 148±31/99±8
Okin 2003 [57]	ECG LVH	LOS ATEN	4 285 4 248	174±14/98±9 174±14/98±9

	Follow-up SBP/DBP	Within- group change	Within- group change in %	p-value	Between- group change	Between- group change in %
	135±?/86±?	-28±13/-16±7	-17/-16	<0.001	-1/0	0/0
	136±?/85±?	-27±12/-16±7	-17/-16	<0.001	Reference	
	141±13/87±9	-8/-11	-5/-11	<0.001	0/+2	0/+3
	141±17/85±10	-7/-14	-5/-14	<0.001	Reference	
	144±16/81±9	-30/-17	-17/-17	<0.001	-1/0	0/0
	145±17/81±9	-29/-17	-17/-17	<0.001	Reference	Reference

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Abbreviations for Appendix 3, Tables 1–13

BMI	=	Body mass index
CHD	=	Coronary heart disease
CV	=	Cardiovascular
CVD	=	Cardiovascular disease
DBP	=	Diastolic blood pressure
ECG	=	Electrocardiography
LVH	=	Left ventricular hypertrophy
SBP	=	Systolic blood pressure
Rx	=	Prescribed therapy
TIA	=	Transitoric ischemic attack

Appendix 3, Table 1
MRFIT [2,3,7,10,13,16]

	Incidence per 1,000 patient years		Relative benefit, %	Absolute benefit, number of prevented cases per 1,000 patient years
	Active	Control		
Mortality in coronary heart disease				
DBP (without Rx)				
90–99	2.6	2.2	–18	–0.4
≥100	2.8	4.3	39	1.5
Cholesterol				
<6.5 mmol/L	2.3	2.8	18	0.5
≥6.5 mmol/L	3.4	2.9	–19	–0.5
BMI				
<25	2.7	2.8	4	0.1
25–30.5	2.7	2.9	7	0.2
>30.5	3.8	2.8	–36	–1.0
Smoking				
No	2.0	2.4	18	0.4
Yes	3.6	3.2	–12	–0.4
ECG-changes during rest or exercise				
No	2.2	2.3	3	0.1
Yes	3.3	3.6	9	0.3
Chol <6.5 + Non-smokers*	0.5	2.5	82	2.0
Chol ≥6.5 + Non-smokers*	2.8	2.3	–18	–0.5
Chol <6.5 + Smokers*	3.1	2.9	–5	–0.2
Chol ≥6.5 + Smokers*	4.3	3.6	–21	–0.7

* The greatest benefit of treatment was observed in patients with normal cholesterol who did not smoke. Only men included in the study.

	Number needed to treat to prevent 1 endpoint per year	Probability to remain free from endpoint during 1 year		Probability to remain free from endpoint during 5 years	
		Active	Control	Active	Control
	–	99.7	99.8	98.7	98.9
	667	99.7	99.6	98.6	97.9
	2 000	99.8	99.7	98.9	98.6
	–	99.7	99.7	98.3	98.6
	10 000	99.7	99.7	98.7	98.6
	5 000	99.7	99.7	98.7	98.6
	–	99.6	99.7	98.1	98.4
	2 500	99.8	99.7	99.0	98.8
	–	99.6	99.7	98.2	98.4
	10 000	99.8	99.8	98.9	98.9
	3 333	99.7	99.6	98.4	98.2
	500	99.9	99.7	99.8	98.8
	–	99.7	99.8	98.6	98.9
	–	99.7	99.7	98.5	98.6
	–	99.6	99.6	97.8	98.2

The table continues on the next page.

Appendix 3, Table 1 *continued*
MRFIT [2,3,7,10,13,16]

	Incidence per 1,000 patient years		Relative benefit, %	Absolute benefit, number of prevented cases per 1,000 patient years
	Active	Control		
Morbidity in coronary heart disease				
DBP (without Rx)				0.6
90–99	8.6	9.2	7	1.5
≥100	9.1	10.6	14	
Cholesterol*				
<6.5 mmol/L	7.7	8.9	13	1.2
≥6.5 mmol/L	10.4	10.9	5	0.5
Smoking				
No	7.3	8.8	17	1.5
Yes	10.5	10.8	3	0.3

* The greatest benefit of treatment was observed in patients with normal cholesterol who did not smoke. Only men included in the study.

	Number needed to treat to prevent 1 endpoint per year	Probability to remain free from endpoint during 1 year		Probability to remain free from endpoint during 5 years	
		Active	Control	Active	Control
	1 667	99.1	99.4	95.7	96.8
	667	99.1	98.9	95.5	94.7
	834	99.2	99.1	96.2	95.6
	2 000	99.0	98.9	94.8	94.6
	667	99.3	99.1	96.4	95.6
	3 334	99.0	98.9	94.8	94.6

Appendix 3, Table 2
MRC – Older [9]

	Incidence per 1,000 patient years		Relative benefit, %	Absolute benefit, number of prevented cases per 1,000 patient years
	Active	Control		
Cardiovascular morbidity				
Age				
65–74	21.0	25.2	17	4.2
Sex				
Men	29.1	36.9	21	7.8
Women	15.7	17.3	9	1.6
Smoking				
No	17.0	23.3	27	6.3
Yes	37.0	32.2	–15	–4.8

	Number needed to treat to prevent 1 endpoint per year	Probability to remain free from endpoint during 1 year		Probability to remain free from endpoint during 5 years	
		Active	Control	Active	Control
	239	97.9	97.5	89.5	87.4
	129	97.1	96.3	85.4	81.6
	625	98.4	98.3	92.1	91.4
	159	98.3	97.7	91.5	88.4
	—	96.3	96.8	81.5	83.9

Appendix 3, Table 3
MRC [4,12,24]

	Incidence per 1,000 patient years		Relative benefit, %	Absolute benefit, number of prevented cases per 1,000 patient years
	Active	Control		
Cardiovascular morbidity (only CHD, stroke and CVD; angina pectoris, TIA and ECG abnormalities not included), and stroke morbidity [12,24]				
Age				
35–54	0.8	1.4	43	0.6
55–64	2.3	4.2	45	1.9
Sex				
Men	10.2	12.3	19	2.1
Women	2.9	3.9	26	1.0
SBP				
<160	1.0	1.6	38	0.6
≥160	1.7	3.2	47	1.5
DBP				
<100	1.3	1.9	32	0.6
≥100	1.5	3.8	61	2.3
Smoking				
No	4.5	6.3	29	1.8
Yes	12.2	13.2	8	1.0

Results reported for age and blood pressures are only valid for stroke incidence

	Number needed to treat to prevent 1 endpoint per year	Probability to remain free from endpoint during 1 year		Probability to remain free from endpoint during 5 years	
		Active	Control	Active	Control
	1 667	99.9	99.9	99.6	99.3
	527	99.8	99.6	98.8	97.9
	477	99.0	98.8	94.9	93.9
	1 000	99.7	99.6	98.6	98.0
	1 667	99.9	99.8	99.5	99.2
	667	99.8	99.7	99.2	98.4
	1 667	99.9	99.8	99.4	99.1
	434	99.9	99.6	99.2	98.1
	555	99.6	99.4	97.8	96.9
	1 000	98.8	98.7	93.9	93.4

The table continues on the next page.

Appendix 3, Table 3 *continued*
MRC [4,12,24]

	Incidence per 1,000 patient years		Relative benefit, %	Absolute benefit, number of prevented cases per 1,000 patient years
	Active	Control		
Morbidity in coronary heart disease [4,12,24]				
Age				
35–54	2.9	3.4	15	0.5
55–64	7.4	8.0	8	0.6
Sex				
Men	8.3	9.0	8	0.7
Women	1.8	1.7	–6	–0.1
SBP				
<160	4.2	4.3	2	0.1
≥160	6.3	6.8	7	0.5
Cholesterol				
<6.5 mmol/L	3.7	4.4	16	0.7
≥6.5 mmol/L	7.1	6.6	–8	–0.5
Smoking				
No	3.5	4.3	19	0.8
Yes	9.0	8.1	–11	–0.9
Ischemic ECG				
No	4.9	5.0	2	0.1
Yes	8.3	11.9	30	3.6

Incidence rate approximately calculated from the mean values of the whole study population and reported incidence rates in some subgroups

	Number needed to treat to prevent 1 endpoint per year	Probability to remain free from endpoint during 1 year		Probability to remain free from endpoint during 5 years	
		Active	Control	Active	Control
	2 000 1 667	99.7 99.3	99.7 99.2	98.6 97.7	98.3 96.0
	1 429 –	99.2 99.8	99.1 99.8	95.9 99.1	95.5 99.2
	1 000 2 000	99.6 99.5	99.6 99.3	97.9 96.9	97.8 96.6
	1 429 –	99.6 99.3	99.6 99.3	98.2 96.4	97.8 96.7
	1 250 –	99.7 99.1	99.6 99.2	98.2 95.3	99.2 95.8
	10 000 278	99.5 99.2	99.5 98.8	97.6 95.9	97.5 94.0

Appendix 3, Table 4
ANBPS [1,15]

	Incidence per 1,000 patient years		Relative benefit, %	Absolute benefit, number of prevented cases per 1,000 patient years
	Active	Control		
All cause mortality and cardiovascular morbidity				
Age				
30–49	9.4	14.0	23	4.6
50–69	23.4	32.3	28	8.9
Sex				
Men	19.8	27.2	27	7.4
Women	12.6	19.6	36	7.0
SBP				
<160	11.0	20.6	47	9.6
≥160	25.2	30.1	16	4.9
DBP				
95–99	15.6	22.3	30	6.7
100–104	17.5	24.5	28	7.0
105–109	20.7	30.5	32	9.8
Cholesterol				
<5.7 mmol/L	11.0	24.6	55	13.6
≥5.7 mmol/L	21.3	24.4	13	3.1
BMI				
<26	18.1	28.3	36	10.2
≥26	16.5	21.2	22	4.7
Smoking				
No	15.4	21.1	27	5.7
Yes	23.4	35.7	34	12.3

	Number need- ed to treat to prevent 1 endpoint per year	Probability to remain free from endpoint during 1 year		Probability to remain free from endpoint during 5 years	
		Active	Control	Active	Control
	218	99.1	98.6	95.3	93.0
	113	97.7	96.8	88.3	83.9
	135	98.0	97.3	90.1	86.4
	143	98.7	98.0	93.7	90.2
	104	98.9	97.9	94.5	89.7
	205	97.5	97.0	87.4	85.0
	150	98.4	97.8	92.2	88.9
	143	98.3	97.6	91.2	87.8
	102	97.9	97.0	89.7	84.8
	74	98.9	97.5	94.5	87.7
	323	97.9	97.6	89.4	87.8
	98	98.2	97.2	91.0	85.9
	213	98.4	97.9	91.8	89.4
	176	98.5	97.9	92.3	89.5
	82	97.7	96.4	88.3	82.2

The table continues on the next page.

Appendix 3, Table 4 *continued*
ANBPS [1,15]

	Incidence per 1,000 patient years		Relative benefit, %	Absolute benefit, number of prevented cases per 1,000 patient years
	Active	Control		
Smoking men*				
BMI <26	34.5	50.0	31	15.5
BMI ≥26	24.1	27.0	11	2.9
Smoking women*				
BMI <26	10.8	56.6	81	46.8
BMI ≥26	7.2	10.8	33	3.6

* The greatest benefit of treatment was observed in smokers (men and women) with low BMI

	Number need- ed to treat to prevent 1 endpoint per year	Probability to remain free from endpoint during 1 year		Probability to remain free from endpoint during 5 years	
		Active	Control	Active	Control
	65	96.6	95.0	82.8	75.0
	345	97.6	97.3	88.0	86.5
	22	98.0	94.3	94.6	71.7
	278	99.3	98.9	96.4	94.6

Appendix 3, Table 5
EWPHE [17–19]

	Incidence per 1,000 patient years		Relative benefit, %	Absolute benefit, number of prevented cases per 1,000 patient years
	Active	Control		
Cardiovascular morbidity				
Age				
60–69	14	31	53	17
70–97	66	111	41	45
Sex				
Men	40	72	44	32
Women	37	66	44	29
Smoking				
No	38	67	43	29
Yes	37	76	51	39
Previous CVD				
No	25	50	49	25
Yes	64	106	39	42
Cardiovascular mortality				
Age				
60–69	12	19	38	7
70–79	35	65	46	30
80–97	140	130	–8	–10
Sex				
Men	28	52	47	24
Women	37	45	18	8
SBP				
<180	23	32	28	9
≥180	43	64	33	21

	Number need- ed to treat to prevent 1 endpoint per year	Probability to remain free from endpoint during 1 year		Probability to remain free from endpoint during 5 years	
		Active	Control	Active	Control
	59	98.6	96.9	93.0	84.5
	23	93.4	88.9	67.0	44.5
	32	96.0	92.8	80.0	64.0
	35	96.3	93.4	81.5	67.0
	35	96.2	93.3	81.0	66.5
	26	96.3	92.4	81.5	62.0
	40	97.5	95.0	87.5	75.0
	24	93.6	89.4	68.0	47.0
	143	98.8	98.1	94.0	90.5
	34	96.5	93.5	82.5	67.5
	—	86.0	87.0	30.0	35.0
	42	97.2	94.8	86.0	74.0
	125	96.3	95.5	81.5	77.5
	112	97.7	96.8	88.5	84.0
	48	95.7	93.6	78.5	68.0

The table continues on the next page.

Appendix 3, Table 5 *continued*
 EWPHE [17–19]

	Incidence per 1,000 patient years		Relative benefit, %	Absolute benefit, number of prevented cases per 1,000 patient years
	Active	Control		
DBP				
90–99	40	64	38	24
100–119	39	82	52	43
Smoking				
No	36	46	22	10
Yes	27	54	50	27
Previous CVD				
No	27	37	27	10
Yes	50	68	27	18
Women <70 yrs*	12	21	43	9
Women ≥70 yrs*	66	61	8	5

* The lowest benefit of treatment was observed in females over 70 years at entry with and without cardiovascular complications at entry

	Number need- ed to treat to prevent 1 endpoint per year	Probability to remain free from endpoint during 1 year		Probability to remain free from endpoint during 5 years	
		Active	Control	Active	Control
	42	96.0	93.6	80.0	68.0
	23	96.1	91.8	80.5	59.0
	100	96.4	95.4	82.0	77.0
	38	97.3	94.6	86.5	73.0
	100	97.3	96.3	86.5	81.5
	56	95.0	93.2	75.0	66.0
	112	98.8	97.9	94.0	89.5
	200	94.4	93.9	72.0	69.5

Appendix 3, Table 6
HEP [20]

	Incidence per 1,000 patient years		Relative benefit, %	Absolute benefit, number of prevented cases per 1,000 patient years
	Active	Control		
Stroke morbidity				
Age				
60–69	7.5	14.3	48	6.8
70–79	18.7	34.4	46	15.7
Sex				
Men	16.8	31.9	47	15.1
Women	10.7	16.5	35	5.8

	Number need- ed to treat to prevent 1 endpoint per year	Probability to remain free from endpoint during 1 year		Probability to remain free from endpoint during 5 years	
		Active	Control	Active	Control
	148	99.2	98.5	96.3	92.9
	64	98.1	96.6	90.7	82.8
	67	98.3	96.8	91.6	84.0
	173	98.9	98.4	94.7	91.8

Appendix 3, Table 7
HDFP [8]

	Incidence per 1,000 patient years		Relative benefit, %	Absolute benefit, number of prevented cases per 1,000 patient years
	Active	Control		
Stroke morbidity				
Age*				
30–49	2.2	3.0	27	0.8
50–59	4.4	6.2	29	1.8
60–69	6.0	11.0	46	5.0
Sex				
White men	2.9	5.1	43	2.2
White women	3.2	4.5	29	1.3
DBP**				
90–104	3.0	4.4	32	1.4
105–114	4.8	7.4	35	2.6
≥115	7.0	12.8	45	5.8
Organ damage**				
No	2.6	4.4	41	1.8
Yes	10.0	12.6	21	2.6

* Incidence rates adjusted for race, sex and blood pressure

** Incidence rates adjusted for age, race and sex

	Number needed to treat to prevent 1 endpoint per year	Probability to remain free from endpoint during 1 year		Probability to remain free from endpoint during 5 years	
		Active	Control	Active	Control
	1 250	99.8	99.7	98.9	98.5
	556	99.6	99.4	97.8	96.9
	200	99.4	98.9	97.0	94.5
	455	99.7	99.5	98.6	97.5
	770	99.7	99.5	98.4	97.8
	714	99.7	99.6	98.5	97.8
	385	99.5	99.3	97.6	96.3
	173	99.3	98.7	96.5	93.6
	556	99.7	99.6	98.7	97.8
	385	99.0	98.7	95.0	93.7

The table continues on the next page.

Appendix 3, Table 7 continued

90–104 mm Hg DBT and no antihypertensive treatment = mild hypertension [11]

	Incidence per 1,000 patient years		Relative benefit, %	Absolute benefit, number of prevented cases per 1,000 patient years
	Active	Control		
Total mortality				
DBP				
90–99	9.4	12.6	25	3.2
100–104	14.0	14.8	5	0.8
Cholesterol*				
<6.5 mmol/L	11.3	14.4	27	3.1
≥6.5 mmol/L	10.6	15.5	32	4.9
BMI**				
<24	14.6	22.7	36	8.1
24–29	9.9	13.9	29	4.0
>29	10.0	11.0	9	1.0
Smoking*				2.7
No	8.2	10.9	25	3.2
Yes	16.1	19.2	16	
Diabetes mellitus*				
No	11.2	14.2	21	3.0
Yes	11.6	15.8	27	4.2

* Incidence rates adjusted for race, sex and blood pressure

** The high mortality in patients with low BMI was due to smoking [26]

	Number needed to treat to prevent 1 endpoint per year	Probability to remain free from endpoint during 1 year		Probability to remain free from endpoint during 5 years	
		Active	Control	Active	Control
	313	99.1	98.7	95.3	93.7
	1 250	98.6	98.5	93.0	92.6
	323	98.9	98.6	94.3	92.8
	205	98.9	98.5	94.7	92.3
	124	98.5	97.7	92.7	88.7
	250	99.0	98.6	95.0	93.0
	1 000	99.0	98.9	95.0	94.5
	371	99.2	98.9	95.9	94.5
	313	98.4	98.1	91.9	90.4
	334	98.9	98.6	94.8	93.5
	239	98.8	98.4	94.2	92.1

Appendix 3, Table 8
VA II [5,6,25]

	Incidence per 1,000 patient years		Relative benefit, %	Absolute benefit, number of prevented cases per 1,000 patient years
	Active	Control		
Cardiovascular morbidity				
Age				
24–50	20.9	47.5	56	26.6
50–59	27.2	84.1	68	56.9
60–79	87.6	196.3	55	108.7
SBP				
<165	29.1	46.4	37	17.3
≥165	48.1	129.4	63	81.3
DBP				
90–104	50.9	75.8	33	24.9
105–114	25.0	96.4	74	71.4
Organ disease				
No	25.3	48.8	48	23.5
Yes	44.7	119.1	62	74.4
Only DBP 90–104*	21.6	20.0	8	1.6
1 risk factor	27.2	51.8	47	24.6
3 risk factors	52.4	154.2	66	101.8

* The greatest benefit of treatment in patients with at least one more additional risk factor (≥50 years, WHO II–III, DBP ≥105)

	Number needed to treat to prevent 1 endpoint per year	Probability to remain free from endpoint during 1 year		Probability to remain free from endpoint during 5 years	
		Active	Control	Active	Control
	36	97.9	95.3	89.6	76.3
	18	97.3	91.6	86.4	58.0
	9	91.2	80.4	56.2	1.9
	58	97.1	95.4	85.4	76.8
	12	95.2	87.1	75.9	353.0
	40	94.9	92.4	74.6	62.1
	14	97.5	90.4	87.5	51.8
	42	97.5	95.1	87.4	75.6
	13	95.5	88.1	77.7	40.4
	625	97.8	98.0	89.2	90.0
	41	97.3	94.8	86.4	74.1
	10	94.8	84.6	73.8	22.9

Appendix 3, Table 9
SHEP [14,21,30]

	Incidence per 1,000 patient years		Relative benefit, %	Absolute benefit, number of prevented cases per 1,000 patient years
	Active	Control		
Cardiovascular morbidity				
Age 60+ (average 72 yrs)	27.1	38.8	32	11.7
Total mortality				
Diabetes mellitus				
No	19.4	21.8	11	2.4
Yes	35	35.6	2	0.6
BMI				
>30	67.9	32.1	112	35.8
26.3–27.9	38	46.8	19	8.8
<24	51.4	90.9	43	39.5
Acute myocardial infarction				
Diabetes mellitus				
No	10.2	11.4	11	1.2
Yes	15.4	26.2	41	10.8
Stroke incidence				
Diabetes mellitus				
No	8.8	15.0	41	6.2
Yes	19.4	28.8	33	9.4
BMI				
>30	30.9	66.3	53	35.4
26.3–27.9	36.5	62.6	42	26.1
<24	49.0	72.3	32	23.3

	Number need- ed to treat to prevent 1 endpoint per year	Probability to remain free from endpoint during 1 year		Probability to remain free from endpoint during 5 years	
		Active	Control	Active	Control
	86	93.3	96.1	86.5	80.6
	417	98.1	97.8	90.3	89.1
	1 667	96.5	96.4	82.5	82.2
	28	93.2	96.8	66.0	84.0
	114	96.2	95.3	81.0	76.6
	25	94.9	90.9	74.3	54.6
	833	99.0	98.9	94.9	94.3
	93	98.5	97.4	92.3	86.9
	161	99.1	98.5	95.6	92.5
	106	98.1	97.1	90.3	85.6
	28	96.9	93.4	84.6	66.9
	38	96.3	93.7	81.8	68.7
	43	95.1	92.8	75.5	63.9

Appendix 3, Table 10
STOP [22]

	Incidence per 1,000 patient years		Relative benefit, %	Absolute benefit, number of prevented cases per 1,000 patient years
	Active	Control		
Cardiovascular morbidity				
Age				
Not reported in specific age intervals				
70–84 (average 76 yrs)	33.5	55.5	40	22.0

	Number need- ed to treat to prevent 1 endpoint per year	Probability to remain free from endpoint during 1 year		Probability to remain free from endpoint during 5 years	
		Active	Control	Active	Control
	46	96.7	94.5	83.3	72.3

Appendix 3, Table 11
OSLO Mild hypertension [23]

	Incidence per 1,000 patient years		Relative benefit, %	Absolute benefit, number of prevented cases per 1,000 patient years
	Active	Control		
Cardiovascular morbidity (angina pectoris and LVH-ECG also included)				
Sex				
Only men included				
SBP				
≤160	8.8	12.2	28	3.4
>160	19.1	31.8	40	12.7
DBP				
≤100	9.5	10.4	9	0.9
>100	13.9	29.8	53	15.9

	Number need- ed to treat to prevent 1 endpoint per year	Probability to remain free from endpoint during 1 year		Probability to remain free from endpoint during 5 years	
		Active	Control	Active	Control
	295	99.1	98.8	95.6	93.9
	78	98.1	96.8	90.4	84.1
	1 112	99.0	98.9	95.2	94.8
	63	98.6	97.0	93.0	85.1

Appendix 3, Table 12
Syst-Eur [27]

	Incidence per 1,000 patient years		Relative benefit, %	Absolute benefit, number of prevented cases per 1,000 patient years
	Active	Control		
Cardiovascular morbidity				
Diabetes mellitus				
No	15.4	19.7	22	4.3
Yes	11.7	27.1	57	15.4
Cardiovascular mortality				
Diabetes mellitus				
No	10	11.9	16	1.9
Yes	8.3	27.8	70	19.5
Total mortality				
Diabetes mellitus				
No	19.8	21.6	8	1.8
Yes	26.4	45.1	41	18.7
Stroke incidence				
Diabetes mellitus				
No	7.8	12.3	37	4.5
Yes	8.3	26.6	69	18.3

	Number needed to treat to prevent 1 endpoint per year	Probability to remain free from endpoint during 1 year		Probability to remain free from endpoint during 5 years	
		Active	Control	Active	Control
	233	98.5	98.0	92.3	90.2
	65	98.8	97.3	94.2	86.5
	526	99.0	98.8	95.0	94.0
	51	99.2	97.2	95.8	86.1
	556	98.0	97.8	90.1	89.2
	53	97.4	95.5	86.8	77.4
	222	99.2	98.8	96.1	93.8
	55	99.2	97.3	95.8	86.7

Appendix 3, Table 13
Syst-China [28,29]

	Incidence per 1,000 patient years		Relative benefit, %	Absolute benefit, number of prevented cases per 1,000 patient years
	Active	Control		
Cardiovascular events				
Diabetes mellitus				
No	20.9	31	33	10.1
Yes	32.1	76.4	58	44.3
Stroke incidence				
Smoking				
No	7.5	16	53	8.5
Yes	16.5	24.5	33	8.0

	Number need- ed to treat to prevent 1 endpoint per year	Probability to remain free from endpoint during 1 year		Probability to remain free from endpoint during 5 years	
		Active	Control	Active	Control
	99	97.9	96.90	89.6	84.5
	23	96.8	92.36	84.0	61.8
	118	99.2	98.4	96.2	92.0
	125	98.3	97.6	91.8	87.8

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