

# High Blood Pressure

What is It? How to Check?

What Can Go Wrong....?

How to treat?

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# Declaration of interest

- None to declare

High blood pressure affects **more than 1 in 4** adults in England



High blood pressure is the **3rd biggest risk factor** for premature death and disability in England after smoking and poor diet



People from the most deprived areas in England are **30%** more likely than the least-deprived to have high blood pressure



**At least half** of all heart attacks and strokes are associated with high BP and it is a major risk factor for chronic kidney disease, heart failure and dementia

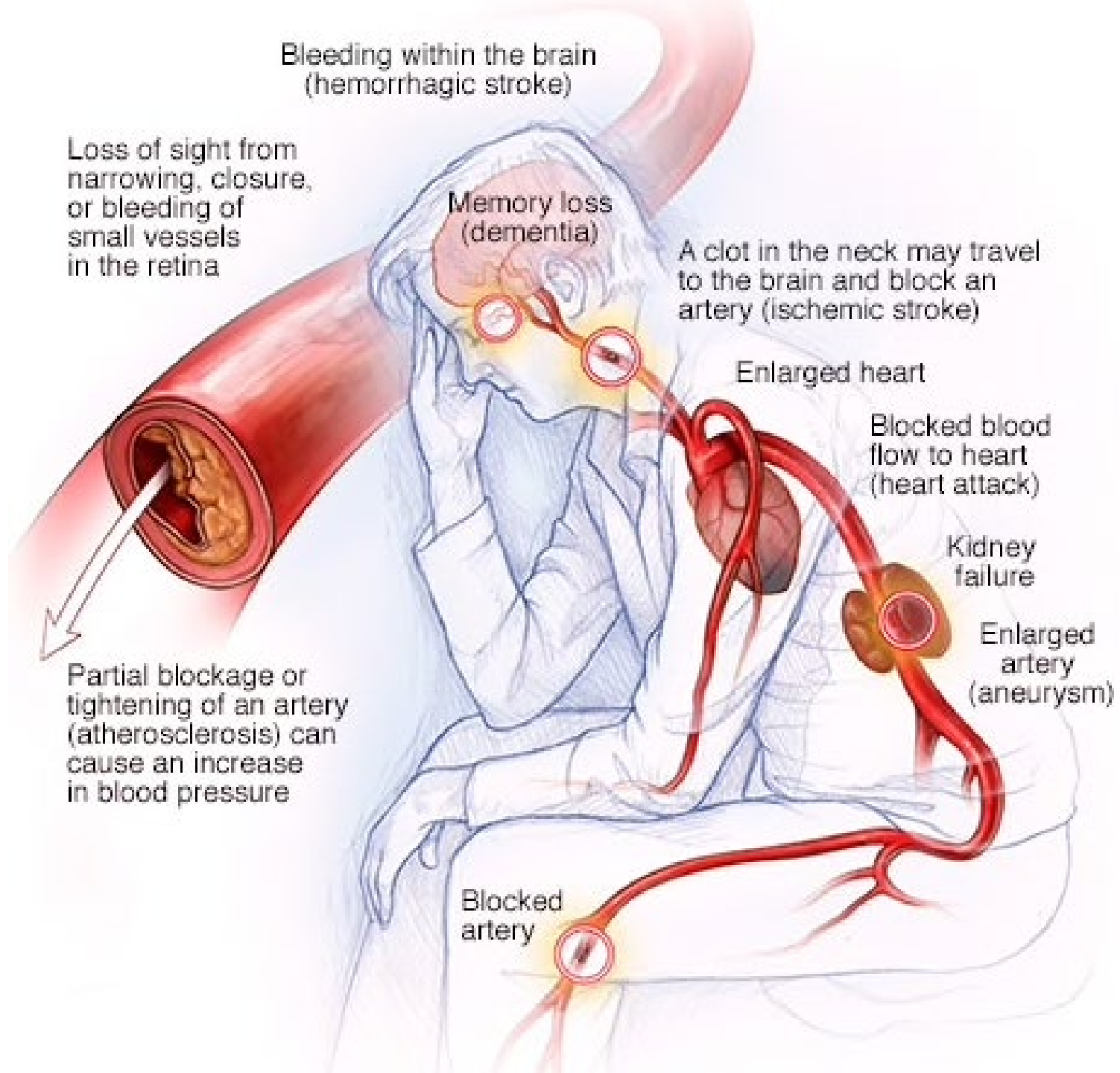


*“What's wrong with high blood pressure – I think mine is ok”*

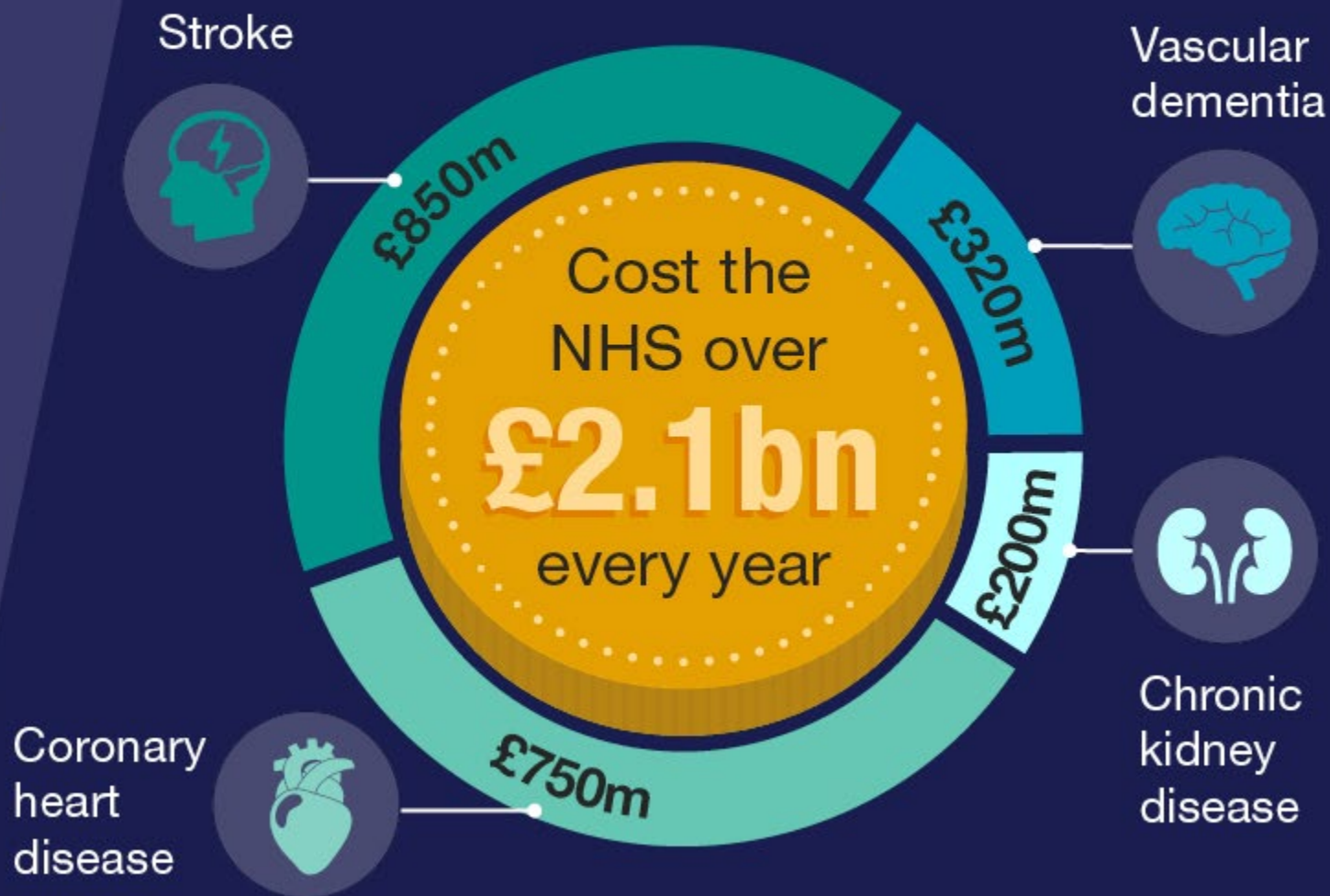


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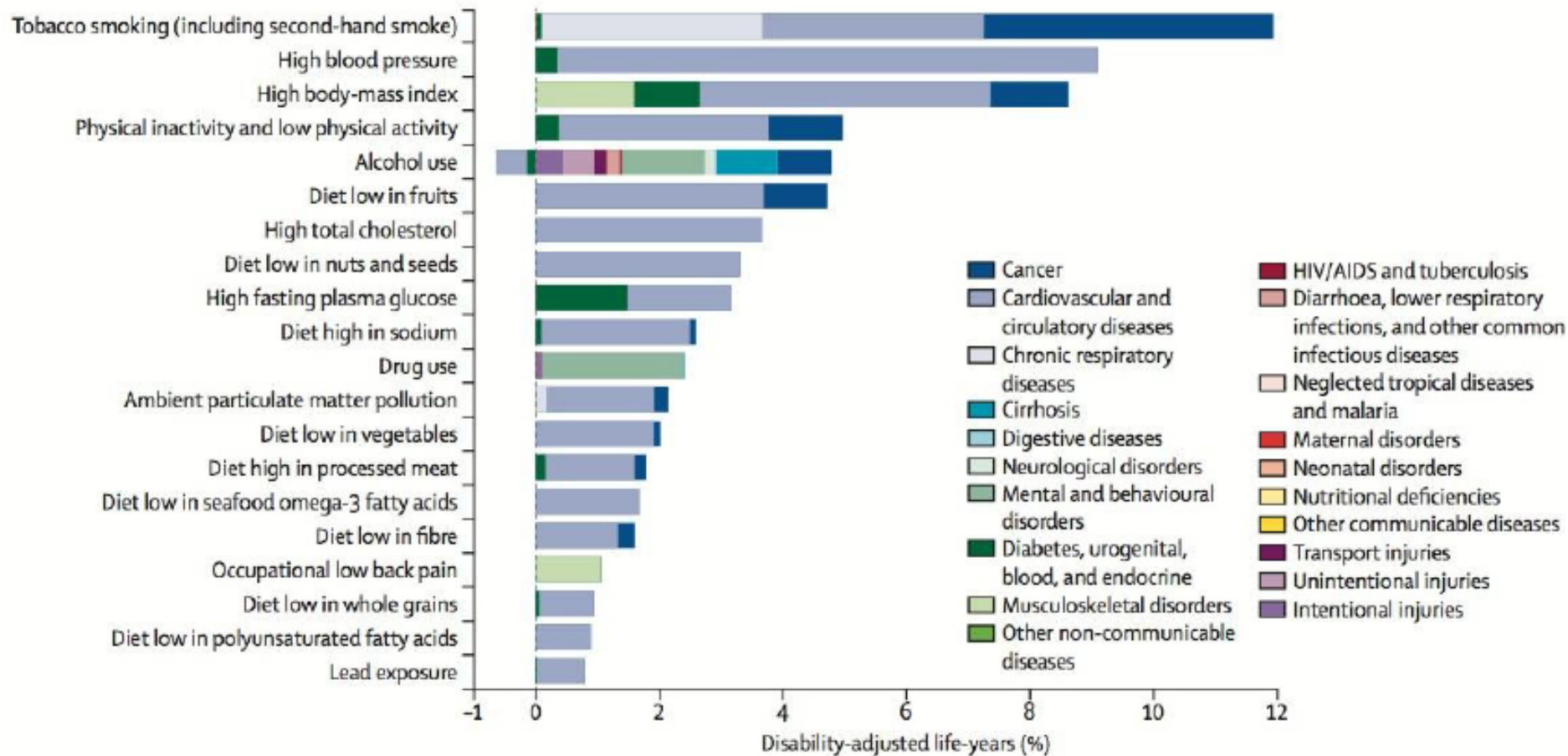


Diseases  
caused by  
high blood  
pressure:

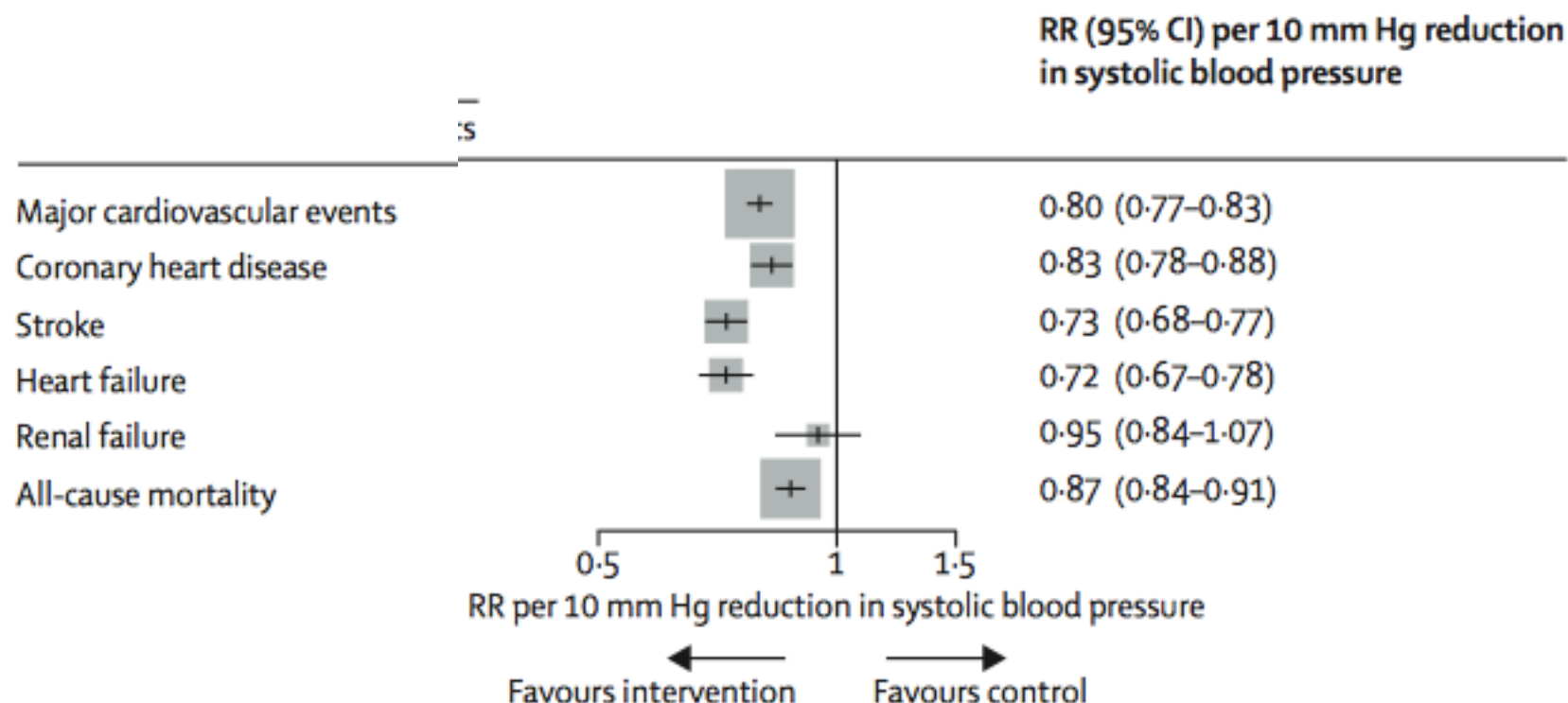


# DALYs Attributable to 20 Risk Factors (UK)

Global Burden of Disease Study. Lancet 2013;381:997-1020



**Figure 7: Burden of disease attributable to 20 leading risk factors for both sexes in 2010, expressed as a percentage of UK disability-adjusted life-years**  
The negative percentage for alcohol is the protective effect of mild alcohol use on ischaemic heart disease and diabetes.



**Figure 3: Standardised effects of a 10 mm Hg reduction in systolic blood pressure**  
 RR=relative risk.

## The NHS Long Term Plan



#NHSLongTermPlan

[www.longtermplan.nhs.uk](http://www.longtermplan.nhs.uk)

- The NHS Long term plan is a new plan for the NHS to improve the quality of patient care and health outcomes.
- It sets out how the £20.5 billion budget settlement for the NHS , announced by the prime minister in summer 2018 will be spent over the next 5 years
- The plan focuses on building an NHS fit for the future by:
  - enabling everyone to get the best start in life
  - helping communities to live well
  - helping people to age well

# The Size of the Prize in Cardiovascular Disease (CVD) Prevention

## England

### 1. The diagnosis and treatment gap



#### Hypertension

Estimated adult population with hypertension	13,550,700
Estimated adult population with undiagnosed hypertension	5,601,600
GP registered hypertensives not treated to 150/90 mmHg target	1,618,900



#### Atrial Fibrillation (AF)

GP registered population with Atrial Fibrillation (AF)	983,300
Estimated GP registered population with undiagnosed AF	422,600
GP registered high risk AF patients (CHA2DS2VASc $\geq 2$ ) not anticoagulated	177,800



#### CVD risk

Estimated adult population 30 to 85 years with 10 year CVD risk $>20\%$	3,960,200
Estimated percentage of people with CVD risk $\geq 20\%$ treated with statins	49

### 2. The burden: first ever CVD events



Coronary Heart disease	128,750
Stroke	66,450
Heart Failure	48,350

### 3. The opportunity: potential events averted and savings over 3 years by optimising treatment in AF and hypertension



Optimal anti-hypertensive treatment of diagnosed hypertensives averts within 3 years:	9,710 heart attacks	Up to £72.5 million saved
	14,500 strokes	Up to £201.7 million saved
Optimally treating high risk AF patients averts within 3 years:	14,220 strokes	Up to £241.6 million saved

# Multiple Risk Factors

- There are two other important cardiovascular risk factors
  - raised blood lipids - hyperlipidaemia
  - smoking

all three factors have a multiplicative effect on each other

# How do we diagnose hypertension?

- **Clinic Blood Pressure Checks**
  - 2 or 3 readings on each occasion & take average
  - Repeated monthly for 3 months
  - If persistently above 140/90mmHg  
= HYPERTENSION
- **Initial Clinic BP measurement (CBPM)**
  - If > 140/90mmHg;
  - refer for either:
- **Ambulatory Blood Pressure Monitor (ABPM) or Home BP monitoring (HBPM)**
  - If BP > 135/85mmHg = HYPERTENSION
- **Diagnosis – The Old Way...**
- **Diagnosis – NICE 2011**

# ABPM

- 24 hour BP monitor
- Readings every half an hour throughout the day, and hourly overnight
- Atleast 14 measurements to confirm dx
- Average of daytime readings used to assess BP for diagnosis
- If  $> 135/85\text{mmHg}$  = hypertension
- Will reduce number of patients with white coat hypertension being treated



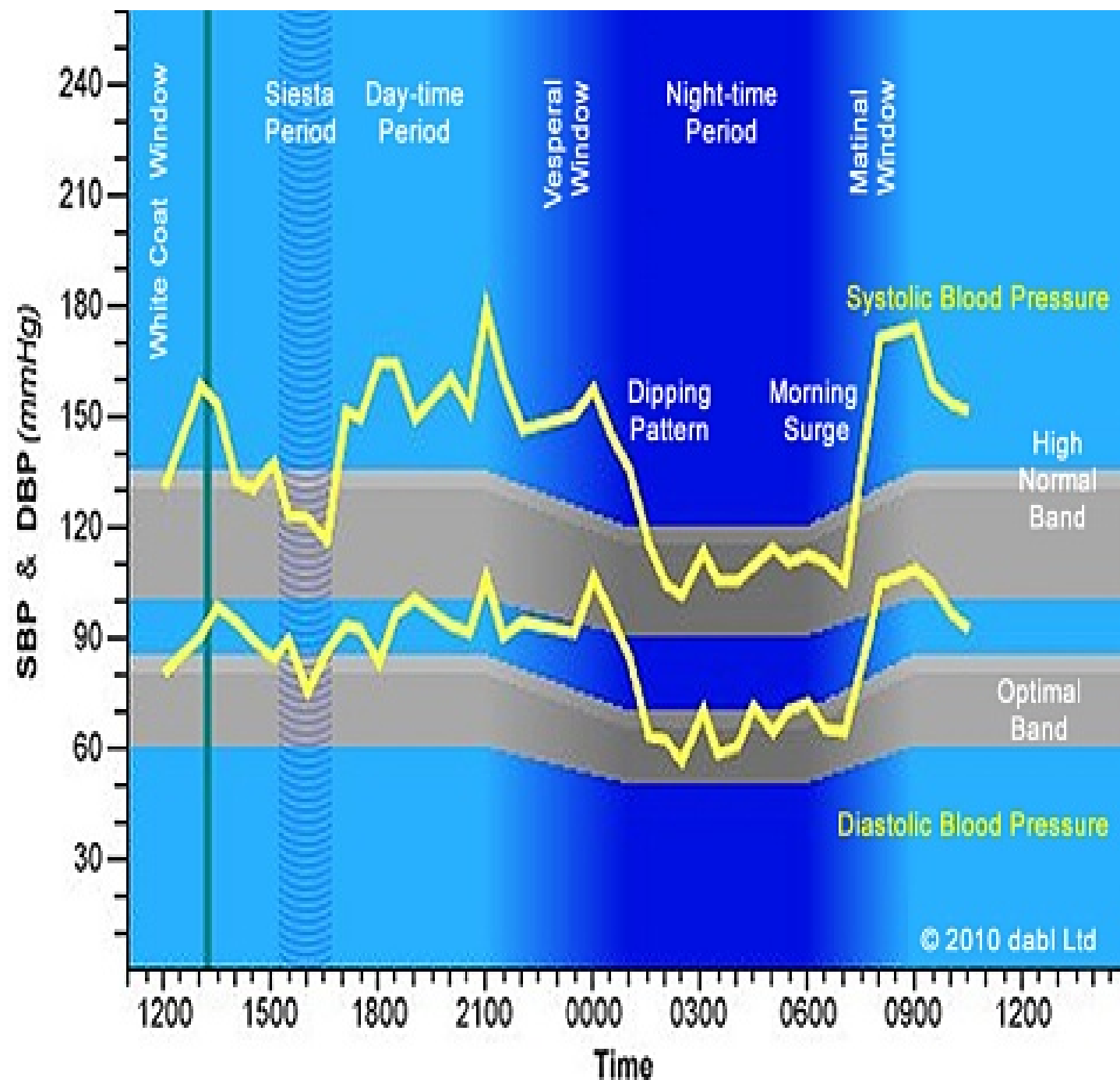
# Home BP monitoring

- Patients loaned a calibrated BP machine
- Takes readings twice daily for 7 days and records results
- Discard first days results and calculate average of all other readings
- If BP > 135/85 = Hypertension



# Do you always follow proper BP measurement technique?

- Environment: quiet, comfortable location at normal room temperature
- Patient:
  - ✓ not needing to pass urine, not recently eaten, smoked or taken caffeine or exercise for at least 30mn before
  - ✓ Seated calmly for 5mn, back supported and feet flat on the floor,
  - ✓ Arm: out-stretched, in line with mid-sternum and supported
- Select cuff size
- Initial BP check: in **both arms**
  - ✓ BP difference of <10mmHg normal
  - ✓ If difference >20 mmHg, repeat measurements
  - ✓ *use the arm with **the higher reading** for subsequent BP measurements*
- Subsequent BP check:
  - ✓ 2 readings, at least 1mn apart,
  - ✓ If more than 5mmHg difference take at least one additional reading, ?average the 2 best readings
- If pulse irregular check BP manually



Date-of-Birth: 07/08/1970

Age: 45 Years

Medications:

Dose:

Time:

Weight:

Race: Unspecified

Physician: admin,admin

Nurse/Technician:

Duration: 21:55

Scan Start: 08/03/2016 13:10 Tue

Scan End: 09/03/2016 11:05 Wed

Successful Reading(s): 35 90%

Indications:

### Overall Summary

	AVG	STD		MIN	MAX	Dipping
Systolic:	128	15.61	mmHg	88 (11:05 Wed)	154 (21:05 Tue)	-5.5%
Diastolic:	81	13.66	mmHg	49 (16:35 Tue)	104 (20:38 Tue)	-11.3%
MAP:	97	15.13	mmHg	56	130	-9.5%
Pulse Pressure:	46	9.19	mmHg	29	73	
Heart Rate:	91	8.81	bpm	73	106	
				Reading(s)	Time	
Percent of Systolic above limits:				45.7%	52.2%	
Percent of Diastolic above limits:				51.4%	56.8%	

### Wake Period(s) 06:00 - 22:00

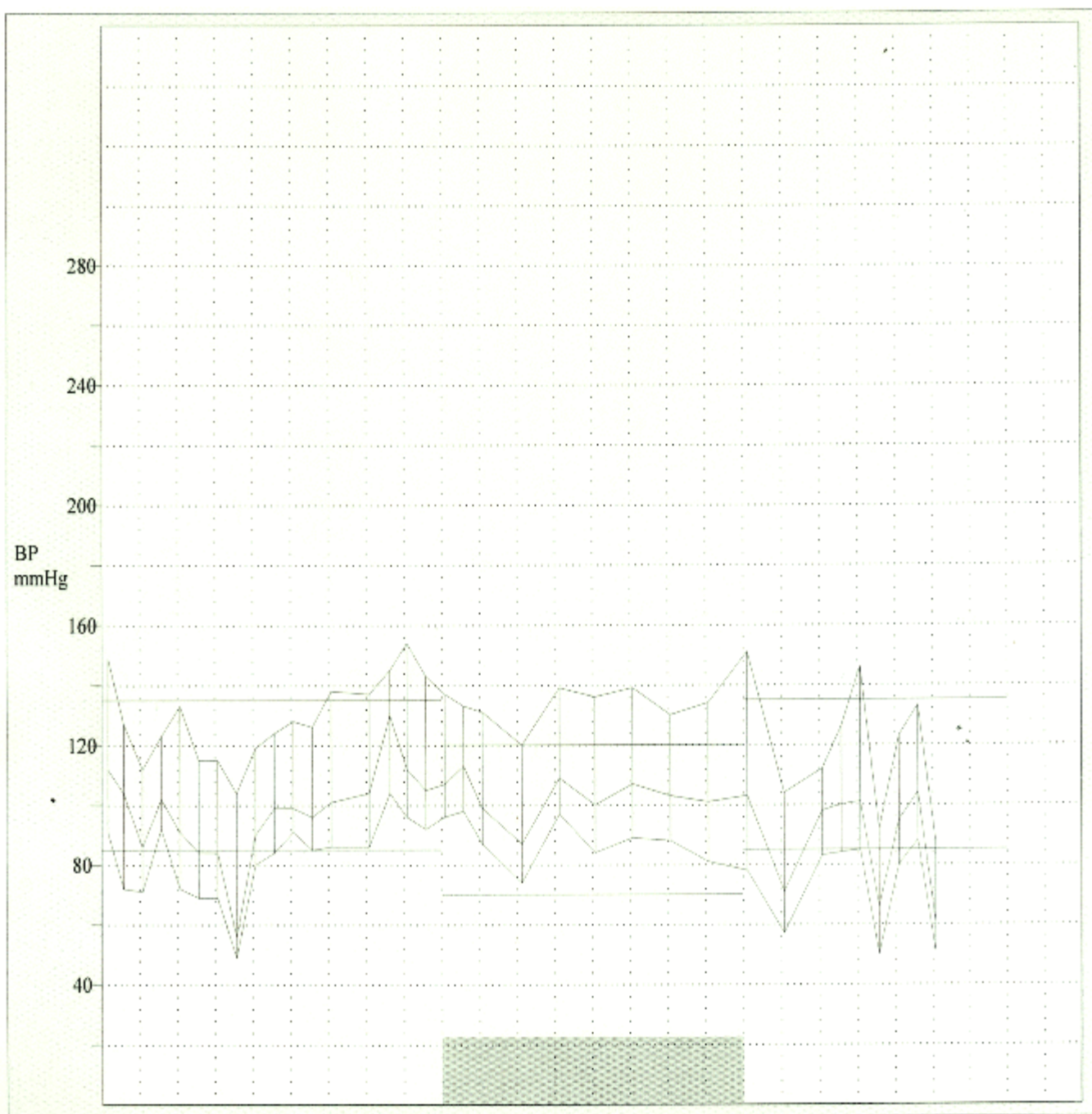
	AVG	STD		MIN	MAX
Systolic:	126	17.47	mmHg	88 (11:05 Wed)	154 (21:05 Tue)
Diastolic:	79	14.46	mmHg	49 (16:35 Tue)	104 (20:38 Tue)
MAP:	94	16.55	mmHg	56	130
Pulse Pressure:	47	10.14	mmHg	29	73
Heart Rate:	91	9.89	bpm	73	106
				Reading(s)	Time
Percent of Systolic readings > 135mmHg:				30.8%	39.2%
Percent of Diastolic readings > 85mmHg:				34.6%	35.5%

Number of Wake Period(s) readings: 26

### Sleep Period(s) 22:00 - 06:00

	AVG	STD		MIN	MAX
Systolic:	133	5.91	mmHg	120 (00:08 Wed)	139 (01:08 Wed)
Diastolic:	88	7.97	mmHg	74 (00:08 Wed)	98 (22:35 Tue)
MAP:	103	7.52	mmHg	87	113
Pulse Pressure:	45	5.85	mmHg	35	53
Heart Rate:	90	4.82	bpm	85	101
				Reading(s)	Time
Percent of Systolic readings > 120mmHg:				88.9%	85.2%
Percent of Diastolic readings > 70mmHg:				100%	100%

Number of Sleep Period(s) readings: 9



# Epworth sleepiness scale



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Use the following scale to choose the most appropriate number for each situation:-

- 0 = would never doze
- 1 = Slight chance of dozing
- 2 = Moderate chance of dozing
- 3 = High chance of dozing

Situation dozing	Chance of
Sitting and reading	<input type="text"/>
Watching TV	<input type="text"/>
Sitting, inactive in a public place (e.g. a theatre or a meeting)	<input type="text"/>
As a passenger in a car for an hour without a break	<input type="text"/>
Lying down to rest in the afternoon when circumstances permit	<input type="text"/>
Sitting and talking to someone	<input type="text"/>
Sitting quietly after a lunch without alcohol	<input type="text"/>
In a car, while stopped for a few minutes in the traffic	<input type="text"/>
<b>Total</b>	<input type="text"/>

Score:

0 – 10 Normal range  
10 – 12 Borderline  
12 – 24 Abnormal

# Office BP measurement - 1

Patients should be seated comfortably in a quiet environment for 5 min before beginning BP measurements.

Three BP measurements should be recorded, 1–2 min apart, and additional measurements only if the first two readings differ by  $> 10$  mmHg.  
BP is recorded as the average of the last two BP readings.

Additional measurements may have to be performed in patients with unstable BP values due to arrhythmias, such as in patients with AF, in whom manual auscultatory methods should be used as most automated devices have not been validated for BP measurement in patients with AF.

Use a standard bladder cuff (12–13 cm wide and 35 cm long) for most patients, but have larger and smaller cuffs available for larger (arm circumference  $> 32$  cm) and thinner arms, respectively.

The cuff should be positioned at the level of the heart with the back and arm supported, to avoid muscle contraction and isometric-exercise dependent increases in BP.

Williams, Mancia et al., J Hypertens 2018;36:1953-2041 and Eur Heart J 2018;39:3021-3104

# Diagnosis (3)

## 1.2.2

Record the lower of the last two measurements as the clinic blood pressure

# Office BP measurement - 1

Patients should be seated comfortably in a quiet environment for 5 min before beginning BP measurements.

Three BP measurements should be recorded, 1–2 min apart, and additional measurements only if the first two readings differ by > 10 mmHg.  
BP is recorded as the average of the last two BP readings.

Additional measurements may have to be performed in patients with unstable BP values due to arrhythmias, such as in patients with AF, in whom manual auscultatory methods should be used as most automated devices have not been validated for BP measurement in patients with AF.

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Williams, Mancia et al., J Hypertens 2018;36:1953-2041 and Eur Heart J 2018;39:3021-3104

## Office BP measurement - 2

When using auscultatory methods, use phase I and V (sudden reduction/disappearance) Korotkoff sounds to identify SBP and DBP, respectively.

Measure BP in both arms at the first visit to detect possible between-arm differences.

Use the arm with the higher value as the reference.

Measure BP 1 minute and 3 min after standing from seated position in all patients

at the first measurement to exclude orthostatic hypotension. Lying and standing BP measurements should also be considered in subsequent visits in older people, in people with diabetes, and in other conditions in which orthostatic hypotension may frequently occur.

Record heart rate and use pulse palpation to exclude arrhythmia.

Williams, Mancia et al., J Hypertens 2018;36:1953-2041 and Eur Heart J  
2018;39:3021-3104

# BP measurement - 3

Recommendations	Class	Level
It is recommended that office BP should be measured in both arms at least at the first visit because a between-arm SBP difference of > 15 mmHg is suggestive of atheromatous disease and is associated with an increased CV risk.	I	A

Williams, Mancia et al., J Hypertens 2018;36:1953-2041 and Eur Heart J 2018;39:3021-3104

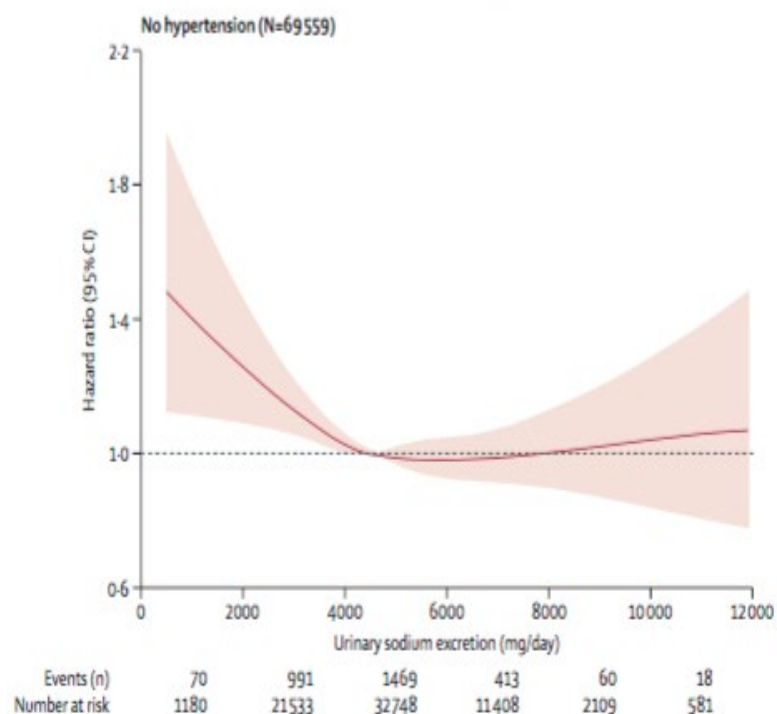
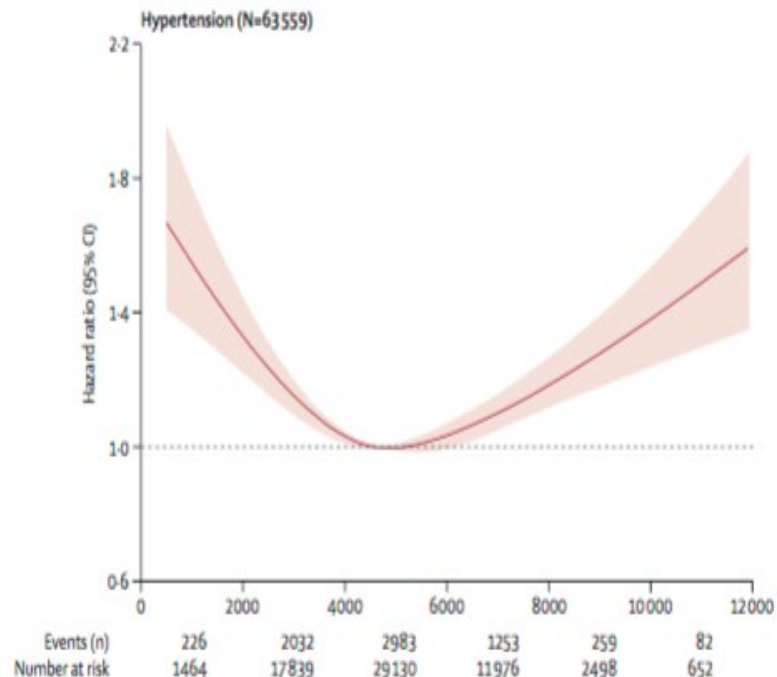
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Record heart rate and use pulse palpation to exclude arrhythmia.

# **NON PHARMACOLOGICAL MEASURES**

# Non-Pharmacological Measures

- Diet
- Lifestyle
  - weight reduction
  - salt reduction
  - moderate alcohol intake
  - exercise
  - smoking cessation
  - cholesterol lowering



## Associations of urinary sodium excretion with cardiovascular events in individuals with and without hypertension: a pooled analysis of data from four studies



Andrew Mente, Martin O'Donnell, Sumathy Rangarajan, Gilles Dagenais, Scott Lear, Matthew McQueen, Rafael Diaz, Alvaro Avezum, Patricio Lopez-Jaramillo, Fernando Lanas, Wei Li, Yin Lu, Sun Yi, Lei Rensheng, Romaina Iqbal, Prem Mory, Rita Yusuf, Khalid Yusoff, Andrzej Szuba, Aytekin Oguz, Annika Rosengren, Ahmad Bahonar, Afzalhussein Yusufali, Aletta Elisabeth Schutte, Jephth Chifamba, Johannes F E Mann, Sonia S Anand, Koon Teo, S Yusuf, for the PURE, EPIDREAM, and ONTARGET/TRANSCEND Investigators

Lancet 2016; 388: 465-75

# Lifestyle modifications

MODIFICATION	RECOMMENDATION	APPROXIMATE SBP REDUCTION (RANGE) <sup>†</sup>
Weight reduction	Maintain normal body weight (body mass index 18.5–24.9 kg/m <sup>2</sup> ).	5–20 mmHg/10kg <sup>92-93</sup>
Adopt DASH eating plan	Consume a diet rich in fruits, vegetables, and lowfat dairy products with a reduced content of saturated and total fat.	8–14 mmHg <sup>94-95</sup>
Dietary sodium reduction	Reduce dietary sodium intake to no more than 100 mmol per day (2.4 g sodium or 6 g sodium chloride).	2–8 mmHg <sup>94-96</sup>
Physical activity	Engage in regular aerobic physical activity such as brisk walking (at least 30 min per day, most days of the week).	4–9 mmHg <sup>97-98</sup>
Moderation of alcohol consumption	Limit consumption to no more than 2 drinks (e.g., 24 oz beer, 10 oz wine, or 3 oz 80-proof whiskey) per day in most men, and to no more than 1 drink per day in women and lighter weight persons.	2–4 mmHg <sup>99</sup>

# What to do while your waiting!



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- Test for presence of protein in the urine
- Take a blood sample to measure
  - Glycated haemoglobin (HbA1C),
  - Electrolytes,
  - Creatinine,
  - Estimated glomerular filtration rate,
  - Total cholesterol and HDL cholesterol
- Examine the fundi for the presence of hypertensive retinopathy
- Arrange for a 12-lead electrocardiograph to be performed.

And while your waiting for these  
results to come back .....

This calculator is only valid if you do not already have a diagnosis of coronary heart disease (including angina or heart attack) or stroke/transient ischaemic attack.

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## About you

Age (25-84):

Sex:

☒ Male ☐ Female

Ethnicity:

UK postcode: leave blank if unknown

Postcode:

## Clinical information

Smoking status:

Diabetes status:

Angina or heart attack in a 1st degree relative < 60? ☐

Chronic kidney disease (stage 3, 4 or 5)? ☐

Atrial fibrillation? ☐

On blood pressure treatment? ☐

Do you have migraines? ☐

Rheumatoid arthritis? ☐

Systemic lupus erythematosus (SLE)? ☐

Severe mental illness?

(this includes schizophrenia, bipolar disorder and moderate/severe depression)

☐

On atypical antipsychotic medication? ☐

Are you on regular steroid tablets? ☐

A diagnosis of or treatment for erectile dysfunction? ☐

Leave blank if unknown

## Welcome to the QRISK<sup>®</sup>3-2018 risk calculator

Welcome to the QRISK<sup>®</sup>3-2018 Web Calculator. The QRISK<sup>®</sup>3 algorithm calculates a person's risk of developing a heart attack or stroke over the next 10 years. It presents the average risk of people with the same risk factors as those entered for that person.

The QRISK<sup>®</sup>3 algorithm has been developed by doctors and academics working in the UK National Health Service and is based on routinely collected data from many thousands of GPs across the country who have freely contributed data to the QResearch database for medical research.

QRISK<sup>®</sup>3 has been developed for the UK population, and is intended for use in the UK. All medical decisions need to be taken by a patient in consultation with their doctor. The authors and the sponsors accept no responsibility for clinical use or misuse of this score.

The science underpinning QRISK<sup>®</sup>3 has been published in the BMJ -- see the publications tab for details.

## What is the difference between QRISK<sup>®</sup>3 and QRISK<sup>®</sup>2?

QRISK<sup>®</sup>3 includes more factors than QRISK<sup>®</sup>2 to help enable doctors to identify those at most risk of heart disease and stroke. These are

- Chronic kidney disease, which now includes stage 3 CKD
- Migraine
- Corticosteroids
- Systemic lupus erythematosus (SLE)
- atypical antipsychotics
- severe mental illness
- erectile dysfunction
- a measure of systolic blood pressure variability

About you

Age (25-84):

Sex: ☒ Male ☐ Female

Ethnicity:

UK postcode: leave blank if unknown

Postcode:

**Your results**

Postcode: EC1

A diagnosis of or treatment for erect

Standard deviation of at least two most recent systolic blood pressure readings (mmHg):

Your risk of having a heart attack or stroke within the next 10 years is:

In other words, in a crowd of 100 people with the same risk factors as you, 20 are likely to have a heart attack or stroke within the next 10 years.



Your body mass index was calculated as 29.98 kg/m<sup>2</sup>.

About you

Age (25-84):

Sex:☒ Male ☐ Female

Ethnicity:

UK postcode: leave blank if unknown

Postcode:

Leave blank if unknown

Cholesterol/HDL ratio:

Systolic blood pressure (mmHg):

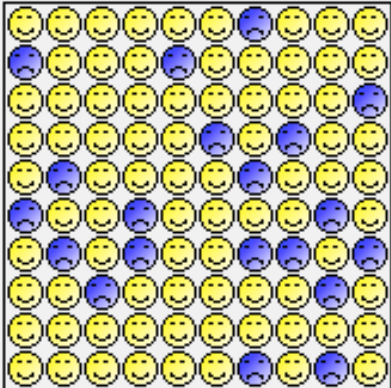
Standard deviation of at least two most recent systolic blood pressure readings (mmHg):

Your results

Your risk of having a heart attack or stroke within the next 10 years is:

20.3%

In other words, in a crowd of 100 people with the same risk factors as you, 20 are likely to have a heart attack or stroke within the next 10 years.



Risk of  
a heart attack or stroke

Clinical information

Smoking status:

Diabetes status:

Angina or heart attack in a 1st degree

Chronic kidney disease (stage 3, 4 or 5)

Atrial fibrillation? ☐

On blood pressure treatment? ☒

Do you have migraines? ☐

Rheumatoid arthritis? ☐

Systemic lupus erythematosus (SLE)

Severe mental illness?  
(this includes schizophrenia, bipolar disorder, moderate/severe depression)

On atypical antipsychotic medication

Are you on regular steroid tablets?

A diagnosis of or treatment for erectile dysfunction

Your score has been calculated using estimated data, as some information was left blank.

Your body mass index was calculated as 29.98 kg/m<sup>2</sup>.

About you

Age (25-84):

Sex: ☒ Male ☐ Female

Ethnicity:

UK postcode: leave blank

Postcode:

Leave blank if unknown

Cholesterol/HDL ratio:

Systolic blood pressure (mmHg):

**Your results**

Your risk of having a heart attack or stroke within the next 10 years is:

**8.5%**

**Clinical information**

Smoking status:

Diabetes status:

Angina or heart attack in the last 10 years? ☐

Chronic kidney disease (stage 3 or worse)? ☐

Atrial fibrillation? ☐

On blood pressure treatment? ☐

Do you have migraines? ☐

Rheumatoid arthritis? ☐

Systemic lupus erythematosus? ☐

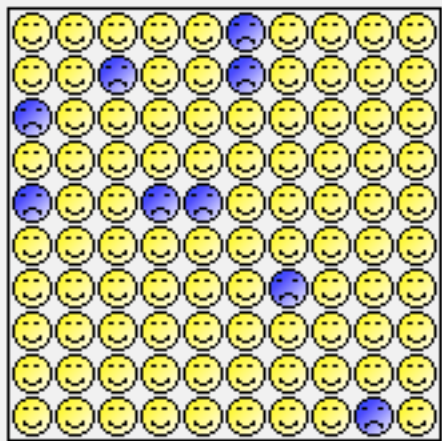
Severe mental illness? (this includes schizophrenia, bipolar disorder, moderate/severe depression) ☐

On atypical antipsychotic medication? ☐

Are you on regular steroid treatment? ☐

A diagnosis of or treatment for cancer in the last 10 years? ☐

In other words, in a crowd of 100 people with the same risk factors as you, 9 are likely to have a heart attack or stroke within the next 10 years.



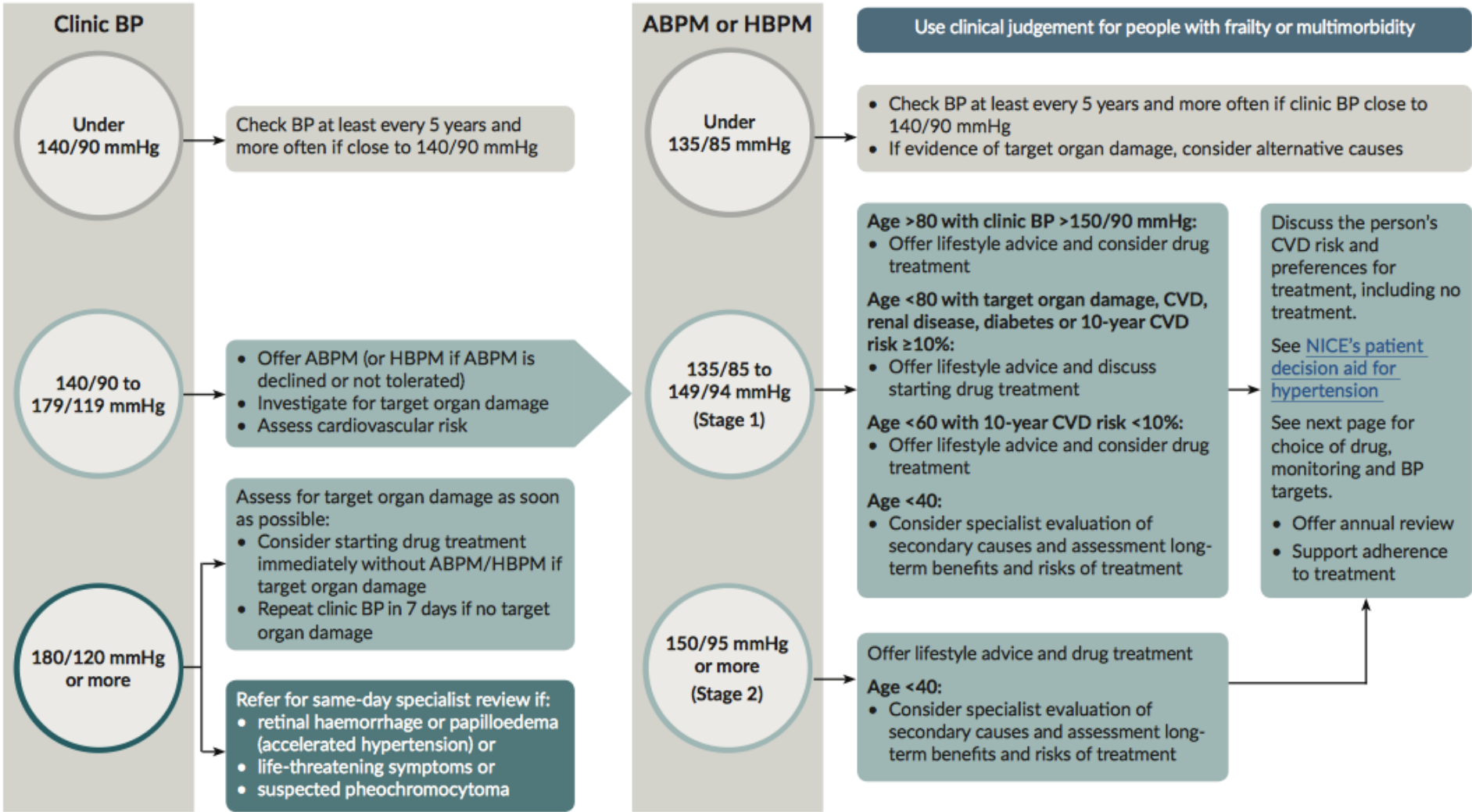
**Risk of  
a heart attack or stroke**

Your score has been calculated using estimated data, as some information was left blank.

Your body mass index was calculated as 26.83 kg/m<sup>2</sup>.

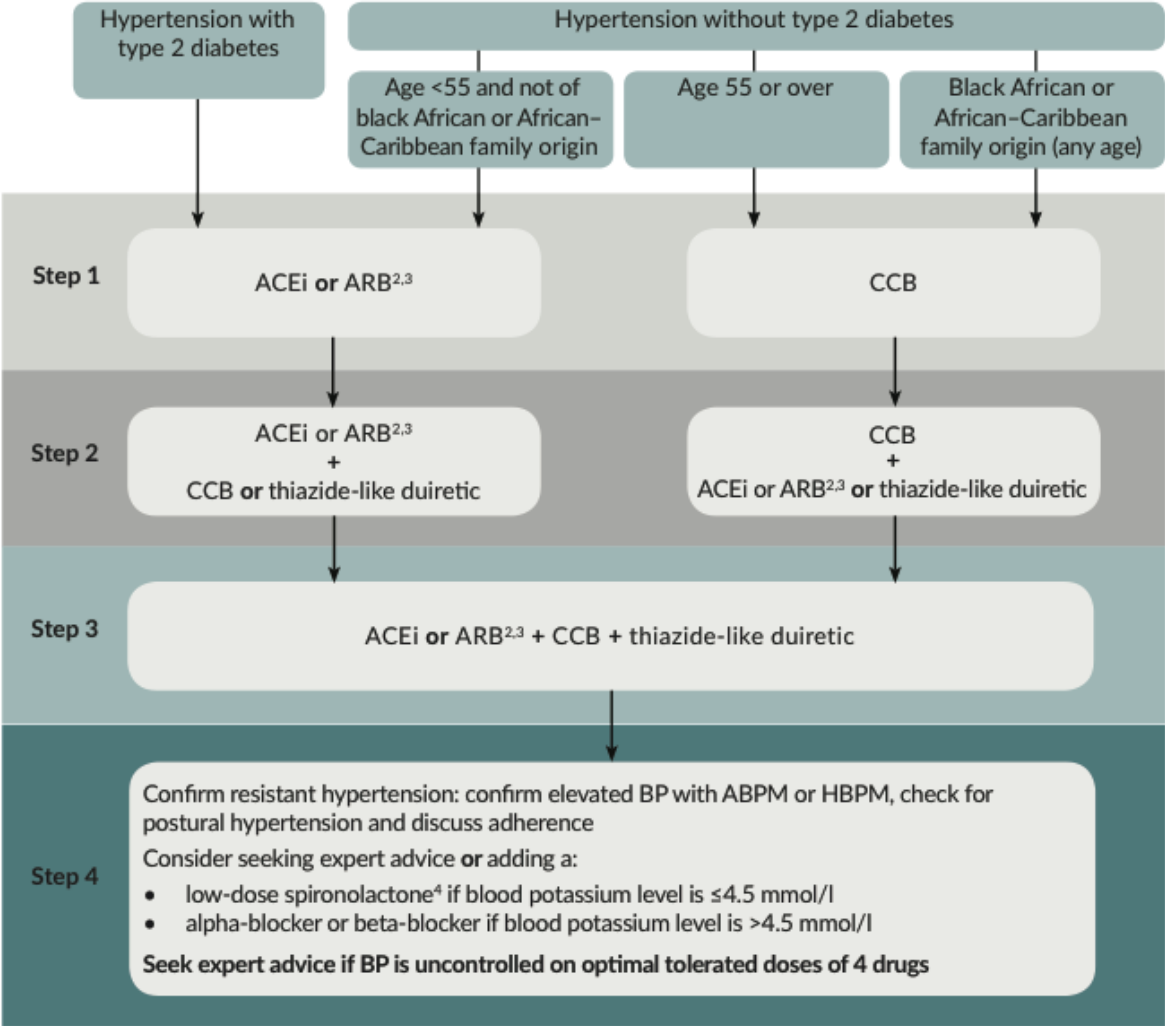
# Hypertension in adults: diagnosis and treatment

Offer lifestyle advice and continue to offer it periodically



# Treatment the NICE way

# Choice of antihypertensive drug<sup>1</sup>, monitoring treatment and BP targets



Use clinical judgement for people with frailty or multimorbidity

Offer lifestyle advice and continue to offer it periodically

## Monitoring treatment

Use clinic BP to monitor treatment.

Measure standing and sitting BP in people with:

- type 2 diabetes or
- symptoms of postural hypotension or
- aged 80 and over.

Advise people who want to self-monitor to use HBPM. Provide training and advice.

Consider ABPM or HBPM, in addition to clinic BP, for people with white-coat effect or masked hypertension.

## BP targets

Reduce and maintain BP to the following targets:

**Age <80 years:**

- Clinic BP  $<140/90$  mmHg
- ABPM/HBPM  $<135/85$  mmHg

**Age  $\geq 80$  years:**

- Clinic BP  $<150/90$  mmHg
- ABPM/HBPM  $<145/85$  mmHg

**Postural hypotension:**

- Base target on standing BP

**Frailty or multimorbidity:**

- Use clinical judgement

<sup>1</sup> For women considering pregnancy or who are pregnant or breastfeeding, see NICE's guideline on [hypertension in pregnancy](#). For people with chronic kidney disease, see NICE's guideline on [chronic kidney disease](#). For people with heart failure, see NICE's guideline on [chronic heart failure](#)

<sup>2</sup> See MHRA drug safety updates on [ACE inhibitors and angiotensin-II receptor antagonists: not for use in pregnancy](#), which states 'Use in women who are planning pregnancy should be avoided unless absolutely necessary, in which case the potential risks and benefits should be discussed', [ACE inhibitors and angiotensin II receptor antagonists: use during breastfeeding](#) and [clarification: ACE inhibitors and angiotensin II receptor antagonists](#). See also NICE's guideline on [hypertension in pregnancy](#).

<sup>3</sup> Consider an ARB, in preference to an ACE inhibitor in adults of African and Caribbean family origin.

<sup>4</sup> At the time of publication (August 2019), not all preparations of spironolactone have a UK marketing authorisation for this indication.

Abbreviations: ABPM, ambulatory blood pressure monitoring; ACEi, ACE inhibitor; ARB, angiotensin-II receptor blocker; BP, blood pressure; CCB, calcium-channel blocker; HBPM, home blood pressure monitoring.



This visual summary builds on and updates previous work on treatment [published by the BIHS](#) (formerly BHS)

# Office BP treatment target range



Age group	Office SBP treatment target ranges (mmHg)					Office DBP treatment target range (mmHg)
	Hypertension	+ Diabetes	+ CKD	+ CAD	+ Stroke/TIA	
18–65 years	<b>Target to 130</b> <i>or lower if tolerated</i>  Not < 120	<b>Target to 130</b> <i>or lower if tolerated</i>  Not < 120	<b>Target to 130</b> <i>or lower if tolerated</i>  Not < 120	<b>Target to 130</b> <i>or lower if tolerated</i>  Not < 120	<b>Target to 130</b> <i>or lower if tolerated</i>  Not < 120	70-79
65–79 years	<b>Target to &lt; 140 to 130</b> <i>if tolerated</i>	<b>Target to &lt; 140 to 130</b> <i>if tolerated</i>	<b>Target to &lt; 140 to 130</b> <i>if tolerated</i>	<b>Target to &lt; 140 to 130</b> <i>if tolerated</i>	<b>Target to &lt; 140 to 130</b> <i>if tolerated</i>	70-79
≥ 80 years	<b>Target to &lt; 140 to 130</b> <i>if tolerated</i>	<b>Target to &lt; 140 to 130</b> <i>if tolerated</i>	<b>Target to &lt; 140 to 130</b> <i>if tolerated</i>	<b>Target to &lt; 140 to 130</b> <i>if tolerated</i>	<b>Target to &lt; 140 to 130</b> <i>if tolerated</i>	70-79
<b>Office DBP treatment target range(mmHg)</b>	70-79	70-79	70-79	70-79	70-79	

Williams, Mancia et al., J Hypertens 2018;36:1953-2041 and Eur Heart J 2018;39:3021-3104

# A Randomized Trial of Intensive versus Standard Blood-Pressure Control

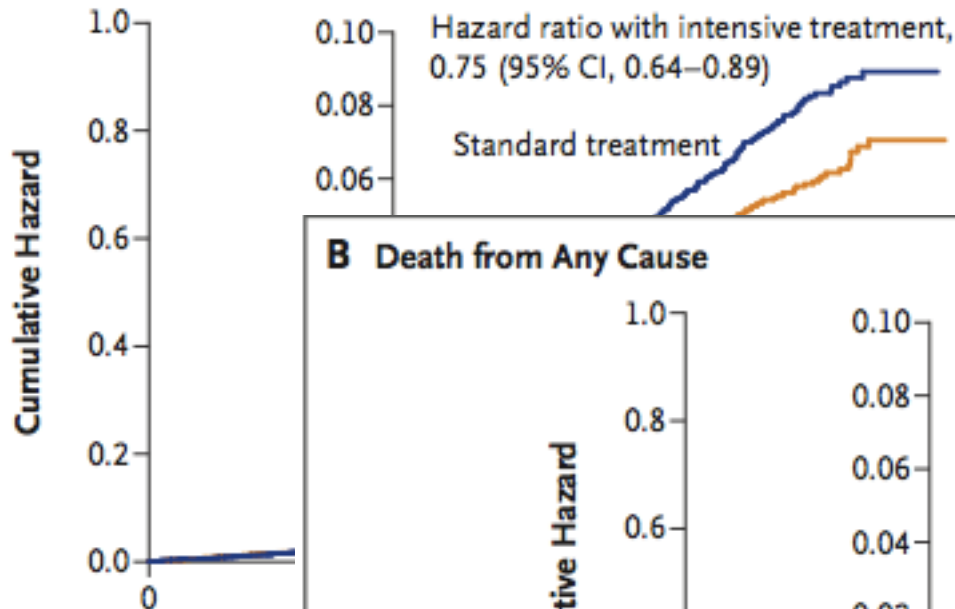
The SPRINT Research Group\*

- RCT with 9361 pts with BP >130mmHg, increased CV risk with out diabetes
- Randomise to BP target <120 vs <140mmHg
- No guide to use as such – open formulary!
- 1ry outcome composite of MI, ACS, stroke, HF or CV death
- Stopped after median 3.2yr



# SPRINT Results

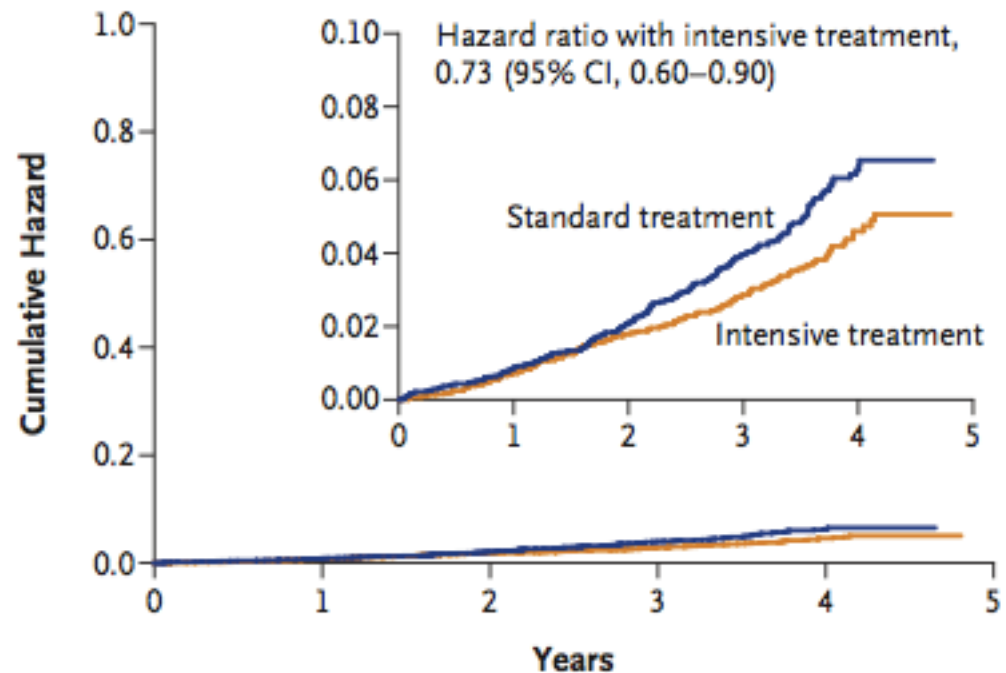
## A Primary Outcome



### No. at Risk

Standard treatment	4683	4
Intensive treatment	4678	4

## B Death from Any Cause



### No. at Risk

Standard treatment	4683	4528	4383	2998	789
Intensive treatment	4678	4516	4390	3016	807

# SPRINT Results

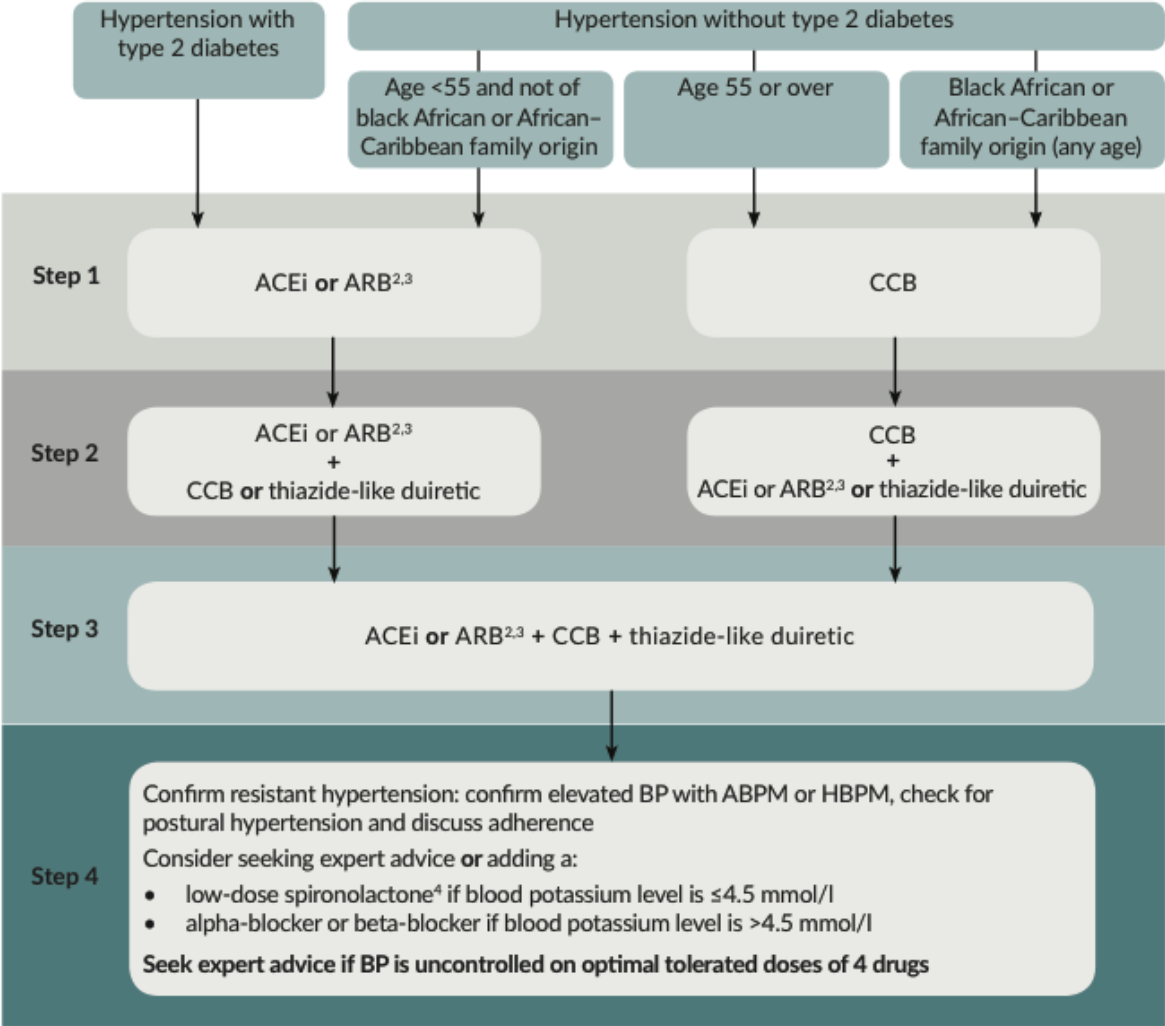


Barts Health

**Table 3. Serious Adverse Events, Conditions of Interest, and Monitored Clinical Events.**

Variable	Intensive Treatment (N = 4678) <i>no. of patients (%)</i>	Standard Treatment (N = 4683) <i>no. of patients (%)</i>	Hazard Ratio	P Value
Serious adverse event*	1793 (38.3)	1736 (37.1)	1.04	0.25
Conditions of interest				
Serious adverse event only				
Hypotension	110 (2.4)	66 (1.4)	1.67	0.001
Syncope	107 (2.3)	80 (1.7)	1.33	0.05
Bradycardia	87 (1.9)	73 (1.6)	1.19	0.28
Electrolyte abnormality	144 (3.1)	107 (2.3)	1.35	0.02
Injurious fall†	105 (2.2)	110 (2.3)	0.95	0.71
Acute kidney injury or acute renal failure‡	193 (4.1)	117 (2.5)	1.66	<0.001
Emergency department visit or serious adverse event				
Hypotension	158 (3.4)	93 (2.0)	1.70	<0.001
Syncope	163 (3.5)	113 (2.4)	1.44	0.003
Bradycardia	104 (2.2)	83 (1.8)	1.25	0.13
Electrolyte abnormality	177 (3.8)	129 (2.8)	1.38	0.006
Injurious fall†	334 (7.1)	332 (7.1)	1.00	0.97
Acute kidney injury or acute renal failure‡	204 (4.4)	120 (2.6)	1.71	<0.001

# Choice of antihypertensive drug<sup>1</sup>, monitoring treatment and BP targets



Use clinical judgement for people with frailty or multimorbidity

Offer lifestyle advice and continue to offer it periodically

## Monitoring treatment

Use clinic BP to monitor treatment.

Measure standing and sitting BP in people with:

- type 2 diabetes or
- symptoms of postural hypotension or
- aged 80 and over.

Advise people who want to self-monitor to use HBPM. Provide training and advice.

Consider ABPM or HBPM, in addition to clinic BP, for people with white-coat effect or masked hypertension.

## BP targets

Reduce and maintain BP to the following targets:

**Age <80 years:**

- Clinic BP  $<140/90$  mmHg
- ABPM/HBPM  $<135/85$  mmHg

**Age  $\geq 80$  years:**

- Clinic BP  $<150/90$  mmHg
- ABPM/HBPM  $<145/85$  mmHg

**Postural hypotension:**

- Base target on standing BP

**Frailty or multimorbidity:**

- Use clinical judgement

<sup>1</sup> For women considering pregnancy or who are pregnant or breastfeeding, see NICE's guideline on [hypertension in pregnancy](#). For people with chronic kidney disease, see NICE's guideline on [chronic kidney disease](#). For people with heart failure, see NICE's guideline on [chronic heart failure](#)

<sup>2</sup> See MHRA drug safety updates on [ACE inhibitors and angiotensin-II receptor antagonists: not for use in pregnancy](#), which states 'Use in women who are planning pregnancy should be avoided unless absolutely necessary, in which case the potential risks and benefits should be discussed', [ACE inhibitors and angiotensin II receptor antagonists: use during breastfeeding](#) and [clarification: ACE inhibitors and angiotensin II receptor antagonists](#). See also NICE's guideline on [hypertension in pregnancy](#).

<sup>3</sup> Consider an ARB, in preference to an ACE inhibitor in adults of African and Caribbean family origin.

<sup>4</sup> At the time of publication (August 2019), not all preparations of spironolactone have a UK marketing authorisation for this indication.

Abbreviations: ABPM, ambulatory blood pressure monitoring; ACEi, ACE inhibitor; ARB, angiotensin-II receptor blocker; BP, blood pressure; CCB, calcium-channel blocker; HBPM, home blood pressure monitoring.

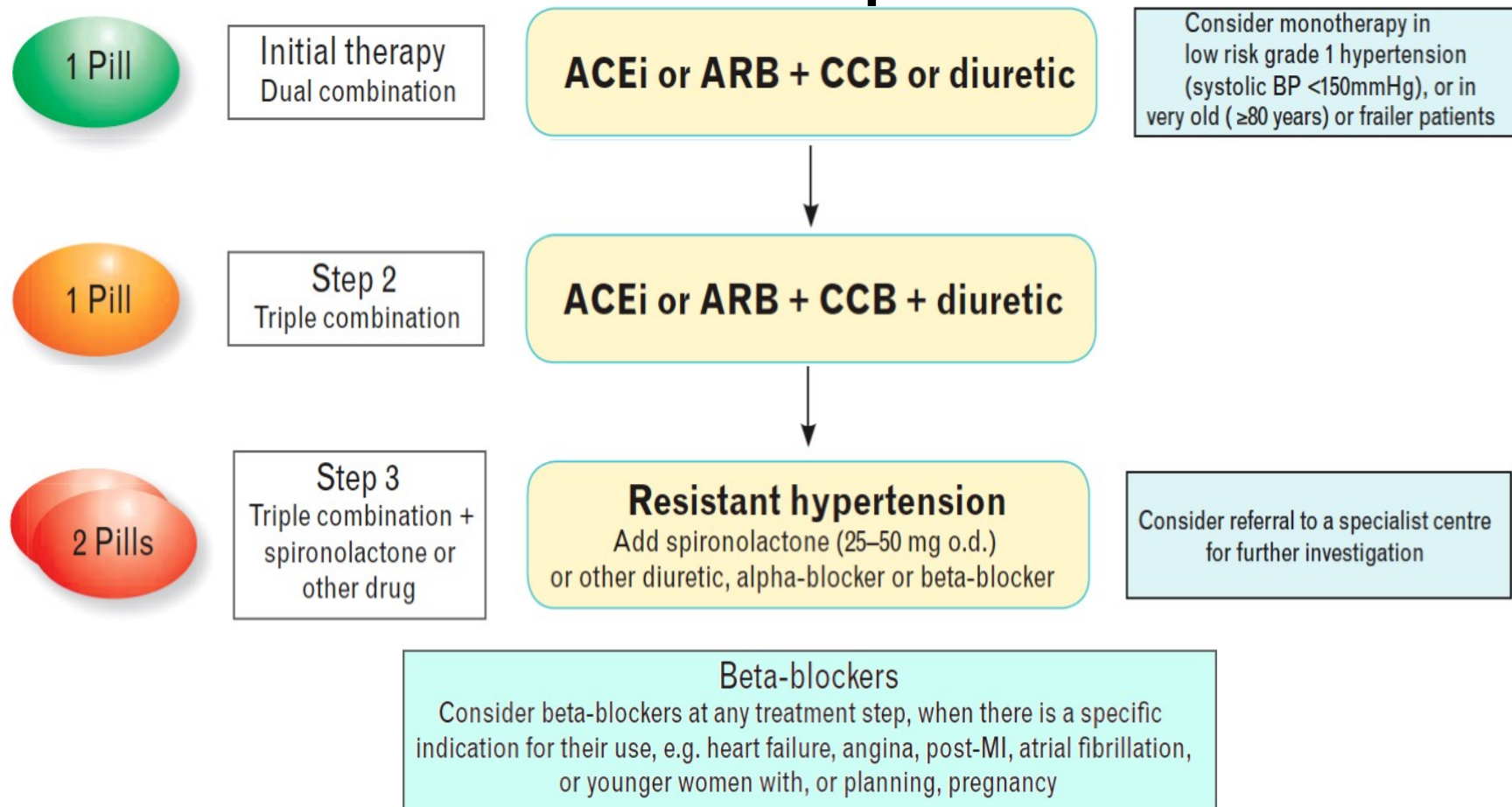


This visual summary builds on and updates previous work on treatment [published by the BIHS](#) (formerly BHS)

# Core drug-treatment strategy for uncomplicated



Barts Health  
NHS Trust



*The core algorithm is also appropriate for most patients with HMOD, cerebrovascular disease, diabetes, or PAD*

# Compelling and possible contraindications to the use of specific antihypertensive drugs

Drug	Contraindications	
	Compelling	Possible
Diuretics (thiazides/thiazide-type, e.g. chlorthalidone and indapamide)	<ul style="list-style-type: none"> <li>Gout</li> </ul>	<ul style="list-style-type: none"> <li>Metabolic syndrome</li> <li>Glucose intolerance</li> <li>Pregnancy</li> <li>Hypercalcemia</li> <li>Hypokalemia</li> </ul>
Beta-blockers	<ul style="list-style-type: none"> <li>Asthma</li> <li>Any high-grade sino-atrial or atrioventricular block</li> <li>Bradycardia (heart rate &lt; 60 beats per min)</li> </ul>	<ul style="list-style-type: none"> <li>Metabolic syndrome</li> <li>Glucose intolerance</li> <li>Athletes and physically active patients</li> </ul>
Calcium antagonists (dihydropyridines)		<ul style="list-style-type: none"> <li>Tachyarrhythmia</li> <li>Heart failure (HFrEF, class III or IV)</li> <li>Pre-existing severe leg oedema</li> </ul>
Calcium antagonists (verapamil, diltiazem)	<ul style="list-style-type: none"> <li>Any high-grade sino-atrial or AV block</li> <li>Severe LV dysfunction (LV EF &lt; 40%)</li> <li>Bradycardia (heart rate &lt; 60 beats per min)</li> </ul>	<ul style="list-style-type: none"> <li>Constipation</li> </ul>
ACE inhibitors	<ul style="list-style-type: none"> <li>Pregnancy</li> <li>Previous angioneurotic oedema</li> <li>Hyperkalemia (potassium &gt; 5.5 mmol/L)</li> <li>Bilateral renal artery stenosis</li> </ul>	<ul style="list-style-type: none"> <li>Women of child-bearing potential without reliable contraception</li> </ul>
ARBs	<ul style="list-style-type: none"> <li>Pregnancy</li> <li>Hyperkalemia (potassium &gt; 5.5 mmol/L)</li> <li>Bilateral renal artery stenosis</li> </ul>	<ul style="list-style-type: none"> <li>Women of child-bearing potential without reliable contraception</li> </ul>

# Medications and other substances that may increase BP

Medication/substance	
Oral contraceptive pill	Especially oestrogen containing; cause hypertension in 5% of women, usually mild but can be severe
Diet pills	For example, phenylpropanolamine and sibutramine
Nasal decongestants	For example, phenylephrine hydrochloride and naphazoline hydrochloride
Stimulant drugs	Amphetamine, cocaine, and ecstasy – these substances usually cause acute rather than chronic hypertension
Liquorice	Chronic excessive liquorice use mimics hyperaldosteronism by stimulating the mineralocorticoid receptor and inhibiting cortisol metabolism
Immunosuppressive medications	For example, cyclosporin A (tacrolimus has less effect on BP and rapamycin has almost no effect on BP), and steroids (e.g. corticosteroids, hydrocortisone)
Antiangiogenic cancer therapies	Antiangiogenic drugs, such as VEGF inhibitors (e.g. bevacizumab), tyrosine kinase inhibitors (e.g. sunitinib), and sorafenib, have been reported to increase BP
Other drugs and substances that may raise BP	Anabolic steroids, erythropoietin, non-steroidal anti-inflammatory drugs, herbal remedies (e.g. ephedra, ma huang)

# Not to do messages from the guidelines

Withdrawal of BP-lowering drug treatment on the basis of age, even when patients attain an age of $\geq 80$ years, is not recommended, provided that treatment is well tolerated.	<b>III</b>	<b>A</b>
The combination of two RAS blockers is not recommended.	<b>III</b>	<b>A</b>
Aspirin is not recommended for primary prevention in hypertensive patients without CVD.	<b>III</b>	<b>A</b>
Routine genetic testing for hypertensive patients is not recommended.	<b>III</b>	<b>C</b>
Use of device-based therapies is not recommended for the routine treatment of hypertension, unless in the context of clinical studies and RCTs, until further evidence regarding their safety and efficacy becomes available.	<b>III</b>	<b>B</b>
It is recommended to avoid binge drinking.	<b>III</b>	<b>A</b>
Routine drug treatment is not indicated for white coat hypertension.	<b>III</b>	<b>C</b>

# RESISTANT HYPERTENSION

# Resistant hypertension

Clinic blood pressure > 140 or > 90 mmHg with

the optimal or *best tolerated* doses of:

ACE inhibitor (or angiotensin-II receptor blocker) +  
calcium channel blocker +  
diuretic

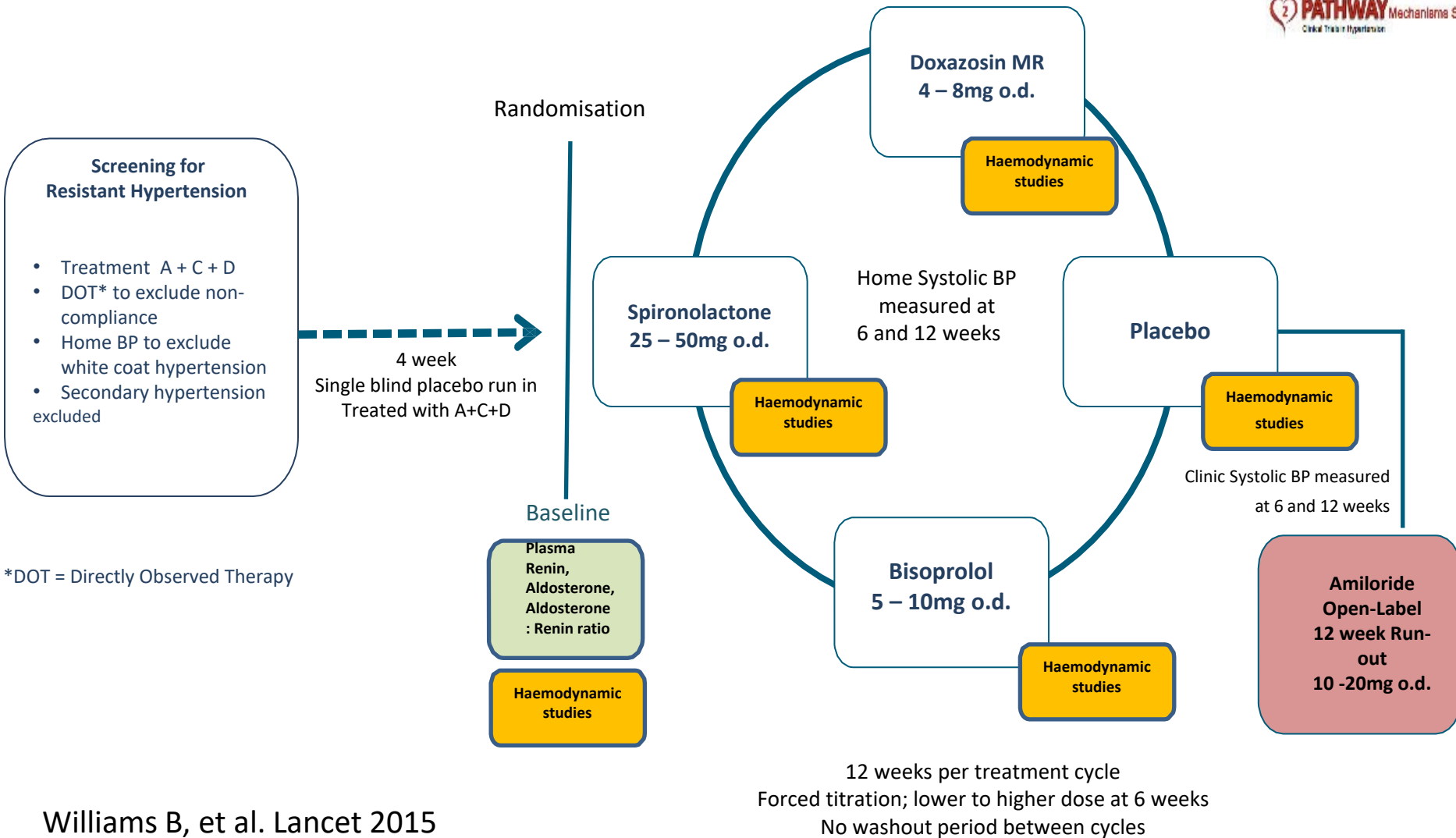
# Resistant hypertension

## The PATHWAY-2 study hypothesis:

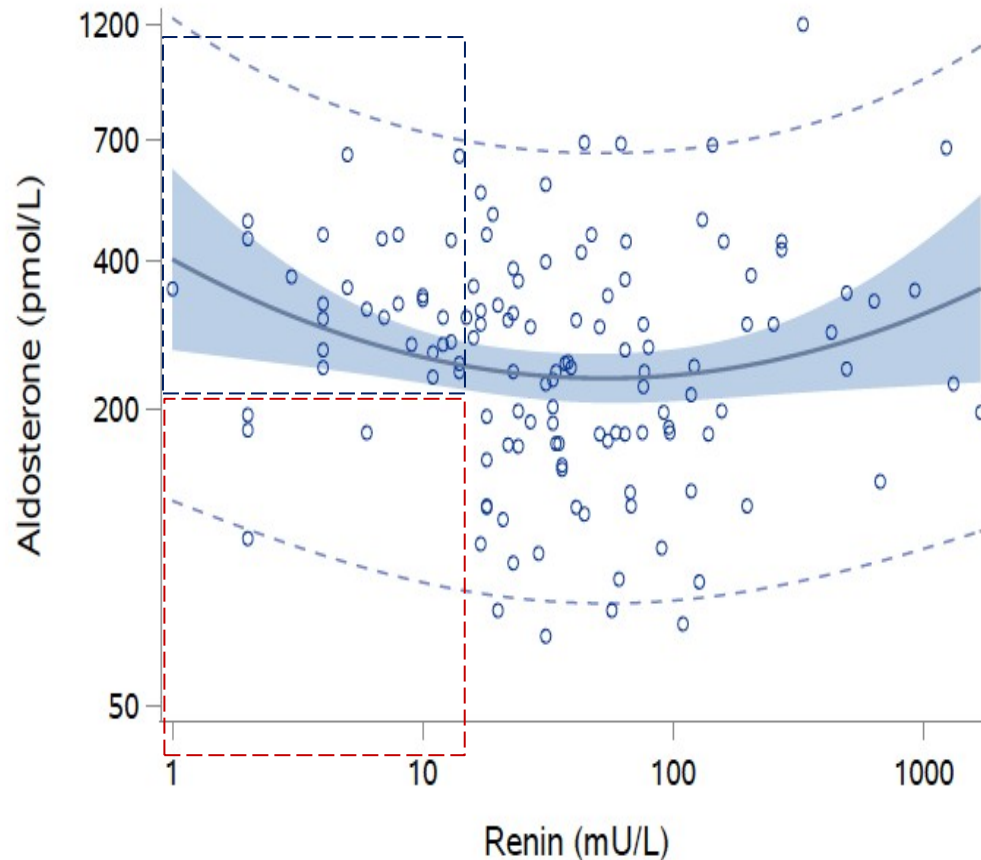
- That resistant hypertension is predominantly a sodium-retaining state
- That, further diuretic therapy with spironolactone would be the most effective additional treatment to lower blood pressure
- When added to therapy with at least 3 medications; ACE-inhibitor or ARB (A), a CCB (C) and a diuretic (D), i.e. A+C+D.

# PATHWAY-2 Mechanisms study

**PATHWAY** Mechanisms Study  
Clinical Trial in Hypertension



# Relationship between renin and aldosterone levels in resistant hypertension

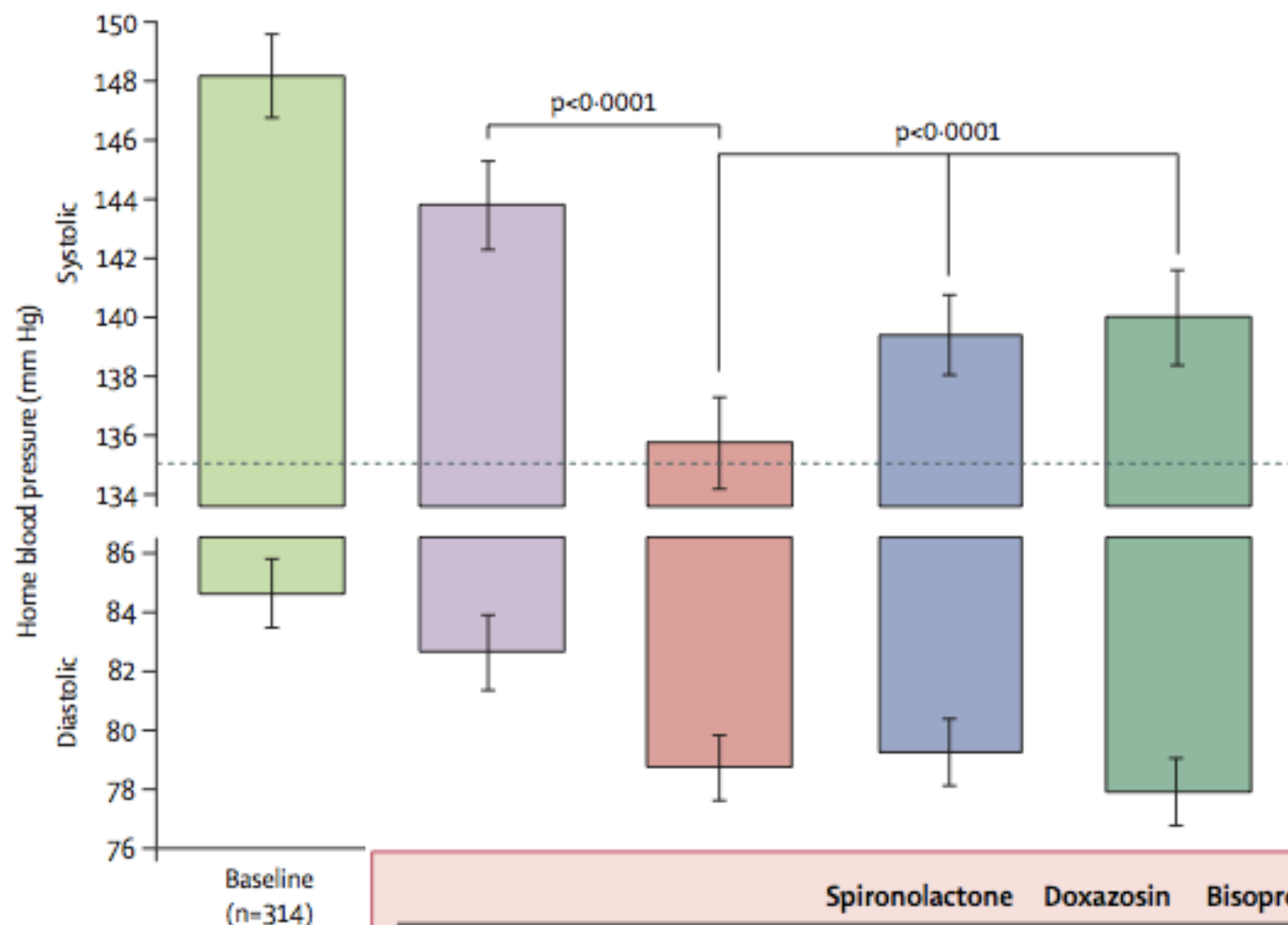


$p=0.340$  for the linear term  
 $p=0.0215$  for the quadratic term\*

- Very few patients with low renin and low aldosterone
- Many more patients with a relative increase in aldosterone despite a low renin

\*Quadratic equation:  
 $\text{aldosterone} = 2.365 -$   
 $0.0309 * \text{renin} + 0.0806 * \text{renin} * \text{renin}$

■ 95% Confidence Limits    - - - 95% Prediction Limits    — Regression



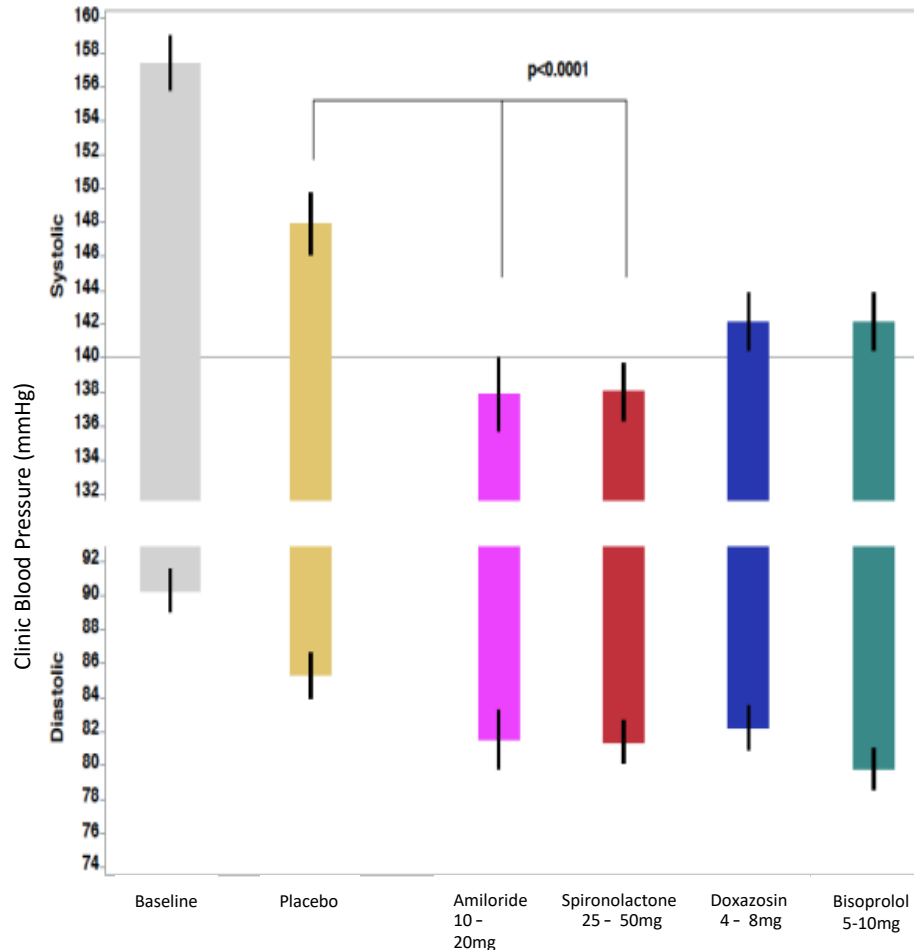
**Figure 2: Home systolic and diastolic blood pressure over other cycles**

	Spironolactone	Doxazosin	Bisoprolol	Placebo	p value*
Serious adverse events	7 (2%)	5 (2%)	8 (3%)	5 (2%)	0.82
Any adverse event	58 (19%)	67 (23%)	68 (23%)	42 (15%)	0.036
Withdrawals for adverse events	4 (1%)	9 (3%)	4 (1%)	3 (1%)	0.28

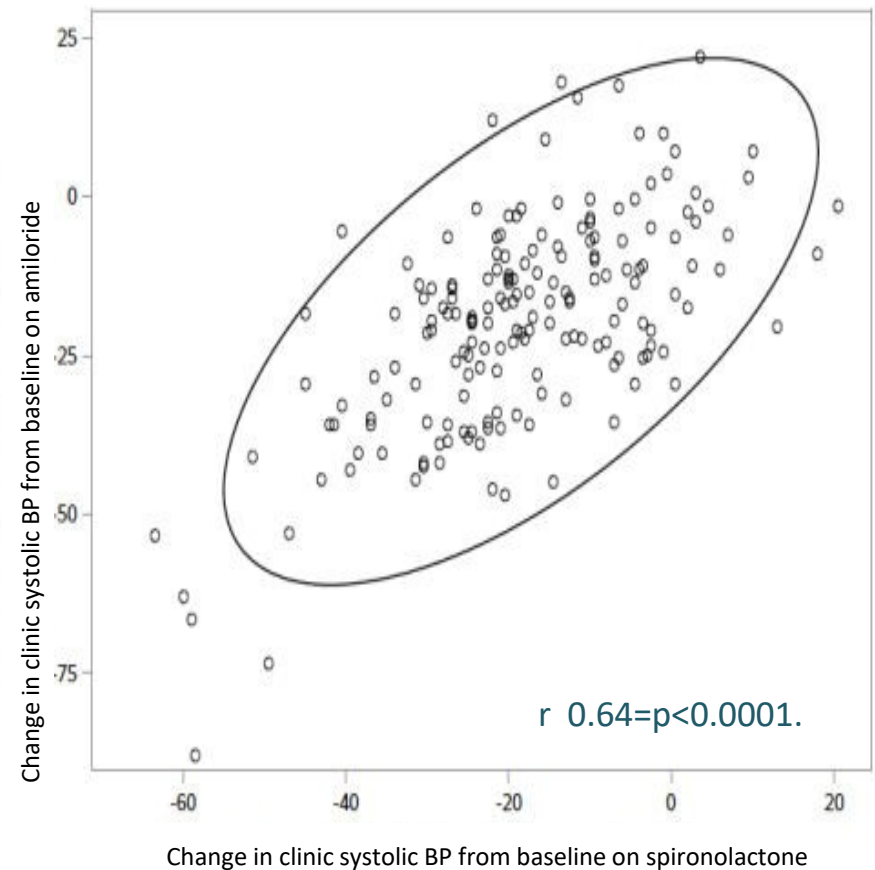
Data are n (%). \*p values for Fisher's exact test. The most common adverse events in at least 5% of patients on any treatment are shown in appendix p 12.

**Table 5: Adverse events and withdrawals**

# Effects of amiloride versus spironolactone on clinic systolic BP in resistant hypertension



Correlation of BP reduction with amiloride vs spironolactone



# Summary and Conclusions

- Resistant Hypertension is predominantly a sodium retaining state, characterised by low plasma renin, inappropriately elevated aldosterone, with the most effective treatment associated with a reduction in systemic volume, i.e. a diuretic
- Spironolactone (25-50mg daily) appears to act primarily as a diuretic to reduce blood pressure in resistant hypertension
- This effect is replicated by amiloride 10-20mg daily
- We speculate that a significant proportion of patients with resistant hypertension have inappropriate aldosterone excess due to aldosterone-producing microadenomas that are poorly detected by conventional imaging, explaining the quadratic relationship between aldosterone and renin levels and the superior response to anti-aldosterone diuretic therapy in these patients

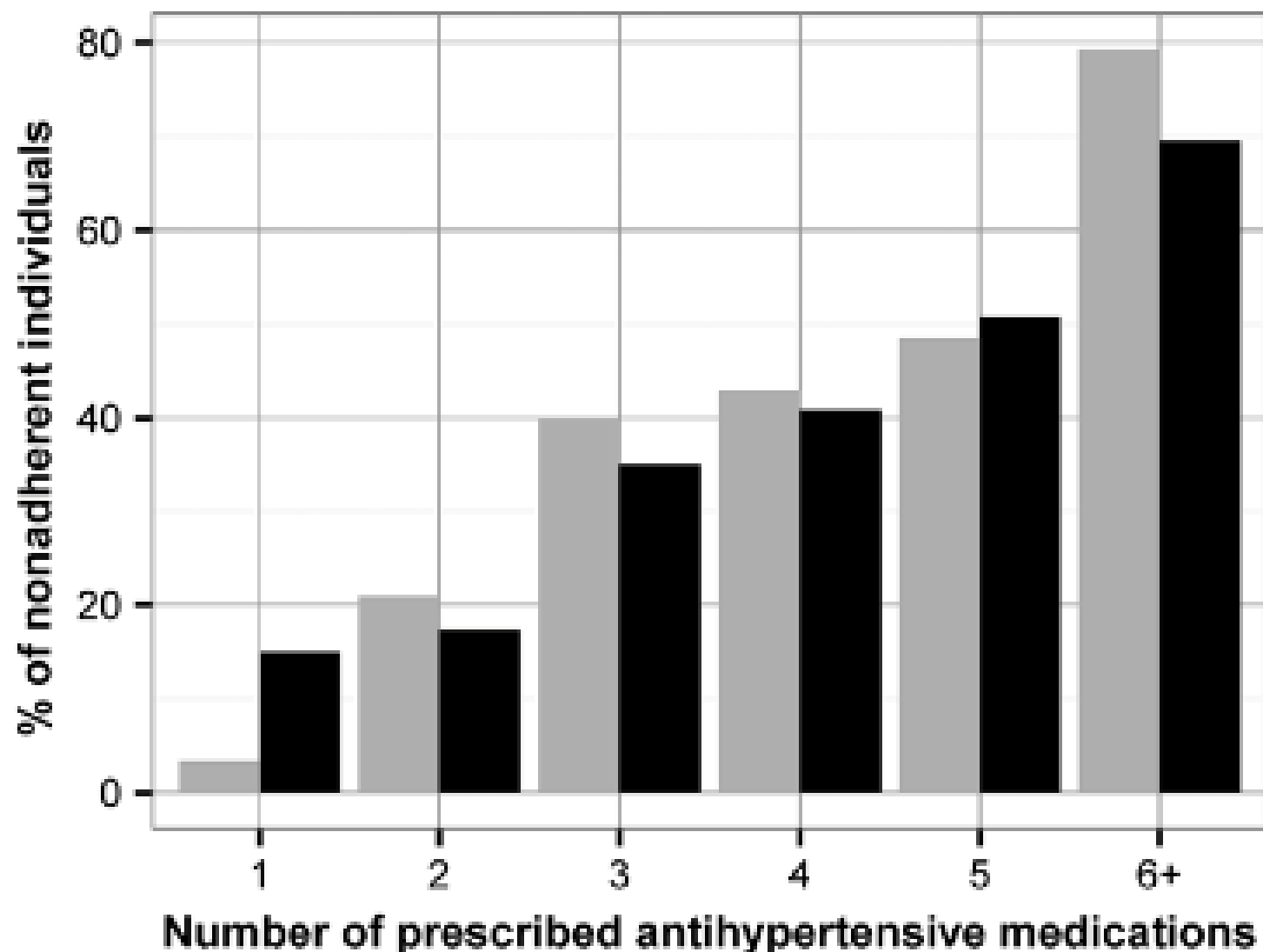
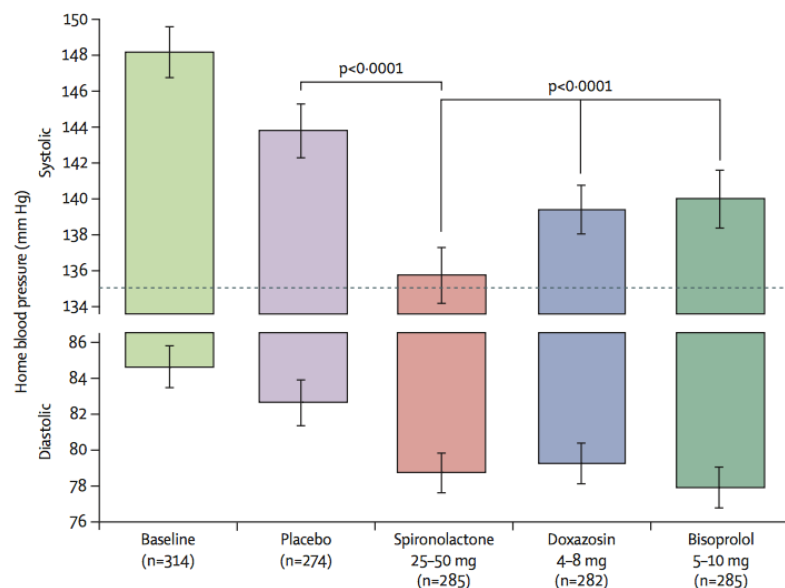


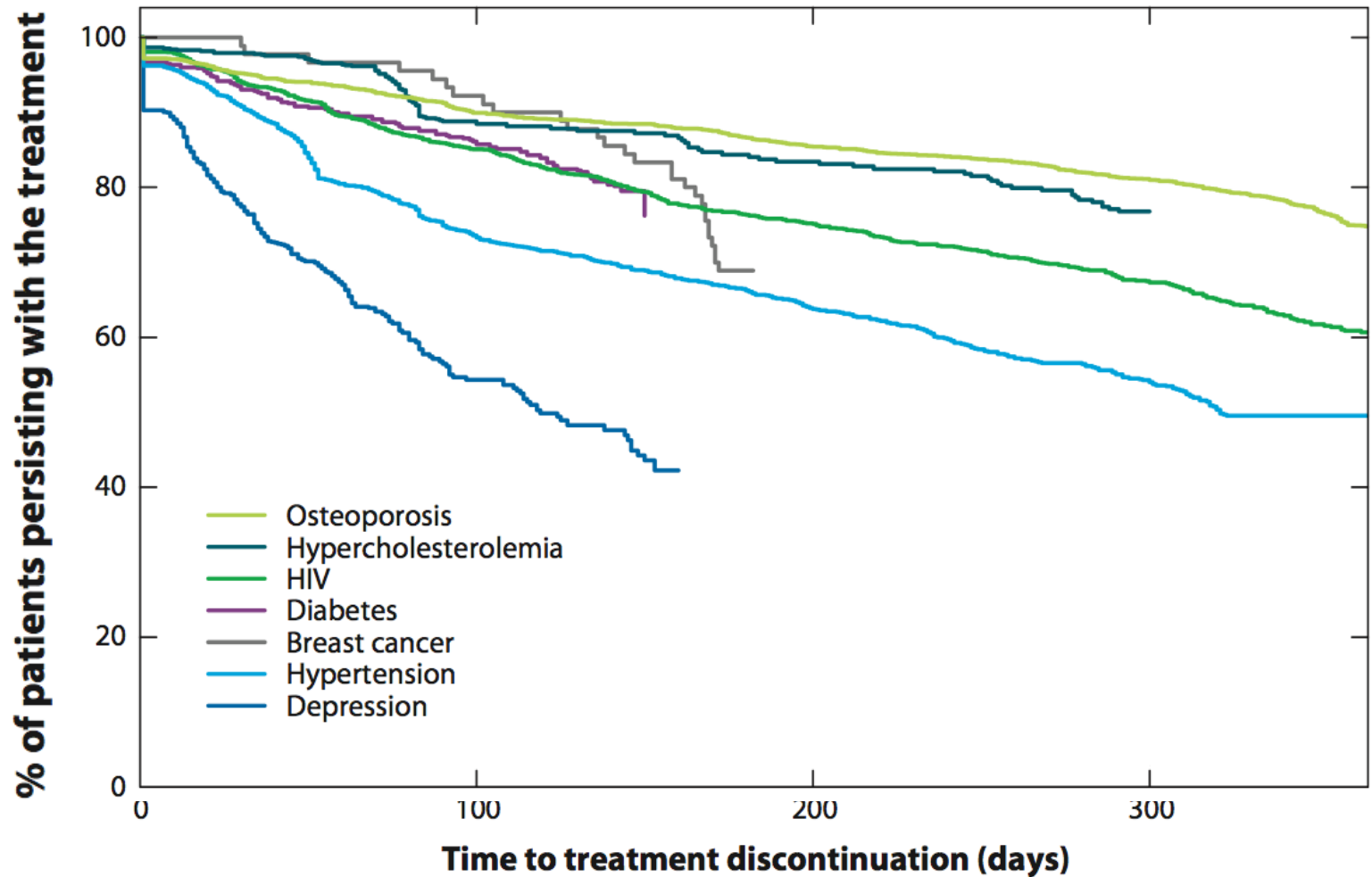
Figure. Association between the number of prescribed antihypertensive medications and the risk of nonadherence by population (gray, United Kingdom; black, Czech Republic).

# Resistant hypertension: *medications work*



	Blood pressure (mm Hg)	Change from baseline (mm Hg)
<b>Mean</b>		
Spironolactone	134.9 (134.0 to 135.9)	-12.8 (-13.8 to -11.8)
Doxazosin	139.0 (138.0 to 140.0)	-8.7 (-9.7 to -7.7)
Bisoprolol	139.4 (138.4 to 140.4)	-8.3 (-9.3 to -7.3)
Placebo	143.6 (142.6 to 144.6)	-4.1 (-5.1 to -3.1)
<b>Mean differences</b>		
Spironolactone vs placebo	8.70 (-9.72 to -7.69)	p<0.0001
Spironolactone vs mean bisoprolol and doxazosin	-4.26 (-5.13 to -3.38)	p<0.0001
Spironolactone vs doxazosin	-4.03 (-5.04 to -3.02)	p<0.0001
Spironolactone vs bisoprolol	-4.48 (-5.50 to -3.46)	p<0.0001

# Poor adherence in HTN: epidemiology



# **Pharmacological strategies to lower BP: tips and tricks**

Can be based on 4 principles:

# Management principles

Can be based on 4 principles:

1. Most ADRs to anti-hypertensive medications are dose dependent

# Systematic review – drug related adverse events

Table 3. Safety Outcomes

	Type of Antihypertensive Drug						ARB	AAB	Placebo
	Diuretics	BB	ACE	Calcium Channel Blocker					
				Total	DHP	non-DHP			
% of patients with adverse events	39.3	32.3	36.1	34.3	34.4	34.0	38.8	36.1	37.3
No. analyzed	694	2164	3869	4418	3865	553	1614	820	948
% of discontinuations	12.7	11.6	10.5	15.3	14.2	17.2	6.8	17.0	11.7
No. analyzed	1628	3759	5411	6441	4756	1409	2044	1103	1717
% of DAEs	3.1	4.5	4.7	6.7	6.9	5.7	3.1	6.0	4.3
No. analyzed	1799	4386	6531	9253	7485	1768	2994	1103	2132
% of DAEs in studies ≤ 1 mo	NR	3.2	1.8	3.0	2.9	3.8	3.3	5.6	1.9
No. of pts with event		9	12	27	24	3	2	6	5
No. analyzed		285	650	896	818	78	60	107	259
% of DAEs in studies > 1 mo	3.0	4.5	5.1	7.1	7.5	5.4	3.1	5.9	4.5
No. of pts with event	55	187	297	589	498	91	90	60	87
No. analyzed	1814	4143	5870	8354	6660	1694	2937	1013	1929
DAEs risk difference <sup>a</sup>	0.027	0.018	0.014	-0.005	NC	NC	0.02	NC	NC
95% CI	(0.001, 0.053)	(-0.008, 0.044)	(-0.002, 0.029)	(-0.022, 0.012)			(0.001, 0.038)		
p value	0.038	0.171	0.085	0.577			0.038		
No. of studies	5	6	17	14			7		

BB =  $\beta$ -blocker; ACE = angiotensin-converting enzyme inhibitor; DHP = dihydropyridine; ARB = angiotensin receptor blocker; AAB =  $\alpha$ -adrenergic blocker; No. analyzed = total number of patients evaluated for safety in each outcome category; NR = not reported; ; NC = not calculated.

<sup>a</sup>Results of random effects model in placebo comparisons.

# Systematic review – drug related adverse events

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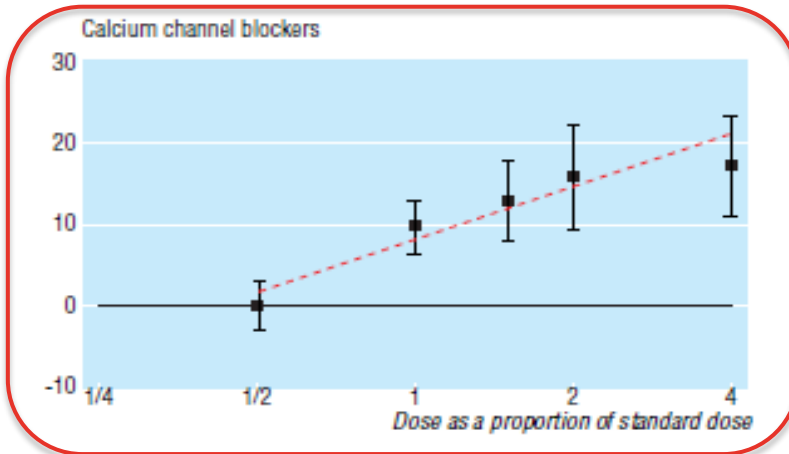
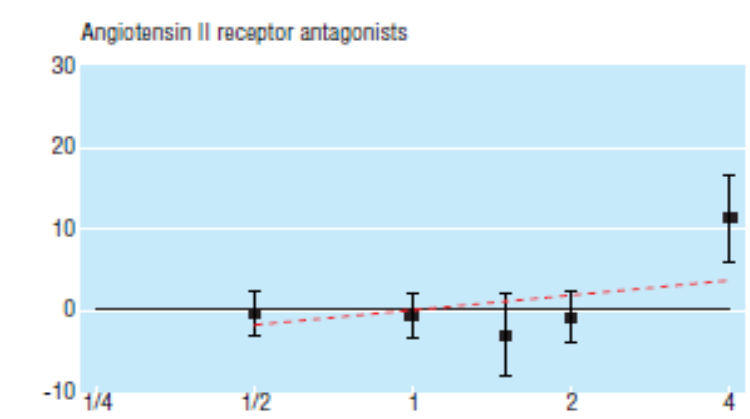
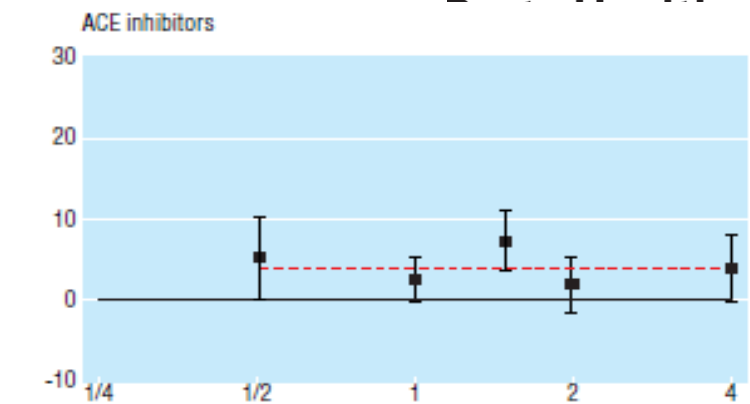
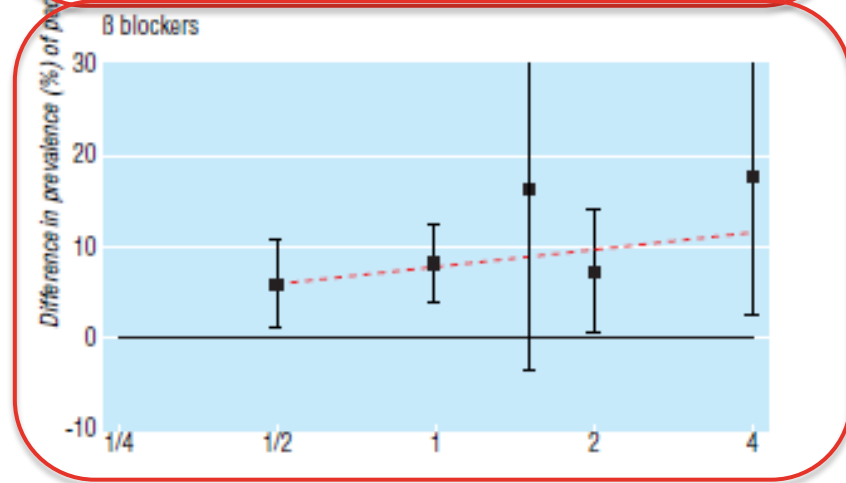
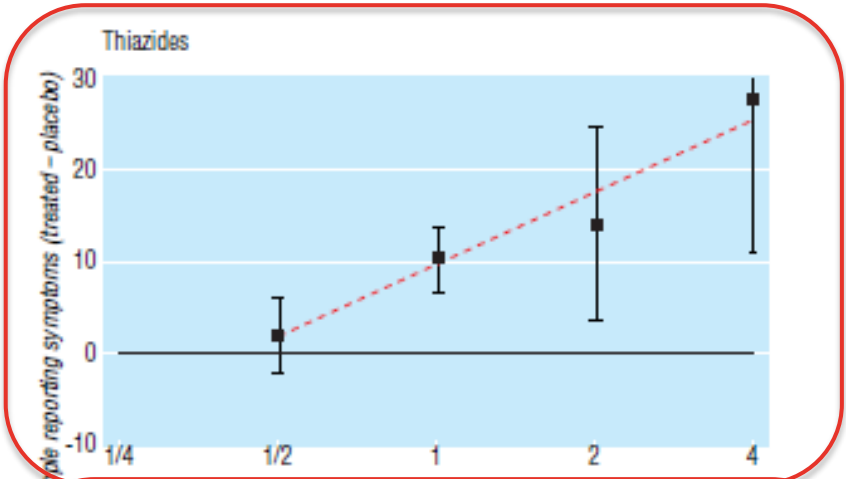
PHARMACOTHERAPY Volume 21, Number 8, 2001

Table 2. Type of Antihypertensive Drug and Adverse Events by Organ System

Organ System	Event	No. of Patients Analyzed (% of patients with this event)						
		Diuretics	BB	ACE	CCB	ARB	AAB	Placebo
Whole body	Total AEs	1081 (10.0)	3349 (9.2)	3938 (5.6)	6883 (13.2)	1438 (6.1)	624 (7.1)	1425 (6.8)
	Total DAEs	702 (0.4)	1746 (1.7)	2268 (1.0)	3775 (2.2)	863 (0.2)	114 (0.9)	908 (0.6)
Respiratory	Total AEs	978 (7.5)	2519 (6.0)	4683 (12.7)	1764 (7.8)	2182 (7.3)	537 (4.7)	1030 (5.7)
	Total DAEs	353 (0.3)	761 (0.4)	3181 (2.0)	1038 (0)	1003 (0.2)	85 (1.2)	537 (0.4)
Cardiovascular	Total AEs	867 (1.3)	2486 (4.1)	2411 (4.1)	5347 (11.9)	660 (1.2)	476 (10.5)	1058 (3.2)
	Total DAEs	413 (1.0)	994 (0.8)	1721 (8.5)	2723 (1.3)	298 (0.7)	99 (6.1)	593 (1.2)
Dermatologic	Total AEs	234 (3.8)	1017 (4.1)	2108 (3.5)	1583 (6.8)	236 (0.4)	252 (1.2)	189 (2.6)
	Total DAEs	49 (2.0)	669 (0.6)	1196 (0.5)	990 (0.8)	616 (0.3)	NR	220 (0.5)
Metabolic	Total AEs	286 (12.6)	264 (0)	862 (3.2)	230 (0.9)	212 (11.8)	47 (8.5)	287 (2.4)
	Total DAEs	295 (0.3)	43 (0)	397 (0.5)	265 (0.4)	212 (0)	NR	242 (0.8)
Neurologic	Total AEs	1106 (16.9)	2991 (11.0)	4092 (10.7)	6502 (17.6)	1888 (9.9)	839 (19.9)	1701 (11.8)
	Total DAEs	512 (1.8)	1175 (1.3)	2653 (1.5)	3645 (2.3)	1252 (0.8)	89 (1.1)	1230 (1.5)
Psychiatric	Total AEs	296 (3.7)	2125 (4.9)	1342 (4.7)	1437 (3.4)	257 (1.6)	159 (6.9)	346 (3.5)
	Total DAEs	352 (0.3)	832 (4.3)	1050 (3.0)	884 (0.7)	212 (0.5)	47 (0)	231 (0.4)
Gastrointestinal	Total AEs	828 (5.6)	2068 (8.9)	2509 (5.1)	4337 (5.9)	1476 (4.1)	500 (6.4)	862 (5.0)
	Total DAEs	511 (1.6)	1177 (0.6)	2184 (1.1)	1915 (0.6)	539 (0.6)	69 (1.4)	318 (0.3)

BB =  $\beta$ -blocker; ACE = angiotensin-converting enzyme inhibitor; CCB = calcium channel blocker; ARB = angiotensin receptor blocker; AAB =  $\alpha$ -adrenergic blocker; NR = not reported.

# Proportion of People reporting one or more symptoms attributable to treatment according to Drug class and Dose as a proportion of standard



# Management principles

Can be based on 4 principles:

1. Most ADRs to anti-hypertensive medications are dose dependent therefore

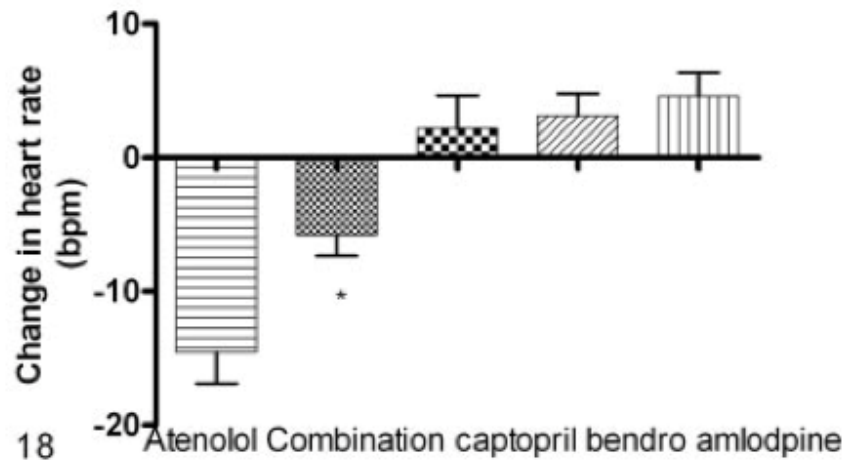
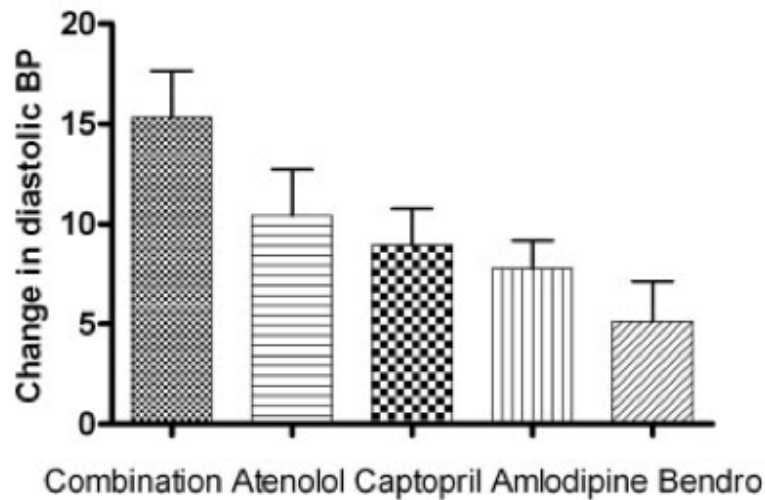
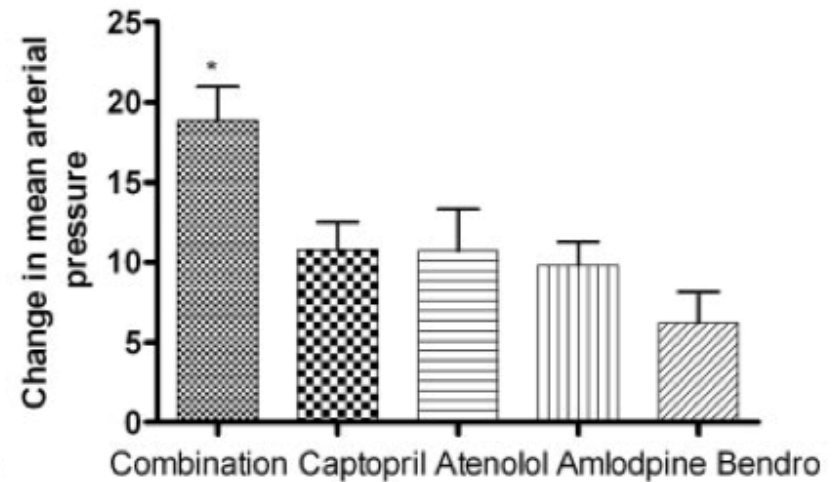
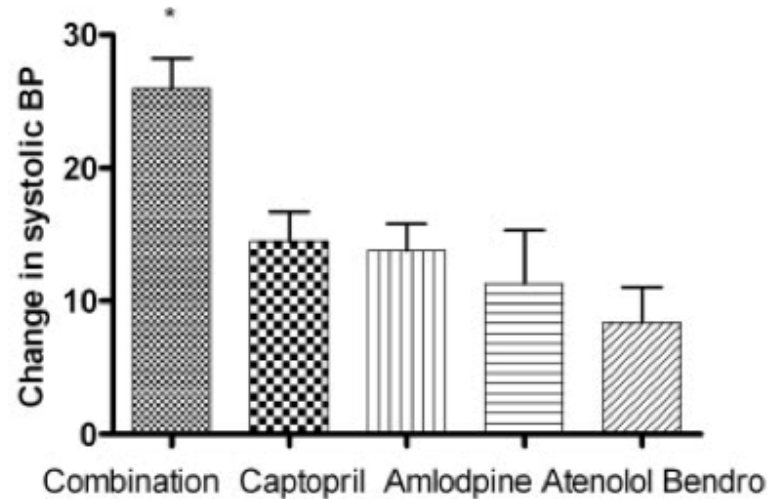
**fractional dosing** below the smallest whole pill weight [and not titrating] may allow patients to tolerate classes previously intolerant of

# Management principles

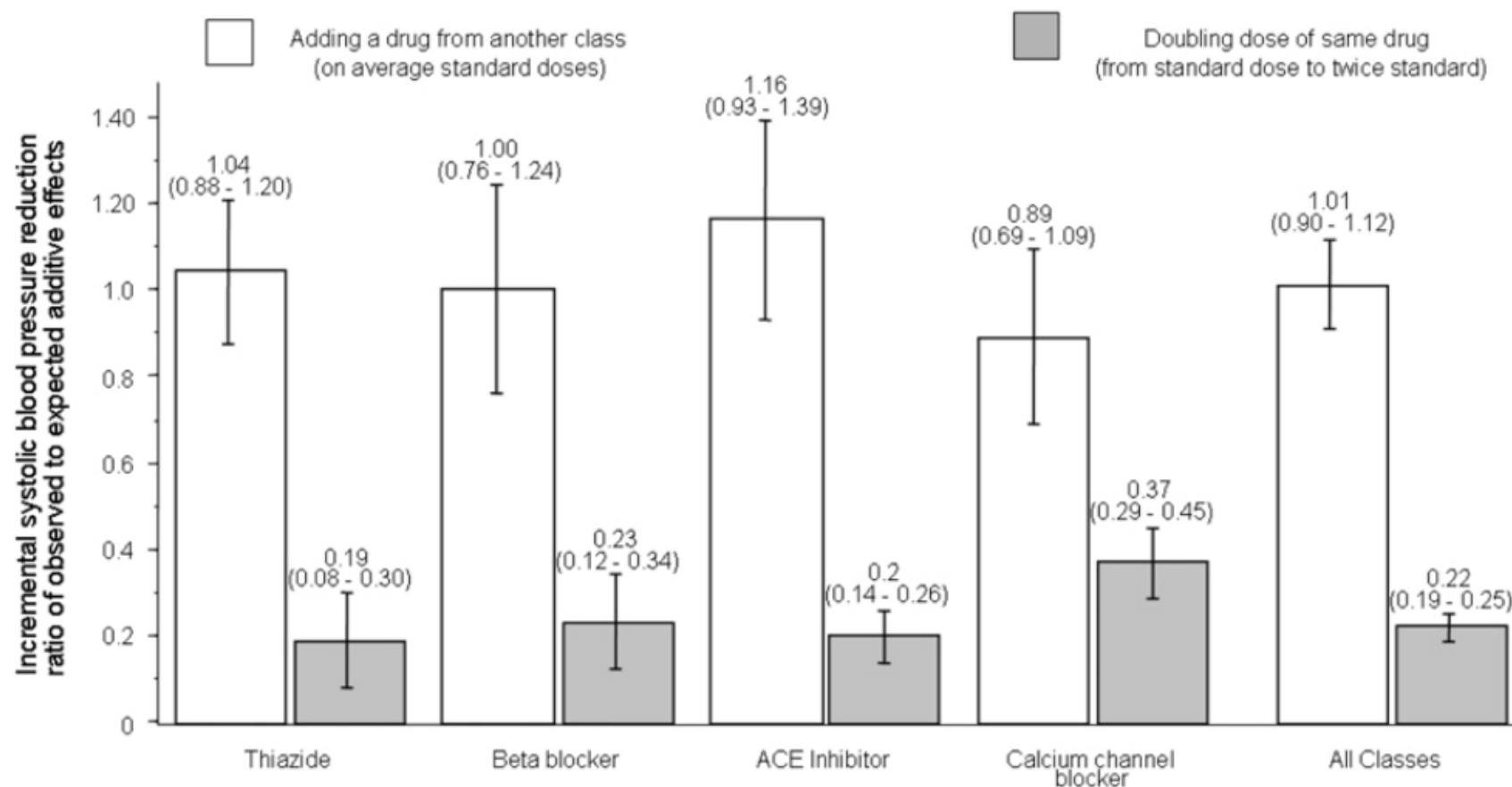
Can be based on 4 principles:

2. Combination of anti-hypertensive medications at low dose is more efficacious than increasing individual medication dose

# Low-dose combination



# Low-dose combination



# Management principles

Can be based on 4 principles:

2. Combination of anti-hypertensive medications at low dose is more efficacious than increasing individual medication dose therefore

**combine medications** at fractional doses including **ultra low doses via liquid formulations** [and not titrating to standard doses] may allow patients greater hypotensive efficacy without increasing ADR likelihood

# Management principles

Can be based on 4 principles:

3. Some patients may not be able to tolerate excipients in solid dosage formulations

# Excipients

<u>Excipient</u>	<u>Frequency</u>	<u>Adverse effects</u>
Sucrose	25%	DM; problematic in fructose intolerance
Saccharin	24%	urticaria; photosensitivity
Lactose	23%	stomach cramps; bloating & flatulence; diarrhoea; muscle cramps; headaches
Silica	23%	sarcoidosis
Parabens	16%	contact dermatitis
Sorbitol	10%	laxative
Aspartame	9%	problematic in PKU
Ethanol	7%	classical alcohol intoxication
Propylene glycol	7%	cardio-renal failure
Mannitol	6%	laxative
Menthol	6%	laryngospasm; GI disturbance

# Liquid formulations

- Avoiding tablet excipients
- community pharmacies
- £ liquids > generics

AVAILABLE IN ALL COLORS



**Retail Price List**  
The source of liquid solutions.  
Rosemont®  
A Portage Company

Products	Storage Instructions	Shelf Life	Pack Size
Accovir Oral Suspension 200mg/5ml (S/F)	Do not store above 25°C	24 months / 1 month	125ml
Accovir Oral Suspension 400mg/5ml (S/F)	Do not store above 25°C	24 months / 1 month	100ml
Alendronic Acid Oral Solution 70mg/100ml (S/F)	Do not store above 25°C	24 months / Immediate use	4 x 100ml
Amlodipine Hydrochloride Oral Solution 5mg/5ml (S/F)	Do not store above 25°C	18 months / 28 days	150ml
Amlodipine Hydrochloride Oral Solution 25mg/5ml (S/F)	Do not store above 25°C	24 months / 6 months	150ml
Amlodipine Oral Solution 1mg/ml (S/F)	Do not store above 25°C	12 months / 28 days	150ml
Amlodipine Oral Solution 2mg/ml (S/F)	Store in a refrigerator (2 - 8°C) Keep the bottle stored upright	12 months / 28 days	150ml
Chlorpromazine Hydrochloride Oral Syrup	Store in a refrigerator (2 - 8°C) Keep the bottle stored upright	24 months / 6 months	150ml
	Do not store above 25°C		150ml

To place



# Management principles

Can be based on 4 principles:

3. Some patients may not be able to tolerate excipients in solid dosage formulations

**liquid/transdermal formulations** may avoid these issues

# Management principles

Can be based on 4 principles:

4. Patients may be reluctant to be rechallenged with previously tried medications or have persistent intolerance

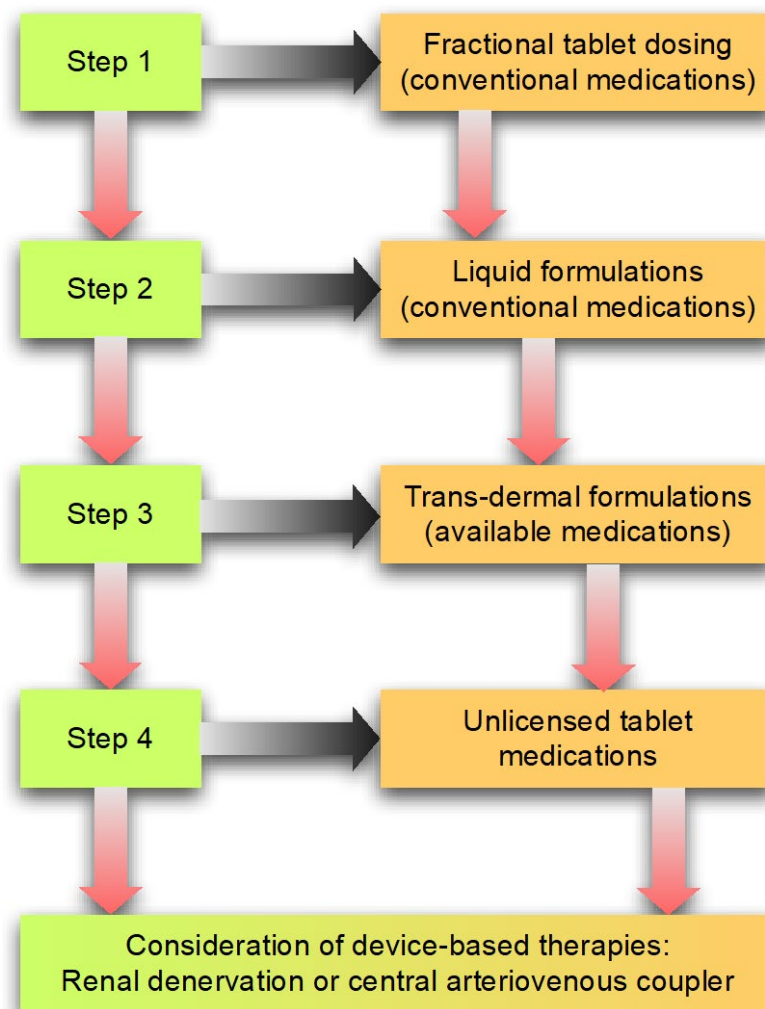
# Management principles

Can be based on 4 principles:

4. Patients may be reluctant to be rechallenged with previously tried medications or have persistent intolerance

repurposing of medications with licensed indications apart from hypertension, such as **phosphodiesterase inhibitors** and **long-acting organic nitrates**, that lower BP in small clinical trials

Can be based on 4 principles:



# Summary

Risk factors – non pharmacological factors are important

Detection – opportunities everywhere!

Management – drugs work!

Also think about overall CV risk

Resistant hypertension is common and associated with high levels of CV morbidity

Adherence is a significant problem that is easy to detect but difficult to manage

Lifestyle changes can make very large differences to BP control

Defined treatment algorithms can improve BP control

Tips and tricks

# High Blood Pressure

What is It? How to Check?

What Can Go Wrong....?

How to treat?

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