Moderately Elevated Blood Pressure

A Systematic Literature Review

Volume 2 – Tables

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The Swedish Council on Technology Assessment in Health Care

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Project Group

Lars Hjalmar Lindholm (Chair)
Ingegerd Agenäs
Bo Carlberg
Helena Dahlgren (Project Director)
Ulf de Faire
Bo Hedblad
Paul Hjemdahl
Thomas Kahan
Lars Lindholm
Karin Manhem
Mats Persson
Mats Ribacke
Ewalotte Ränzlöv (Project Assistant)
Ola Samuelsson
Kurt Svärdsudd

Other Contributors

Hans Melander
Mats Halldin

Scientific Reviewers

Anders Ahlbom (Chapter 5)
Anders Alvestrand (Chapter 13)
Lars Borqquist
Frej Fyhrqvist
Hans Herlitz (Chapter 13)
Peter Nilsson
Ingrid Os
Annika Rosengren

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Contents

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 Insuficienca Renal en Paricentes no Diabeticos (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
TONE	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 cilexitil
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 Treat–Control/Control x 100.

Further abbreviations

ACEi = Angiotensin converting enzyme inhibitors
AE = Subjective adverse effects, biochemical adverse effects not included
Alpha-B = Alpha1-receptor blockers
AP = Angina pectoris
ARB = Angiotensin receptor blocker
BB = Beta-adrenoceptor blocker based
BMI = Body mass index
BP = Blood pressure
CCB = Calcium channel blockers
CHD = Coronary heart disease
CHF = Congestive heart failure
CV = Cardiovascular
D = Diuretics
DBP = Diastolic blood pressure
ECG = Electrocardiography
FH = Fundus hypertonicus
HT = Hypertension
LVH = Left ventricular hypertrophy
MAP = Mean arterial pressure
MI = Myocardial infarction
Non-BB = Non beta-adrenoceptor blocker based
NYHA = New York Heart Association
Rx = Prescribed therapy
SC = Stepped care
SR = Slow release
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)
Pharmacological				
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 athero-sclerosis		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)
EWPHE, 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 antihypertensive 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 placebo 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, previous CV complication, 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. ctn *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)
Multifactorial and non-pharmacological				
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)
Hypertension after a cerebrovascular event				
HSCSG, 1974 [8]	Prior stroke or TIA, and hypertension	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 hypertension	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
Hypertension and kidney				
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

The table continues on the next page.

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), *and* 1. ram *vs* met *vs* aml; 2. add fur, cln, dox, vasodilators
Hypertension and diabetes mellitus				
UKPDS, 1998 [14]	Diabetes mellitus type 2 and HT	O	UC	Intensive (<150/ 85 mm Hg) *vs* moderate (<180/ 105 mm Hg), *and* 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), *and* 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±08; 2.3±0.3	Medium
	5.3[1]	Creatine clearence	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 microalbuminuria, 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 mortality	13.9±0.5; 3.9±0.3	High
	4.2	CV mortality, non-fatal CHD	All cause mortality, 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
Multifactorial and non-pharmacological			
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 antihypertensive 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
Hypertension after a cerebrovascular event			
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
Hypertension and cardiovascular risk			
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 ≥90 mm Hg on each of 3 weekly visits on placebo and ≥1 early atherosclerotic lesion(s) in extra-cranial carotid arteries (by ultrasonography).
VHAS, 1997 [81]	SBP ≥160 and DBP ≥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.
CAPPP, 1999 [59,77]	DBP ≥100 mm Hg in untreated patients (supine, 2 readings) on 2 occasions 1 week apart; in treated patients DBP ≥100 mm Hg must be documented in previous medical records.
STOP-2, 1999 [58,67]	Supine DBP ≥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 antihypertensive 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 ≥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 ≤40%, aortic stenosis, serum creatinine >160 µmol/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 ≥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 ≥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 ≥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 *and* 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, *and* serum creatinine (133–442 µmol/L).
AASK, 2002 [98]	Afro-Americans with DBP ≥95 mm Hg, *and* 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, *and* 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/m^2, >33 kg/m^2 (males) or >37 kg/m^2 (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, *and* diabetes mellitus type 2.
ABCD, 2000 [50,51,82]	DBP ≥80 mm Hg, *and* diabetes mellitus type 2.
RENAAL, 2001 [42]	SBP 100–200 and DBP ≤110 mm Hg (seated), *and* 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, *and* diabetes mellitus *and* proteinuria >900 mg/24h.
J-MIND, 2001 [39]	SBP ≥140 and/or DBP ≥90 mm Hg (supine), *and* 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	Intervention	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		186	157	24–75; 51
	Control		194	167	
USPHS, 1977 [83]	Treatment	>1 600	193	142	21–55; 44
	Control		196	146	
VA-NHLBI, 1978 [15]	Treatment	118 157	508	410	21–50; 38
	Control		504	400	
HDFP, 1979 [7,9,10,17–19, 23,26,87]					
Strata I–III	Treatment	159	5 485	5 477	30–69; 51
	Control	468	5 455	5 439	
Stratum I	Treatment		3 903	3 895	--; 51
	Control		3 922	3 911	
ANBPS, 1980 [1,29,35]	Treatment	104 171	1 721	1 679	30–69; 50
	Control		1 706	1 660	
Oslo, 1980 [61]	Treatment	16 200	406	406	40–49; 45
	Control		379	379	
MRC, 1985 [5,24,75]	Treatment	515 000	8 700	≈7 000	35–64; 52
	Control		8 654	≈7 000[5]	
EWPHE, 1985 [36–38]	Treatment		416	404	≥60; 72
	Control		424	412	
HEP, 1986 [45]	Treatment	10 718	419		60–79; 69
	Control		468		
SHEP, 1991 [28,46,53, 55,65]	Treatment	447 921	2 365		>60; 72
	Control		2 371		

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

% 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	3/2	63
			124/70	3/1	73
			122/68	5/3	65
			127/71		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	Intervention	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	Intervention	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	Intervention	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	Intervention	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 25	90 112	123 130	213 242	Yes	69 56
3 6	17 41	19 22	36 63	Yes	84 77
39 28	161[4] 180[4]	140[4] 135[4]	301 315	Yes[4]	44 47
				Yes	72 59
				Yes	
3 4	59 77	64 60	123 137	Yes	
	87 90 96	101 104 111	188 194 207	Yes	
4[7] 1[7]	33 44	28 38	61 82	Yes	
103 108	141 152	114 114	259 26	Yes	ARB: 26 Placebo: 18
	23 22 19	7 5 3	30 27 22	Yes	
0 0	45 56	63 58	108 114	Yes	76 72
	65 69	55 59	120 128	Yes	37 52

The table continues on the next page.

Appendix 1, Table 5 *continued*

Study, year Reference	Intervention	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	Intervention	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
684 438 435	1 145 697 708	1 058 559 606	2 203 1 256 1 314	Yes	
		317 561	769 1 258		
	4 8		13 17	Yes	
	152 143		337 319		
15 15	84 82	111 128	195 210	Yes	58 62
	431 431		873 893	Yes	
			841 818	Yes	
			1 293 1 318	Yes	
	101 94	74 77	175 171	Yes	77 65
	0 1	2 1	2 2	Yes	≈20? --
0[11] 0[12]; 0[13]	2[11] 0[12]; 2[13]	1[11] 0[12]; 0[13]	3[11] 0[12]; 2[13]	Yes	44[11] 7[12]; 100[13]
12 4	42 24	22 17	64 41	Yes	

The table continues on the next page.

Appendix 1, Table 5 *continued*

Study, year Reference	Intervention	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
Hypertension after a cerebrovascular event							
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
Hypertension and kidney							
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 2	15 19	11 5	26 24	No	
	2 1	41 33	23 25	64 58	Yes	
				51 60		
	16 17	93 107	53 51	146 158	Yes	
	81 86	181 198	125 121	306 319	Yes	
					Yes	
		0.6[14] 0.7[14]		1.6[14] 1.9[14]		
		0.5[14] 0.9[14] 0.8[14]		1.5[14] 1.7[14] 2.0[14]		

The table continues on the next page.

Appendix 1, Table 5 *continued*

Study, year Reference	Intervention	Stroke			Coronary heart disease		
		fatal	non-fatal	all	fatal	non-fatal	all
Hypertension and diabetes mellitus							
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	Intervention	Stroke			Coronary heart disease		
		fatal	non-fatal	all	fatal	non-fatal	all
Hypertension and cardiovascular risk							
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 and 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	Treatment	1.4	5.7	7.1
[12,13,80,89]	Control	9.5	17.6	27.1
	% Change	–85	–68	–74
USPHS, 1977	Treatment	0.0	0	0
[83]	Control	0.0	1.5	1.5
	% Change		–100	–100
VA-NHLBI, 1978	Treatment	0.0	0.0	0.0
[15]	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	Treatment	0.4	1.5	1.9
[1,29,35]	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	Treatment	0.0	0.0	0.0
[61]	Control	1.0	1.4	2.4
	% Change	–100	–100	–100
MRC, 1985	Treatment	0.4	1.0	1.4
[5,24,75]	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			10.3
	CCB			8.8
	% Change			17
Multifactorial and non-pharmacological				
GPPT, 1986 [96]	Treatment	0.6	1.4	2.0
	Control	0.7	1.3	2.0
	% Change	–17	13	2
MRFIT, 1990 [2,4,16,22,25,32]	Treatment			
	Control			
	% Change			
Patel, 1985 [78]	Treatment			
	Control			
	% Change			
Stamler, 1987 [88]	Treatment	2.5[8]		
	Control	0.0[9]; 0.0[10]		
RIS, 1998 [52]	Treatment	1.8	7.8	9.6
	Control	4.2	14.9	19
	% Change	–56	–48	–50
TONE, 1998 [93]	Na^+ reduction			1.2
	Control			2.3
	% Change			–50
	Weight reduction			0
	Control			2.3
	% Change			–100
	Their combination			2.7
	Control			2.3
	% Change			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[8]	5.0[8]	2.5[8]	7.6[8]
0.0[9]; 10.4[10]			0.0[9]; 0.0[10]	0.0[9]; 10.4[10]	0.0[9]; 0.0[10]	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
Hypertension after a cerebrovascular event				
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
Hypertension and kidney				
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
Hypertension and diabetes mellitus				
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**
Hypertension and cardiovascular risk				
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
Hypertension after a cerebrovascular event				
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	*	*
Hypertension and kidney				
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 therapy 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
Hypertension and diabetes mellitus				
UKPDS, 1998 [14]	Intensive Moderate			*
	BB; ACEi			ns
FACET, 1998 [90]	ACEi CCB			ns
ABCD, 2000 [50,51,82]	Intensive Moderate			ns
	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
Hypertension and cardiovascular risk				
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 (%)	Normotensive[1] 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
		33	21[2]	12
	12			
				17
	17			
		30–50[3]	18[4]	12
	≈12			
				10
	10			
	9			
				15
	44			
		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
HAPPHY,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 ACEi Placebo		16 13

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

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

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]	4.4	0.9[1,2]	
	BB			
	CCB			
	D			
	Alpha-B			
	ACEi			
	Placebo[6]			
BBB, 1994 [56]	Tight	4.9	0	6
	Less tight			
Syst-Eur, 1997 [84–86,91]	CCB	2	5	
	Placebo		5	
HOT, 1998 [60,63,64]	DBP ≤80	3.8	2	
	DBP ≤85		2	
	DBP ≤90		2	
Syst-China, 2000 [70,92]	CCB	3.0	9	
	Placebo		11	
SCOPE, 2003 [69]	ARB	3.6	0.2	
	Placebo			
HYVET Pilot, 2003 [44]	D	1.1	2	
	ACEi		1.6	
	Placebo		2	
Comparing drug treatments				
IPPPSH, 1985 [3]	BB	4.0	0.6	
	Non-BB		0.5	
HAPPHY, 1987 [95]	BB	3.8	1	
	Non-BB			
MAPHY, 1988 [94]	BB	5.0	0	
	Non-BB		0.1	

	Total withdrawn from randomized Rx (%)	Withdrawn from randomized Rx due to AE (%)	Total AE frequency (%)	Change in treatment 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 treatment 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 18	9.3 8.2		
		11.4 11.4	57 55	
	9.8 11.8	2.9 4.2	17.2 18.1	
	39 30	22.6 16	49 42	
	15 19	13 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 treatment Rx group due to AE
	37 38	16.3 15.3		
	9.1 8.8	2.8 2.3		
	35 30	15 8	21 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		
	Less tight			
	ACEi		Several patients, numbers not reported	
	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 treatment 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 (%)
Hypertension and cardiovascular risk				
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] Referes 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 symtoms during follow-up.

[12] Refused follow-up.

	Total withdrawn from randomized Rx (%)	Withdrawn from randomized Rx due to AE (%)	Total AE frequency (%)	Change in treatment 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 = Candersartan
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

Alpha$_1$-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

Further abbreviations

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

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	% randomized 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	– Previouly 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	% randomized 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 – ↑ LVMI	Echo	CAPT PLAC	Double-blind
	52	– DBP ≥95–120 – ↑ 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 – ↑ LVMI (M >134; F >110)	Echo	CELI ATEN	Double-blind
70	– BP ≥170/95–120 – ↑ 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 ≥160/95	Echo	CAPT LISI QUIN	Unclear blinding
59	– DBP ≥95–115 – ↑ 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 – ↑ LVMI (M >120; F >98)	Echo	RAMI (1.5 mg) RAMI (5 mg) PLAC	Double-blind All pts treated with furosomid
?	– 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

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)
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 – ↑ LVMI (M >130; F >110)	Echo	FOSI NIF	Double-blind
67	– DBP ≥95–114 – ↑ LVM (PWT ≥10 or IST ≥11 mm)	Echo	ATEN RAMI	Unclear blinding
65	– BP ≥160/95 – ↑ LVM (PWT ≥12)	Echo	ENAL LISI	Unclear blinding
59	– DBP ≥95–115 – ↑ LVMI (M >120; F >98)	Echo	RAMI ATEN	PROBE design
?	DBP ≥95–114	Echo	LISI DIL	Double-blind
100	– DBP ≥95 – ↑ LVMI (≥131)	Echo	LISI HYDR	Double-blind Atenolol/ Chlorthalidone added if BP not controlled
50	– Amb BP >140/>90 – ↑ LVMI (M >130; F >110)	Echo	ISRA PERI	Unclear blinding All pts BMI <26
67	DBP ≥95–114	Echo	BUNA METO	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)
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 ≥160/90 – ↑ LVMI (M ≥119; F ≥110)	Echo	ALE NIC	Unclear blinding
75	– ↑ LVMI (≥75) – DM2 (HbA1c <8%)	Echo	NITR CAPT	BP not specified Unclear blinding All pts with DM2
63	– DBP ≥95–114 – ↑ 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 ≥160/90/≥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 ≥160/95 or DBP ≥90–114	Echo	BUNA METO	Double-blind
81	– DBP ≥95–114 – ↑ LVMI (M ≥119; F ≥98)	Echo	HCTZ ISRA	Unclear blinding 2:1 randomization
44	BP ≥160/95	Echo	NILV TEMO CADR	Unclear blinding
51	BP ≥160/90	Echo	CHLT PLAC	Double-blind
82	DBP ≥95–115	Echo	LOS VERA	Double-blind
87	DBP ≥95 – ↑ LVM (LVWT ≥1.2 cm)	Echo	ATEN CAPT	PROBE design All pts HCTZ if DBP >90
74	DBP ≥95–114	Echo	HCTZ RAMI	Double-blind
79	DBP ≥95–114 – ↑ LVMI (M >102; F>88)	Echo	MIBE ATEN	Double-blind
53	– DBP ≥95–114 – ↑ LVMI (M ≥130; F ≥110)	Echo	LOS HCTZ	Double-blind
70 (PP: 66)	– DBP ≥95–114 – ↑ LVMI (M >134; F >110)	Echo	RILM NIF	Double-blind Per protocol (PP) analysis
62	DBP ≥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	Inter-vention	Comments
84	– Pts with no LVH: DBP ≥100 and Amb DBP ≥95 – Other pts: BP ≥165/100	Echo	ISRA HCTZ + Amilorid	Unclear blinding Atenolol or hydralazine added if DBP >90 Complicated design!
23	BP ≥160/<95	Echo	QUIN HCTZ/ Triam	Double-blind All pts prev untreated
42	– BP ≥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 – ↑ 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 – ↑ 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 – ↑ LVMI (M >130; F >110)	Echo	ENAL LOS ENAL + LOS	Unclear blinding
56	– SBP ≥160–209 – ↑ LVMI (M >120; F >100)	Echo	INDAP ENAL	Double-blind Per protocol (PP) analyses
43	– Fasting-Glucose <7.8 – BMI >27–45 – BP ≥160/≥95–114 – ↑ LVMI (M >100; F >75)	Echo	ATEN PERI	Double-blind Indapamide or amlodipine added if BP not controlled
77	– DBP >100 – No CAD – ↑ 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 – ↑ 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 ≥140/90 – Prev untreated pts: BP ≥150/90 – ↑ LVMI (M >116; F >116; if <65 yrs; >104 if ≥65 yrs)	Echo	NIF ENAL	Double-blind
54	– BP ≥140/90 – ↑ LVMI (M >134; F >110)	Echo	ENAL HCTZ ATEN VERA	Unclear blinding
61	BP ≥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	Inter-vention	Comments
	45	– BP ≥130–180/ ≥95–110 – BMI ≥25–37 – Sedentary physical activity	Echo	Exercise + weight control Exercise only Control group	Life style modifica-tions
	50	DBP ≥95–114	Echo	LOS ENAL	Double-blind
	62	– BP ≥140–200/ ≥95–115 – ↑ LVMI (M >120; F >100)	Echo	CAND ENAL	Double-blind HCTZ added if DBP ≥140/90
	63	– SBP ≥140–200/ ≥95–115 – ↑ LVMI (M >120; F >105)	Echo	LOS ATEN	Double-blind HCTZ added if BP ≥140/90
	46	– BP ≥160–200/ ≥95–114 – ↑ 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 NIF	12 10	326.3±126.2 293.6±35.7
Dahlöf 1992 [10]	LVMI (g/m)	ENAL HCTZ	14 14	146.3±10.3 137.5±11.2
Schulte 1992 [68]	LVMI (g/m^2)	NIF PERI	14 16	141±6 148±5
Studies 1993 to 2003				
Salcedo 1993 [63]	LVMI (g/m^2)	VERA Alpha-MET ATEN ENAL	15 15 15 15	180±27 176±30 170±23 178±28
Gonzalez-Fernandez 1993 [23]	LVMI (g/m^2)	CAPT PLAC	14 13	149±17 155±40
Senior 1993 [71]	LVMI (g/m^2)	HCTZ INDAP NIF INDAP ATE INDAP ENAL INDAP	20 20 19 22 12 17 9 9	141.3±6.6 151.4±6.3 170.4±6.6 144.1±5.3 156.7±8.4 146.2±5.1 142.0±6.7 155.1±6.3
Gonzales-Juanatey 1994 [24]	LVMI (g/m^2)	VERA NITR	14 14	159±31 167±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 38	123±26 115±23
Wambach 1994 [81]	LVMI (g/m^2)	CELI ATEN	8 8	186±43 164±24
Komsuoglu 1994 [39]	LVMI (g/m^2)	NITR VERA	16 14	155±28 160±32
Henderson 1994 [31]	LVM (g)	CAPT PLAC	12 14	205±12 207±14
Diez 1994 [16]	LVMI (g/m^2)	CAPT LISI QUIN	30 37 20	102±6 92±6 103±6
Machnig 1994 [48]	LVMI (g/m^2)	NITR CAPT NITR + CAPT	18 15 18	134±15 148±23 185±57
Agabiti-Rosei 1994 [2]	LVMI (g/m^2)	AMLO ENAL	12 12	154±34 134±30
Lièvre 1995 [46]	LVMI (g/m^2)	RAMI (1.5 mg) RAMI (5 mg) PLAC	35 33 35	134±8 143±6 134±5
Liebson 1995 [45]	LVM (g)	*At 12 mo:* CHLT ACEB DOXA AMLO ENAL PLAC	 111 103 113 100 105 186	 207.6 203.7 199.1 191.7 202.2 205.0

Follow-up LVH	Within-group change	Within-group change in %	p-value	Between-group change	Between-group change in %
117±22	–6	–5	<0.05	–6	–6
116±22	+1	+1		Reference	
157±34	–27	–15	<0.05	–14	–7
151±27	–13	–8	NS	Reference	
151±23	–4	–3	NS	0	0
155±28	–4	–3	NS	Reference	
202±12	–3	–3.5	NS	–22	–13
232±16	+25	+12	<0.05	Reference	
89±4	–13	–13	<0.05	–2	–2
77±4	–15	–16	<0.05	–4	–5
92±5	–11	–11	<0.05	Reference	
115±19	–19	–14	<0.001	Reference	
118±23	–30	–20	<0.001	–6	–6
131±23	–54	–29	<0.001	–12	–12
132±29	–22	–14	<0.01	–5	–1
117±21	–17	–13	<0.05	Reference	
127±?	–7±4	–4	NS	–11	–7
132±?	–11±4	–8	0.004	–15	–11
138±?	+4±4	+3		Reference	
At 12 mo:					
172.8	–34.8±4.6	–17	<0.05	–17	–8
187.0	–16.7±4.5	–8	<0.05	+2	+1
177.1	–22.0±3.6	–12	<0.05	–4	–3
165.1	–26.6±3.6	–14	<0.05	–8	–5
184.9	–17.3±4.6	–9	<0.05	+1	0
186.8	–18.2±3.1	–9	<0.05	Reference	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 20	140±14 144±19
Kirpizidis 1995 [36]	LVMI (g/m^2)	FOSI NIF	16 15	146±17 146±14
Rosatti 1995 [61]	LVMI (g/m^2)	ATEN RAMI	10 11	145±2 147±7
Kohno 1995 [38]	LVMI (g/m^2)	ENAL LISI	16 15	166±26 167±28
Agabiti-Rosei 1995 [1]	LVMI (g/m^2)	RAMI ATEN	56 55	135±6 132±4
Van Leeuwen 1995 [82]	LVMI (g/m^2)	LISI DIL	20 16	92±? 98±?
Fogari 1995 [19]	LVMI (g/m^2)	LISI HYDR	15 15	172±19 171±15
Grandi 1995 [28]	LVMI (g/m^2)	ISRA PERI	18 18	139±15 142±14
Schobel 1996 [67]	LVMI (g/m^2)	BUNA METO	23 20	284±80 282±74

Follow-up LVH	Within-group change	Within-group change in %	p-value	Between-group change	Between-group change in %
124±14	–16	–11.8±4.0	<0.001	–7	–5
135±22	–9	–5.7±7.0	0.002	Reference	
124±9	–22	–15	<0.001	–9	–6
133±13	–13	–9	<0.001	Reference	
117±4	–28	–19	<0.01	–3	–2
116±3	–31	–21	<0.01	Reference	
128±?	–38	–23	<0.05	–1	–1
130±?	–37	–22	<0.05	Reference	
121±7	–14	–10	<0.001	–12	–8
130±4	–2	–2	NS	Reference	
82±?	–9 (–16 to –2)	–11	<0.01	–8	–9
96±?	–2 (–14 to 10)	–2	NS	Reference	
147±17	–25	–14	0.005	–17	–9
163±20	–8	–5	NS	Reference	
119±18	–20	–14.5±4.7	<0.005	–10	–7
112±19	–30	–21.1±4.3	<0.005	Reference	
259±67	–25±42	–9	<0.05	+3	–1
254±70	–28±44	–10	<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
Gottdiener 1997 [27]	LVM (g)	ATEN CAPT CLON DIL HCTZ PRAZ	36 40 36 52 38 28	325±98 302±62 329±69 314±94 310±83 348±86
Sumimoto 1997 [74]	LVMI (g/m^2)	ALE NIC	10 10	136±15 132±11
Scognamiglio 1997 [70]	LVMI (g/m^2)	NITR CAPT	37 36	87±2 89±2
Lacourciere 1997 [42]	LVMI (g/m^2)	HCTZ AMLO HCTZ + AMLO	7 18 13	149±7 150±4 155±5
Giugliano 1997 [22]	LVMI (g/m^2)	CARVE ATEN	22 20	110±15 107±14
Kribben 1997 [40]	ECG	HCTZ ATEN NITR ENAL	No individual data	No individual data
Fagard 1997 [18]	LVM (g)	HCTZ + TRIA TRAN	11 14	239±78 278±91
Lombardo 1997 [47]	LVMI (g/m^2)	FOSI AMLO	12 12	125±32 106±18
Leenen 1996 [44]	LVMI (g/m^2)	DIL AMLO	13 17	108±8 107±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 METO	20 16	146±34 144±26
Papademetriou 1997 [58]	LVMI (g/m^2)	HCTZ ISRA	45 89	165±36 170±36
Ueno 1997 [80]	LVMI (g/m^2)	NIVA TEMO CADR	12 12 12	129±48 117±39 110±30
Ofili 1998 [56]	LVMI (g/m^2)	CHLT PLAC	47 47	109±33 102±24
Cuspidi 1998 [9]	LVMI (g/m^2)	LOS VERA	8 9	124±21 117±17
Laufer 1998 [43]	LVMI (g/m^2)	ATEN CAPT	13 15	127±22 126±21
Roman 1998 [60]	LVMI (g/m^2)	HCTZ RAMI	28 22	93±20 104±20
Höglund 1998 [33]	LVMI (g/m^2)	MIBE ATEN	31 29	117±12 123±18
Tedesco 1998 [75]	LVM (g/m^2)	HCTZ LOS	28 42	140±23 139±19

Follow-up LVH	Within-group change	Within-group change in %	p-value	Between-group change	Between-group change in %
132±25	–20±37	–10	<0.05	+1	0
129±26	–32±42	–10	<0.05	Reference	
145±?	–19.8±21.2	–12	<0.001	–14	–8
164±?	–5.8±24.7	–4	0.12	Reference	
115±39	–14	–8.5±12.3	<0.05	–42	–36
88±20	–29	–22.8±13.5	<0.01	–57	–50
138±27	+28	+31.8±33.1	<0.01	Reference	
93±28	–16	–17 (–4 to –28)	<0.001	–24	–19
110±26	+8	+4 (–5 to +14)	<0.01	Reference	
103±16	–21	–17	<0.05	–11	–8
107±20	–10	–9	NS	Reference	
131±?	+4	+3	NS	+2	+1
128±?	+2	+2	NS	Reference	
92±23	–1	–1	NS	Reference	
95±20	–9	–9	<0.001	–8	–8
103±15	–13.5±16.5	–11	<0.001	–2	–2
111±17	–11.7±14.6	–9	<0.001	Reference	
135±21	–5	–4	NS	Reference	
128±21	–11	–8	<0.02	–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 32	177±41 173±35
Beltman 1998 [4]	LVMI (g/m^2)	AMLO LISI	28 31	88±21 91±16
Sihm 1998 [72]	LVM (g)	ISRA HCTZ + Amilorid	25 25	358±128 311±80
Heesen 1998 [29]	LVMI (g/m^2)	QUIN HCTZ/Triam	21 23	88±9 94±9
Molinero 1998 [54]	LVMI (g/m^2)	VERA HCTZ + Amilorid	11 15	110±33 114±29
Thürmann 1998 [78]	LVMI (g/m^2)	ATEN VALS	29 29	127±25 127±23
Manolis 1998 [51]	LVMI (g/m^2)	ISRA SPIR ISRA + SPIR	10 11 14	140±15 139±15 148±16
Gaudio 1998 [20]	LVMI (g/m^2)	BENA NITR	22 22	143±12 136±6
Gosse 1999 [25]	LVMI (g/m^2)	BISO VERA	23 24	126±27 115±22
Gerritsen 1998 [21]	LVMI (g/m^2)	NITR ENAL PLAC	37 38 34	146±35 141±29 140±32

Follow-up LVH	Within-group change	Within-group change in %	p-value	Between-group change	Between-group change in %
155±40	–22.1±23.3	–12	<0.001	Reference	
146±36	–26.9±29.5	–16	<0.001	–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	–130±75	–37	<0.001	–61	–14
241±55	–70±53	–23	<0.001	Reference	
64±13	–24	–27	<0.001	+4	+3
66±13	–28	–30	<0.001	Reference	
115±21	+5	+5	NS	–8	–6
127±22	+13	+11	NS	Reference	
117±27	–10	–8	<0.01	Reference	
106±25	–21	–17	<0.001	–11	–9
128±13	–12	–9	0.002	+2	+1
125±14	–14	–10	<0.001	Reference	Reference
132±15	–16	–11	0.002	–2	–1
123±11	–20	–14	<0.001	–11	–7
127±8	–9	–7	<0.01	Reference	
124±31	–2	–2	NS	–2	–2
115±27	0	0	NS	Reference	
138±?	–12.0±5.4	–8	<0.01	–23	–14
140±?	–1.0±4.7	–0.1	NS	–10	–6
149±?	+9.3±3.4	+6	<0.01	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
Avanza 2000 [3]	LVMI (g/m^2)	ENAL LOS ENAL + LOS	15 15 16	141±4 147±4 146±3
Modena 1999 [53]	LVMI (g/m)	17-beta-estradiol PLAC	82 79	81±17 84±16
Diamond 1999 [15]	LVMI (g/m)	ENAL EPRO	9 8	118±42 111±37
Topouchian 1999 [79]	LVMI (g/cm)	VERA TRAN VERA + TRAN	21 18 20	51.7±11.3 51.9±11.2 51.4±17.6
Gosse 2000 [26]	LVMI (g/m^2)	ENAL INDAP	206 205	138±36 144±40
Kuperstein 2000 [41]	LVMI (g/m^2)	PERI ATEN	10 11	98±9 101±11
Brilla 2000 [6]	LVMI (g/m^2)	LISI HCTZ	11 14	170±16 160±14
Terpstra 2001 [76]	LVMI (g/m^2)	AMLO LISI	61 63	109±20 114±23
Malmqvist 2001 [50]	LVMI (g/m^2)	CAPT METO	22 25	113±23 116±19
Malmqvist 2001 [49]	LVMI (g/m^2)	IRBE ATEN	44 50	154.3±35.0 143.5±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)			*No of subjects with LVH:*
		RAMI	4 135	321 (7.8%)
		PLAC	4 146	355 (8.6%)
Black 2001 [5]	LVMI (g/m^2)	FELO	54	96±18
		PLAC	57	100±30
Devereux 2001 [14]	LVMI (g/m^2)	NIF	122	133±25
		ENAL	113	130±23
Novo 2001 [55]	LVMI (g/m^2)	ENAL	10	140±11
		HCTZ	10	143±15
		ATEN	13	142±10
		VERA	13	136±10
Pontremoli 2001 [59]	LVMI (g/m^2)	LISI	16	56±3
		NIF	15	63±3
Heesen 2001 [30]	LVMI (g/m^2)	LISI	30	104±18
		PLAC	32	92±20
Schussheim 2001 [69]	LVM (g)	VERA	14	190±13
		NIF	15	200±15
Hinderliter 2002 [32]	LVMI (g/m)	Exercise + weight control	36	48±10
		Exercise only	27	50±11
		Control group	19	51±14
De Rosa 2002 [13]	LVMI (g/m^2)	LOS	22	176±24
		ENAL	20	170±19

Follow-up LVH	Within-group change	Within-group change in %	p-value	Between-group change	Between-group change in %
No of subjects with LVH:					
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±?	–15.0±22.6	–11	<0.001	–2	–2
130±?	–13.2±23.4	–9	<0.001	Reference	
143±?	–6.6±20	–4	<0.001	–3	–2
144±?	–3.7±21	–2	NS	Reference	
2 547±1 077	–288	–10.2	<0.001	–163	–6
2 700±1 147	–125	–4.4	<0.001	Reference	

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 %
DBP:					
90±?	–11±15	–11	0.02	+4	+2
97±?	–15±9	–13	0.001	Reference	
Mean BP:					
96.9±2.8	–16	–14	<0.001	–8	–7
101.5±2.0	–8	–7	<0.006	Reference	
140±4/92±3	–9/–12	–6/–12	<0.01	+12/+1	+7/+1
136±3/93±2	–21/–13	–13/–13	<0.01	Reference	
154±8/87±11	–30/–10	–16/–10	<0.01	–	–
156±25/88±13	–21/–15	–12/–15	<0.01	–	–
149±18/88±7	–23/–14	–13/–14	<0.01	–	–
158±23/87±9	–26/–17	–14/–16	<0.01	–	–
136±10/85±5	–31/–18	–19/–18	<0.001	–33/–17	–18/–17
160±8/100±16	–2/–1	–1/–1	NS	Reference	
DBP:					
85.3±2.1	–14.4	–14.4	<0.001	+0.3	–0.1
87.6±2.1	–14.7	–14.3	<0.001	Reference	Reference
91.3±1.6	–12.3	–11.9	<0.001	–0.8	–0.8
89.3±1.8	–11.1	–11.1	<0.001	Reference	Reference
85.7±1.9	–17.1	–16.6	<0.001	–0.6	–0.5
86.3±1.7	–16.5	–16.1	<0.001	Reference	Reference
85.7±2.0	–17.4	–16.9	<0.001	–1.9	–1.8
87.4±2.1	–15.5	–15.1	<0.001	Reference	Reference
134±8/84±4	–34/–10	–20/–10	<0.001	–3/+4	–1/+4
133±8/88±5	–31/–14	–19/–14	<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
Jula 1994 [35]	Echo LVMI	Non-PH PLAC	38 38	149±15/98±6 144±12/97±5
Wambach 1994 [81]	Echo LVMI	CELI ATEN	8 8	145±15/91±7 150±16/95±10
Komsuoglu 1994 [39]	Echo LVMI	NITR VERA	16 14	180±6/111±4 183±7/113±3
Henderson 1994 [31]	Echo LVM	CAPT PLAC	12 14	139±5/88±7 137±9/92±7
Diez 1994 [16]	Echo LVMI	CAPT LISI QUIN	30 37 20	126±1 (×BP) 121±2 (×BP) 119±3 (×BP)
Machnig 1994 [48]	Echo LVMI	NITR CAPT NITR + CAPT	18 15 18	152±11/101±7 147±11/99±6 160±12/101±9
Agabiti-Rosei 1994 [2]	Echo LVMI	AMLO ENAL	12 12	170±21/104±6 162±18/105±16
Lièvre 1995 [46]	Echo LVMI	RAMI (1.5) RAMI (5) PLAC	35 33 35	161±2/95±2 161±2/95±2 166±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	–15/–9	–10/–9	<0.001	–6/–4	–4/–4
135±10/92±5	–9/–5	–6/–5	<0.001	Reference	
136±12/86±5	–9/–5	–6/–5	NS	+9/+7	+6/+8
132±15/83±7	–18/–12	–12/–13	<0.001	Reference	
156±6/91±1	–24/–20	–13/–18	<0.001	+7/0	+4/0
152±5/93±2	–31/–20	–17/–18	<0.001	Reference	
126±9/81±9	–13/–7	–9/–8	<0.01	–6/–1	–4/–1
130±11/86±11	–7/–6	–5/–7	<0.01	Reference	
112±1 (×BP)	–14	–11	<0.001	0	+1
103±1 (×BP)	–18	–15	<0.001	–4	–3
105±3 (×BP)	–14	–12	<0.001	Reference	
137±13/87±10	–15/–14	–10/–14	<0.05	Reference	
134±13/89±9	–13/–10	–9/–10	<0.05	+2/+4	+1/+4
143±8/89±8	–17/–12	–11/–12	<0.05	–2/+2	–1/+2
137±9/85±3	–33/–19	–19/–18	<0.001	–13/0	–7/0
142±12/86±8	–20/–19	–12/–18	<0.01	Reference	
153±?/90±?	–8±2/–5±1	–5/–5	NS	+1/–1	0/–1
147±?/88±?	–12±2/–7±2	–8/–7	NS	–3/–3	–3/–3
157±?/91±?	–9±2/–4±2	–5/–4	NS	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
Liebson 1995 [45]	Echo LVM (12 mo)	CHLT ACEB DOXA AMLO ENAL PLAC	111 103 113 100 105 186	?/? ?/? ?/? ?/? ?/? ?/?
Vyssoulis 1995 [83]	Echo LVMI	CELI METO	19 21	160±15/103±5 160±13/105±5
Kirpizidis 1995 [36]	Echo LVMI	 FOSI NIF	 16 15	*DBP:* 103±7 104±6
Rosatti 1995 [61]	Echo LVM	ATEN RAMI	10 11	172±6/96±4 175±5/100±6
Kohno 1995 [38]	Echo LVMI	ENAL LISI	16 15	182±11/104±6 182±12/103±5
Agabiti-Rosei 1995 [1]	Echo LVMI	RAMI ATEN	56 55	161±2/103±1 165±2/104±1
van Leeuwen 1995 [82]	Echo LVMI	LISI DIL	20 16	161±? 103±? 155±? 102±?
Fogari 1995 [19]	Echo LVMI	LISI HYDR	15 15	157±7/97±5 157±7/97±4
Grandi 1995 [28]	Echo LVMI	ISRA PERI	18 18	155±8/106±7 156±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	<0.001	Reference	
		–16±6/			
		–17±5			
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			*24-h BP:*
		DIL	13	157±4/103±2
		AMLO	17	158±3/102±2
Schobel 1996 [67]	Echo LVMI	BUNA	23	144±12/92±9
		METO	20	145±15/92±5
Gottdiener 1997 [27]	Echo LVM			*SBP:*
		ATEN	36	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	No ind data	No individual data
		ATEN		
		NITR		
		ENAL		
Fagard 1997 [18]	Echo LVM	HCTZ + TRIA	11	163±14/104±9
		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			*24-h BP:*
		FOSI	12	141±13/95±7
		AMLO	12	137±8/91±8
Schmieder 1997 [64]	Echo LVMI			*24-h BP:*
		BUNA	20	144±12/92±9
		METO	16	148±14/96±7
Papademetriou 1997 [58]	Echo LVMI	HCTZ	45	161±17/101±6
		ISRA	89	158±16/101±7
Ueno 1997 [80]	Echo LVMI	NILV	12	174±10/104±7
		TEMO	12	173±18/103±8
		CADR	12	171±16/103±7
Ofili 1998 [56]	Echo LVMI	CHLT	47	169±11/79±8
		PLAC	47	172±13/79±8
Cuspidi 1998 [9]	Echo LVMI	LOS	8	149±11/99±4
		VERA	9	156±13/103±7
Laufer 1998 [43]	Echo LVM	ATEN	13	153±10/102±6
		CAPT	15	154±13/101±5
Roman 1998 [60]	Echo LVMI			*24-h BP:*
		HCTZ	28	146±?/93±?
		RAMI	22	153±?/96±?
Höglund 1998 [33]	Echo LVMI	MIBE	31	163±14/103±6
		ATEN	29	163±18/103±6
Tedesco 1998 [75]	Echo LVM			*24-h BP:*
		HCTZ	28	156±11/96±8
		LOS	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	–18/–14	–13/–15	<0.001	–2/–4	–1/–4
121±6/81±4	–16/–10	–12/–11	<0.001	Reference	
24-h BP:					
135±17/85±6	–9/–7	–6/–8	<0.01	+4/+5	+3/+5
135±17/84±8	–13/–12	–9/–13	<0.01	Reference	
136±?/88±?	–25±17/–13±7	–15/–13	<0.001	–7/–1	–4/–1
140±?/89±?	–18±16/–12±9	–11/–12	<0.001	Reference	
141±12/87±8	–33/–17	–19/–16	<0.01	–2/+2	–1/+2
140±5/86±6	–33/–17	–19/–17	<0.01	–2/+2	–1/+1
140±7/84±7	–31/–19	–18/–18	<0.01	Reference	
144±14/62±8	–25/–17	–14/–18	<0.001	–16/–13	–6/–17
163±21/75±9	–9/–4	–8/–5	<0.05	Reference	
132±13/89±5	–17/–10	–11/–10	<0.05	–2/+3	–1/+3
141±14/90±6	–15/–13	–10/–13	<0.05	Reference	
132±?/85±?	–21/–17	–14/–17	<0.001	–7/–4	–5/–4
140±?/88±?	–14/–13	–9/–13	<0.001	Reference	
24-h BP:					
132±?/84±?	–14/–9	–10/–10	<0.001	Reference	
147±?/91±?	–6/–5	–4/–5	<0.001	+8/+4	+6/+5
145±15/89±7	–18±14/–14±7	–11/–14	<0.001	–7/–4	–4/–4
152±23/93±9	–11±19/–11±9	–7/–10	<0.001	Reference	
24-h BP:					
145±13/89±12	–11/–7	–7/–7	<0.01	Reference	
133±11/84±6	–22/–11	–14/–11	<0.001	–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 NIF	24 32	164±20/103±5 158±20/103±5
Beltman 1998 [4]	Echo LVMI	AMLO LISI	28 31	158±16/102±5 161±15/100±4
Sihm 1998 [72]	Echo LVM	ISRA HCTZ + Amilor	25 25	174±17/111±7 168±14/109±7
Heesen 1998 [29]	Echo LVMI	QUIN HCTZ/ TRIA	21 23	179±5/90±2 178±5/90±2
Molinero 1998 [54]	Echo LVMI	VERA HCTZ + Amilor	11 15	169±8/101±6 168±13/103±3
Manolis 1998 [51]	Echo LVMI	ISRA SPIR ISRA + SPIR	10 11 14	157±14/103±6 153±13/100±4 164±19/105±7
Gaudio 1998 [20]	Echo LVMI	BENA NITR	22 22	155±11/102±3 159±12/102±3
Gerritsen 1998 [21]	Echo LVMI	NITR ENAL PLAC	37 38 34	168±18/90±9 165±15/92±8 166±18/93±8
Thürmann 1999 [77]	Echo LVMI	ATEN VALS	29 29	160±14/103±6 163±12/101±6
Gosse 1999 [25]	Echo LVMI	BISO VERA	23 24	174±10/99±6 168±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	–15/–14	–9/–14	<0.001	Reference	
136±13/86±8	–22/–17	–14/–17	<0.001	–7/–3	–5/–3
143±?/90±?	–16±17/–13±8 –17±14/–9±6	–9/–12	<0.05	Reference	
146±?/91±?		–10/–9	<0.05	–1/+3	–1/+3
133±13/85±9	–41/–26	–24/–23	<0.001	–1/–2	0/–1
128±12/85±6	–40/–24	–24/–22	<0.001	Reference	
156±7/87±4	–26/–3	–15/–3	<0.001	–1/+1	–1/+1
153±6/86±4	–25/–4	–14/–4	<0.001	Reference	
157±9/89±4	–12/–12	–7/–12	<0.001	–3/–3	–2/–3
159±9/94±4	–9/–9	–5/–9	<0.001	Reference	
137±13/89±8	–20/–14	–13/–13	<0.001	–5/–1	–3/0
138±16/87±8	–15/–13	–10/–13	<0.001	Reference	Reference
134±17/81±8	–30/–24	–18/–23	<0.001	–15/–10	–8/–10
137±8/83±4	–18/–19	–12/–19	<0.001	+5/–2	+2/–2
136±6/85±3	–23/–17	–14/–17	<0.001	Reference	
153±?/81±?	–15 ±/–9±2	–9/–10	<0.01	–12/–5	–7/–6
154±2/84±?	–11±2/–8±1	–7/–9	<0.01	–8/–4	–5/–5
163±?/89±?	–3±2/–4±1	–2/–4	NS	Reference	
147±18/90±7	–13/–13	–8/–13	<0.001	Reference	
146±13/90±7	–17/–11	–10/–11	<0.001	–4/–2	–2/–2
150±?/92±?	–24/–7	–14/–7	<0.001	–8/0	–4/0
152±?/94±?	–16/–7	–10/–7	<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
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±?	–28±3/–19±1	–17 /–18	<0.001	–7/–3	–4/–2
138±?/86±?	–21±2/–16±1	–13/–16	<0.001	Reference	
336 (8.1%)	+15	+0.3		–39	–0.9
406 (9.8%)	+54	+1.2		Reference	
137±?/80±?	–12±12/–3±7	–8/–4	<0.01	–14/–3	–7/–4
148±?/84±?	–2±14/0.1±9	–1/0	NS	Reference	
150±?/85±?	–21±23/–13±11	–12/–13	<0.001	+1/–1	+1/–1
150±?/86±?	–22±24/–12±11	–13/–12	<0.001	Reference	
130±12/85±8	–30/–21	–19/–20	<0.001	–12/–5	–7/–5
135±12/88±8	–18/–16	–12/–15	<0.01	Reference	
131±12/84±8	–27/–20	–17/–19	<0.001	–9/–4	–5/–4
139±12/88±6	–19/–14	–12/–14	<0.01	–1/+2	0/+1
135±2/87±1	–26/–18	–16/–17	<0.001	–3/–3	–2/–2
138±2/87±2	–23/–15	–14/–15	<0.001	Reference	
161±16/81±7	–16/–6	–9/–7	<0.001	–5/+1	–3/+1
163±17/80±9	–11/–7	–6/–8	<0.001	Reference	
143±4/91±2	–21/–14	–13/–14	<0.01	+2/+1	0/0
151±5/90±3	–23/–15	–13/–14	<0.01	Reference	
134/88	–8/–5	–6/–5	NS	–3/–3	–3/–3
136/89	–1/–5	–1/–5	NS	+3/–3	+2/–3
139/92	–4/–2	–3/–2	NS		
140±?/92±?	–15 (–23 to –6)	–10	<0.001	0	0
	–11 (–14 to –8)	–11		0	0
144±?/91±?	–11 (–28 to –2)	–10	<0.001	Reference	
	–15 (–14 to –8)	–11			

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±? 136±?/85±?	–28±13/–16±7 –27±12/–16±7	–17/–16 –17/–16	<0.001 <0.001	–1/0 Reference	0/0
	141±13/87±9 141±17/85±10	–8/–11 –7/–14	–5/–11 –5/–14	<0.001 <0.001	0/+2 Reference	0/+3
	144±16/81±9 145±17/81±9	–30/–17 –29/–17	–17/–17 –17/–17	<0.001 <0.001	–1/0 Reference	0/0 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	99.7	99.7	98.6	98.3
	1 667	99.3	99.2	97.7	96.0
	1 429	99.2	99.1	95.9	95.5
	–	99.8	99.8	99.1	99.2
	1 000	99.6	99.6	97.9	97.8
	2 000	99.5	99.3	96.9	96.6
	1 429	99.6	99.6	98.2	97.8
	–	99.3	99.3	96.4	96.7
	1 250	99.7	99.6	98.2	99.2
	–	99.1	99.2	95.3	95.8
	10 000	99.5	99.5	97.6	97.5
	278	99.2	98.8	95.9	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 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
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 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
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 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
	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 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
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 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
	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 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
	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 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
	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 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
	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 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	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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