Dr Patrick Kay

General & Interventional Cardiologist

Middlemore & Auckland City Hospitals

Ambulatory BP Monitoring - Concurrent Workshop Repeated

Sunday, 23 June 2013	Start 8:30am	Duration: 55mins	Works
	Start 9:35am	Duration: 55mins	Works

HYPERTENSION

Patrick Kay, Interventional Cardiologist
Auckland

Rotorua 2013

HYPERTENSION

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Rotorua 2013

1. Who is this man?

- (A) Wolfgang Amadeus Mozart
- (B) Daniel Bernoulli
- (C) Stephen Harper
- (D) Stephen Hales

New European Guidelines for BP released 14 June 2014

New Aspects of the Guidelines

1.2 New aspects

- Strengthening of the prognostic value of home blood pressure monitoring (HBPM) and of its role for diagnosis and management of hypertension, next to ambulatory blood pressure monitoring (ABPM).
- Update of the prognostic significance of night-time BP, white-coat hypertension and masked hypertension.
- Re-emphasis on integration of BP, cardiovascular (CV) risk factors, asymptomatic organ damage (OD) and clinical complications for total CV risk assessment.
- Update of the prognostic significance of asymptomatic OD, including heart, blood vessels, kidney, eye and brain.
- Reconsideration of the risk of overweight and target body mass index (BMI) in hypertension.
- Hypertension in young people.
- Initiation of antihypertensive treatment. More evidence-based criteria and no drug treatment of high normal BP.
- Target BP for treatment. More evidence-based criteria and unified target systolic blood pressure (SBP) (<140 mmHg) in both higher and lower CV risk patients.
- Liberal approach to initial monotherapy, without any all-ranking purpose.
- Revised schema for priorital two-drug combinations.
- New therapeutic algorithms for achieving target BP.
- Extended section on therapeutic strategies in special conditions.
- Revised recommendations on treatment of hypertension in the elderly.
- Drug treatment of octogenarians.
- Special attention to resistant hypertension and new treatment approaches.
- Increased attention to OD-guided therapy.
- New approaches to chronic management of hypertensive disease.

Premise

- The initial evaluation of a patient with hypertension should
- 1. confirm the diagnosis of hypertension
- 2. detect causes of secondary hypertension
- 3. Assess CV risk and end-organ damage

Stratification of total CV risk in categories of low, moderate, high and very high risk according to SBP and DBP and prevalence of RFs, asymptomatic OD, diabetes, CKD stage or symptomatic CVD. Subjects with a high normal office but a raised out-of-office BP (masked hypertension) have a CV risk in the hypertension range.

Other risk factors, asymptomatic organ damage or disease	Blood Pressure (mmHg)			
	High normal SBP 130–139 or DBP 85–89	Grade 1 HT SBP 140–159 or DBP 90–99	Grade 2 HT SBP 160–179 or DBP 100–109	Grade 3 HT SBP ≥180 or DBP ≥110
No other RF		Low risk	Moderate risk	High risk
1–2 RF	Low risk	Moderate risk	Moderate to high risk	High risk
≥3 RF	Low to Moderate risk	Moderate to high risk	High Risk	High risk
OD, CKD stage 3 or diabetes	Moderate to high risk	High risk	High risk	High to very high risk
Symptomatic CVD, CKD stage ≥4 or diabetes with OD/RFs	Very high risk	Very high risk	Very high risk	Very high risk

BP = blood pressure; CKD = chronic kidney disease; CV = cardiovascular; CVD = cardiovascular disease; DBP = diastolic blood pressure; HT = hypertension; OD = organ damage; RF = risk factor; SBP = systolic blood pressure.

Authors/Task Force Members et al. Eur Heart J 2013;eurheartj.eht151

European Heart Journal

Office blood pressure measurement

When measuring BP in the office, care should be taken:
• To allow the patients to sit for 3–5 minutes before beginning BP measurements.
• To take at least two BP measurements, in the sitting position, spaced 1–2 min apart, and additional measurements if the first two are quite different. Consider the average BP if deemed appropriate.
• To take repeated measurements of BP to improve accuracy in patients with arrhythmias, such as atrial fibrillation.
• To use a standard bladder (12–13 cm wide and 35 cm long), but have a larger and a smaller bladder available for large (arm circumference >32 cm) and thin arms, respectively.
• To have the cuff at the heart level, whatever the position of the patient.
• When adopting the auscultatory method, use phase I and V (disappearance) Korotkoff sounds to identify systolic and diastolic BP, respectively.
• To measure BP in both arms at first visit to detect possible differences. In this instance, take the arm with the higher value as the reference.
• To measure at the first visit, BP 1 and 3 min after assumption of the standing position in elderly subjects, diabetic patients, and in other conditions in which orthostatic hypotension may be frequent or suspected.
• To measure, in case of conventional BP measurement, heart rate by pulse palpation (at least 30 s) after the second measurement in the sitting position.

In-Office-Most reproducible BP

- Electronic device
- Multiple recordings
- Quietened room

Definitions and classification of office blood pressure levels (mmHg)

Category	Systolic		Diastolic
Optimal	<120	and	<80
Normal	120–129	and/or	80–84
High normal	130–139	and/or	85–89
Grade 1 hypertension	140–159	and/or	90–99
Grade 2 hypertension	160–179	and/or	100–109
Grade 3 hypertension	≥180	and/or	≥110
Isolated systolic hypertension	≥140	and	<90

Definitions of hypertension by office and out-of-office blood pressure levels

Category	Systolic BP (mmHg)		Diastolic BP (mmHg)
Office BP	≥140	and/or	≥90
Ambulatory BP			
Daytime (or awake)	≥135	and/or	≥85
Nighttime (or asleep)	≥120	and/or	≥70
24-h	≥130	and/or	≥80
Home BP	≥135	and/or	≥85

Out of Office Blood Pressure Assessment

- Ambulatory BP assessment
- Home BP assessment
- Correlation between these 2 modalities is fair to moderate!

Clinical indications for out-of-office blood pressure measurement for diagnostic purposes

Clinical indications for HBPM or ABPM
• Suspicion of white-coat hypertension
- Grade I hypertension in the office
- High office BP in individuals without asymptomatic organ damage and at low total CV risk
• Suspicion of masked hypertension
- High normal BP in the office
- Normal office BP in individuals with asymptomatic organ damage or at high total CV risk
• Identification of white-coat effect in hypertensive patients
• Considerable variability of office BP over the same or different visits
• Autonomic, postural, post-prandial, siesta- and drug-induced hypotension
• Elevated office BP or suspected pre-eclampsia in pregnant women
• Identification of true and false resistant hypertension
Specific indications for ABPM
• Marked discordance between office BP and home BP
• Assessment of dipping status
• Suspicion of nocturnal hypertension or absence of dipping, such as in patients with sleep apnoea, CKD, or diabetes
• Assessment of BP variability

Example of ABPs

Case 1

37 yr old male
Well, semi-pro golfer.
+ve family history of ischemic heart disease
GP – BP=150/90mmHg, P=70
Clinic BP – 150/100mmHg, both arms. Repeated after 10 mins.

ABPM applied

AMBULATORY BLOOD PRESSURE REPORT

Dr P Kay

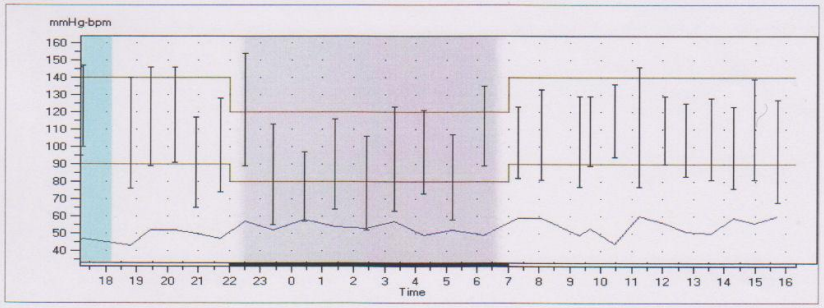
Patient Name: **Patient ID:** qay9355 **Test Date:** 02-Nov-2012

Interpretive Summary

Based upon ESH and AHA recommendations, the ABPM data suggests

- Normal 24 hour SYS and DIA pressure (129/77 mmHg)
- Normal awake SYS and DIA pressure (134/83 mmHg)
- Normal asleep SYS and DIA pressure (119/67 mmHg)

1st hour max (147/100 mmHg) and available literature suggest white coat syndrome.
Asleep dip is 10.8% SYS and 19.3% DIA, Dipper (normal)



Period	Time	Samples	Mean Sys mmHg (+/- Std.Dev.)	Mean Dia mmHg (+/- Std.Dev.)	Mean HR BPM (+/- Std.Dev.)	BP Load Sys %	BP Load Dia %
Overall	17:12-15:44 (22:32)	28	129 (13.9)	77 (13.2)	53 (4.9)	32	21
Awake Period	07:00-22:00	19	134 (9.5)	83 (9.3)	52 (5.6)	26	21
Asleep Period	22:00-07:00	9	119 (17.1)	67 (14.0)	53 (3.4)	44	22
White Coat Period	17:12-18:12 (1st Hr)	2				100	100
Maximum			147	100	47	-	-
Mean			146	98	46	-	-

Asleep Dip: Sys = 10.8% Dia = 19.3%

Current Medications

Physician Interpretation

Referring physician: **Interpreting physician:**

Signature Date Signature Date

AMBULATORY BLOOD PRESSURE REPORT

Dr P Kay

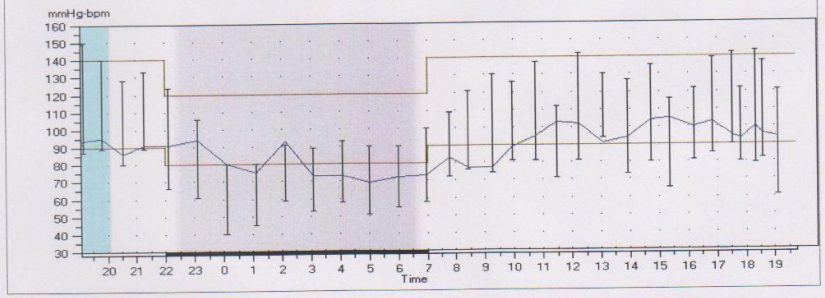
Patient Name: s [redacted] **Patient ID:** 14 october 2 **Test Date:** 13-Oct-2010

Interpretive Summary

Based upon ESH and AHA recommendations, the ABPM data suggests

- Optimal 24 hour SYS and DIA pressure (120/72 mmHg)
- Normal awake SYS and DIA pressure (131/80 mmHg)
- Optimal asleep SYS and DIA pressure (94/55 mmHg)

1st hour max (150/92 mmHg) and available literature suggest white coat syndrome.
Asleep dip is 28.0% SYS and 31.9% DIA, Dipper (normal)



Period	Time	Samples	Mean Sys mmHg (+/- Std.Dev.)	Mean Dia mmHg (+/- Std.Dev.)	Mean HR BPM (+/- Std.Dev.)	BP Load Sys %	BP Load Dia %
Overall	19:07-19:07 (24:00)	33	120 (20.7)	72 (14.4)	89 (10.7)	18	6
Awake Period	07:00-22:00	23	131 (11.3)	80 (8.3)	94 (7.8)	22	9
Asleep Period	22:00-07:00	10	94 (13.1)	55 (7.7)	79 (9.6)	10	0
White Coat Period	19:07-20:07 (1st Hr)	3				67	33
Maximum			150	92	95	-	-
Mean			146	89	94	-	-

Asleep Dip: Sys = 28.0% Dia = 31.9%

Current Medications

Physician Interpretation

Referring physician:

Signature Date

Interpreting physician:

Signature Date

Case 2

56yr Chinese female. Borderline BP readings last 2 years
Dyslipidemic

GP – 146/94, 136/96, 164/102 over last 6 months
Clinic – 156/98mmHg

ABPM apllied

AMBULATORY BLOOD PRESSURE REPORT

Dr P Kay

SunTech®

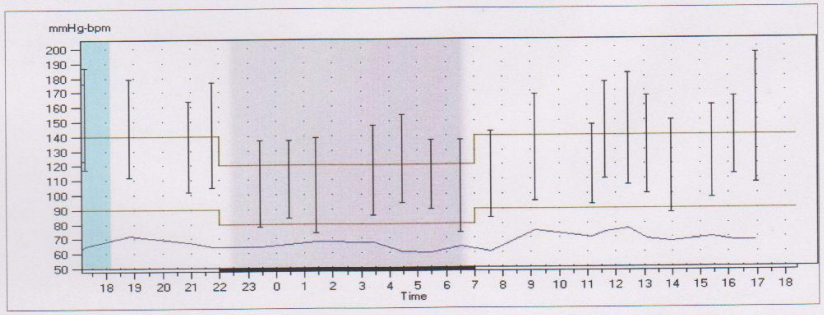
Patient Name: y [redacted] **Patient ID:** 24.08.1956 **Test Date:** 20-Jul-2010

Interpretive Summary

Based upon ESH and AHA recommendations, the ABPM data suggests

- 24 hour SYS and DIA hypertension (160/97 mmHg)
- Awake SYS and DIA hypertension (169/103 mmHg)
- Asleep SYS and DIA hypertension (141/83 mmHg)

Asleep dip is 16.6% SYS and 19.9% DIA, Dipper (normal)



Period	Time	Samples	Mean Sys mmHg (+/- Std.Dev.)	Mean Dia mmHg (+/- Std.Dev.)	Mean HR BPM (+/- Std.Dev.)	BP Load Sys %	BP Load Dia %
Overall	17:09-17:46 (24:37)	22	160 (18.5)	97 (13.9)	67 (4.4)	100	77
Awake Period	07:00-22:00	15	169 (14.9)	103 (11.0)	69 (4.4)	100	87
Asleep Period	22:00-07:00	7	141 (6.7)	83 (7.8)	64 (3.0)	100	57
White Coat Period	17:09-18:09 (1st Hr)	2				100	100
Maximum			187	123	65	-	-
Mean			182	120	64	-	-

Asleep Dip: Sys = 16.6% Dia = 19.9%

Current Medications

Physician Interpretation

Referring physician:

Signature Date

Interpreting physician:

Signature Date

AMBULATORY BLOOD PRESSURE REPORT

Dr P Kay

SunTech®

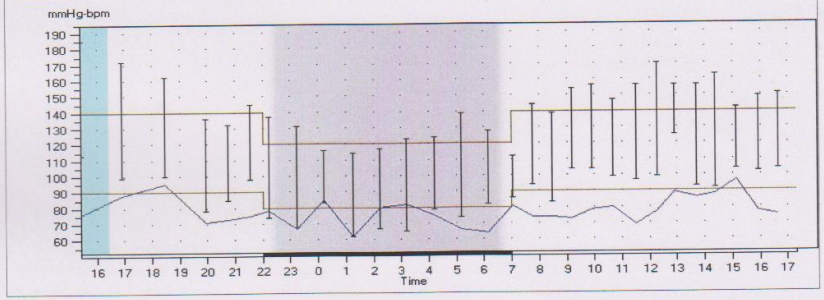
Patient Nam [redacted] **Patient ID:** bny5322 **Test Date:** 16-Sep-2011

Interpretive Summary

Based upon ESH and AHA recommendations, the ABPM data suggests

- 24 hour SYS and DIA hypertension (143/90 mmHg)
- Awake SYS and DIA hypertension (151/98 mmHg)
- Asleep SYS and DIA hypertension (125/73 mmHg)

Asleep dip is 17.1% SYS and 25.8% DIA, Dipper (normal)



Period	Time	Samples	Mean Sys mmHg (+/- Std.Dev.)	Mean Dia mmHg (+/- Std.Dev.)	Mean HR BPM (+/- Std.Dev.)	BP Load Sys %	BP Load Dia %
Overall	15:27-16:40 (25:13)	29	143 (18.5)	90 (15.3)	78 (8.6)	76	62
Awake Period	07:00-22:00	20	151 (15.8)	98 (10.6)	80 (8.0)	80	80
Asleep Period	22:00-07:00	9	125 (9.0)	73 (7.6)	73 (8.6)	67	22
White Coat Period	15:27-16:27 (1st Hr)	1				100	100
Maximum			185	113	76	-	-
Mean			185	113	76	-	-

Asleep Dip: Sys = 17.1% Dia = 25.8%

Current Medications

Physician Interpretation

Referring physician: Patrick Kay

Interpreting physician: Patrick Kay

Signature Date Signature Date

AMBULATORY BLOOD PRESSURE REPORT

Dr P Kay

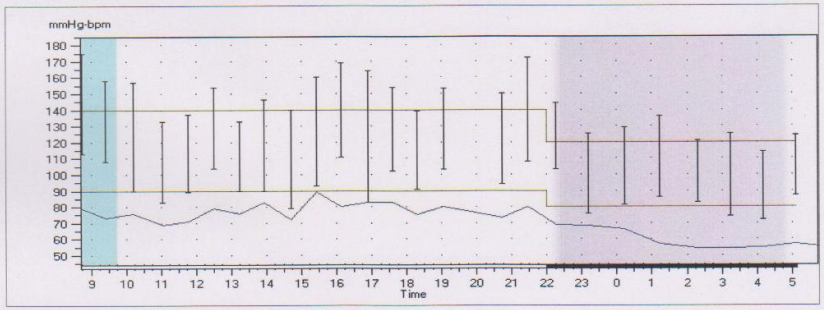
Patient Name: [redacted] **Patient ID:** 22.04.1970 **Test Date:** 15-Feb-2013

Interpretive Summary

Based upon ESH and AHA recommendations, the ABPM data suggests

- 24 hour SYS and DIA hypertension (143/90 mmHg)
- Awake SYS and DIA hypertension (152/95 mmHg)
- Asleep SYS and DIA hypertension (127/81 mmHg)

Asleep dip is 16.4% SYS and 14.6% DIA, Dipper (normal)



Period	Time	Samples	Mean Sys mmHg (+/- Std.Dev.)	Mean Dia mmHg (+/- Std.Dev.)	Mean HR BPM (+/- Std.Dev.)	BP Load Sys %	BP Load Dia %
Overall	08:44-07:43 (22:59)	28	143 (16.7)	90 (12.4)	71 (10.2)	75	57
Awake Period	07:00-22:00	18	152 (13.2)	95 (10.5)	77 (5.4)	67	56
Asleep Period	22:00-07:00	10	127 (8.2)	81 (10.5)	60 (6.0)	90	60
White Coat Period	08:44-09:44 (1st Hr)	2				100	100
Maximum			175	113	79	-	-
Mean			166	110	76	-	-

Asleep Dip: Sys = 16.4% Dia = 14.6%

Current Medications

Physician Interpretation

Referring physician: **Interpreting physician:**

Signature Date Signature Date

Advantages of ABPM

- Overcomes the variability seen in GP/clinic/hospital environments
- Many measurements in a home/work environment
- Allows greater buy-in / understanding from patients
- Closely correlated to end-organ CV events (ARTEMIS STUDY)
- Allows understanding of diurnal variation of blood pressure-dipper
- / non-dipper.
- Non-dippers strongly correlated with CVD events and end organ damage LVH, IMT and CVD death

Home BP recordings

How Do You Do It?

Morning and evening for 7 days
Quiet room rested for 5 mins
Arm and back supported with cuff at the level if the heart
Logbook or preferrably electronic database (avoids editing by patient)
Exclude first day of monitoring
The Home BP is the average of all recordings of the 6/7 days

BUT unlike ABPM does not give data :

- during routine activities
- during sleep

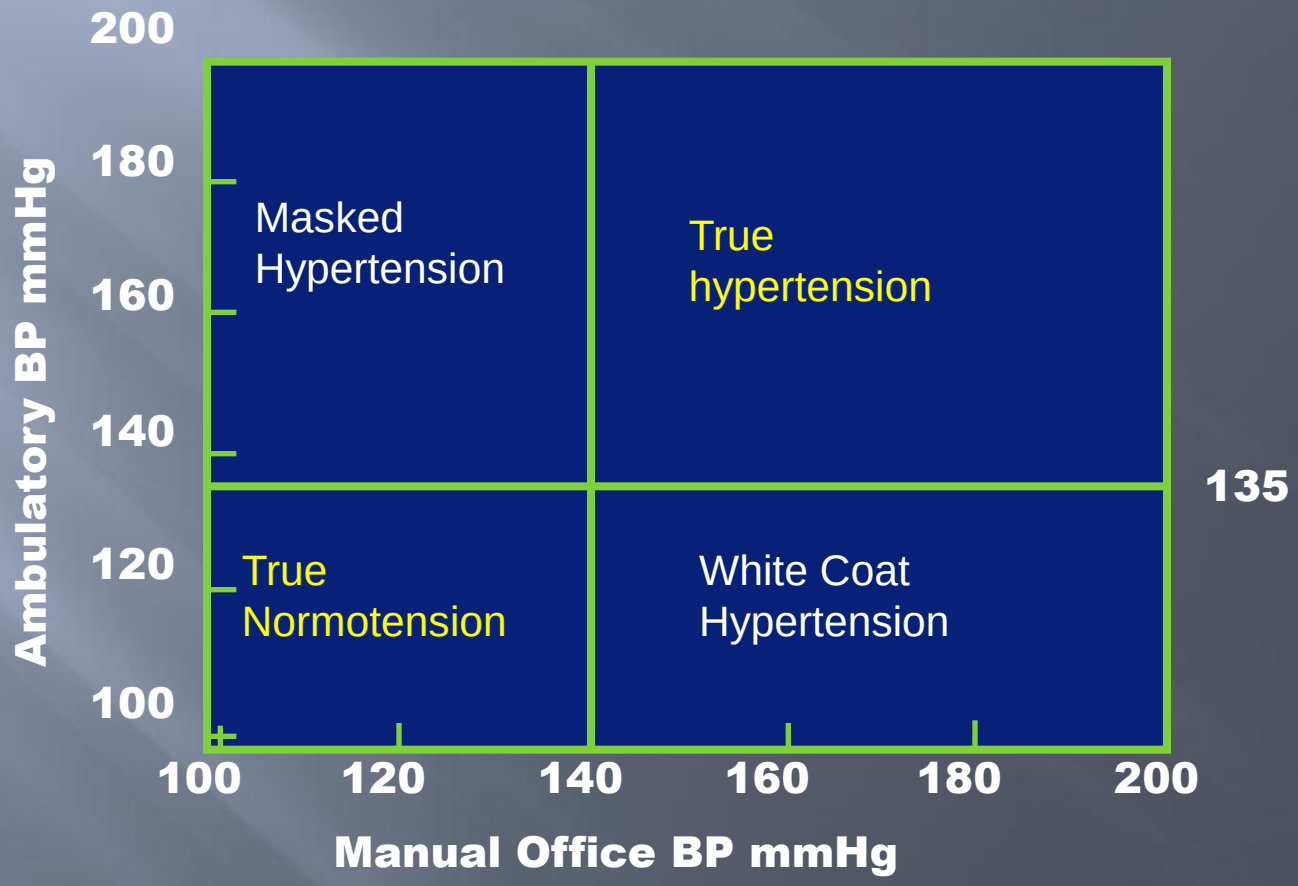
To quantify short –term BP variability

Home BP recordings

Better than office BP at predicting CV events and more closely correlated to development LVH and CV morbidity and mortality

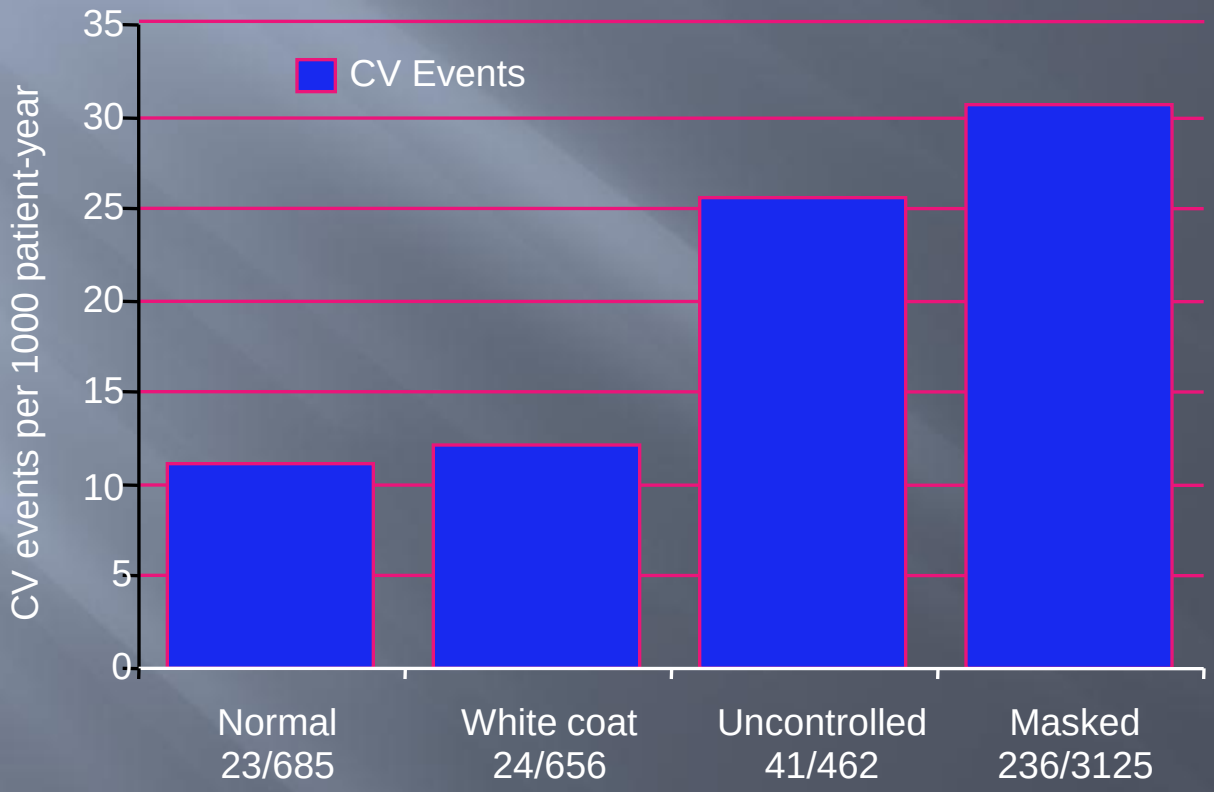
- As good as ABPM for end-organ risk and CV events

Only relying on manual office blood pressures misses out on white coat and masked hypertension



From Pickering, *Hypertension* 1992

The prognosis of masked hypertension



Bobrie et al. *JAMA* 2004;291:1342-9

White Coat and Masked Hypertension

Both seen in 13% hypertensive population

White Coat associations: age, female, non-smoking

Masked hypertension associations: younger age, male, exercise
Obesity, diabetes, CKD, family history of hypertension.
CV events equate to true sustained hypertension. In diabetic patients
Sustained nocturnal hypertension may occur leading to nephropathy

2. Who first described an epidemiological association between high blood pressure and premature death?

- (A) Hippocrates
- (B) Nikolai Korotkoff
- (C) New York Insurance Company Actuaries in the 1920s
- (D) The Framingham Study Group in 1961

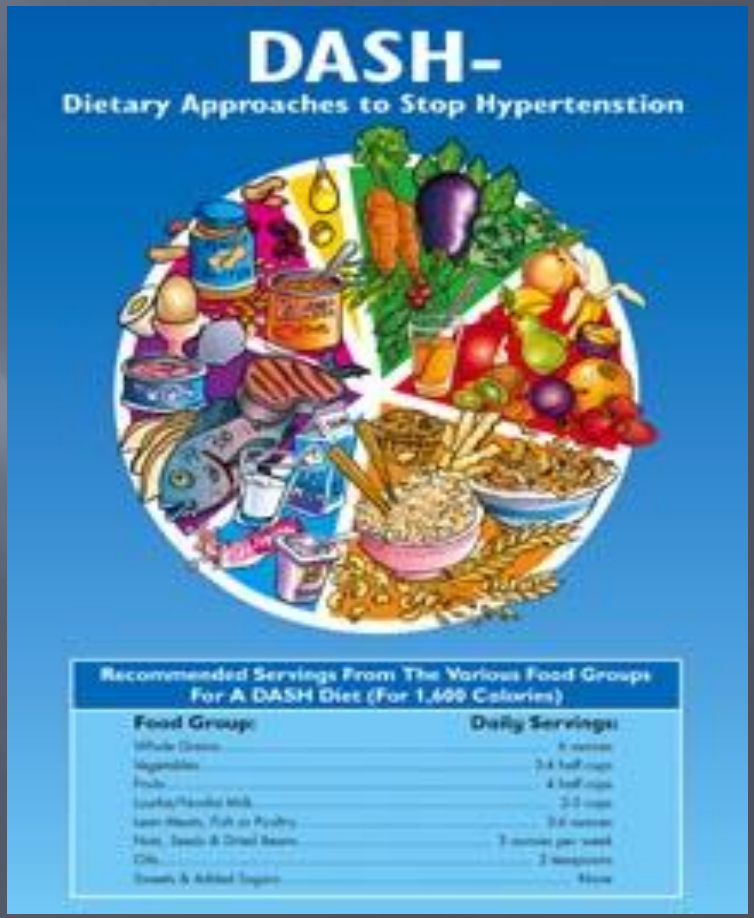
3. What was the largest antihypertensive drug trial ever conducted?

- (A) ALLHAT
- (B) CAPPP
- (C) STOP-Hypertension-2
- (D) CAMELOT

TREATMENT

Non-pharmacologic therapy

- Dietary salt restriction
- Weight loss
- DASH diet
- Exercise
- Limited alcohol intake
- Vitamin D
- Patient education
- Smoking / NSAIDs



Lifestyle modifications in the management of hypertension

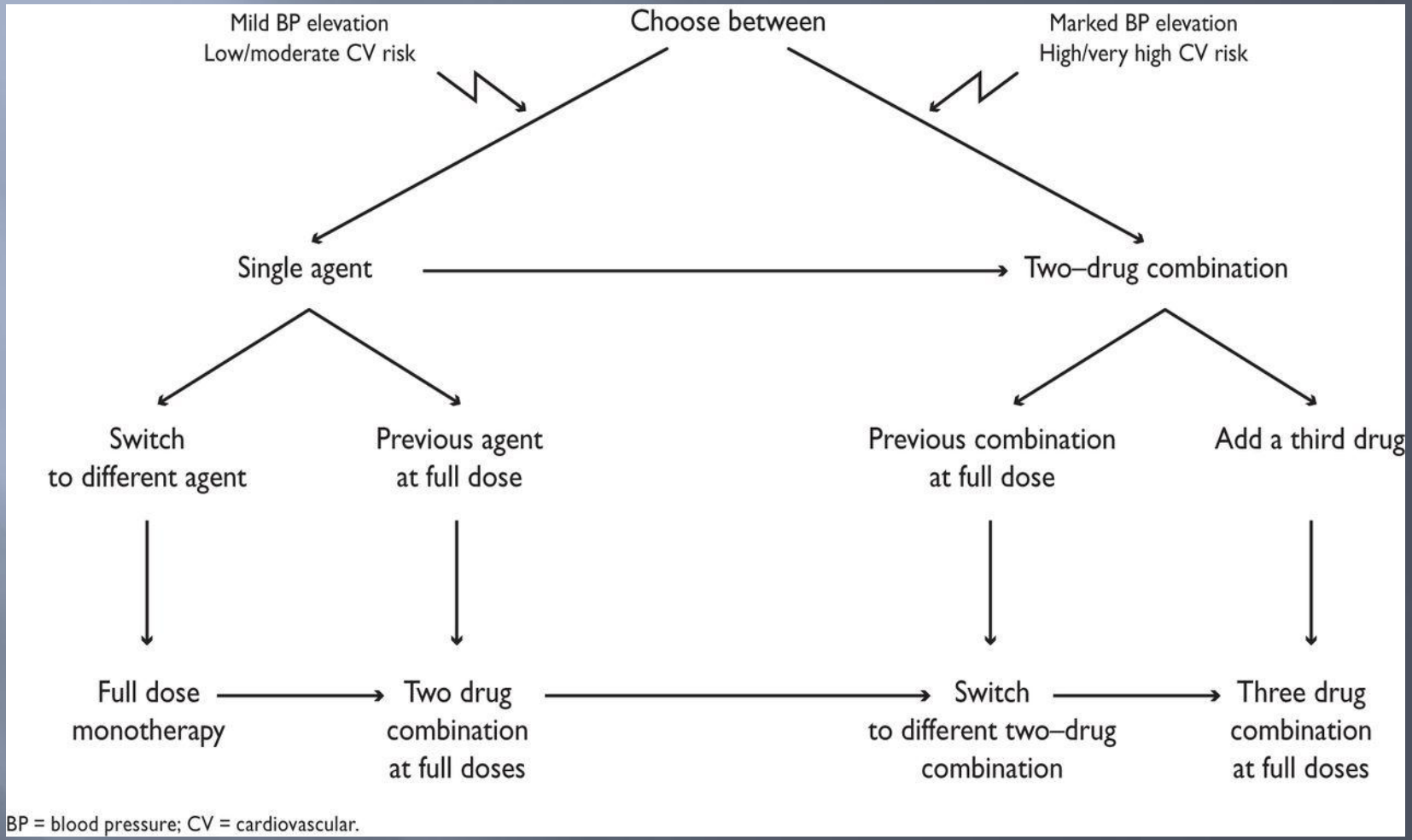
Modification	Recommendation	Approximate systolic BP reduction, range*
Weight reduction	Maintain normal body weight (BMI, 18.5 to 24.9 kg/m2)	5 to 20 mmHg per 10-kg weight loss
Adopt DASH eating plan	Consume a diet rich in fruits, vegetables, and low-fat dairy products with a reduced content of saturated and total fat	8 to 14 mmHg
Dietary sodium reduction	Reduce dietary sodium intake to no more than 100 meq/day (2.4 g sodium or 6 g sodium chloride)	2 to 8 mmHg
Physical activity	Engage in regular aerobic physical activity such as brisk walking (at least 30 minutes per day, most days of the week)	4 to 9 mmHg
Moderation of alcohol consumption	Limit consumption to no more than 2 drinks per day in most men and no more than 1 drink per day in women and lighter-weight persons	2 to 4 mmHg

For overall cardiovascular risk reduction, stop smoking. The effects of implementing these modifications are dose and time dependent and could be higher for some individuals; they are not all additive.

BMI: body mass index; BP: blood pressure; DASH: Dietary Approaches to Stop Hypertension.

Reproduced from: The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Available at http://www.nhlbi.nih.gov/guidelines/hypertension/jnc7full.pdf.

Monotherapy vs. drug combination strategies to achieve target BP. Moving from a less intensive to a more intensive therapeutic strategy should be done whenever BP target is not achieved.



BP = blood pressure; CV = cardiovascular.

Authors/Task Force Members et al. Eur Heart J 2013;eurheartj.eht151

European Heart Journal

Recommended Medications

- The first choice for initial therapy should be either a calcium-channel blocker or ACE inhibitor/ARB or a thiazide-type diuretic [chlorthalidone].
- If initial therapy was with a calcium-channel blocker or a thiazide-type diuretic and a second drug is required, an ACE inhibitor should be added. If initial therapy was with an ACE inhibitor, a calcium-channel blocker or thiazide-type diuretic should be added.
- If treatment with three drugs is required, the combination of ACE inhibitor, calcium-channel blocker, and thiazide-type diuretic should be used.
- If blood pressure remains uncontrolled on adequate doses of three drugs, physicians should consider adding a fourth and/or seeking expert advice. Consider use of Spironolactone.
- If a fith drug is required, one of the following should be considered; a higher dose of a thiazide-type diuretic, the addition of another diuretic (careful monitoring is recommended), beta blockers, and/or selective alpha blockers.
- Beta blockers are not a preferred initial therapy for hypertension. However, beta blockers may be considered in younger people, particularly those with an intolerance or contraindication to ACE inhibitors and angiotensin II receptor blockers (ARBS), women of child-bearing potential, or patients with evidence of increased sympathetic drive.
- In patients whose blood pressure is well controlled (ie< 140/90mm Hg) with a regimen that includes a beta blocker; long term management should be considered as part of their routine review. In these patients, there is no absolute need to replace the beta blocker with an alternative agent.
- With use of betablocker consider co-administraion with alpha bocker.

Considerations for individualizing antihypertensive therapy

Indication	Antihypertensive drugs
Compelling indications (major improvement in outcome independent of blood pressure)	
Systolic heart failure	ACE inhibitor or ARB, beta blocker, diuretic, aldosterone antagonist*
Post-myocardial infarction	ACE inhibitor, beta blocker, aldosterone antagonist
Proteinuric chronic kidney disease	ACE inhibitor and/or ARB
Angina pectoris	Beta blocker, calcium channel blocker
Atrial fibrillation rate control	Beta blocker, nondihydropyridine calcium channel blocker
Atrial flutter rate control	Beta blocker, nondihydropyridine calcium channel blocker
Likely to have a favorable effect on symptoms in comorbid conditions	
Benign prostatic hypertrophy	Alpha blocker
Essential tremor	Beta blocker (noncardioselective)
Hyperthyroidism	Beta blocker
Migraine	Beta blocker, calcium channel blocker
Osteoporosis	Thiazide diuretic
Perioperative hypertension	Beta blocker
Raynaud's syndrome	Dihydropyridine calcium channel blocker
Contraindications	
Angioedema	ACE inhibitor
Bronchospastic disease	Beta blocker
Depression	Reserpine
Liver disease	Methyldopa
Pregnancy	ACE inhibitor, ARB (includes women likely to become pregnant)
Second or third degree heart block	Beta blocker, nondihydropyridine calcium channel blocker
May have adverse effect on comorbid conditions	
Depression	Beta blocker, central alpha agonist
Gout	Diuretic
Hyperkalemia	Aldosterone antagonist, ACE inhibitor, ARB
Hyponatremia	Thiazide diuretic
Renovascular disease	ACE inhibitor or ARB

* A survival benefit from an aldosterone antagonist has only been demonstrated in patients with advanced heart failure; in patients with less severe disease, an aldosterone antagonist is primarily given for hypokalemia

Adapted from The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure, JAMA 2003; 289:2560.

Methods to improve adherence to physicians' recommendations

Patient level
Information combined with motivational strategies (see Section 5.1.6 on smoking cessation).
Group sessions.
Self-monitoring of blood pressure.
Self-management with simple patient-guided systems.
Complex interventions.[a]
Drug treatment level
Simplification of the drug regimen.
Reminder packaging.
Health system level
Intensified care (monitoring, telephone follow-up, reminders, home visits, telemonitoring of home blood pressure, social support, computer-aided counselling and packaging).
Interventions directly involving pharmacists.
Reimbursement strategies to improve general practitioners' involvement in evaluation and treatment of hypertension.

Gaps in evidence and need for future trials

- Should antihypertensive drug treatment be given to all patients with grade 1 hypertension when their CV risk is low-to-moderate?
- Should elderly patients with a SBP between 140 and 160 mmHg be given antihypertensive drug treatments?
- Should drug treatment be given to subjects with white-coat hypertension? Can this condition be differentiated into patients needing or not needing treatment?
- Should antihypertensive drug treatment be started in the high normal BP range and, if so, in which patients?
- What are the optimal office BP values (i.e. the most protective and safe) for patients to achieve by treatment in different demographic and clinical conditions?
- Do treatment strategies based on control of out-of-office BP provide an advantage (reduced clinical morbidity and mortality, fewer drugs, fewer side-effects) over strategies based on conventional (office) BP control?
- What are the optimal out-of-office (home and ambulatory) BP values to be reached with treatment and should targets be lower or higher in high risk hypertensives?
- Does central BP add to CV event prediction in untreated and treated hypertensive patients?
- Do invasive procedures for treatment of resistant hypertension compare favourably with the best drug treatment and provide long-term BP control and reduction of morbid and fatal events?
- Do treatment-induced changes in asymptomatic OD predict outcome? Which measures—or combinations of measures—are most valuable?
- Are lifestyle measures known to reduce BP capable of reducing morbidity and mortality in hypertensive patients?
- Does a treatment-induced reduction of 24h BP variability add to CV protection by antihypertensive treatment?
- Does BP reduction substantially lower CV risk in resistant hypertension?

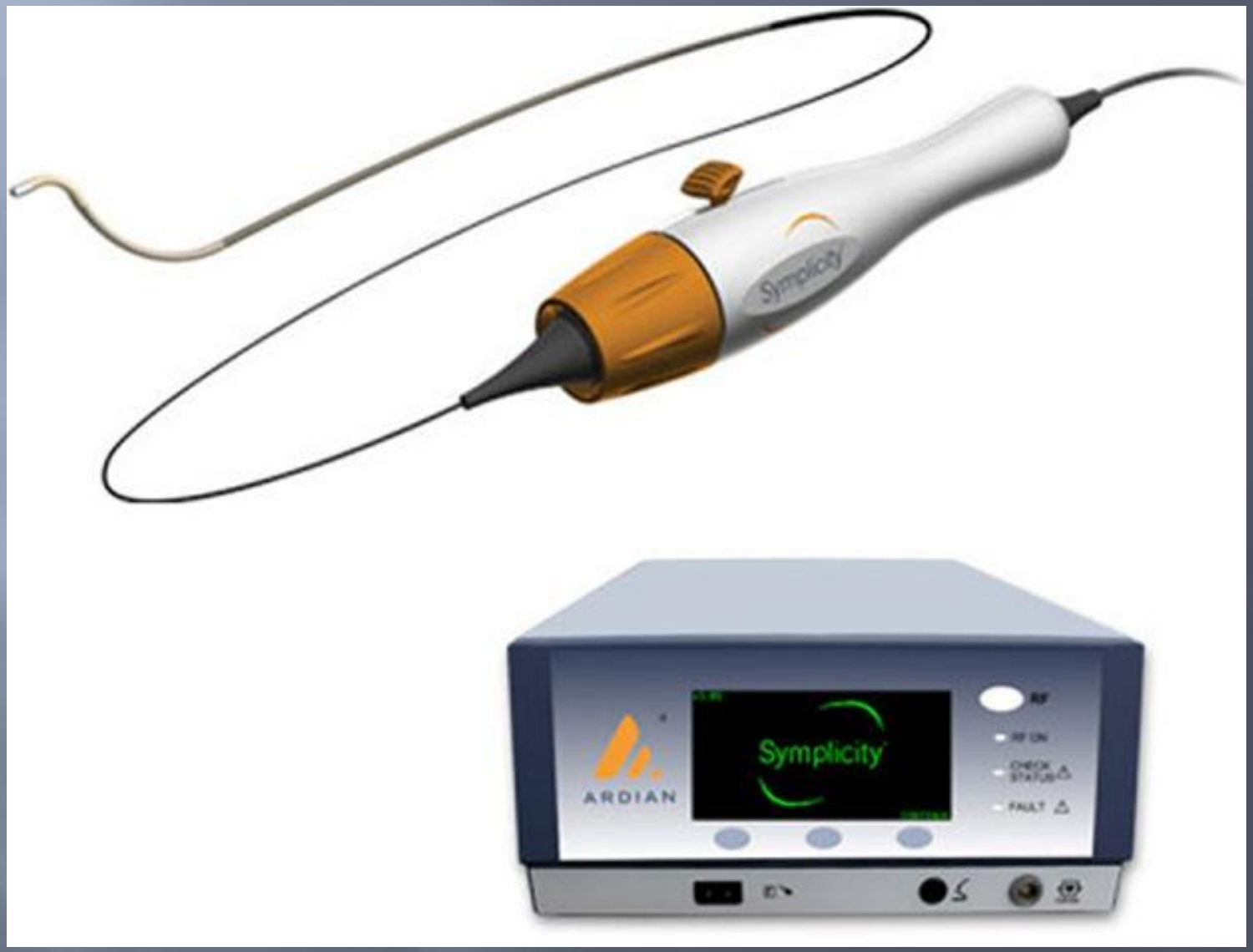
The Symplicity HTN-2 Trial

- Renal sympathetic denervation in patients with treatment-resistant hypertension: a randomised controlled trial

- 106 patients with resistant hypertension
- Randomised to denervation or standard therapy

- Results after 6 months follow-up
  - Mean 32/12 BP reduction in active group
  - cf. 1/0 BP increase in control group

Lancet 2010 ; 376 : 1903-1909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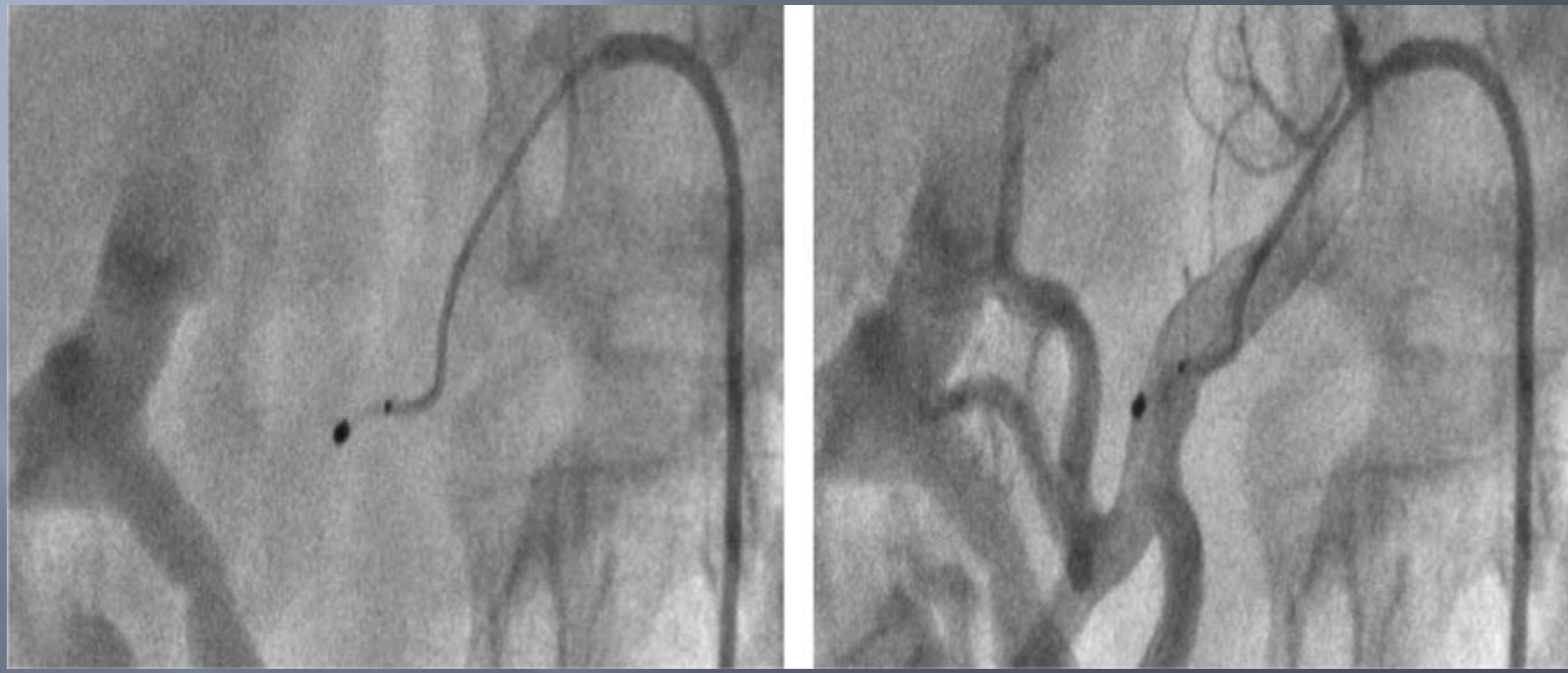
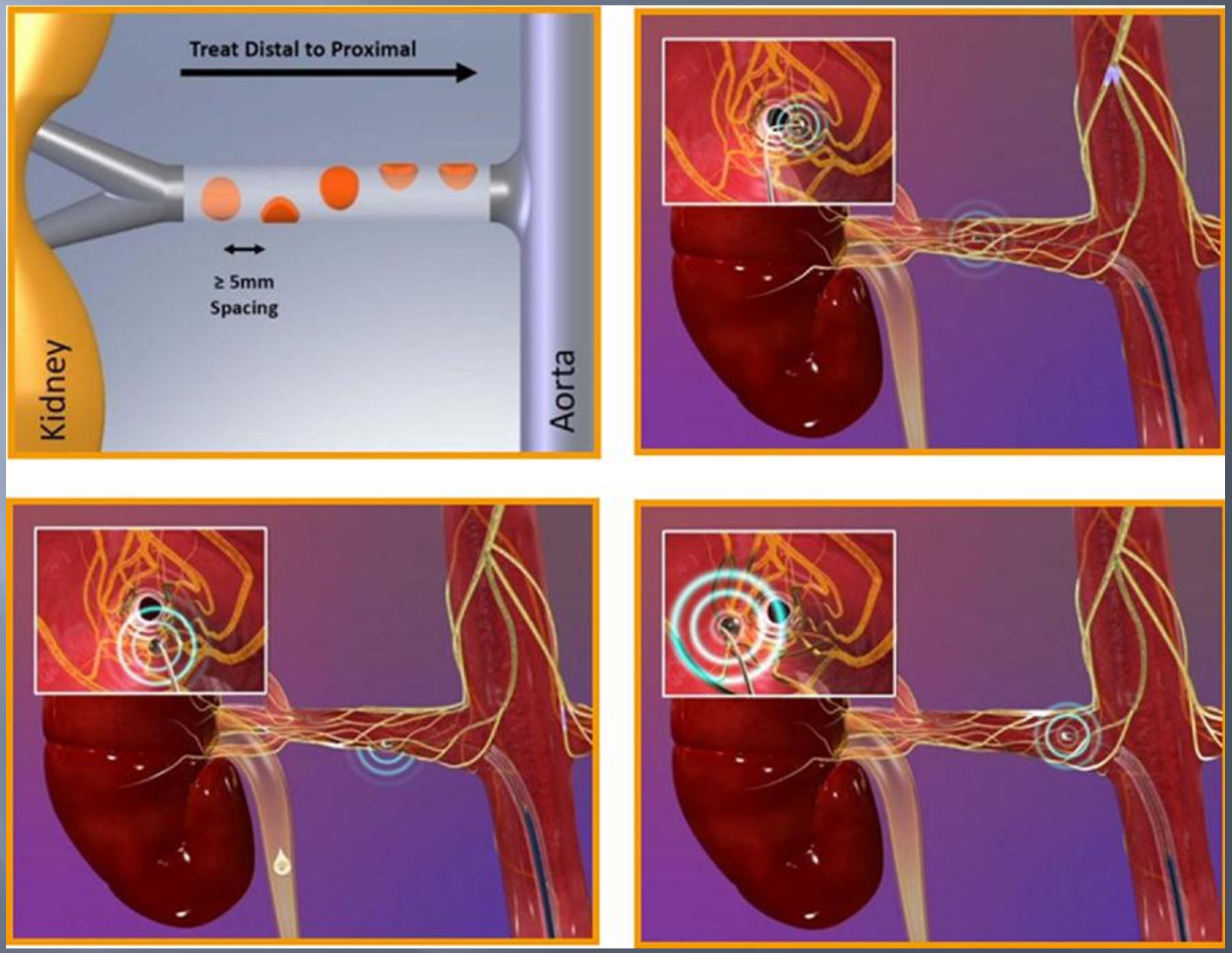
Symplicity




Treat Distal to Proximal
≥ 5mm
Spacing
Kidney
Aorta

- More patients and longer follow-up
- Further validate renal denervation

- Symplicity HTN-3 underway in USA
  → 530 patients, multicentre, prospective, single blind, RCT

Questions

A/Prof I Patrick Kay, Middlemore, Auckland City, Mercy Hospitals
Private Clincs: Apollo, Eastcare, Silverdale, Pukekohe

- First-line agents will normalise BP in 30-50% patients with mild hypertension
- Patient who is relatively unresponsive to one drug → almost 50% likelihood of becoming normotensive on a second drug

? Resistant hypertension

? Candidate for renal denervation

Personal and family medical history

1. Duration and previous level of high BP, including measurements at home.
2. Secondary hypertension
a) Family history of CKD (polycystic kidney).
b) History of renal disease, urinary tract infection, haematuria, analgesic abuse (parenchymal renal disease).
c) Drug/substance intake, e.g. oral contraceptives, liquorice, carbenoxolone, vasoconstrictive nasal drops, cocaine, amphetamines, gluco- and mineralocorticosteroids, non-steroidal anti-inflammatory drugs, erythropoietin, cyclosporine.
d) Repetitive episodes of sweating, headache, anxiety, palpitations (pheochromocytoma).
e) Episodes of muscle weakness and tetany (hyperaldosteronism).
f) Symptoms suggestive of thyroid disease.
3. Risk factors
a) Family and personal history of hypertension and CVD
b) Family and personal history of dyslipidaemia.
c) Family and personal history of diabetes mellitus (medications, blood-glucose levels, polyuria).
d) Smoking habits.
e) Dietary habits.
f) Recent weight changes; obesity.
g) Amount of physical exercise.
h) Snoring; sleep apnoea (information also from partner).
i) Low birth-weight.
4. History and symptoms of organ damage and cardiovascular disease.
a) Brain and eyes: headache, vertigo, impaired vision, TIA, sensory or motor deficit, stroke, carotid revascularization.
b) Heart: chest pain, shortness of breath, swollen ankles, myocardial infarction, revascularization, syncope, history of palpitations, arrhythmias, especially atrial fibrillation.
c) Kidney: thirst, polyuria, nocturia, haematuria.
d) Peripheral arteries: cold extremities, intermittent claudication, pain-free walking distance, peripheral revascularization.
e) History of snoring/chronic lung disease/sleep apnoea.
f) Cognitive dysfunction.
5. Hypertension management
a) Current antihypertensive medication.
b) Past antihypertensive medication.
c) Evidence of adherence or lack of adherence to therapy.
d) Efficacy and adverse effects of drugs.

Physical examination for secondary hypertension, organ damage and obesity

Signs suggesting secondary hypertension
• Features of Cushing syndrome.
• Skin stigmata of neurofibromatosis (pheochromocytoma).
• Palpation of enlarged kidneys (polycystic kidney).
• Auscultation of abdominal murmurs (renovascular hypertension).
• Auscultation of precordial or chest murmurs (aortic coarctation; aortic disease; upper extremity artery disease).
• Diminished and delayed femoral pulses and reduced femoral blood pressure compared to simultaneous arm BP (aortic coarctation; aortic disease; lower extremity artery disease).
• Left–right arm BP difference (aortic coarctation; subclavian artery stenosis).
Signs of organ damage
• Brain: motor or sensory defects.
• Retina: fundoscopic abnormalities.
• Heart: heart rate, 3rd or 4th heart sound, heart murmurs, arrhythmias, location of apical impulse, pulmonary rales, peripheral oedema.
• Peripheral arteries: absence, reduction, or asymmetry of pulses, cold extremities, ischaemic skin lesions.
• Carotid arteries: systolic murmurs.
Evidence of obesity
• Weight and height.
• Calculate BMI: body weight/height^2 (kg/m^2).
• Waist circumference measured in the standing position, at a level midway between the lower border of the costal margin (the lowest rib) and uppermost border of the iliac crest.

Laboratory investigations

Routine tests
• Haemoglobin and/or haematocrit.
• Fasting plasma glucose.
• Serum total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol.
• Fasting serum triglycerides.
• Serum potassium and sodium.
• Serum uric acid.
• Serum creatinine (with estimation of GFR).
• Urine analysis: microscopic examination; urinary protein by dipstick test; test for microalbuminuria.
• 12-lead ECG.
Additional tests, based on history, physical examination, and findings from routine laboratory tests
• Haemoglobin A_{1c} (if fasting plasma glucose is >5.6 mmol/L (102 mg/dL) or previous diagnosis of diabetes).
• Quantitative proteinuria (if dipstick test is positive); urinary potassium and sodium concentration and their ratio.
• Home and 24-h ambulatory BP monitoring.
• Echocardiogram.
• Holter monitoring in case of arrhythmias.
• Carotid ultrasound.
• Peripheral artery/abdominal ultrasound.
• Pulse wave velocity.
• Ankle-brachial index.
• Fundoscopy.
Extended evaluation (mostly domain of the specialist)
• Further search for cerebral, cardiac, renal, and vascular damage, mandatory in resistant and complicated hypertension.
• Search for secondary hypertension when suggested by history, physical examination, or routine and additional tests.

Predictive value, availability, reproducibility and cost–effectiveness of some markers of organ damage

Marker	Cardiovascular predictive value	Availability	Reproducibility	Cost-effectiveness
Electrocardiography	+++	++++	++++	++++
Echocardiography, plus Doppler	++++	+++	+++	+++
Estimated glomerular filtration rate	+++	++++	++++	++++
Microalbuminuria	+++	++++	++	++++
Carotid intima–media thickness and plaque	+++	+++	+++	+++
Arterial stiffness (pulse wave velocity)	+++	++	+++	+++
Ankle–brachial index	+++	+++	+++	+++
Fundoscopy	+++	++++	++	+++
Additional measurements				
Coronary calcium score	++	+	+++	+
Endothelial dysfunction	++	+	+	+
Cerebral lacunae/white matter lesions	++	+	+++	+
Cardiac magnetic resonance	++	+	+++	++

Clinical indications and diagnostics of secondary hypertension

	Clinical indications			Diagnostics	
Common causes	**Clinical history**	**Physical examination**	**Laboratory investigations**	**First-line test(s)**	**Additional/ confirmatory test(s)**
Renal parenchymal disease	History of urinary tract infection or obstruction, haematuria, analgesic abuse; family history of polycystic kidney disease.	Abdominal masses (in case of polycystic kidney disease).	Presence of protein, erythrocytes, or leucocytes in the urine, decreased GFR.	Renal ultrasound	Detailed work-up for kidney disease.
Renal artery stenosis	Fibromuscular dysplasia: early onset hypertension (especially in women). Atherosclerotic stenosis: hypertension of abrupt onset, worsening or increasingly difficult to treat; flash pulmonary oedema.	Abdominal bruit	Difference of >1.5 cm in length between the two kidneys (renal ultrasound), rapid deterioration in renal function (spontaneous or in response to RAA blockers).	Renal Duplex Doppler ultrasonography	Magnetic resonance angiography, spiral computed tomography, intra-arterial digital subtraction angiography.
Primary aldosteronism	Muscle weakness; family history of early onset hypertension and cerebrovascular events at age <40 years.	Arrhythmias (in case of severe hypokalaemia).	Hypokalaemia (spontaneous or diuretic-induced); incidental discovery of adrenal masses.	Aldosterone–renin ratio under standardized conditions (correction of hypokalaemia and withdrawal of drugs affecting RAA system).	Confirmatory tests (oral sodium loading, saline infusion, fludrocortisone suppression, or captopril test); adrenal CT scan; adrenal vein sampling.
Uncommon causes					
Pheochromocytoma	Paroxysmal hypertension or a crisis superimposed to sustained hypertension; headache, sweating, palpitations and pallor; positive family history of pheochromocytoma.	Skin stigmata of neurofibromatosis (café-au-lait spots, neurofibromas).	Incidental discovery of adrenal (or in some cases, extra-adrenal) masses.	Measurement of urinary fractionated metanephrines or plasma-free metanephrines.	CT or MRI of the abdomen and pelvis; 123 I-labelled meta-iodobenzyl-guanidine scanning; genetic screening for pathogenic mutations.
Cushing's syndrome	Rapid weight gain, polyuria, polydipsia, psychological disturbances.	Typical body habitus (central obesity, moon-face, buffalo hump, red striae, hirsutism).	Hyperglycaemia	24-h urinary cortisol excretion	Dexamethasone-suppression tests

Blood pressure goals in hypertensive patients

Recommendations	Class [a]	Level [b]	Ref. [c]
A SBP goal <140 mmHg:			
a) is recommended in patients at low–moderate CV risk;	I	B	266, 269, 270
b) is recommended in patients with diabetes;	I	A	270, 275, 276
c) should be considered in patients with previous stroke or TIA;	IIa	B	296, 297
d) should be considered in patients with CHD;	IIa	B	141, 265
e) should be considered in patients with diabetic or non-diabetic CKD.	IIa	B	312, 313
In elderly hypertensives less than 80 years old with SBP ≥160 mmHg there is solid evidence to recommend reducing SBP to between 150 and 140 mmHg.	I	A	265
In fit elderly patients less than 80 years old SBP values <140 mmHg may be considered, whereas in the fragile elderly population SBP goals should be adapted to individual tolerability.	IIb	C	-
In individuals older than 80 years and with initial SBP ≥160 mmHg, it is recommended to reduce SBP to between 150 and 140 mmHg provided they are in good physical and mental conditions.	I	B	287
A DBP target of <90 mmHg is always recommended, except in patients with diabetes, in whom values <85 mmHg are recommended. It should nevertheless be considered that DBP values between 80 and 85 mmHg are safe and well tolerated.	I	A	269, 290, 293

Major drug combinations used in trials of antihypertensive treatment in a step-up approach or as a Randomized combination

Trial	Comparator	Type of patients	SBP diff (mmHg)	Outcomes
ACE-I and diuretic combination				
PROGRESS[296]	Placebo	Previous stroke or TIA	–9	–28% strokes (P <0.001)
ADVANCE[276]	Placebo	Diabetes	–5.6	–9% micro/macro vascular events (P = 0.04)
HYVET[287]	Placebo	Hypertensives aged ≥80 years	–15	–34% CV events (P <0.001)
CAPPP[455]	BB + D	Hypertensives	+3	+5% CV events (P = NS)
Angiotensin receptor blocker and diuretic combination				
SCOPE[450]	D + placebo	Hypertensives aged ≥70 years	–3.2	–28% non fatal strokes (P = 0.04)
LIFE[457]	BB + D	Hypertensives with LVH	–1	–26% stroke (P <0.001)
Calcium antagonist and diuretic combination				
FEVER[269]	D + placebo	Hypertensives	–4	–27% CV events (P <0.001)
ELSA[186]	BB + D	Hypertensives	0	NS difference in CV events
CONVINCE[458]	BB + D	Hypertensives with risk factors	0	NS difference in CV events
VALUE[456]	ARB + D	High-risk hypertensives	–2.2	–3% CV events (P = NS)
ACE-I and calcium antagonist combination				
SystEur[451]	Placebo	Elderly with ISH	–10	–31% CV events (P <0.001)
SystChina[452]	Placebo	Elderly with ISH	–9	–37% CV events (P <0.004)
NORDIL[461]	BB + D	Hypertensives	+3	NS difference in CV events
INVEST[459]	BB + D	Hypertensives with CHD	0	NS difference in CV events
ASCOT[423]	BB + D	Hypertensives with risk factors	–3	–16% CV events (P <0.001)
ACCOMPLISH[414]	ACE-I + D	Hypertensives with risk factors	–1	–21% CV events (P <0.001)
BB and diuretic combination				
Coope & Warrender[453*]	Placebo	Elderly hypertensives	–18	–42% strokes (P <0.03)
SHEP[449]	Placebo	Elderly with ISH	–13	–36% strokes (P <0.001)
STOP[454]	Placebo	Elderly hypertensives	–23	–40% CV events (P = 0.003)
STOP 2[460]	ACE-I or CA	Hypertensives	0	NS difference in CV events
CAPPP[455]	ACE-I + D	Hypertensives	–3	–5% CV events (P = NS)
LIFE[457]	ARB + D	Hypertensives with LVH	+1	+26% stroke (P <0.001)
ALLHAT[448]	ACE-I + BB	Hypertensives with risk factors	–2	NS difference in CV events
ALLHAT[448]	CA + BB	Hypertensives with risk factors	–1	NS difference in CV events
CONVINCE[458]	CA + D	Hypertensives with risk factors	0	NS difference in CV events
NORDIL[461]	ACE-I + CA	Hypertensives	–3	NS difference in CV events
INVEST[459]	ACE-I + CA	Hypertensives with CHD	0	NS difference in CV events
ASCOT[423]	ACE-I + CA	Hypertensives with risk factors	+3	+16% CV events (P <0.001)
Combination of two renin–angiotensin–system blockers /ACE-I + ARB or RAS blocker + renin inhibitor				
ONTARGET[463]	ACE-I or ARB	High-risk patients	–3	More renal events
ALTITUDE[433]	ACE-I or ARB	High-risk diabetics	–1.3	More renal events

Treatment strategies and choice of drugs

Recommendations	Class [a]	Level [b]	Ref. [c]
Diuretics (thiazides, chlorthalidone and indapamide), beta-blockers, calcium antagonists, ACE inhibitors, and angiotensin receptor blockers are all suitable and recommended for the initiation and maintenance of antihypertensive treatment, either as monotherapy or in some combinations with each other.	I	A	284, 332
Some agents should be considered as the preferential choice in specific conditions because used in trials in those conditions or because of greater effectiveness in specific types of OD.	IIa	C	-
Initiation of antihypertensive therapy with a two-drug combination may be considered in patients with markedly high baseline BP or at high CV risk.	IIb	C	-

Gaps in evidence and need for future trials

- Should antihypertensive drug treatment be given to all patients with grade 1 hypertension when their CV risk is low-to-moderate?
- Should elderly patients with a SBP between 140 and 160 mmHg be given antihypertensive drug treatments?
- Should drug treatment be given to subjects with white-coat hypertension? Can this condition be differentiated into patients needing or not needing treatment?
- Should antihypertensive drug treatment be started in the high normal BP range and, if so, in which patients?
- What are the optimal office BP values (i.e. the most protective and safe) for patients to achieve by treatment in different demographic and clinical conditions?
- Do treatment strategies based on control of out-of-office BP provide an advantage (reduced clinical morbidity and mortality, fewer drugs, fewer side-effects) over strategies based on conventional (office) BP control?
- What are the optimal out-of-office (home and ambulatory) BP values to be reached with treatment and should targets be lower or higher in high risk hypertensives?
- Does central BP add to CV event prediction in untreated and treated hypertensive patients?
- Do invasive procedures for treatment of resistant hypertension compare favourably with the best drug treatment and provide long-term BP control and reduction of morbid and fatal events?
- Do treatment-induced changes in asymptomatic OD predict outcome? Which measures—or combinations of measures—are most valuable?
- Are lifestyle measures known to reduce BP capable of reducing morbidity and mortality in hypertensive patients?
- Does a treatment-induced reduction of 24h BP variability add to CV protection by antihypertensive treatment?
- Does BP reduction substantially lower CV risk in resistant

Definitions and classification of office blood pressure levels (mmHg)

Category	Systolic		Diastolic
Optimal	<120	and	<80
Normal	120–129	and/or	80–84
High normal	130–139	and/or	85–89
Grade 1 hypertension	140–159	and/or	90–99
Grade 2 hypertension	160–179	and/or	100–109
Grade 3 hypertension	≥180	and/or	≥110
Isolated systolic hypertension	≥140	and	<90

Outline

- Introduction
- Definitions
- Pathophysiology
- Risk factors
- Primary versus Secondary
- Complications
- Treatment options
- Studies / Evidence
- . . . ? Future developments

Introduction

- Common presentation to GP
- National Health and Nutrition Examination Survey (NHANES) 2005-2008 USA
  - 30% adults have hypertension
  - 65 million individuals
  - Hypertension defined as:
    - Systolic BP ≥ 140mmHg
    - Diastolic BP ≥90mmHg
    - Taking antihypertensive agents

Definitions

Category	Systolic BP	Diastolic BP
Normal	<120	<80
Prehypertension	120-139	80-89
Stage 1	140-159	90-99
Stage 2	>160	>100

Seventh Report of Joint National Committee (JNC 7) 2003
*Average of 2 or more readings at 2 or more visits
*No antihypertensive agents, not acutely unwell

Systolic BP >220 and diastolic BP >120

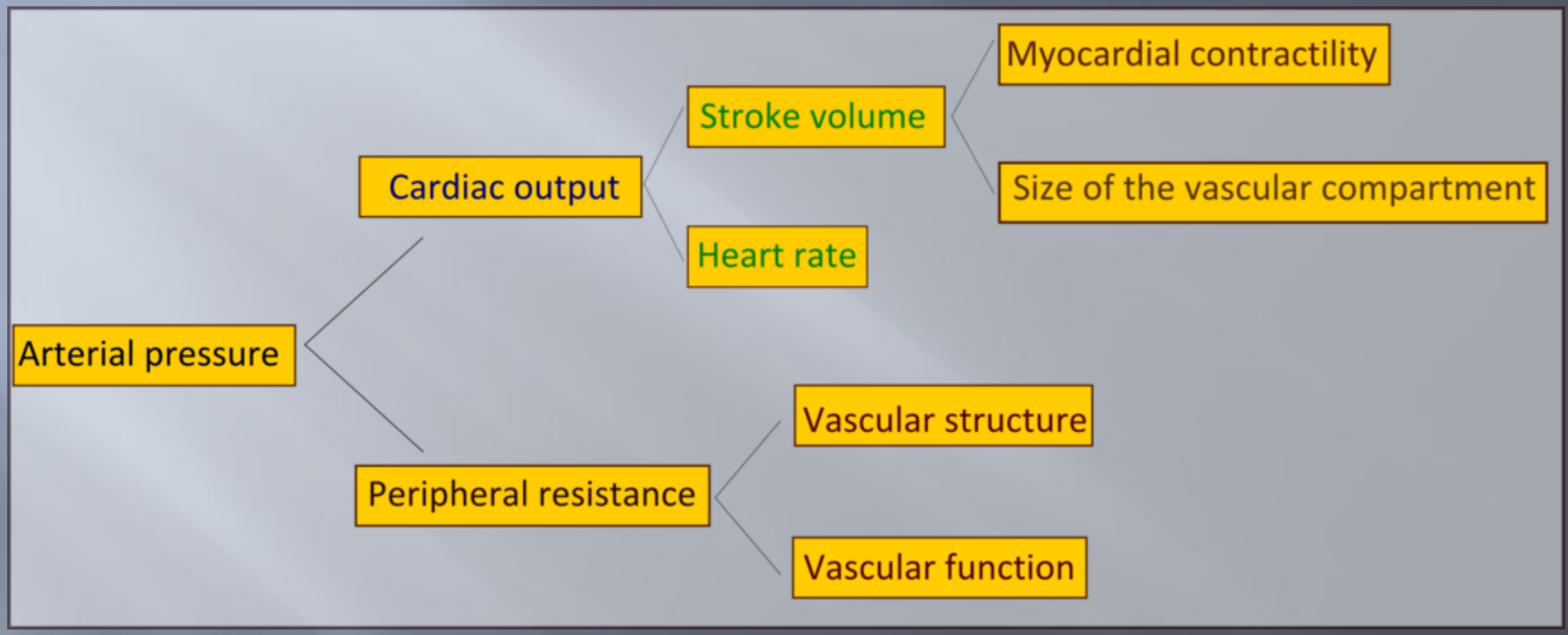
- Hypertensive urgency:
  - Severe hypertension in asymptomatic individual
  - BP control over several days to weeks

- Malignant hypertension:
  - Severe hypertension with acute end organ damage
  - Retinal haemorrhages, exudates or papilloedema
  - Hypertensive encephalopathy

Hypertensive emergencies

- Accelerated-malignant hypertension with papilloedema
- Cerebrovascular
  - Hypertensive encephalopathy
  - Atherothrombotic brain infarction with severe hypertension
  - Intracerebral hemorrhage
  - Subarachnoid hemorrhage
- Cardiac
  - Acute aortic dissection
  - Acute left ventricular failure
  - Acute or impending myocardial infarction
  - After coronary bypass surgery
- Renal
  - Acute glomerulonephritis
  - Renal crises from collagen vascular diseases
  - Severe hypertension after kidney transplantation
- Excessive circulating catecholamines
  - Pheochromocytoma crisis
  - Food or drug interactions with monoamine-oxidase inhibitors
  - Sympathomimetic drug use (cocaine)
  - Rebound hypertension after sudden cessation of antihypertensive drugs
- Eclampsia
- Surgical
  - Severe hypertension in patients requiring immediate surgery
  - Postoperative hypertension
  - Postoperative bleeding from vascular suture lines
- Severe body burns
- Severe epistaxis

Pathophysiology



Risk Factors

- Family history
- Excess sodium intake
- Excess alcohol intake
- Obesity and weight gain
- Physical inactivity
- Dyslipidaemia
- Vitamin D deficiency

Primary versus Secondary

- Secondary hypertension
  - Primary renal disease
  - Oral contraceptives
  - Drug-induced
  - Pheochromocytoma
  - Primary aldosteronism
  - Renovascular disease
  - Cushing's syndrome
  - Endocrine disorders
  - Obstructive sleep apnoea
  - Coarctation of the aorta

Complications

(1) Heart

(2) Brain

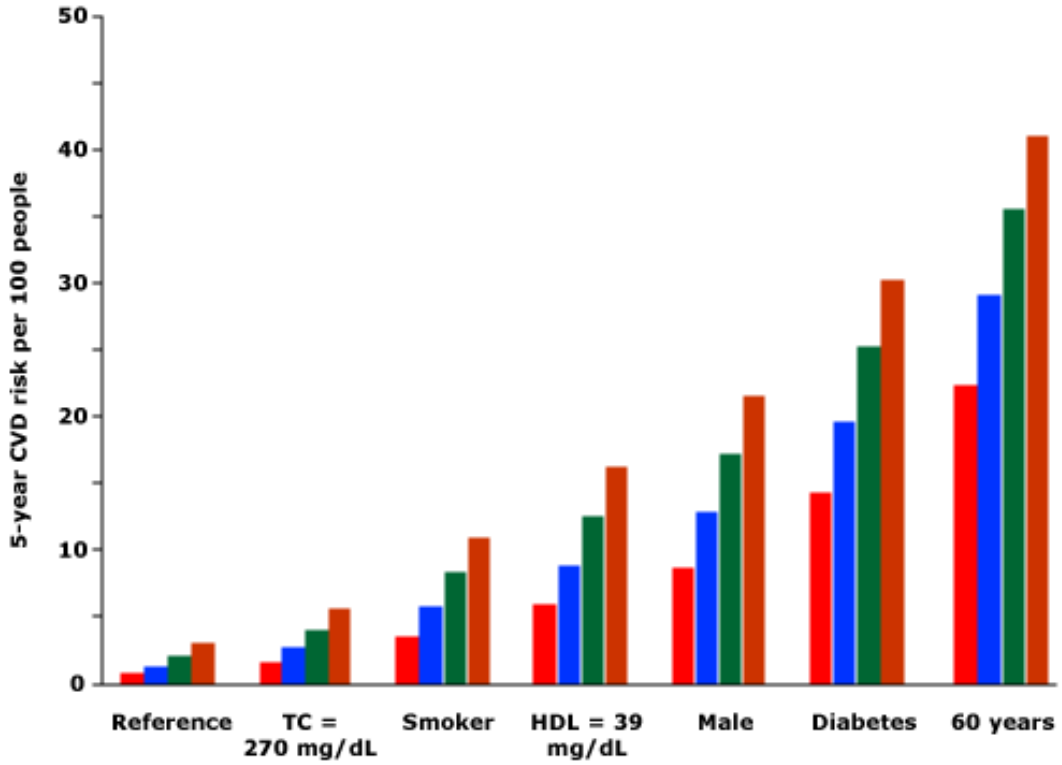
(3) Kidney

(4) Peripheral arteries

(1) Heart

- Hypertensive heart disease
  - Structural / Functional adaptations
  - Left ventricular hypertrophy
  - Congestive heart failure (systolic and diastolic)
  - Atherosclerotic coronary artery disease
  - Microvascular disease
  - Cardiac arrhythmias

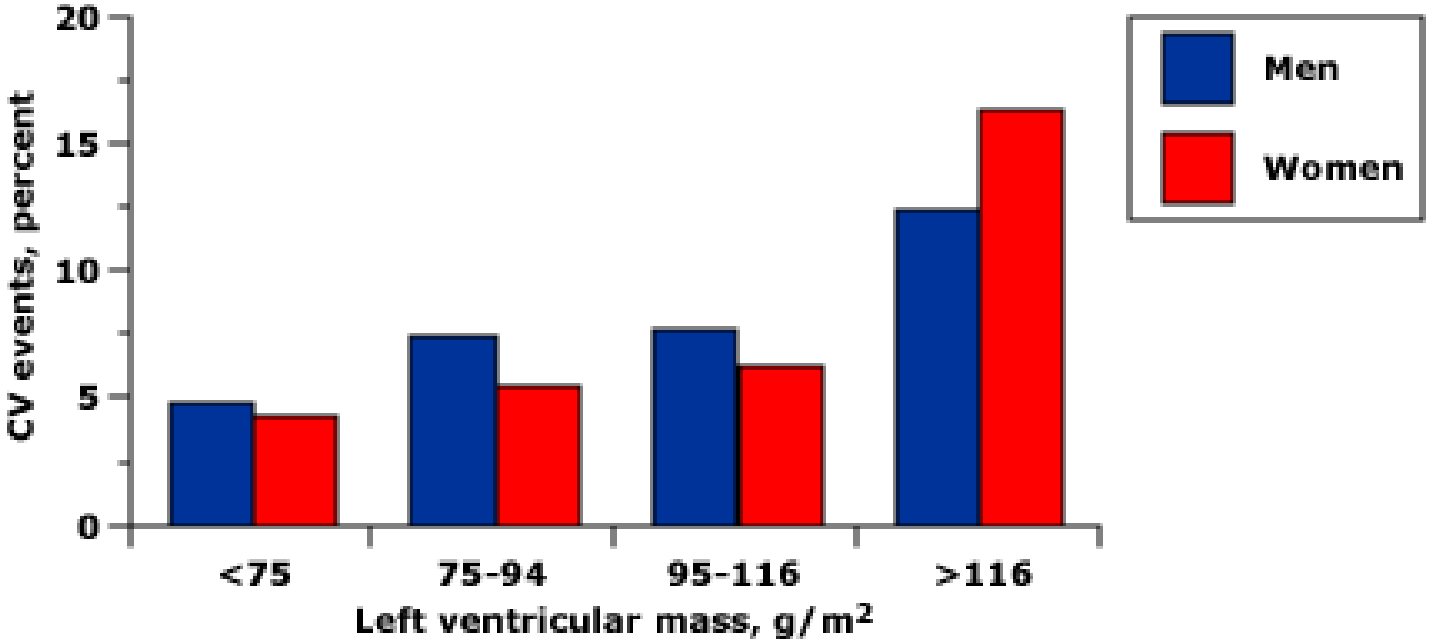
Additive effects of risk factors on cardiovascular disease at five years



Cumulative absolute risk of cardiovascular disease (CVD) at five years according to systolic blood pressure and specified levels of other risk factors. The reference category is a nondiabetic, nonsmoking 50-year-old woman with a serum total cholesterol (TC) of 154 mg/dL (4.0 mmol/L) and HDL-cholesterol of 62 mg/dL (1.6 mmol/L). The CVD risks are given for systolic blood pressure levels of 110, 130, 150, and 170 mmHg. In the other categories, the additional risk factors are added consecutively. As an example, the diabetes category is a 50-year-old diabetic man who is a smoker and has a total cholesterol (TC) of 270 mg/dL (7 mmol/L) and HDL-cholesterol of 39 mg/dL (1 mmol/L).

Adapted from: Jackson R, Lawes CM, Bennett DA, et al, Lancet 2005; 365:434.

Cardiovascular risk with LVH by echocardiography



Four-year, age-adjusted incidence of cardiovascular events in men and women in the Framingham Study according to left ventricular mass determined by echocardiography. Subjects with increased left ventricular mass (far right panel) had a marked increase in cardiovascular risk.

Adapted from Levy, D, Garrison, RJ, Savage, DD, et al, N Engl J Med 1990; 322:1561.

(2) Brain

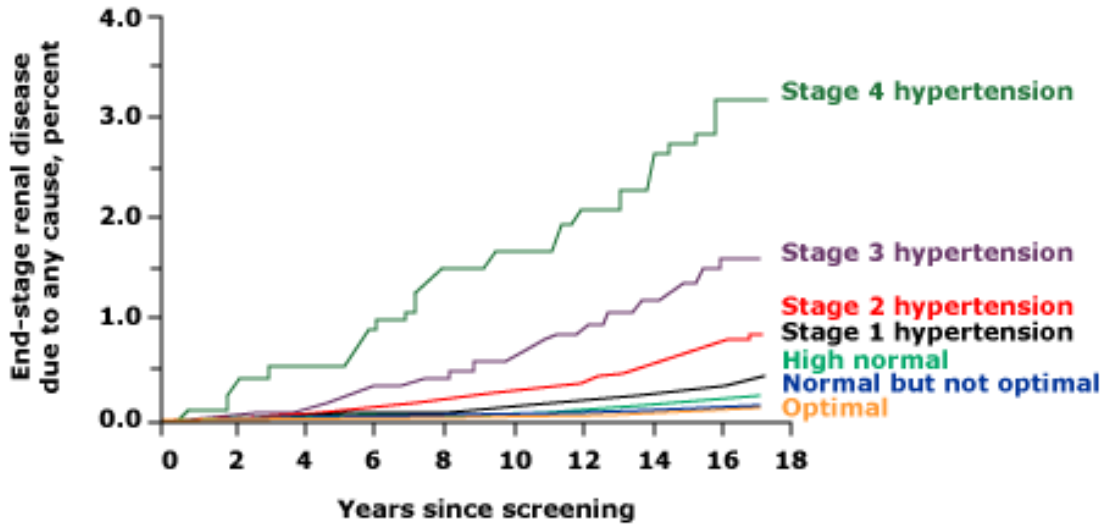
- Stroke
  - Second most frequent cause of death
  - ↑BP is the strongest risk factor for stroke
  - 85% strokes are infarction
  - 15% intracerebral or subarachnoid haemorrhage
- Impaired cognition in aging population
  - Subcortical white matter ischaemia
- Hypertensive encephalopathy
  - Failure of autoregulation
  - Headache, nausea, vomiting, neurological deficit

(3) Kidney

- Target and cause of hypertension
- Risk factor for CKD and ESRF
- ↑BP → ischaemic changes glomeruli
- Loss of autoregulation / GFR → glomerular hyperfiltration → further renal damage → glomerulosclerosis

Hypertension and ESRF - table

Relation between hypertension and development of ESRD

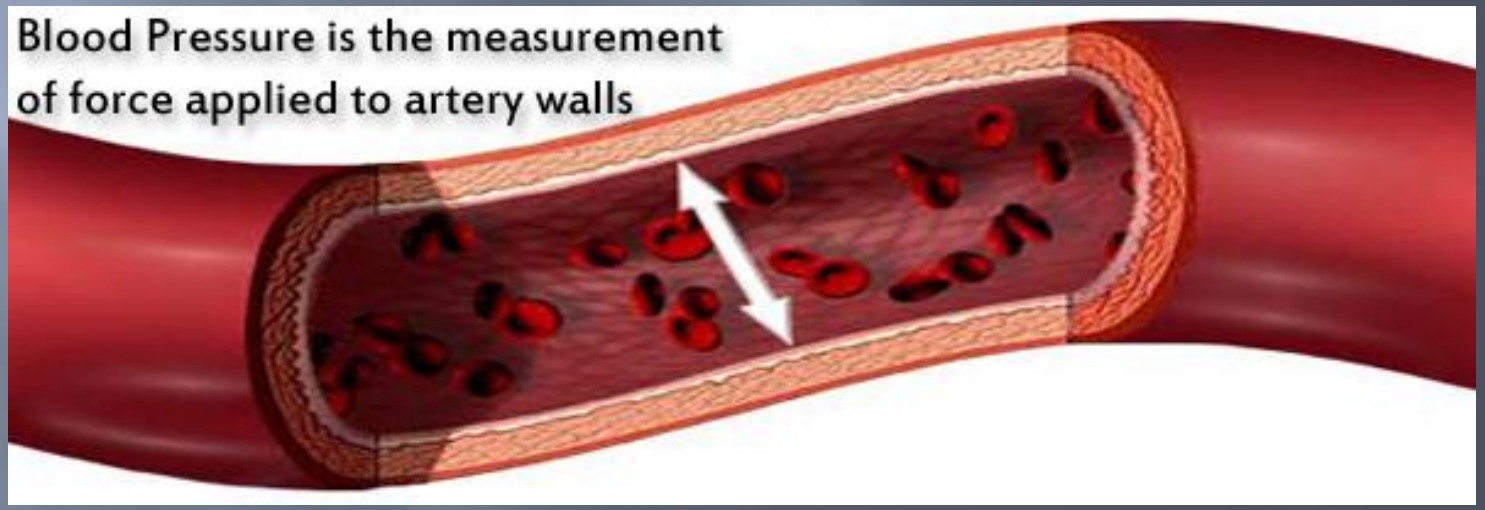


Cumulative incidence of end-stage renal disease (ESRD), due to any cause, according to blood pressure category in 332,544 men screened for the MRFIT trial. The adjusted relative risk increased from 1.0 in those with optimal blood pressure (<120/<80) to 1.9 with high normal blood pressure, 3.1 with mild hypertension, 6.0 with moderate hypertension, and 11.2 with severe hypertension. Patients with stage 1 hypertension or lower blood pressure were at very low risk of ESRD at 16 years (≤0.34 percent).

Redrawn from Klag, MJ, Whelton, PK, Randall, BL, et al, N Engl J Med 1996; 334:13.

(4) Peripheral arteries

- Contribute to the pathogenesis of hypertension
- Target organ for atherosclerotic disease



Treatment

Non-pharmacologic (lifestyle) modification

Drug therapy

MINISTRY OF HEALTH
MANATŪ HAUORA

New Zealand Primary Care Handbook 2012

Cardiovascular risk assessment and diabetes screening

Cardiovascular risk factor management

Management of type 2 diabetes

Smoking cessation

Weight management

Stroke and transient ischaemic attack

Coronary heart disease

Heart failure

Prevention of infective endocarditis

Rheumatic fever

New Zealand Society NZSSD for the Study of Diabetes

Te Hotu

Kidney Health New Zealand

Drug therapy

- Initial therapy:

- Thiazide-type diuretics
- ACE-inhibitors / ARBs
- Calcium channel blockers
- Beta blockers

- Each agent is roughly equally effective at ↓ BP
- Amount of BP ↓ important, not the drug choice
  (assuming there is no indication for a particular drug)

2010 Guidelines - European Society of Hypertension / European Society of Cardiology

e.g. CAPPP, STOP-Hypertension -2, NORDIL, UKPKS

Pertinent Papers in Hypertension

- ALLHAT trial of monotherapy
- ACCOMPLISH trial of combination therapy
- HYVET study for hypertension in elderly
- The Symplicity HTN-2 Trial for renal denervation

ALLHAT Trial

- Antihypertensive and Lipid-Lowering Treatment to prevent Heart Attack Trial
- 41,000 patients
- Randomised prospective study
- 55yrs + with hypertension and at least one coronary risk factor
- Mean BP 146/84

Hypertension 2003; 42:239

- Randomised to 1 of 4 regimes:
  - Chlorthalidone
  - Amlodipine
  - Lisinopril
  - Doxazosin
- Primary outcome:
  - combined fatal CAD and non-fatal MI
- Secondary outcomes:
  - all cause mortality
  - stroke
  - combined cardiovascular events including CHF

- Doxazosin arm discontinued in 2000

  → Excess of heart failure events cf. chlorthalidone arm

  (**Doxazosin 8.1%** risk cf. **Chlorthalidone 4.5%, RR 2.04)**

- Results
  - Mean follow-up 4.9years
  - Mean BP 146/80 – 135/75
- Primary outcome -

  Identical for chlorthalidone, amlodipine and lisinopril groups (6year rate 11%)
- Secondary outcome -

  All cause mortality – identical in the 3 groups

Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High BP (JNC 7) 2003

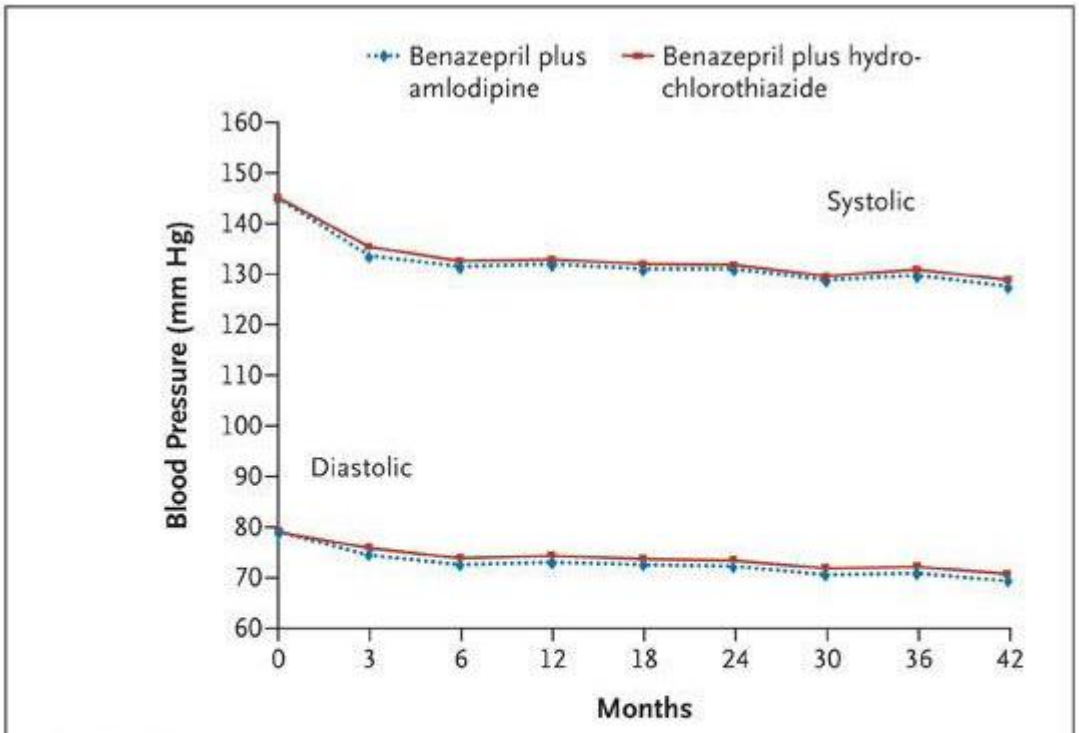
→ low-dose thiazides should be initial drug treatment of most patients with uncomplicated hypertension

ACCOMPLISH Trial

- Directly compared combination regimes (2 drugs)
- 11,506 patients
- Hypertensive, >55yrs and SBP >160mmHg
- Randomised:
  - Benazepril / Hydrochlorothiazide
  - Benazepril / Amlodipine

NEJM 2008 ; 359 : 2417-2428

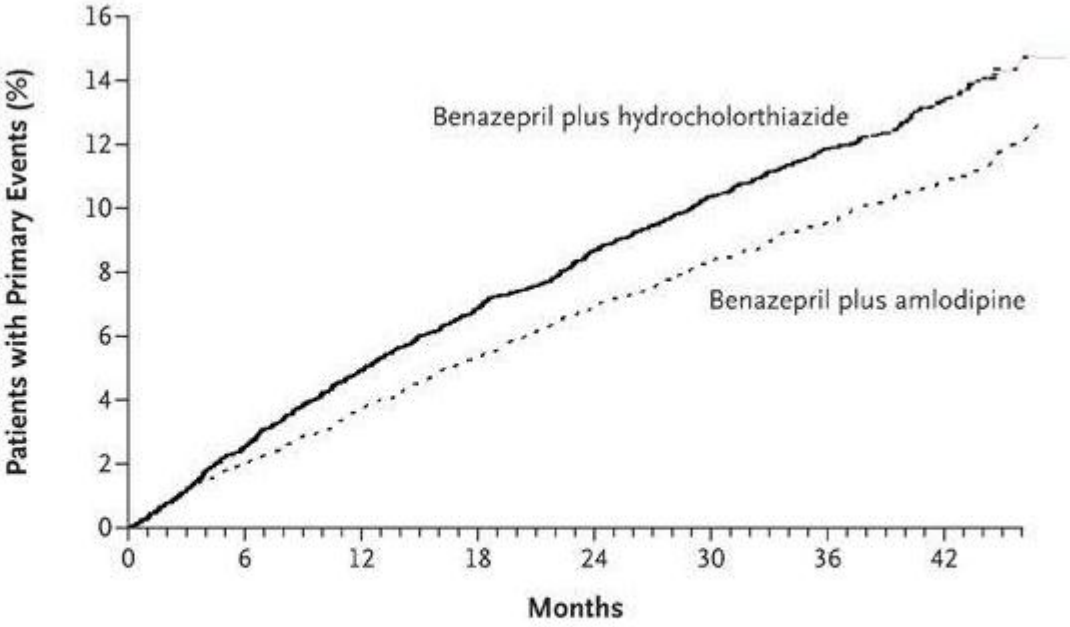
- Primary endpoint
  - Time to first event
  - Death, non-fatal MI, non-fatal stroke, hospitalisation for angina, resuscitation after cardiac event, coronary revascularisation
- Trial started 2003



No. at Risk

Benazepril plus amlodipine	5740	5517	5404	5178	5010	4866	4298	2804	1074
Benazepril plus hydrochlorothiazide	5757	5537	5408	5222	5033	4825	4299	2529	1042

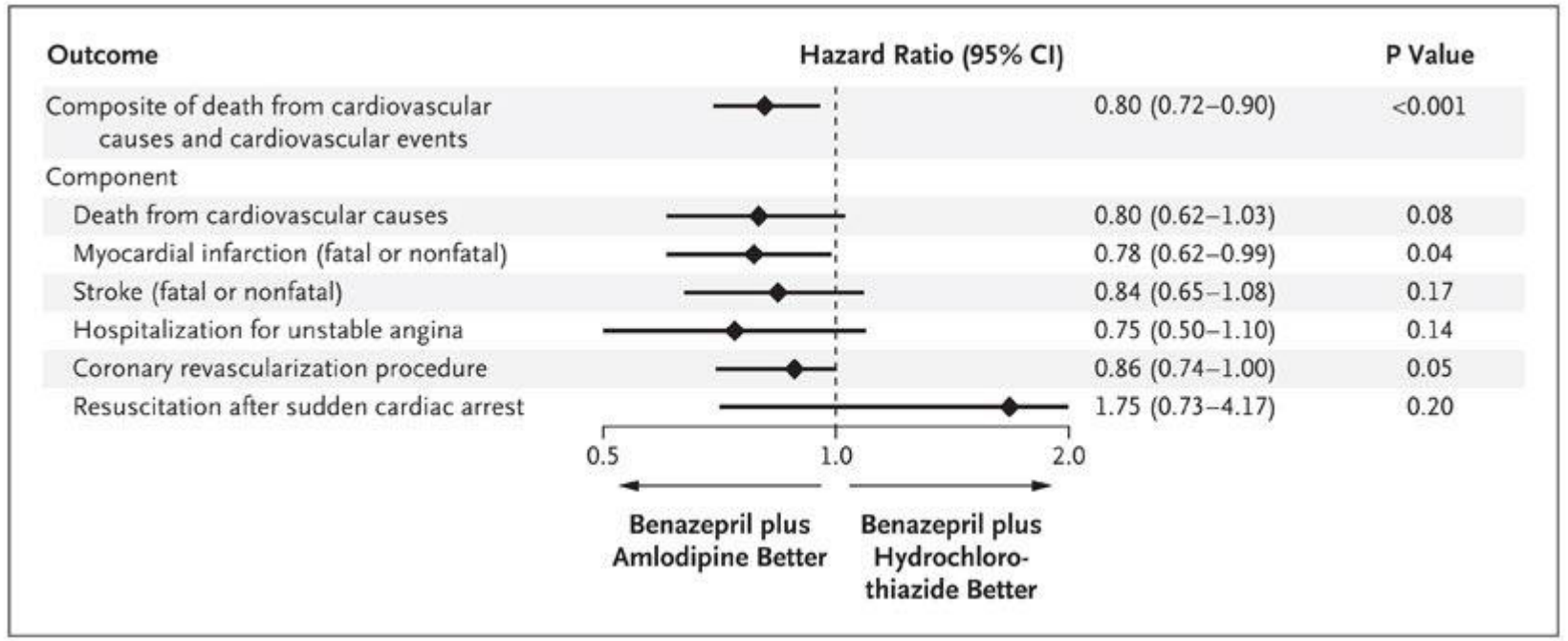
The NEW ENGLAND JOURNAL of MEDICINE



No. at Risk

Benazepril plus amlodipine	5512	5317	5141	4959	4739	2826	1447
Benazepril plus hydrochlorothiazide	5483	5274	5082	4892	4655	2749	1390

The NEW ENGLAND JOURNAL of MEDICINE



The NEW ENGLAND JOURNAL of MEDICINE

- Trial terminated early (October 2007)
- Mean follow-up 39 months
- Cardiovascular morbidity / mortality was reduced by 20% with the ACE-I / CCB compared with the ACE-I / HCTZ

"The benazepril-amlodipine combination was superior to the benazepril-hydrochlorothiazide combination in reducing cardiovascular events in patients with hypertension who were at risk for such events"

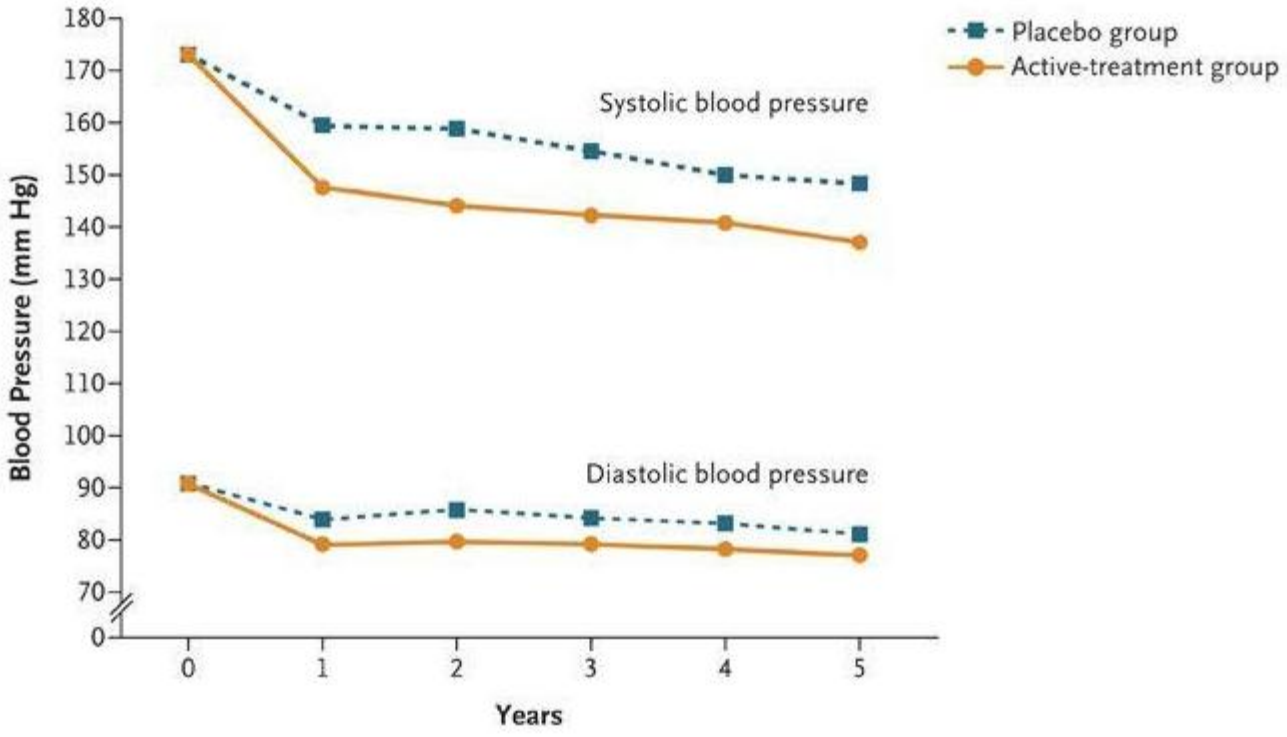
HYVET Study

- Treatment of Hypertension in Patients 80 years of Age or Older
- ≥80 yrs with sustained systolic hypertension
- Randomly assigned:
  - Indapamide +/- Perindopril
  - Or matching Placebos
- Target BP 150/80

NEJM 2008 ; 358 : 1887-98

- 1933 active treatment; 1912 placebo
- Mean age 83.6 yrs
- Mean BP 173/90
- Follow-up for mean 4yrs

- Treatment group:
  - 30% reduction in rate of fatal / non-fatal stroke
  - 21% reduction in rate of death from any cause
  - 23% reduction in death from cardiovascular cause
  - 64% reduction in rate of heart failure



No. at Risk

Placebo group	1912	1468	701	330	191	116
Active-treatment group	1933	1540	754	373	207	118

References

- Up to date online
- www.hypertensiononline.org
- www.symplifybptrial.com/
- Harrison's principles of internal medicine. 15th Edition. McGraw-Hill. *Braunwald, Fauci, Kasper, Hauser, Longo, Jameson*.
- Hypertension (Seminal Papers Presentation) *Dr Walter van der Merwe*, North Shore Hospital