A/Prof Gerard Wilkins

A/Proff of Medicine at Otago University

Cardiac Services at Dunedin Hospital

Ambulatory BP Monitoring - Concurrent Workshop

Saturday, 17 August 2013 Start 4:30pm Duration: 60mins Lounge 1



Hypertension – Ambulatory BP Monitoring

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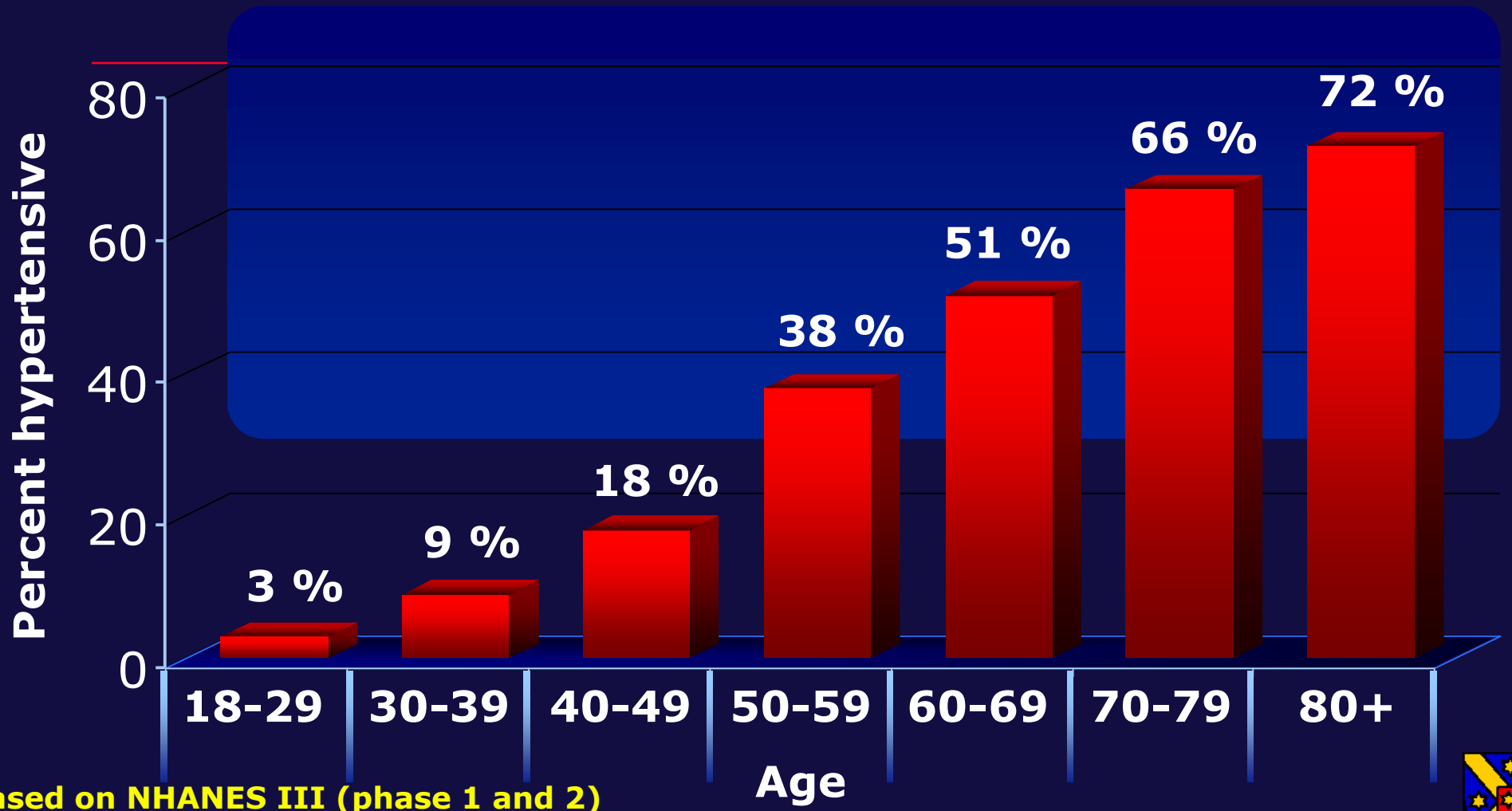
Boring old hypertension ?

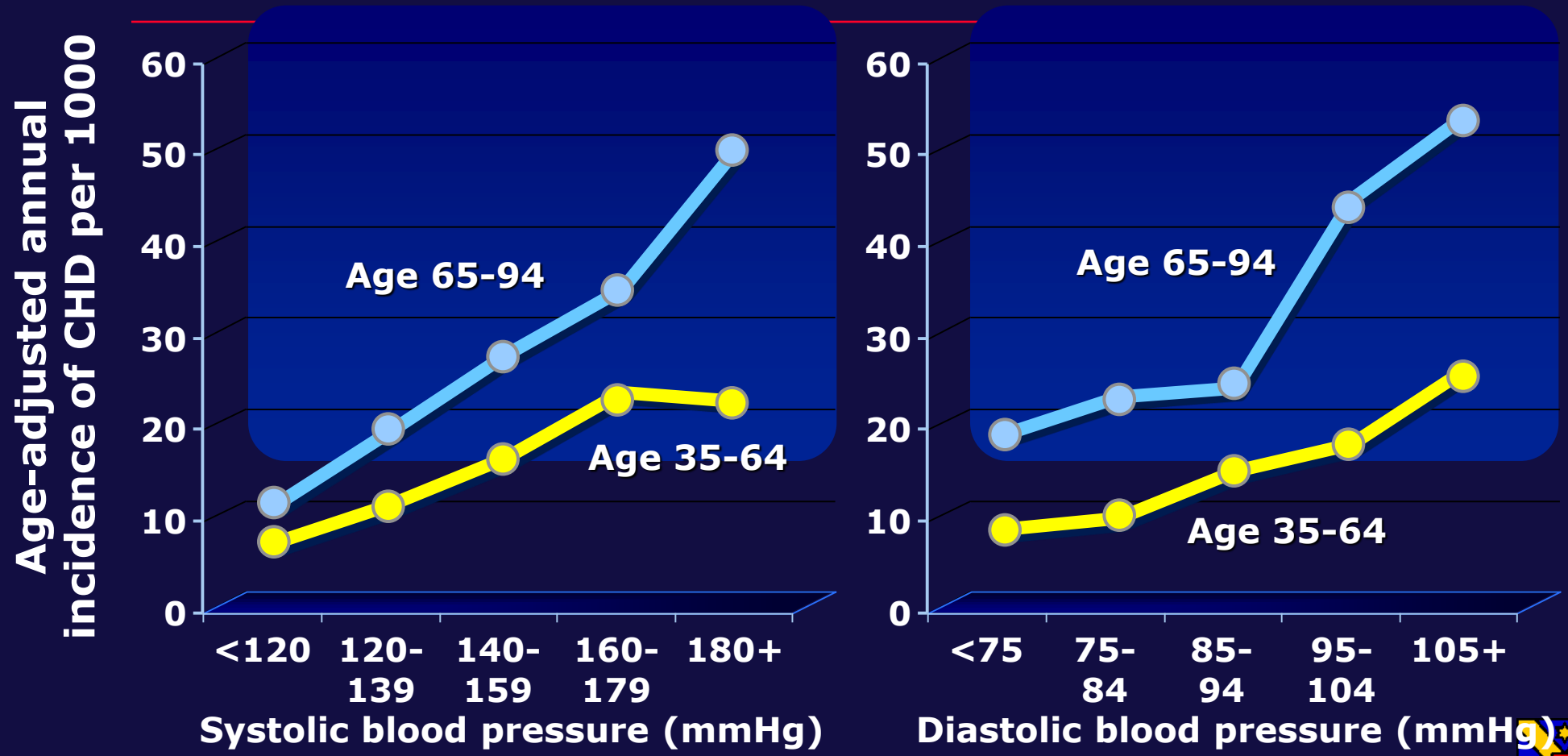
Prevalence of Hypertension in the US



Based on NHANES III (phase 1 and 2)
Hypertension defined as blood pressure ≥140/90 mmHg or treatment

JNC-VI. Arch Intern Med. 1997;157:2413-2446.

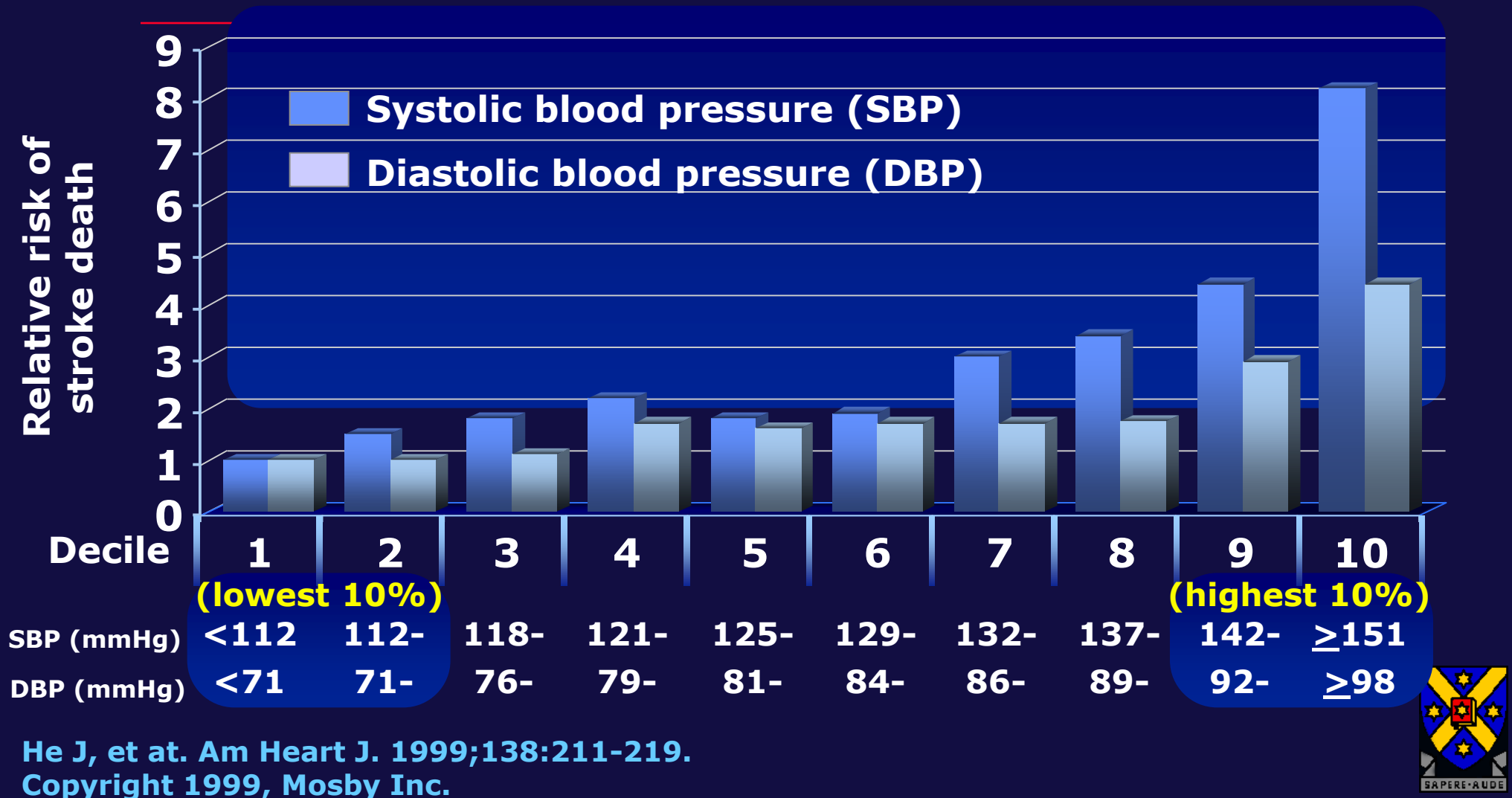
Blood Pressure and Risk for Coronary Heart Disease in Men



Based on 30 year follow-up of Framingham Heart Study subjects free of coronary heart disease (CHD) at baseline

Framingham Heart Study, 30-year Follow-up. NHLBI, 1987.

Risk of Stroke Death According to SBP and DBP in MRFIT



He J, et at. Am Heart J. 1999;138:211-219.

Blood Pressure Classification

BP Classification	SBP mmHg		DBP mmHg
Normal	<120	and	<80
Prehypertension	120–139	or	80–89
Stage 1 Hypertension	140–159	or	90–99
Stage 2 Hypertension	≥160	or	≥100

JNC VII GUIDELINES

CVD Risk

- HTN prevalence ~ 800,000 people in NZ
- The BP relationship to risk of CVD is continuous, consistent, and independent of other risk factors.
- Each increment of 20/10 mm Hg doubles the risk of CVD across the entire BP range starting from 115/75 mm Hg.
- Prehypertension signals the need for increased education to reduce BP in order to prevent hypertension.
  - Wt loss, exercise, Etoh reduction, Salt restriction, Smoking cessation, Dietary change (green vegetables)

JNC VII GUIDELINES

JNC-VI General Goals for BP Control

Pre-existing condition	BP goals (mmHg)
Essential Hypertension	<140/90
Diabetes	<130/85
Renal Disease and proteinuria >1.0 gram/24 h	<125/75

Coresh J, et al. Arch Intern Med. 2001;161(9):1207-1216.

Benefits of Lowering BP

	Average Percent Reduction
Stroke incidence	35–40%
Myocardial infarction	20–25%
Heart failure	50%

JNC VII GUIDELINES

New European Guidelines Released June 14 2013

New Aspects of the Guidelines

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

- Essential hypertension:
  - Older
  - Family history
- Lifestyle
  - Inactivity
  - Obesity
  - Excessive ETOH
  - Excessive salt
  - Fast food
  - Stress
- Secondary Causes
  - Coarctation aorta
  - Renal artery stenosis
    - Atherosclerosis
    - Fibromuscular dysplasia
  - Kidney disease
  - Endocrine disorders
    - Conn's syndrome ↓K
    - Phaeochromacytoma
    - Cushings
    - Polycyctic ovaries

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.

European Heart Journal

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

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

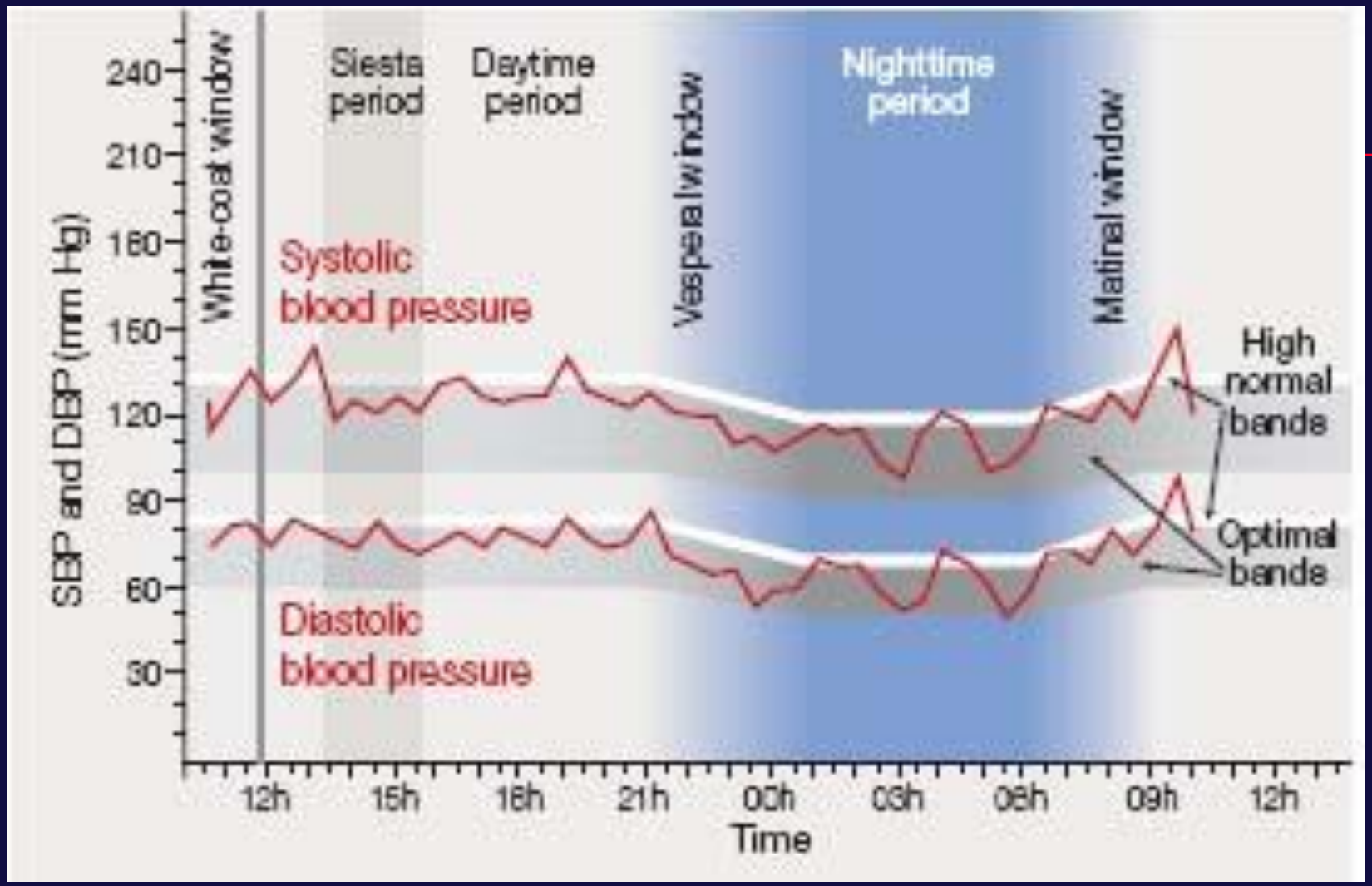
- Ambulatory BP assessment
- Home BP assessment

- 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

Ambulatory Blood Pressure Monitoring


White-coat window
Siesta period
Daytime period
Vesperal window
Nighttime period
Matinal window
Systolic blood pressure
Diastolic blood pressure
High normal bande
Optimal bande
SBP and DBP (mm Hg)
240
210
180
150
120
90
60
30
12h
15h
18h
21h
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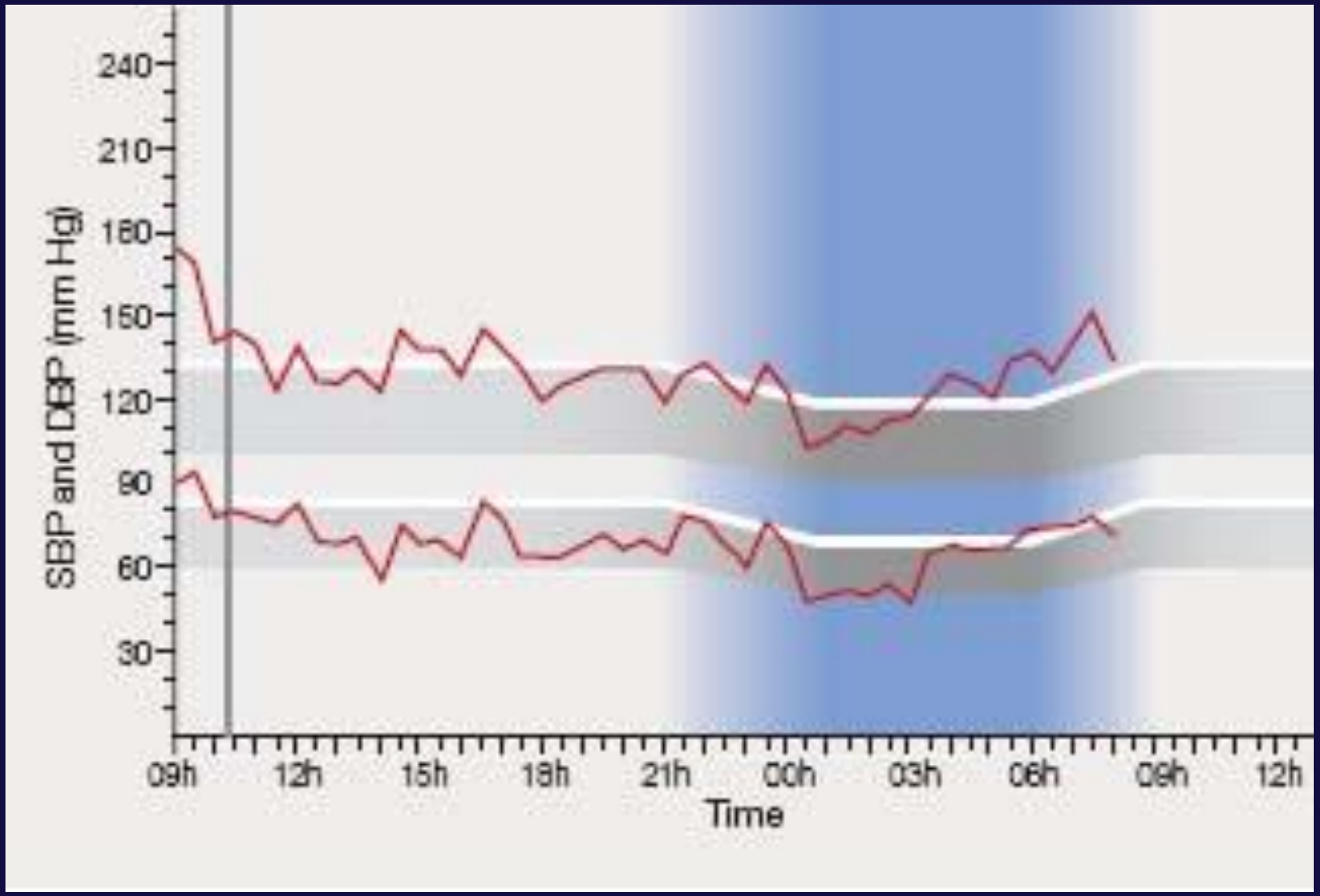
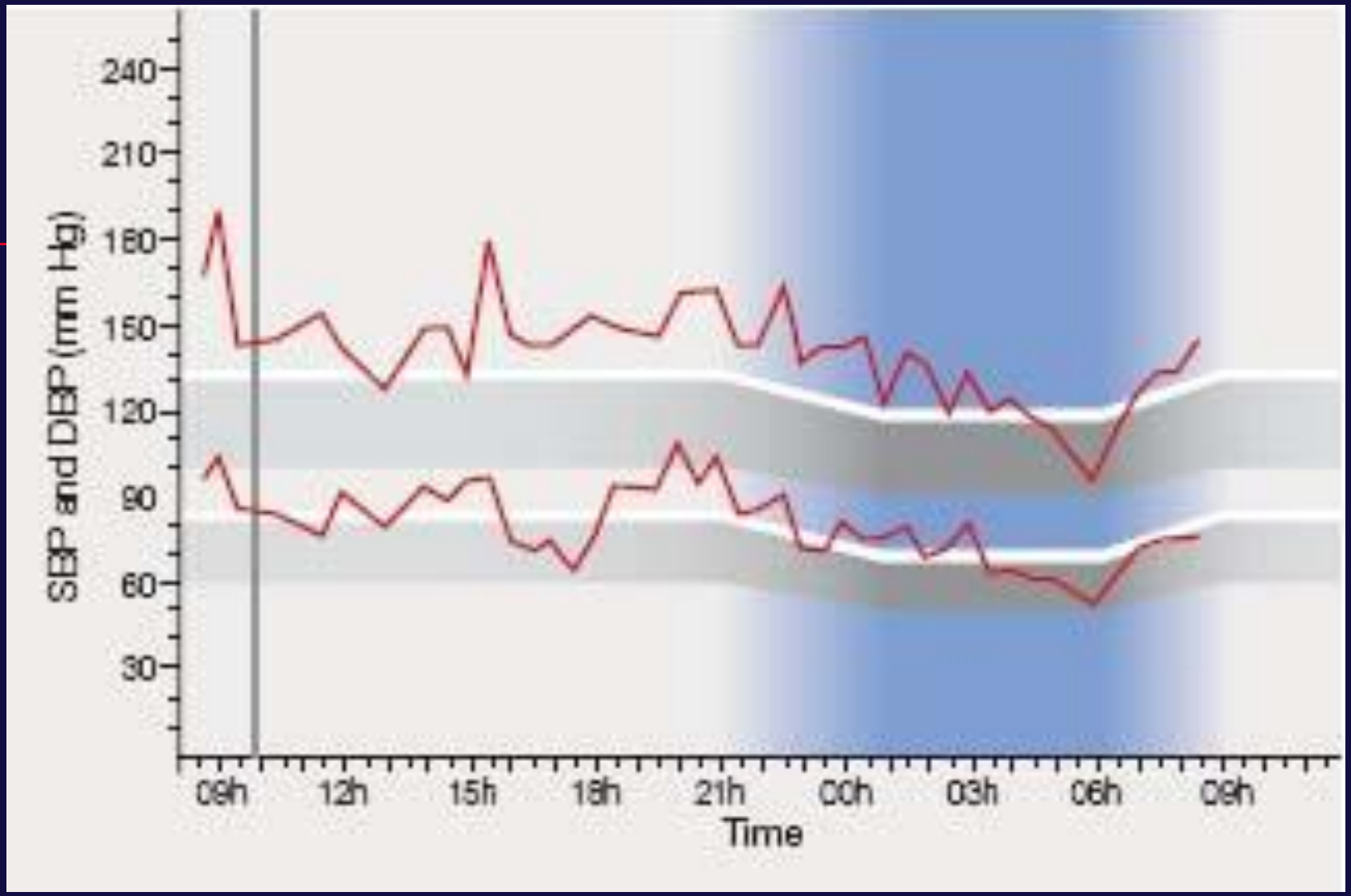
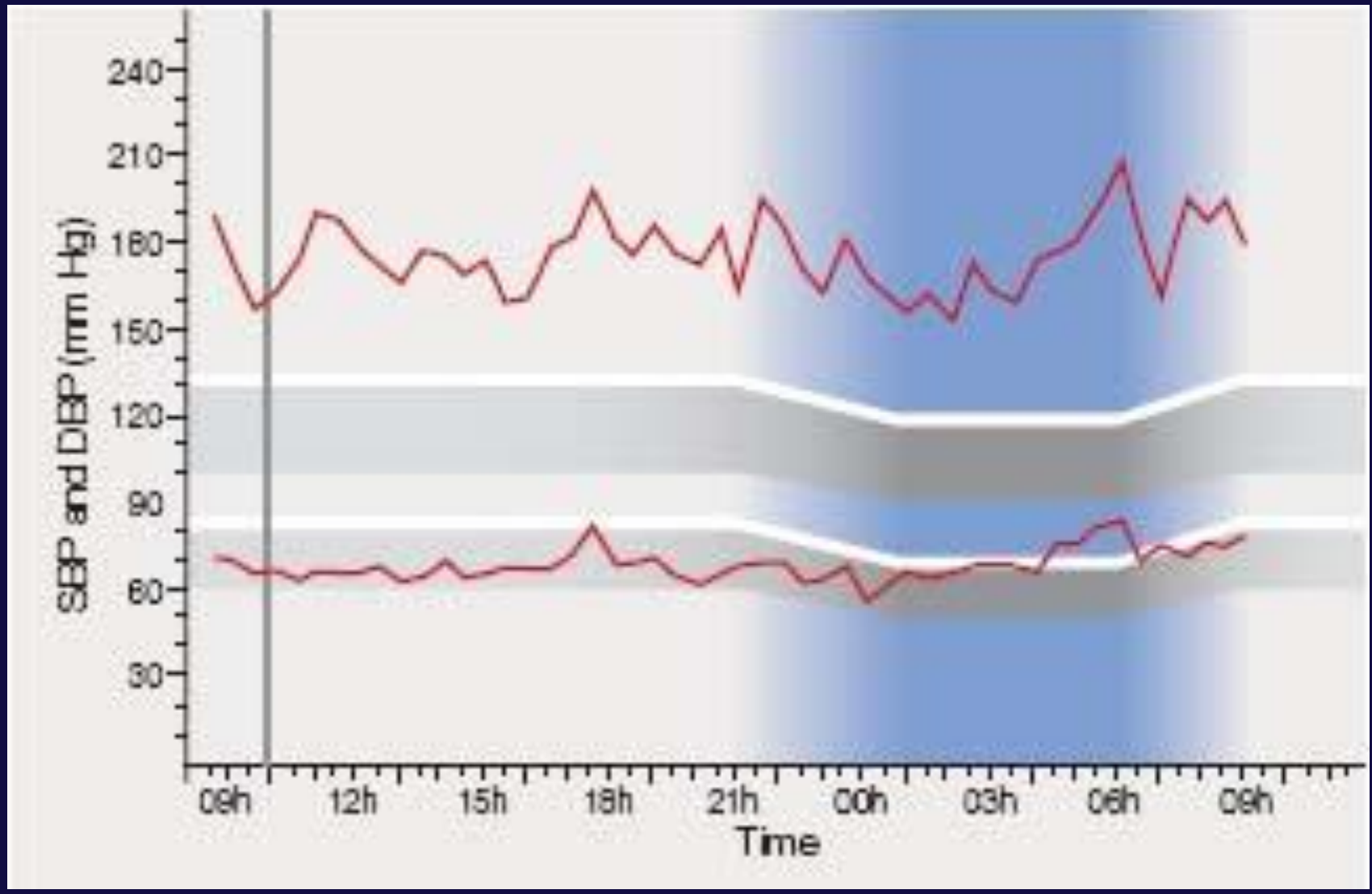
03h
06h
09h
12h
Time



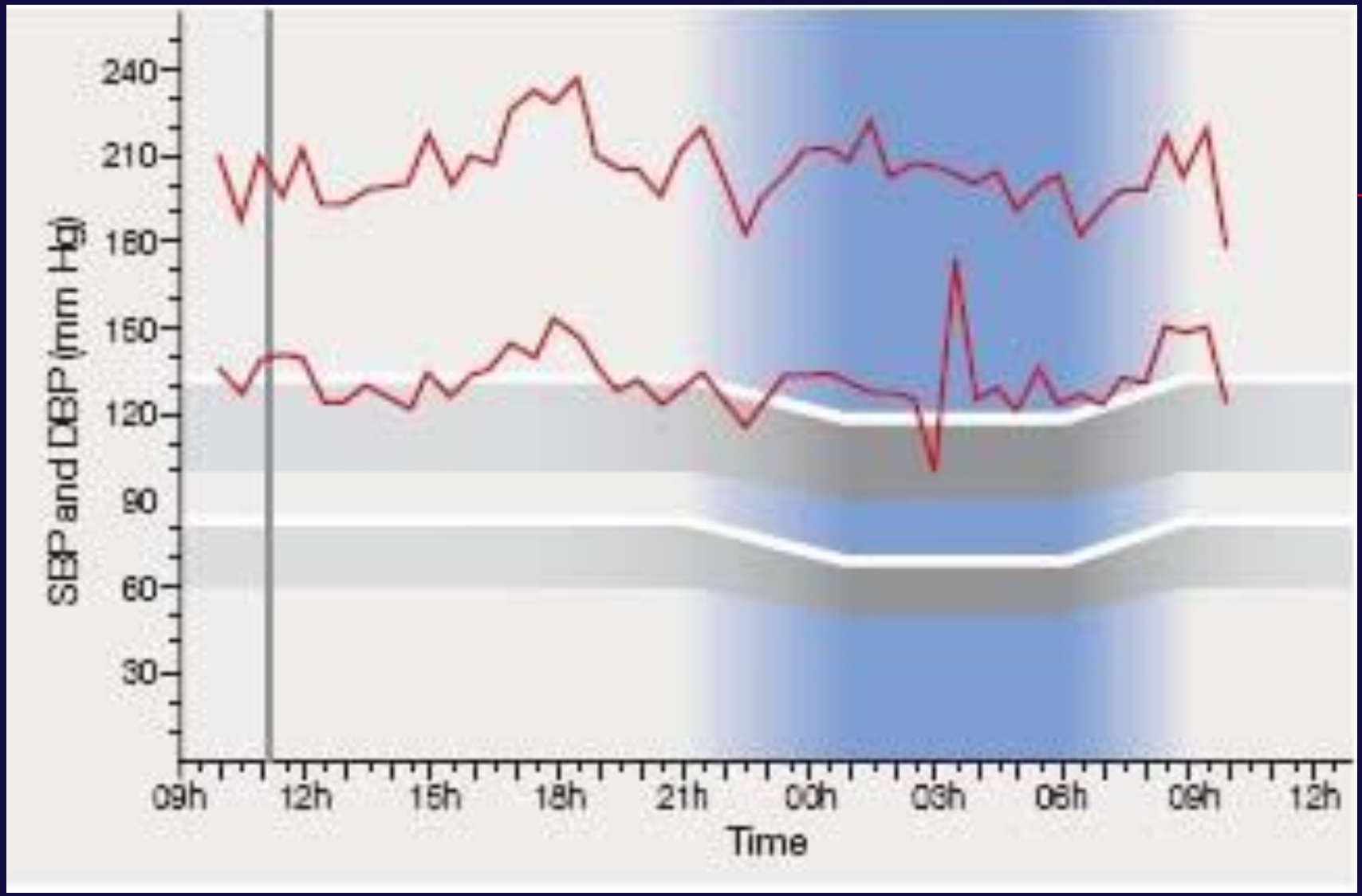
ABPM suggests white-coat hypertension (175 mm Hg/95 mm Hg) with otherwise normal 24-hour systolic blood pressure (133 mm Hg daytime, 119 mm Hg night time) and optimal 24-hour diastolic blood pressure (71 mm Hg daytime, 59 mm Hg nighttime). Normal dipping pattern.



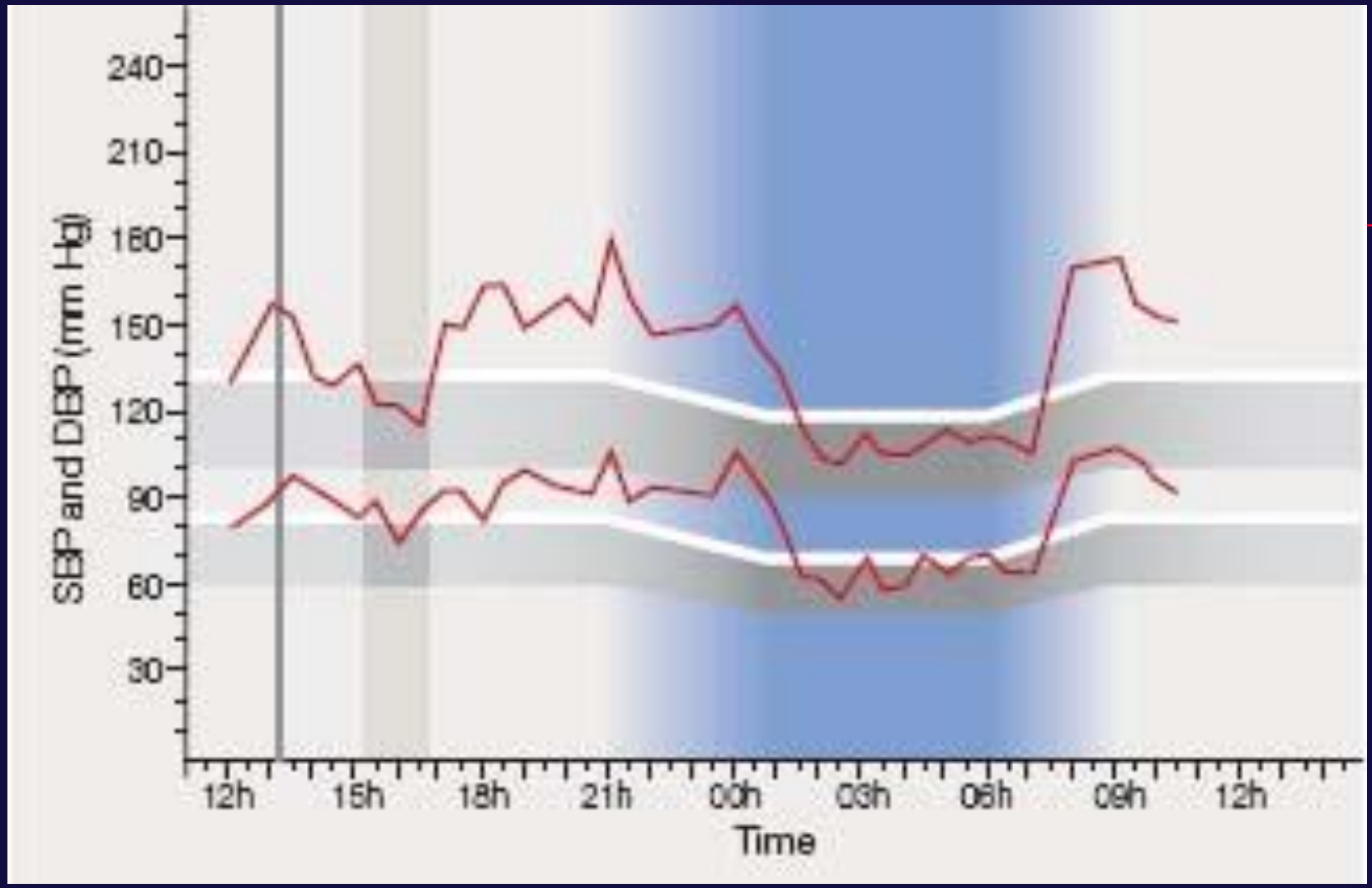
ABPM suggests mild daytime systolic hypertension (150 mm Hg), borderline daytime diastolic hypertension (87 mm Hg), borderline nighttime systolic hypertension (123 mm Hg), and normal nighttime diastolic blood pressure (68 mm Hg) with a whitecoat effect (187 mm Hg/104 mm Hg). Normal dipping pattern.



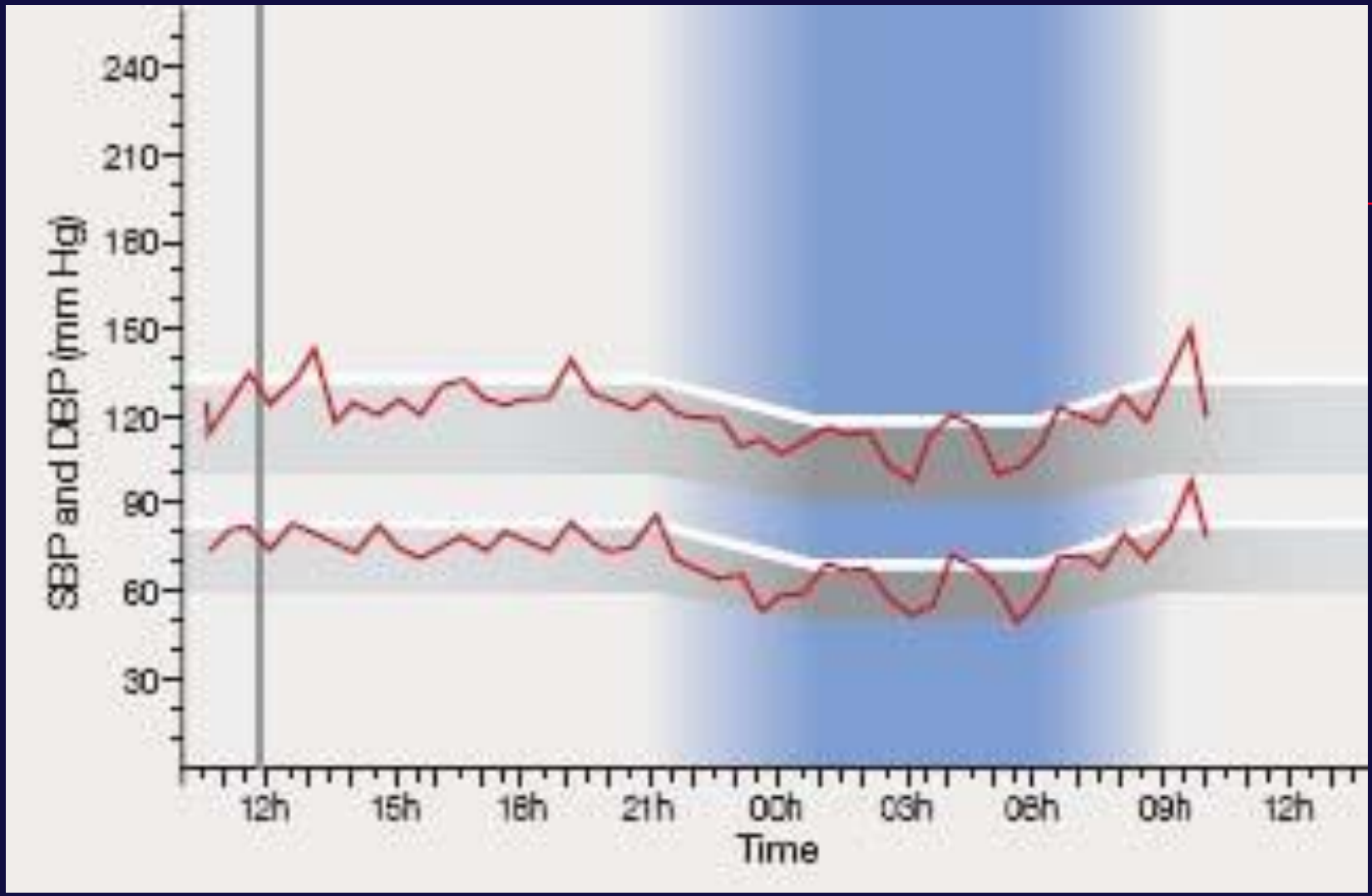
ABPM suggests severe daytime isolated systolic hypertension (176 mm Hg/68 mm Hg), severe nighttime systolic hypertension (169 mm Hg), and borderline nighttime masked diastolic hypertension (70 mm Hg). Nondipping pattern.



ABPM suggests severe 24-hour systolic and diastolic hypertension (209 mm Hg/135 mm Hg daytime, 205 mm Hg/130mm Hg night time). Non-dipping pattern.



ABPM suggests mild daytime systolic and diastolic hypertension (152 mm Hg/94 mm Hg), optimal night-time systolic blood pressure (111 mm Hg), and normal night-time diastolic blood pressure (66 mm Hg) with a white-coat effect (158 mm Hg/90 mm Hg). Measurements taken during the siesta are not included in these averages. Extreme dipping pattern.



ABPM suggests optimal 24-hour blood pressure (128mm Hg/78 mm Hg daytime, 110 mm Hg/62 mm Hg night-time). Normal dipping pattern.

Example of ABPs

Case 1

42 yr old male
Well, athletic with regular exercise
+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

SunTech®

BULATORY BLOOD PRESSURE REPORT

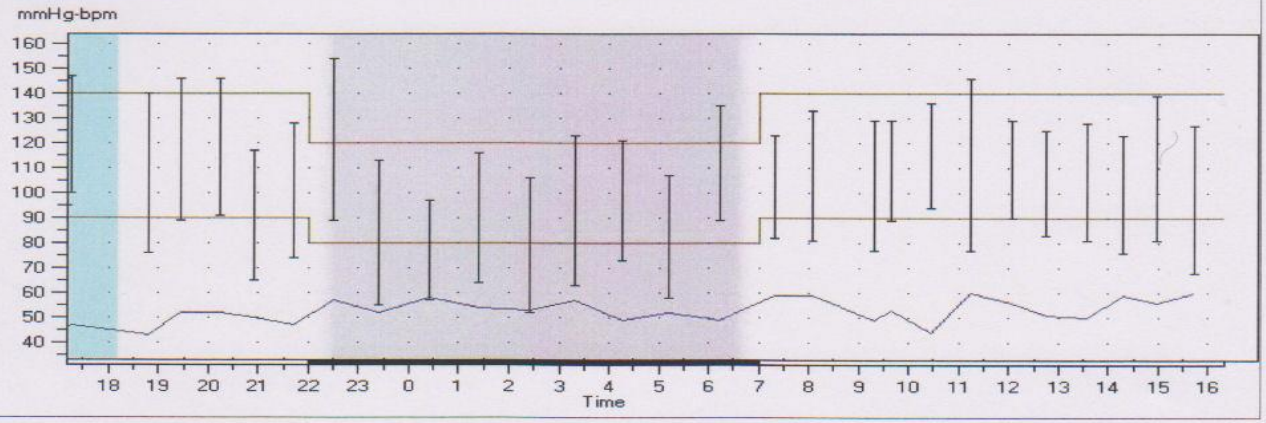
Patient Name: rhys bishop **Patient ID:** **Test Date:** 02-Nov-2012

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

AMBULATORY BLOOD PRESSURE REPORT

SunTech®

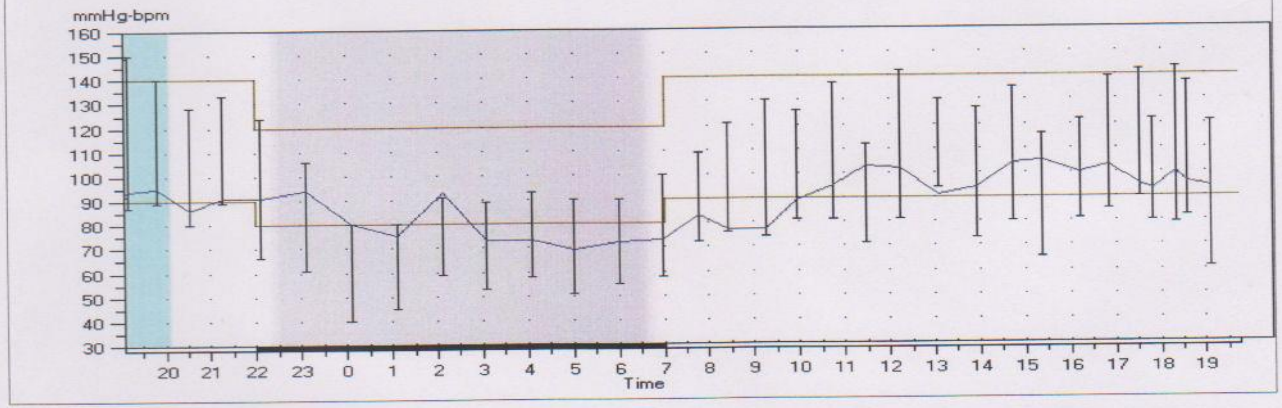
Patient Name: [redacted] **Patient ID:** 14 october 2 **Test Date:** 13-Oct-2010

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

Case 2

57 year old 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

SunTech®

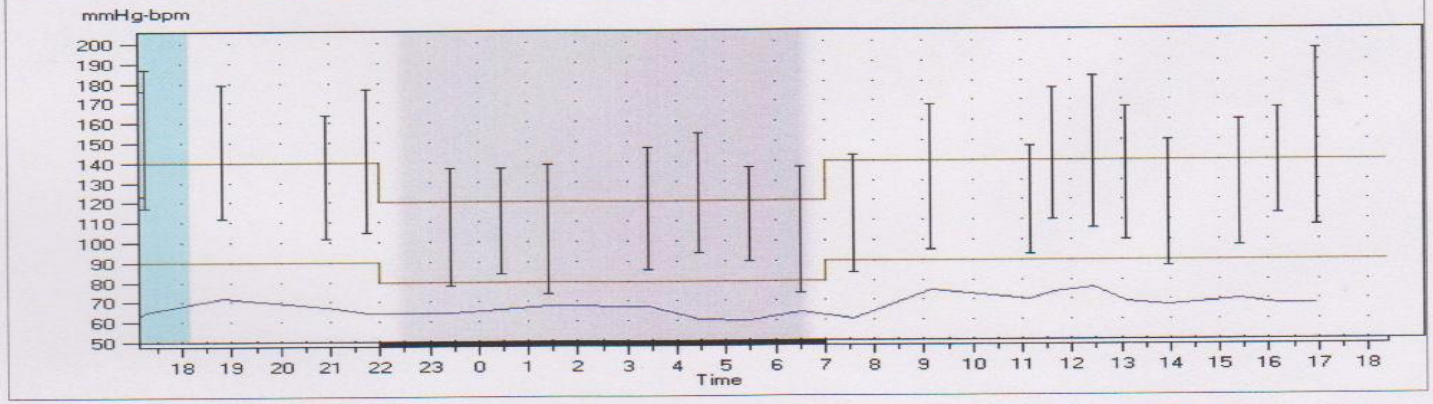
Patient Name: yvonne zhang **Patient ID:** 24.08.1956 **Test Date:** 20-Jul-2010

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

AMBULATORY BLOOD PRESSURE REPORT

SunTech®

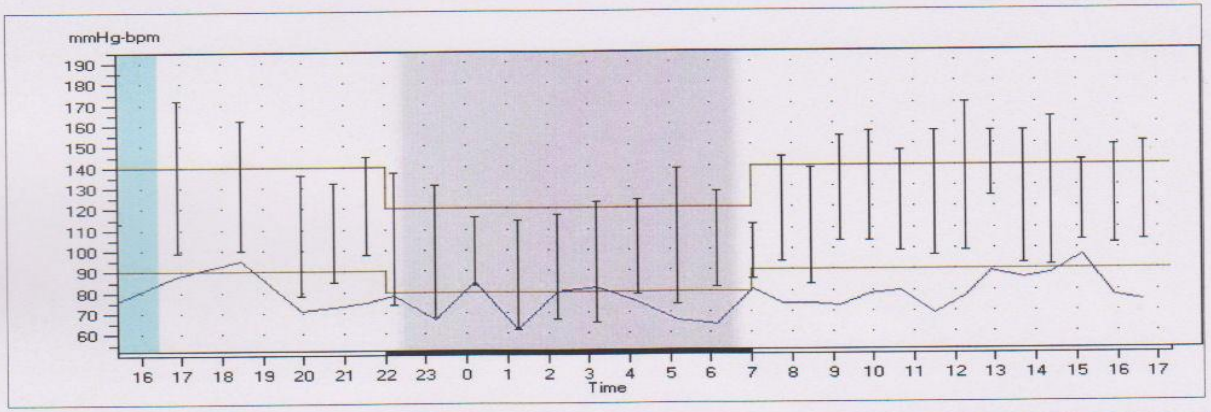
Patient Name: **Patient ID:** **Test Date:** 16-Sep-2011

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

Case F

- A 62 year old male presents for routine prescription of meds. Hypertension has been present for several years. It has been hard to manage adequately. BPs are often high in your rooms. He reports that his home measurements are lower than yours but does not seem to take them very often. He contents that his BP is "scared-up" when you take it. Therapy is Betaloc 95mg and simvastatin 40mg for hypercholesterolaemia. There is a family history of stroke and ischaemic heart disease. He is not overweight and remains reasonably active. His wife runs a health food shop. He doesn't really want to take other medications and complains that he is worried about side-effects. BPs are consistently 160-170/90-95.
- How do you decide if he needs more therapy?
- What is the target?
- How will you get there?

AMBULATORY BLOOD PRESSURE REPORT

SunTech®

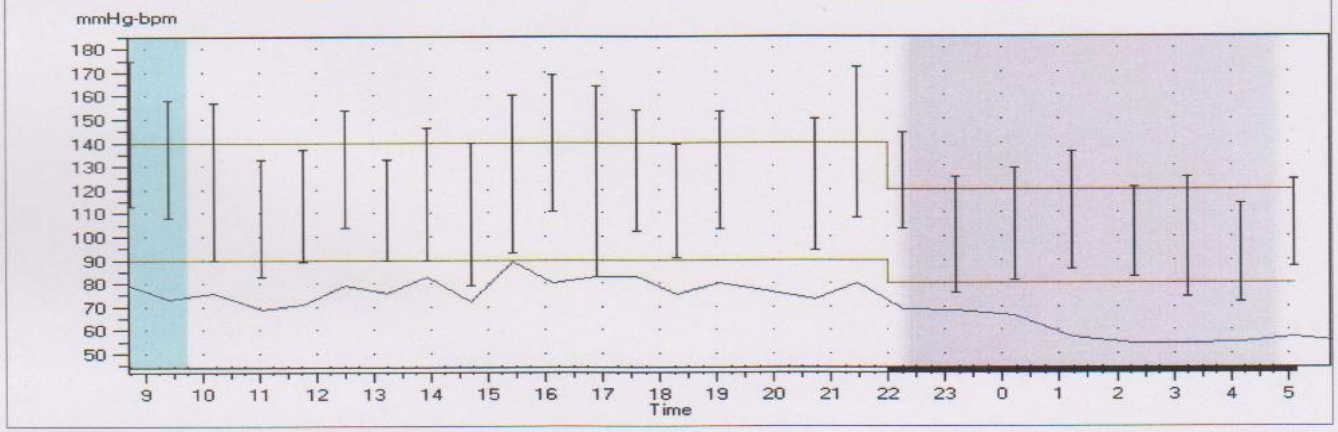
Patient Name: [redacted] **Patient ID** [redacted] **Test Date:** 15-Feb-2013

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

When the BP cuff is confusing you

- Seek evidence of end organ damage
  - Retinopathy, nephropathy, any vascular disease
- Look for LVH
  - ECG (specific?insensitive), ECHO
- Do a 24 hour BP
  - Highly predictive

JNC-VI General Goals for BP Control

Pre-existing condition	BP goals (mmHg)
Essential Hypertension	<140/90
Diabetes	<130/85
Renal Disease and proteinuria >1.0 gram/24 h	<125/75

Coresh J, et al. Arch Intern Med. 2001;161(9):1207-1216.

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 preferably 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

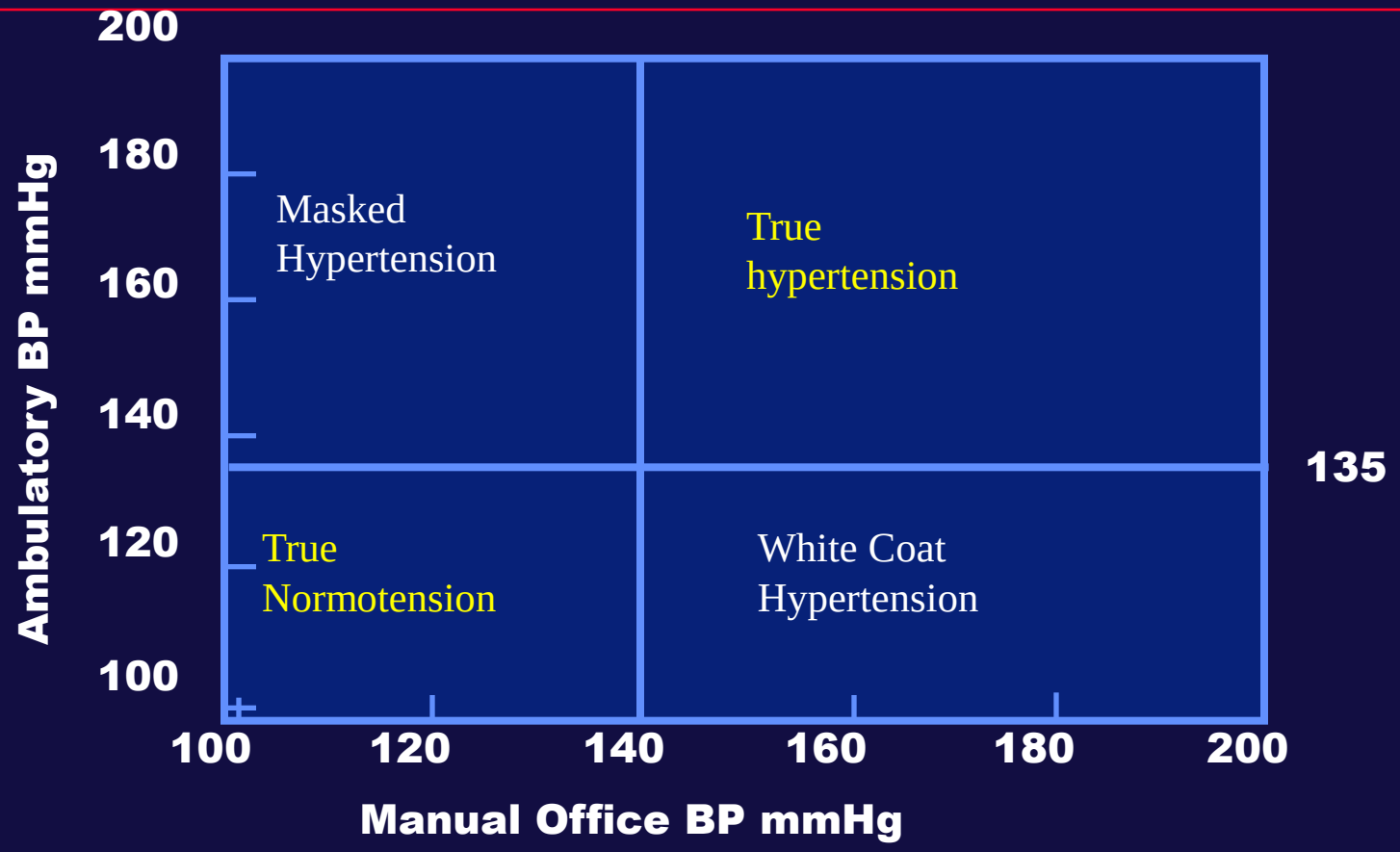
To quantify short –term BP variability

Home BP recordings

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

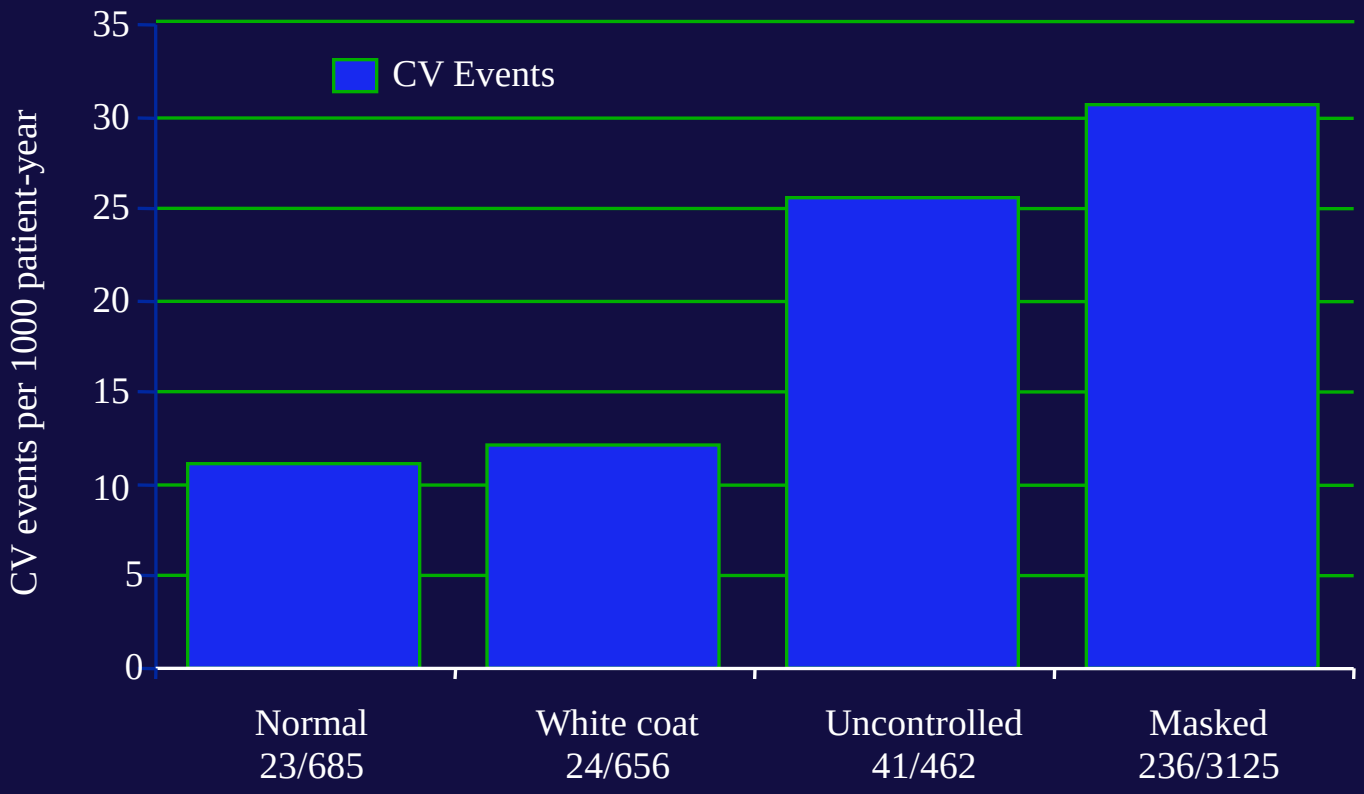
As good as ABPM for end-organ risk and CV events

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

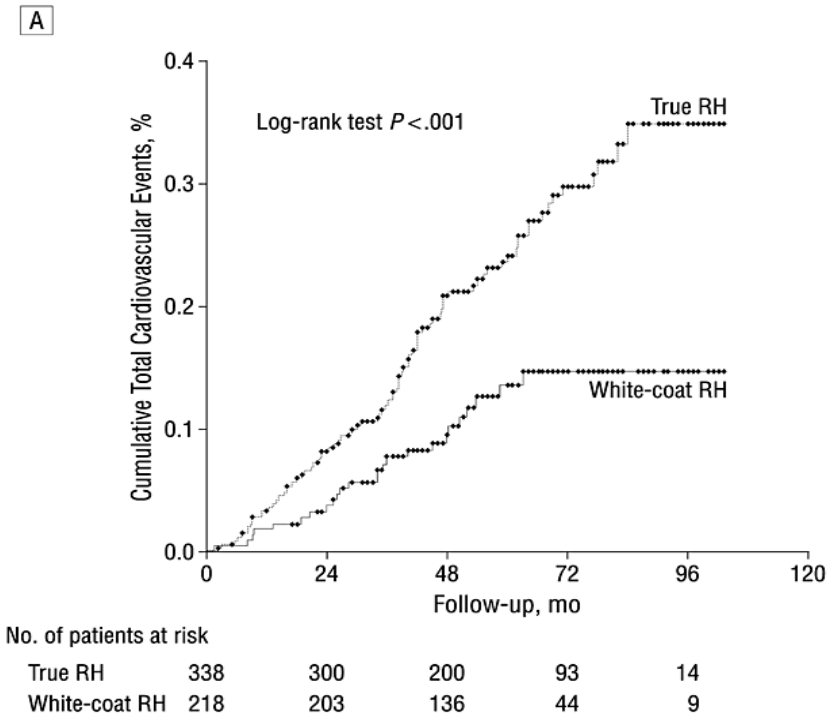
- Both seen in 13% hypertensive population
- White Coat associations: age, female, non-smoking
- Masked hypertension associations:
  - younger age, male, exercise,
  - obesity, diabetes, CKD,
  - family history of hypertension.

CV events in masked hypertension equate to true sustained hypertension.
In diabetic patients sustained nocturnal hypertension may occur leading to nephropathy

Prognostic Influence of Office and Ambulatory Blood Pressures in Resistant Hypertension

- 556 patients, resistant hypertension
- Office and ambulatory BPs done
- 4.8 year follow-up
- Endpoint combined fatal and non-fatal cardiovascular events

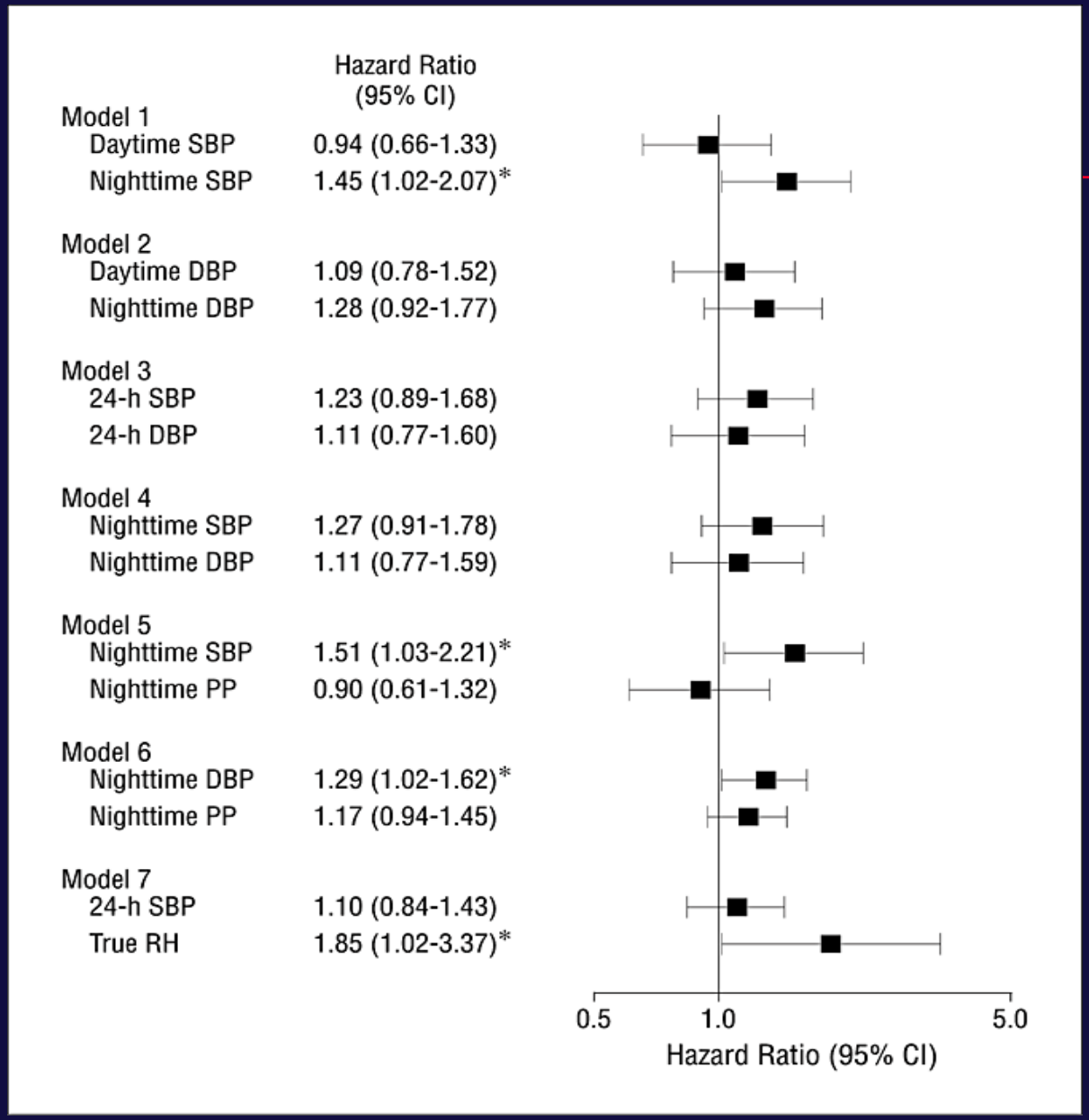
Salles, G. F. et al. Arch Intern Med 2008;168:2340-2346.



Kaplan-Meier estimates of incident total fatal and nonfatal cardiovascular event curves (A), all-cause mortality curves (B), and cardiovascular mortality curves (C) in patients grouped according to ambulatory blood pressure monitoring diagnosis of true or white-coat resistant hypertension (RH)

Salles, G. F. et al. Arch Intern Med 2008;168:2340-2346.

ARCHIVES OF INTERNAL MEDICINE



Hazard ratios (95% confidence intervals [CIs]) when 2 ambulatory blood pressure monitoring variables were included simultaneously in the same multivariate Cox models for prediction of the composite end point

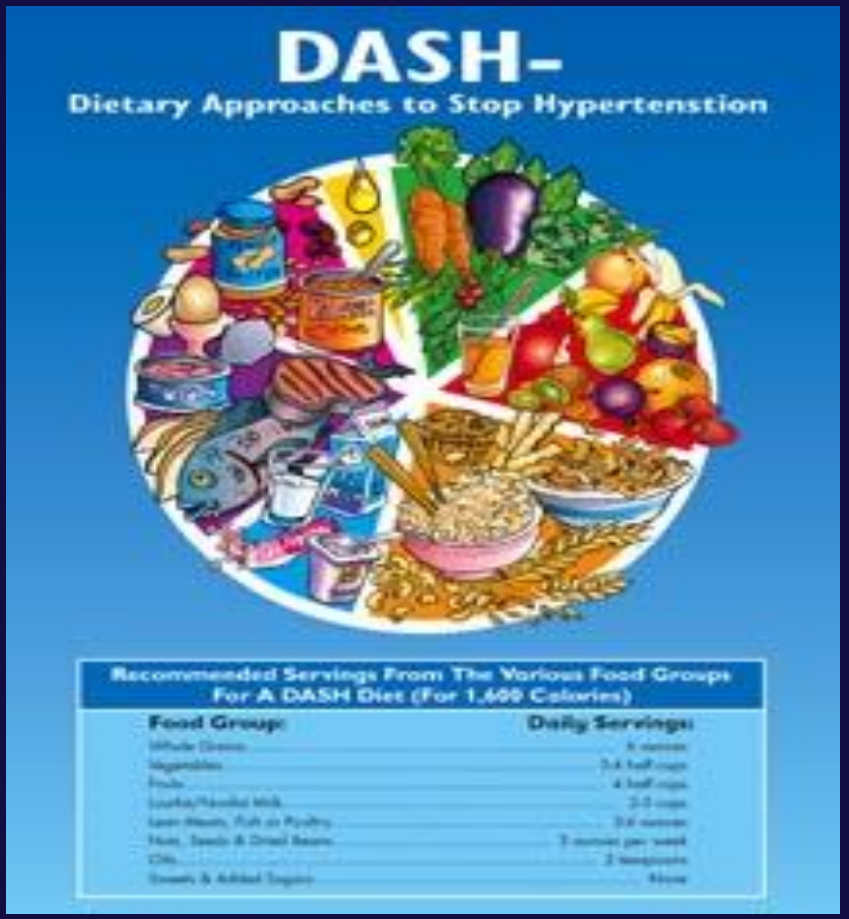
ARCHIVES OF INTERNAL MEDICINE

Salles, G. F. et al. Arch Intern Med 2008;168:2340-2346.

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

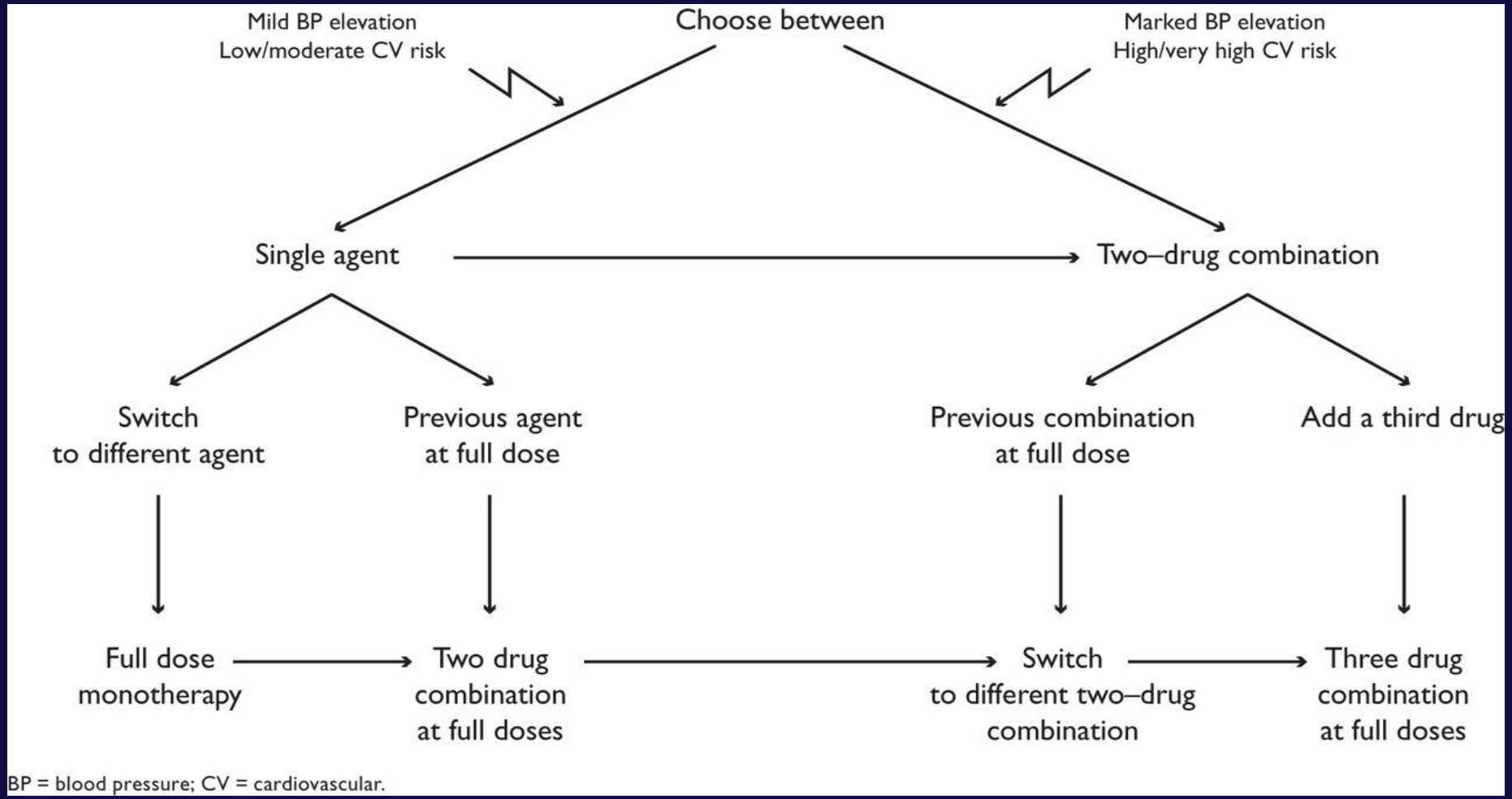
Modification	Recommendation	Approximate systolic BP reduction, range*
Weight reduction	Maintain normal body weight (BMI, 18.5 to 24.9 kg/m2)	5 to 20 mmHg per 10-kg weight loss
Adopt DASH eating plan	Consume a diet rich in fruits, vegetables, and low-fat dairy products with a reduced content of saturated 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 fifth 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.

Average Number of Anti-Hypertensive Agents Used to Achieve Target BP

	MDRD	ABCD	HOT	UKPDS
Goal BP	<92 mmHg MAP*	<75mm Hg DBP	<80 mmHg DBP	<85 mmHg DBP
Achieved BP	93	~75	81	82
Avg # of drugs per patient	3.6	2.7	3.3	2.8

*The goal mean arterial pressure (MAP) of <92 mmHg specified in the MDRD trial corresponds to a systolic/diastolic blood pressure of approximately 125/75 mmHg.

Monotherapy is a myth

Nice Hypertension Guidelines

Under 55 years

Start ACEI

Over 55 years

Start Thiaz or CCB

Inadequate control

ACEI + CCB or ACEI + Thiaz

Inadequate control

ACEI + CCB + Thiaz

Add extra diuretic, alpha blocker **
Consider betablocker

Substitute RAB for ACEI intolerant **

- Chlorthalidone: the forgotten diuretic
- Spironolactone: subclinical Conn’s

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?

Betablockers are dead

Long live Beta-blockers

Cochrane Review
Beta-blockers for hypertension

Authors' conclusions 13 RCTs, 91,561 patients

- The available evidence does not support the use of beta-blockers as first-line drugs in the treatment of hypertension. This conclusion is based on the relatively weak effect of beta-blockers to reduce stroke and the absence of an effect on coronary heart disease when compared to placebo or no treatment. More importantly, it is based on the trend towards worse outcomes in comparison with calcium-channel blockers, renin-angiotensin system inhibitors, and thiazide diuretics. Most of the evidence for these conclusions comes from trials where atenolol was the beta-blocker used (75% of beta-blocker participants in this review). However, it is not known at present whether beta-blockers have differential effects on younger and elderly patients or whether there are differences between the different sub-types of beta-blockers.

ASCOT-BPLA (Anglo-Scandinavian Cardiac Outcomes Trial - Blood Pressure Lowering Arm)

- ASCOT began in 1997, designed to evaluate different treatment strategies for preventing cardiovascular disease in hypertensive patients not considered conventionally dyslipidemic. Conducted in more than 650 general practices and 32 regional medical centers across the United Kingdom, Ireland, and 5 Scandinavian countries.
- N = 19,257 hypertensive patients
- Screening and baseline blood pressure >/= 160/100 mm Hg untreated or >/= 140/90 mm Hg at baseline if treated with 1 or more drugs.
- Patients were started on either amlodipine or atenolol, with the second drug added if and when needed.
- Primary outcome measured for the ASCOT-BPLA was a combined end point of nonfatal MI and fatal CHD.
- Trial stopped Nov '04 due to significant all-cause mortality *benefit* in the amlodipine/perindopril arm.

Results of the ASCOT-BPLA Study

End point	Hazard ratio	95% CI	*P* value
All-cause mortality	0.86	0.78-0.96	.005
Primary end point: nonfatal MI and fatal CHD	0.90	0.78-1.03	.12
Total coronary end point: primary end point + new-onset angina + fatal and nonfatal heart failure	0.86	0.78-0.96	.0048
Fatal and nonfatal stroke	0.77	0.66-0.90	.007
All CV events and revascularization procedures	0.84	0.77-0.90	< .0001
CV mortality	0.76	0.65-0.91	.0017
New-onset diabetes mellitus	0.68	0.60-0.77	< .0001

CHD = coronary heart disease; CI = confidence interval; CV = cardiovascular; MI = myocardial infarction

ASCOT-BPLA: Calcium Blocker/ACE Inhibitor Regimen Superior to Beta-Blocker/Diuretic Regimen

ALLHAT: Study Design

- Randomized, double-blind, multicenter clinical trial
- Determine whether occurrence of fatal CHD or nonfatal MI is lower for high-risk hypertensive patients treated with newer agents (CCB, ACE inhibitor, alpha-blocker) compared with a diuretic
- 623 clinical sites in United States, Canada, Puerto Rico, US Virgin Islands

ALLHAT Officers. *JAMA*. 2002;288:2981-2997.

ALLHAT: Study Design (cont'd)

- 42,418 high-risk hypertensive patients aged ≥ 55 years
- The largest hypertension hard-end point trial
- Diverse patient population: men, women, black individuals, elderly, diabetics

ALLHAT Officers. *JAMA*. 2002;288:2981-2997.

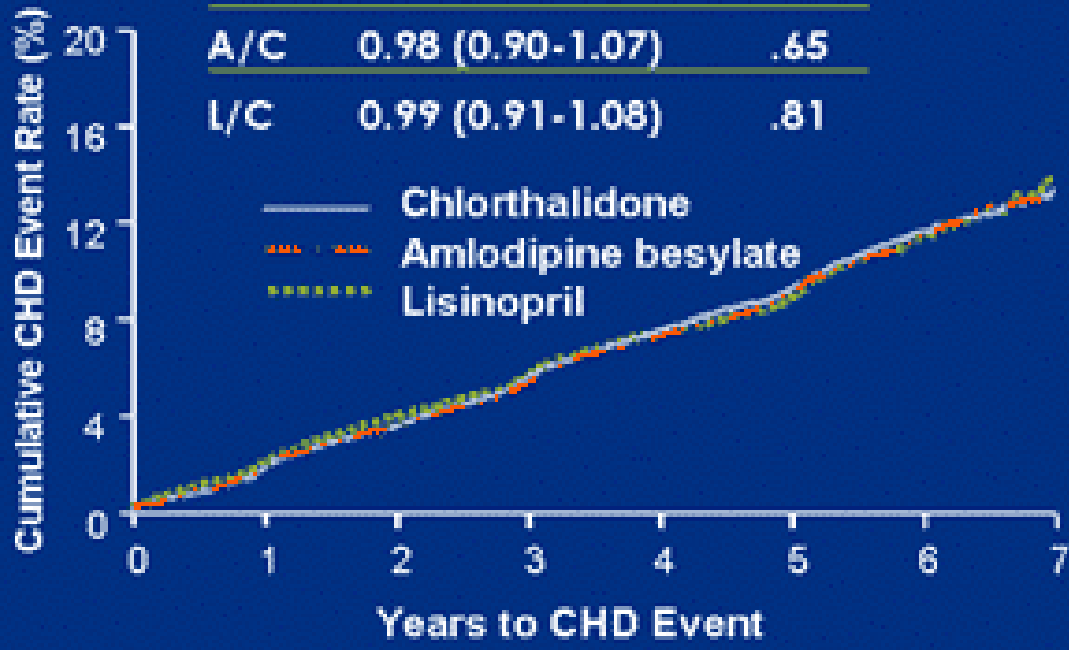
ALLHAT: Patient Baseline Characteristics

	Chlorthalidone (n=15,255)	Amlodipine besylate (n=9048)	Lisinopril (n=9054)
Mean SBP/DBP (mm Hg)	146/84	146/84	146/84
Treated (90%)	145/83	145/83	145/84
Untreated (10%)	156/89	157/90	156/89
Mean age (years)	67	67	67
Black (%)	35	36	36
Hispanic (%)	12	12	12
Women (%)	47	47	46
Current smoking (%)	22	22	22
History of CHD (%)	26	24	25
Type 2 diabetes (%)	36	37	36

ALLHAT Officers. *JAMA*. 2002;288:2981-2997.

ALLHAT Primary End Point: Cumulative Fatal CHD or Nonfatal MI

	RR (95% CI)	P value
A/C	0.98 (0.90-1.07)	.65
L/C	0.99 (0.91-1.08)	.81



Number at Risk:								
Chlorthalidone	15,255	14,477	13,820	13,102	11,362	6340	2956	209
Amlodipine besylate	9048	8576	8218	7843	6824	3870	1878	215
Lisinopril	9054	8535	8123	7711	6662	3832	1770	195

RR=relative risk; CI=confidence interval.

ALLHAT Officers. *JAMA*. 2002;288:2981-2997.

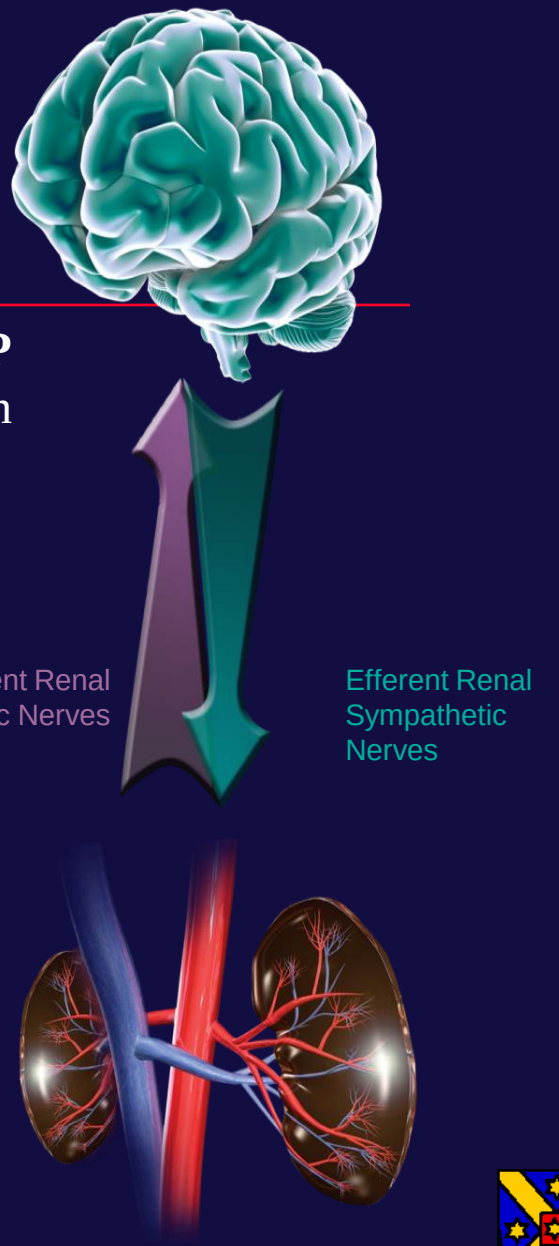
Implication of ALLHAT

- Thiazide diuretic is equal in efficacy to new agents
- Betablocker not tested
- Good control required multiple agents in the majority of patients
- Cross-over may have confused the answer

Sympathetic Nerve Impact

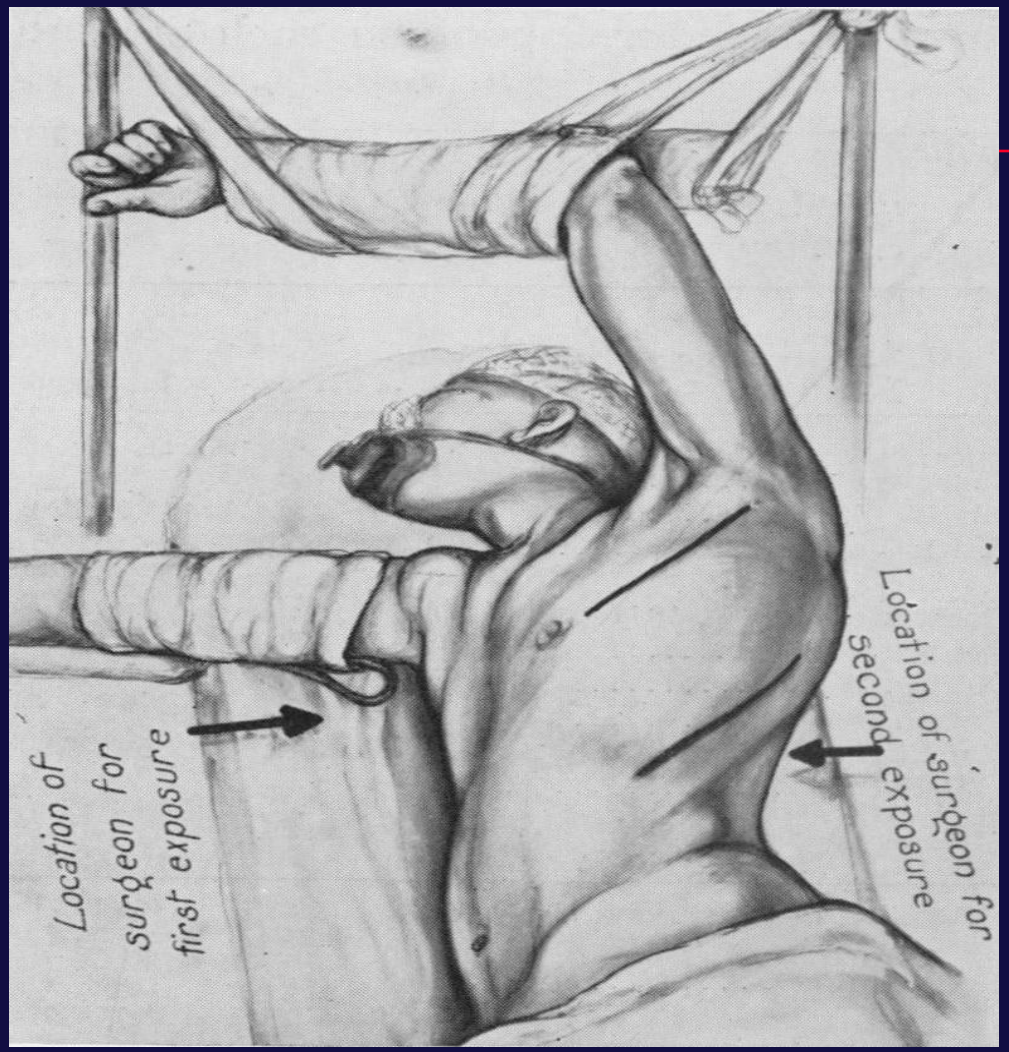
Role of kidney and sympathetic innervation in control of BP

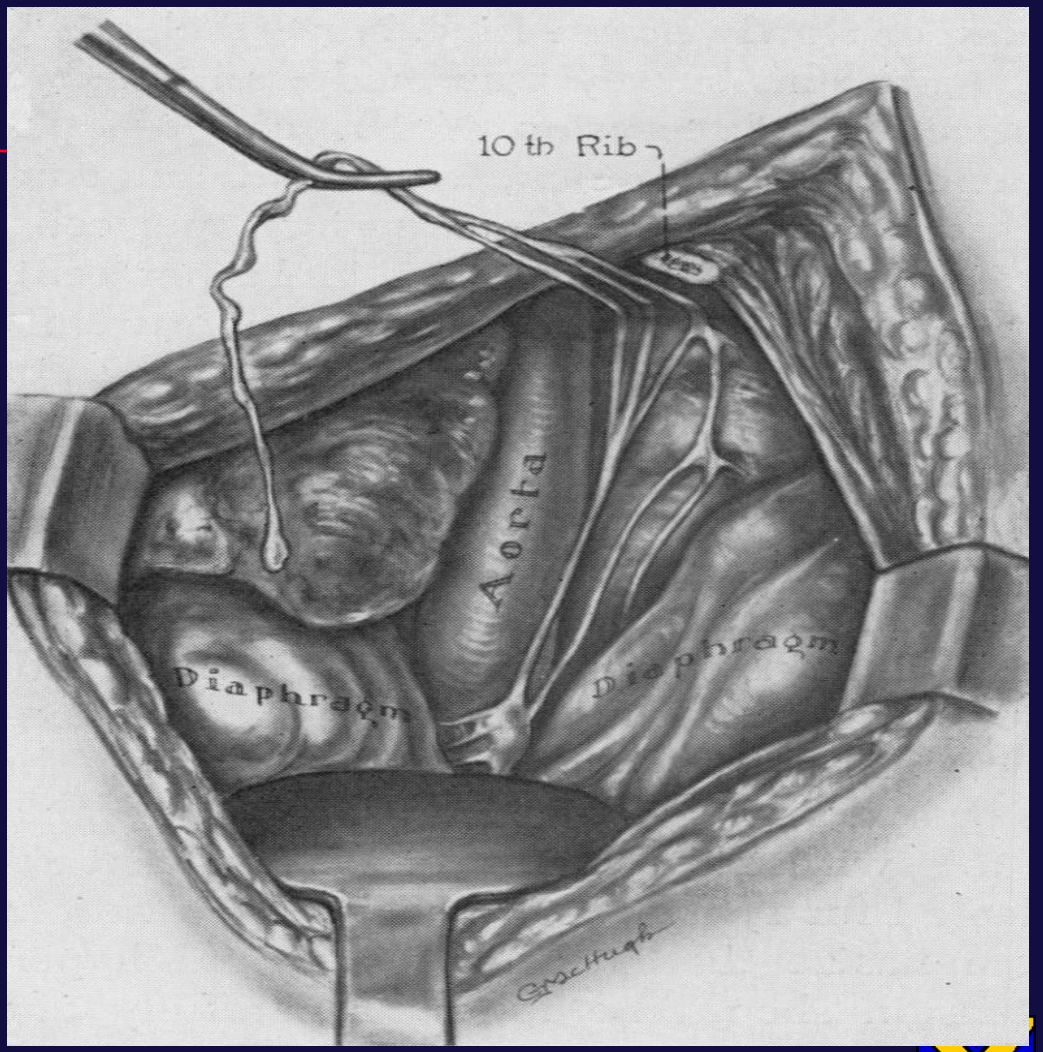
- Renal sympathetic nerves play a critical role in the initiation and maintenance of systemic hypertension. Efferent and afferent renal sympathetic nerves form the renal plexus located in the outer wall of the renal artery[1]
- Activation of the efferent renal sympathetic nerves leads to:[2]
  - Renal insufficiency by decreasing renal blood flow and function
  - Hypertension by increasing vasoconstriction, heart rate and heart contractility
- Activation of the afferent renal sympathetic nerves leads to:[2]
  - Hypertension by increasing the activity of the sympathetic nervous system



1. Doumas M, Faselis C, Papademetriou V. Renal sympathetic denervation and systemic hypertension. *Am J Cardiol.* 2010;105(4):570-6.
2. Esler MD, The sympathetic system and hypertension. *Am J Hypertens.* 2000;13(6 Pt 2):99S-105S.

Surgical Sympathectomy





Grimson KS, Orgain ES, Anderson B, et al. Total thoracic and partial to total lumbar sympathectomy, splanchnicectomy and celiac ganglionectomy for hypertension. *Ann Surg.* 1953;138(4):532-47.

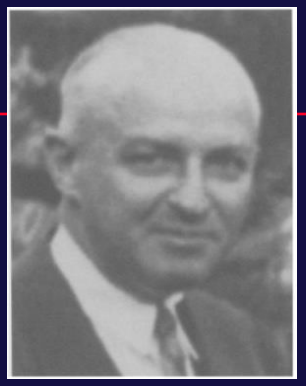
Concept Validated by Surgical History

THE EFFECTS OF PROGRESSIVE SYMPATHECTOMY ON BLOOD PRESSURE

BRADFORD CANNON

From the Laboratories of Physiology in the Harvard Medical School

Received for publication March 24, 1931



Dr. Reginald H. Smithwick

THE EFFECT OF RENAL DENERVATION ON THE LEVEL OF ARTERIAL BLOOD PRESSURE AND RENAL FUNCTION IN ESSENTIAL HYPERTENSION

By IRVINE H. PAGE and GEORGE J. HEUER

(*From the Hospital of the Rockefeller Institute for Medical Research, New York, and the Department of Surgery, New York Hospital, New York*)

(Received for publication September 12, 1934)

THE JOURNAL

of the American Medical Association

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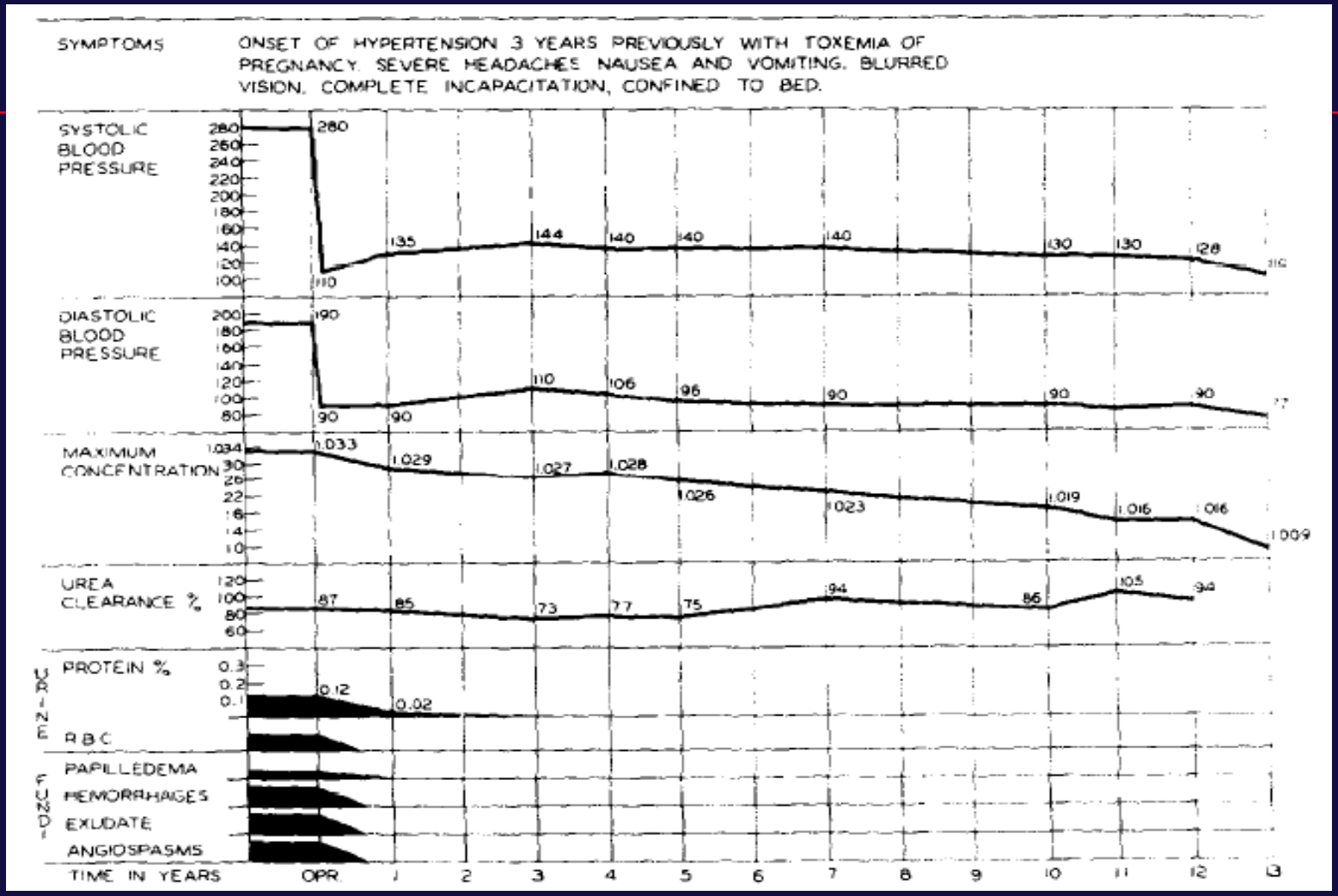
SPLANCHNICECTOMY FOR ESSENTIAL HYPERTENSION

RESULTS IN 1,266 CASES

Reginald H. Smithwick, M.D.
and
Jesse E. Thompson, M.D., Boston

Effective, but significant morbidity

BP Control Maintained Long



Peet, M. Hypertension and its surgical treatment by bilateral supradiaphragmatic splanchnicectomy. *Am J Surg*. 1948;75(1):48-68.

So why did sympathectomy disappear?

- Surgical, highly invasive
- Non-selective ablation
  - Postural hypotension
  - Bowel and bladder incontinence
  - Sexual dysfunction
- Developments in drug therapy

Sir Horace Smirk. Pioneer in drug treatment of hypertension

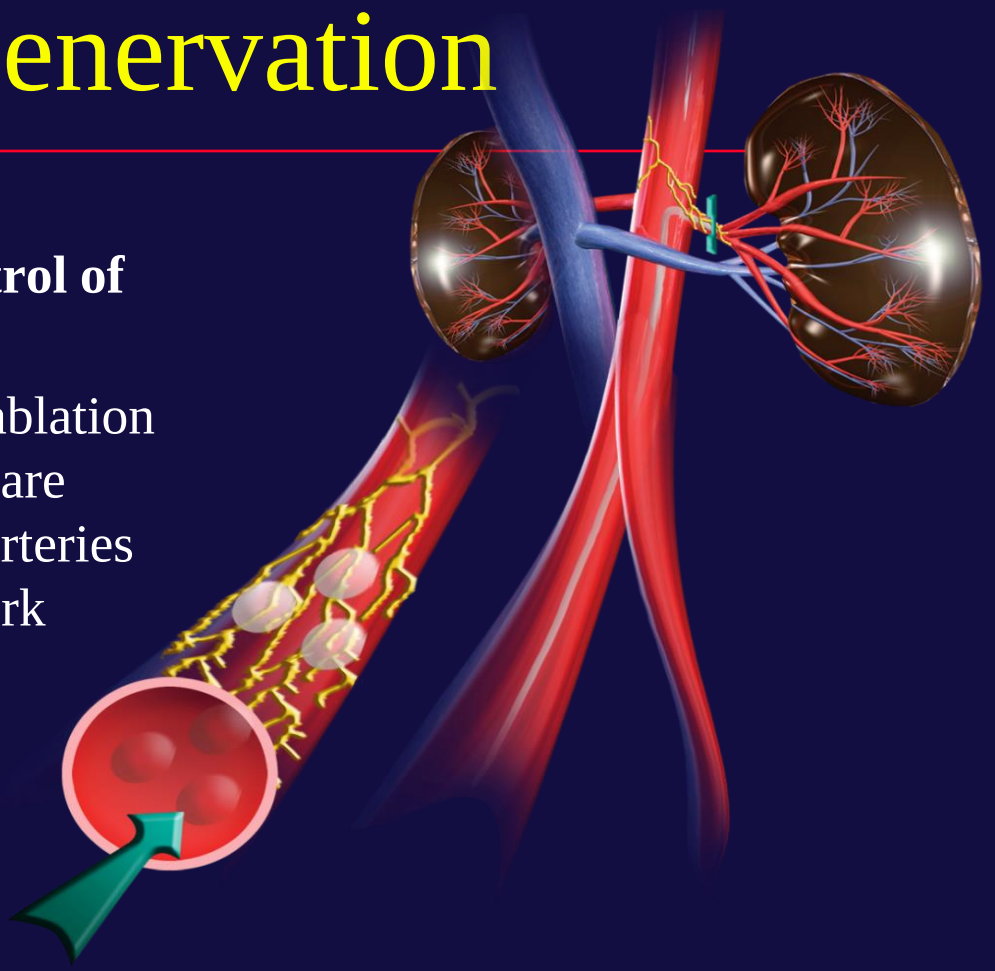
- Smirk FH,Alstad KS. Treatment of Hypertension by Penta-and Hexa-methonium salts. BMJ June 2, 1951.

Doyle AE.. Hypertension
1991 Feb;17(2):247-50

Renal Denervation

Renal sympathetic denervation for control of resistant hypertension[1]

- Renal denervation is a catheter-based ablation procedure in which transmural lesions are delivered along the walls of the renal arteries to disrupt the sympathetic nerve network located within the arterial adventitia



Catheter Delivered Lesions

1. Esler MD, Symplicity HTN-2 Investigators, et al. Renal sympathetic denervation in patients with treatment-resistant hypertension (The Symplicity HTN-2 Trial): A randomised controlled trial. *Lancet.* 2010;376(9756):1903-9.

EnligHTN™ Renal Denervation System

* CE Mark — December 2011
Not for sale in the U.S.

ENLIGHTN I

Procedure Overview

- Initial basket positioning proximal to the bifurcation
- Expand basket and perform generator diagnostic check for electrode contact
- Ablate – 90 seconds per electrode
- For a second set of ablations the basket is collapsed, pulled back 1 cm, rotated and expanded, contact is checked and ablation sequence repeated

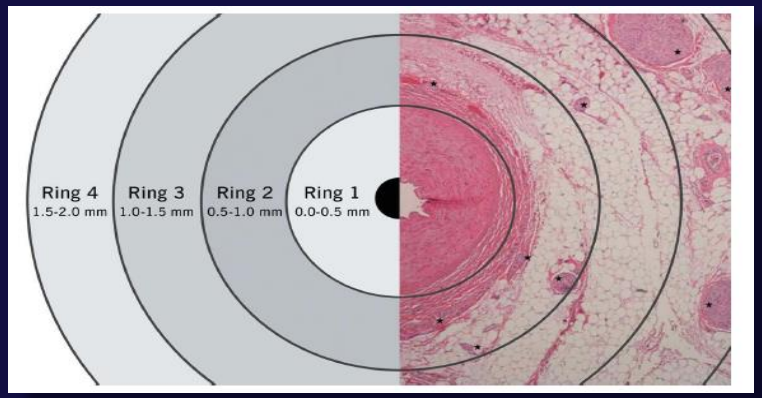
ST. JUDE MEDICAL
MORE CONTROL. LESS RISK.

SAPERE·AUDE

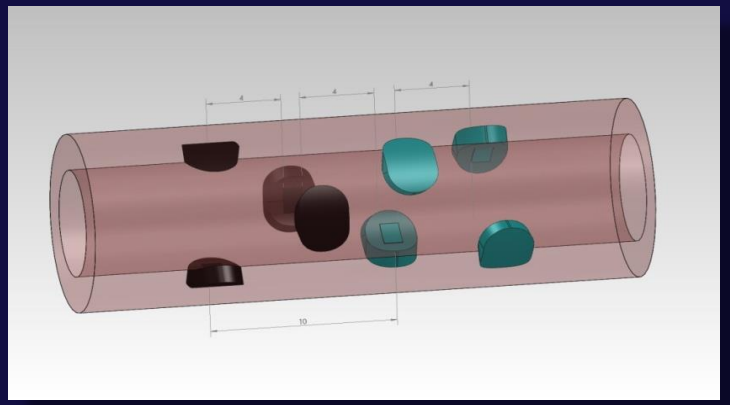
Renal Procedure Goal: Effective Denervation

ENLIGHTN I

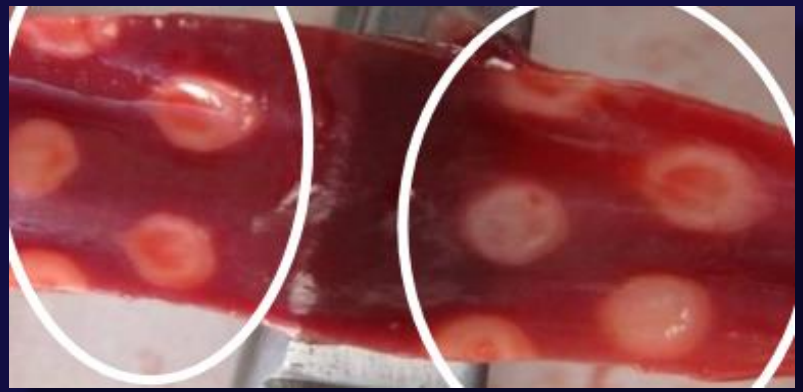
Transmurality*



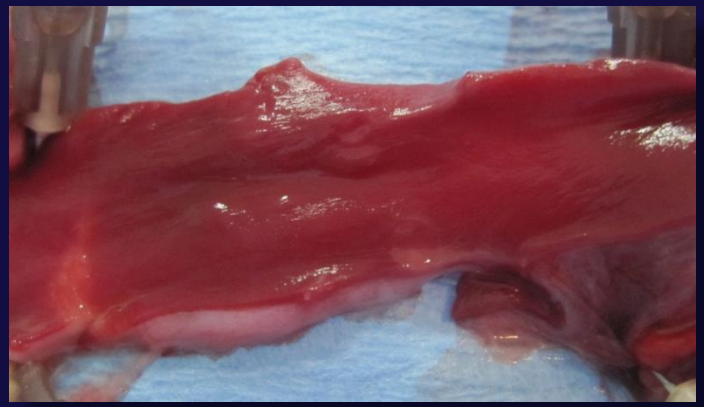
Predictable Pattern



Acute lesion formation**



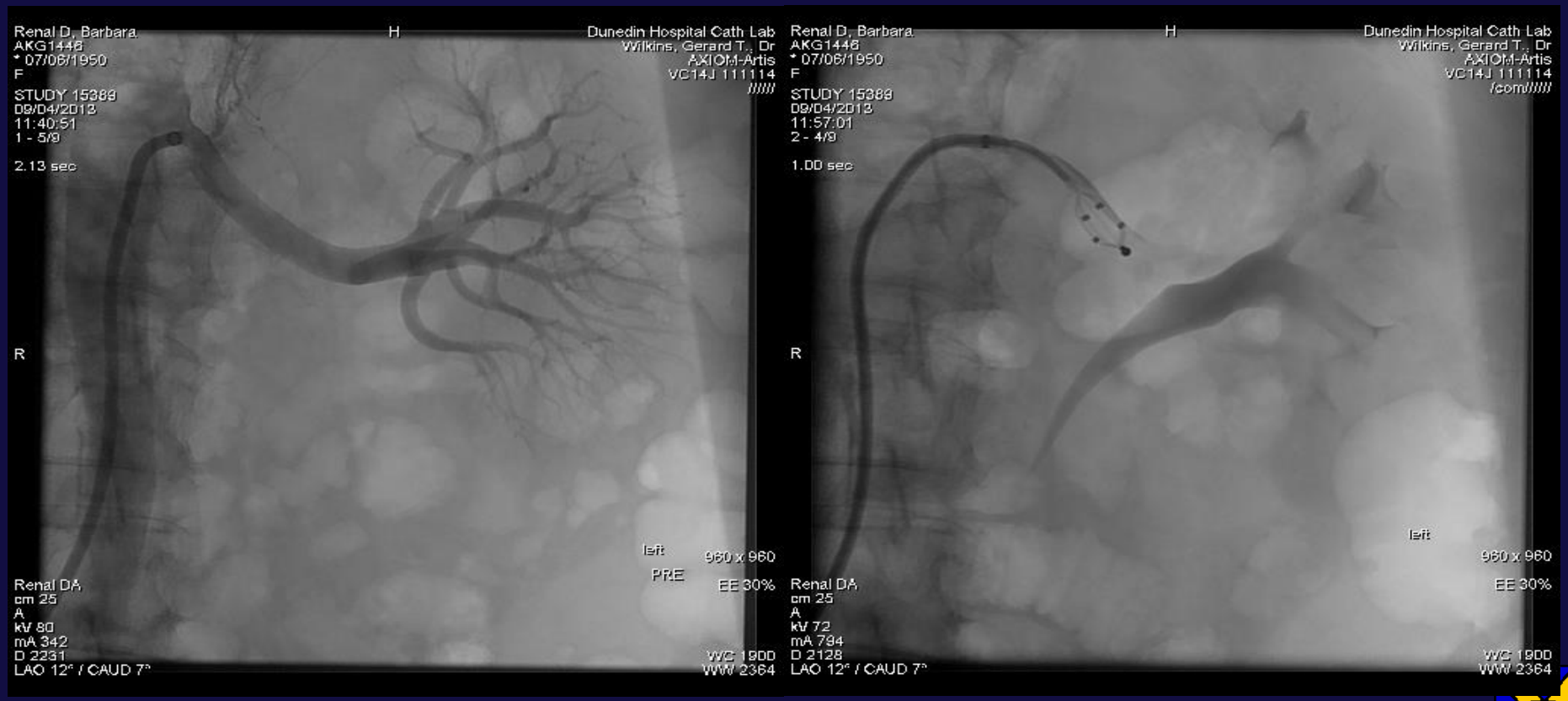
After one month**

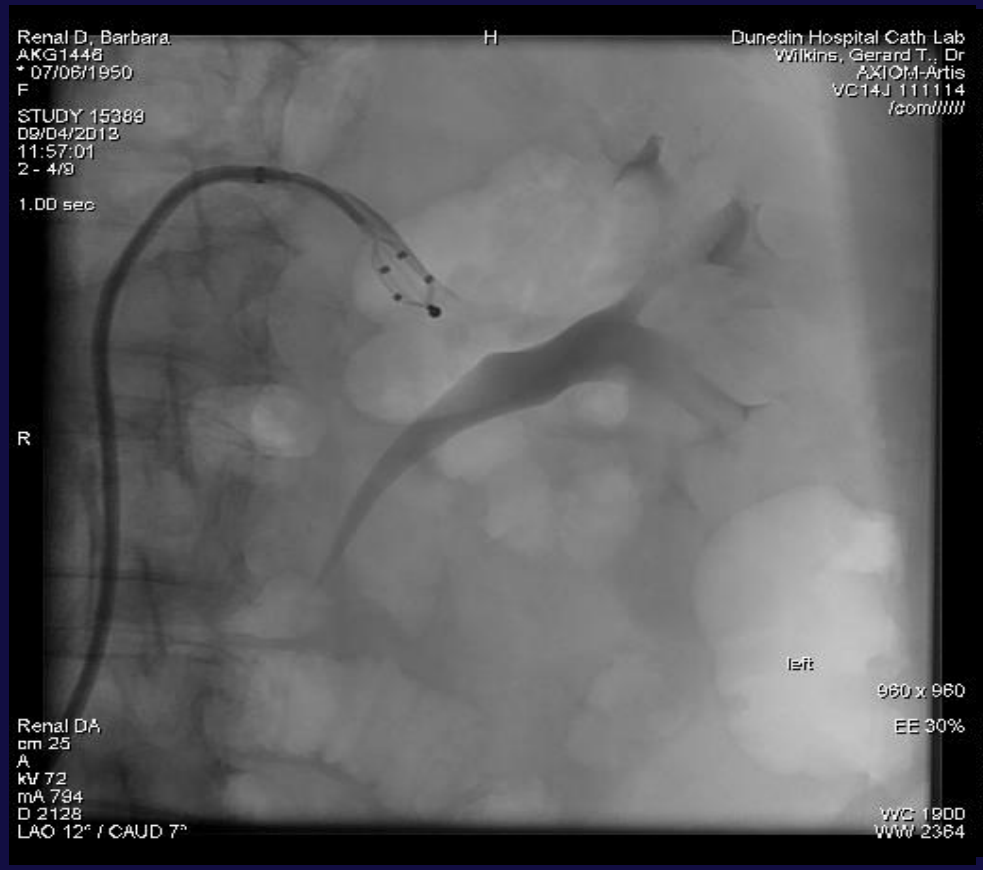


* Atherton DS, Deep NL, Mendelsohn FO, Micro-Anatomy of the Renal Sympathetic Nervous System: A Human Postmortem Histological Study, Clinical Anatomy 2011.

** Animal study. Results on file at St. Jude Medical

Set-up left renal angiogram:

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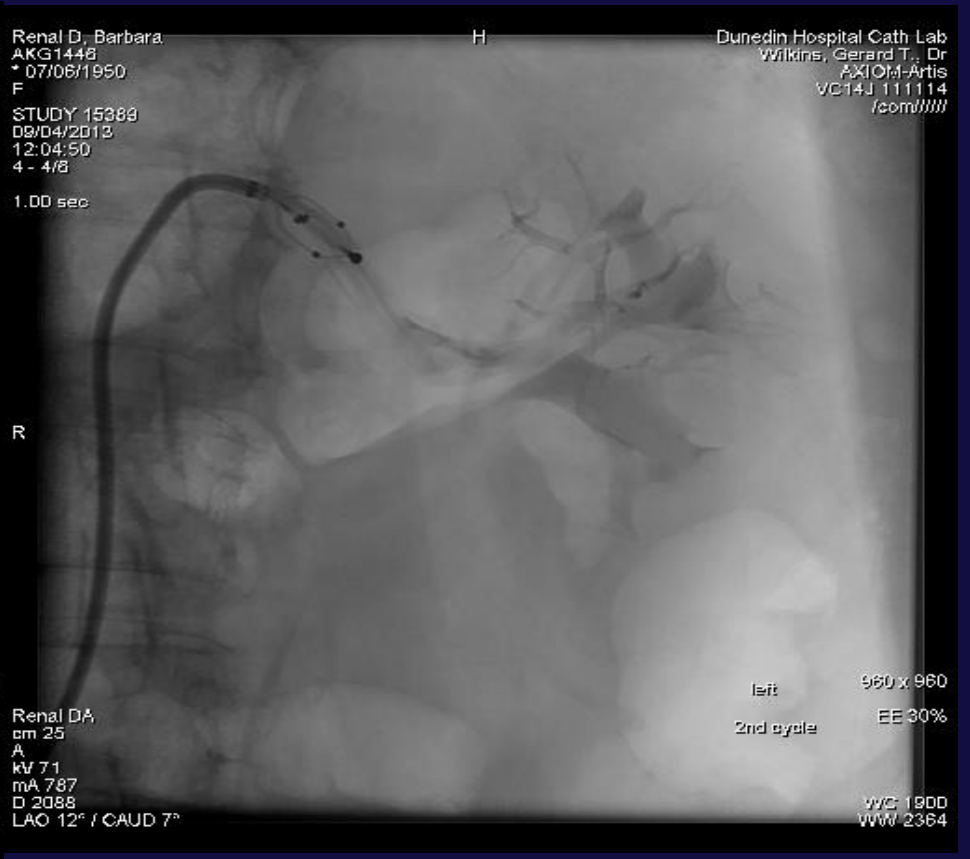
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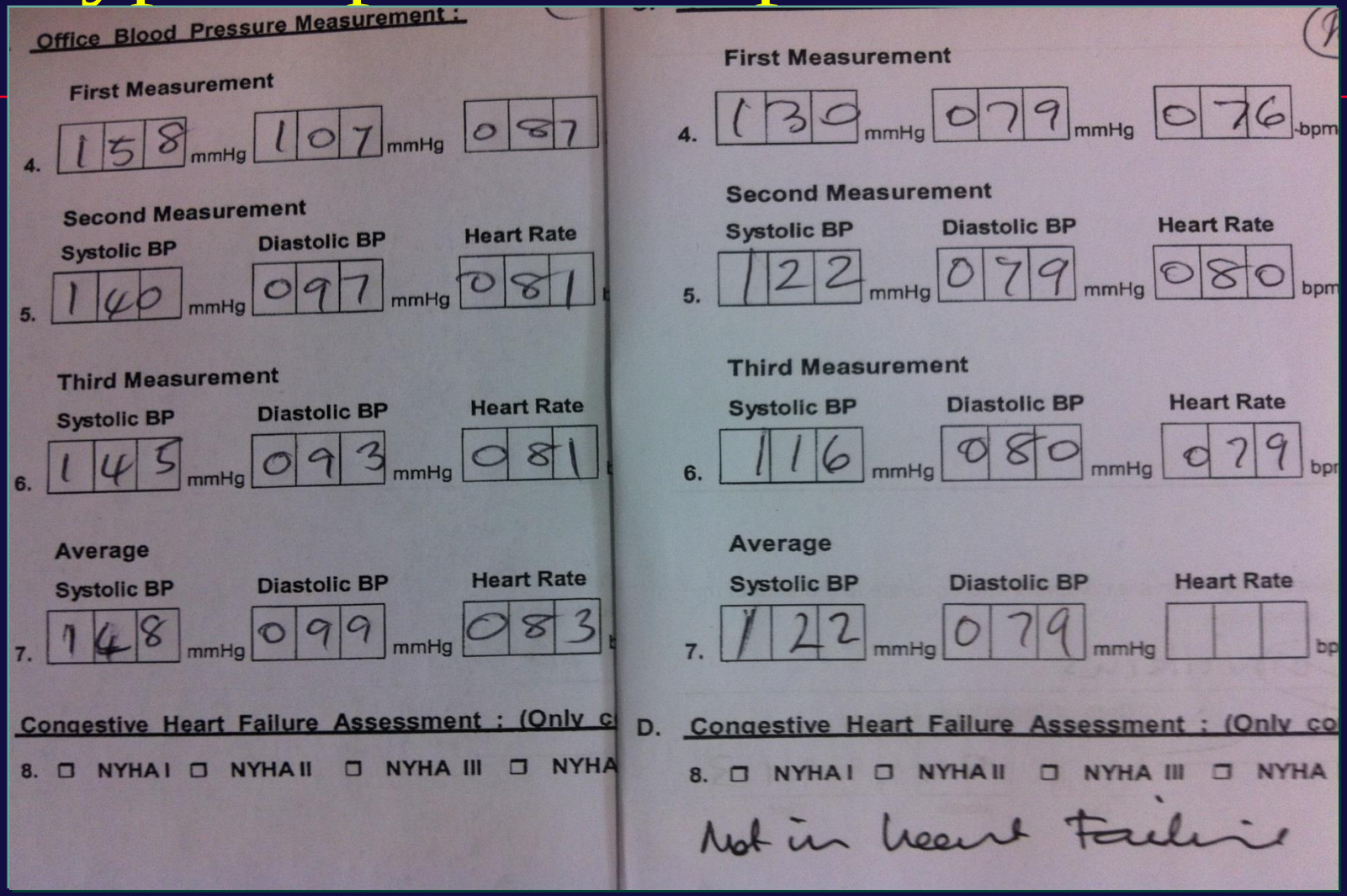
Typical patient response 1month



Office Blood Pressure Measurement :

First Measurement

4. 158 mmHg 107 mmHg 087

Second Measurement

	Systolic BP	Diastolic BP	Heart Rate
5.	140 mmHg	097 mmHg	081

Third Measurement

	Systolic BP	Diastolic BP	Heart Rate
6.	145 mmHg	093 mmHg	081

Average

	Systolic BP	Diastolic BP	Heart Rate
7.	148 mmHg	099 mmHg	083

Congestive Heart Failure Assessment : (Only c

8. ☐ NYHA I ☐ NYHA II ☐ NYHA III ☐ NYHA

First Measurement

4. 130 mmHg 079 mmHg 076 bpm

Second Measurement

	Systolic BP	Diastolic BP	Heart Rate
5.	122 mmHg	079 mmHg	080 bpm

Third Measurement

	Systolic BP	Diastolic BP	Heart Rate
6.	116 mmHg	080 mmHg	079 bpm

Average

	Systolic BP	Diastolic BP	Heart Rate
7.	122 mmHg	079 mmHg	bp

D. Congestive Heart Failure Assessment : (Only co

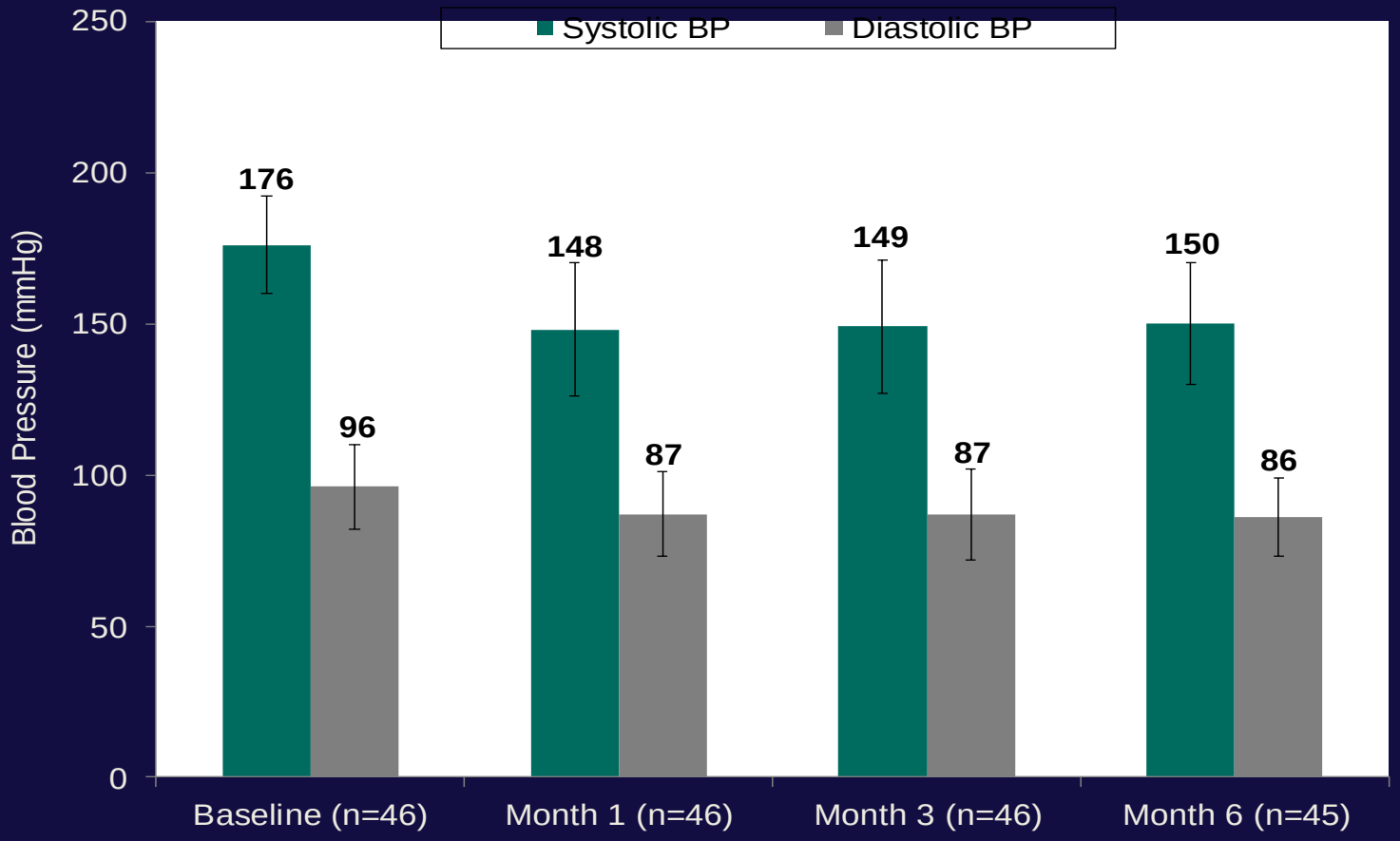
8. ☐ NYHA I ☐ NYHA II ☐ NYHA III ☐ NYHA

Not in heart failure

EnligHTN 2 Study, currently on going

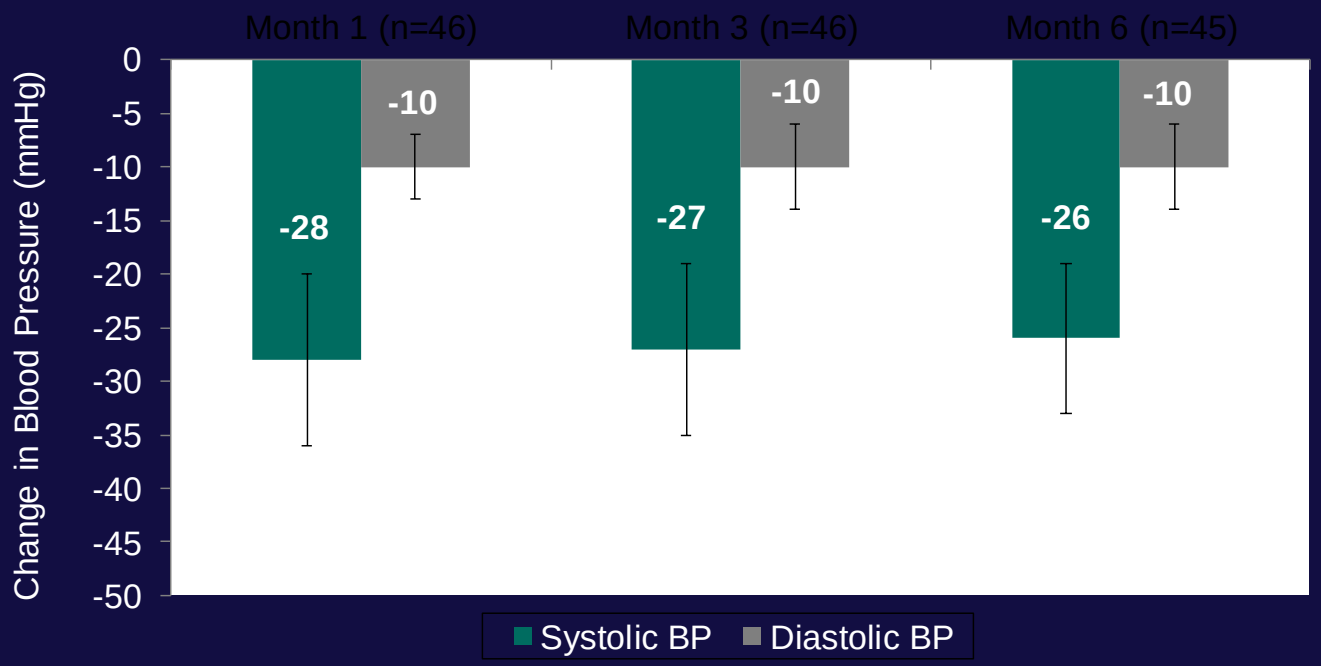
SAPERE·AUDE

Mean Office Blood Pressure



Average 4.3 drugs

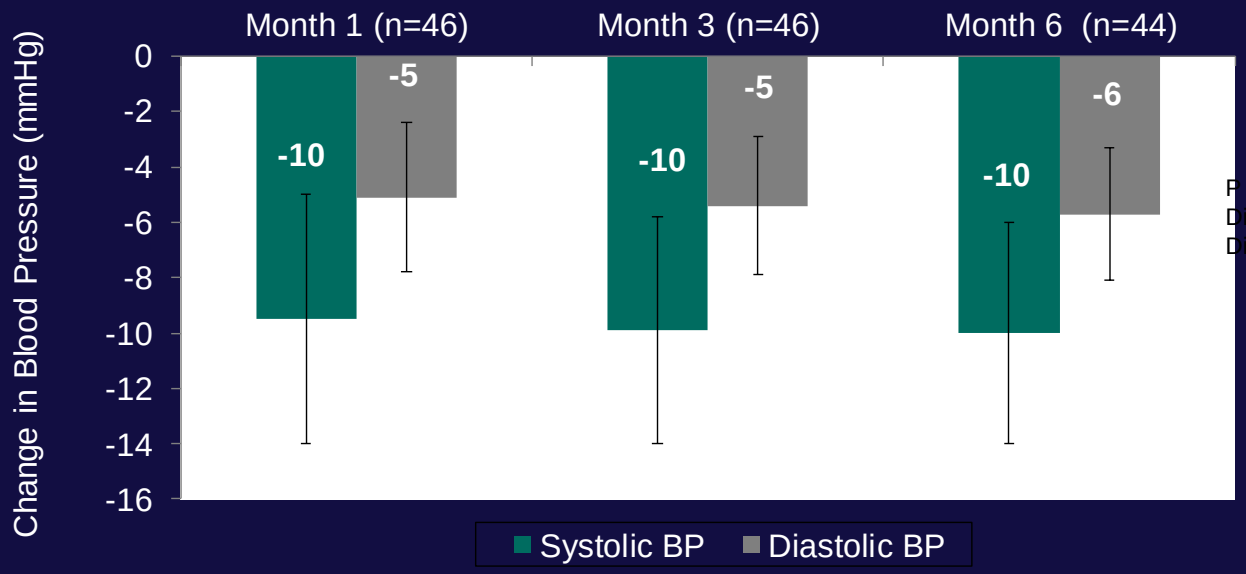
Office BP Reduction from Baseline



p <0.0001

EnligHTN therapy delivers a rapid and significant reduction in Office BP that is sustained through the 6M timeframe

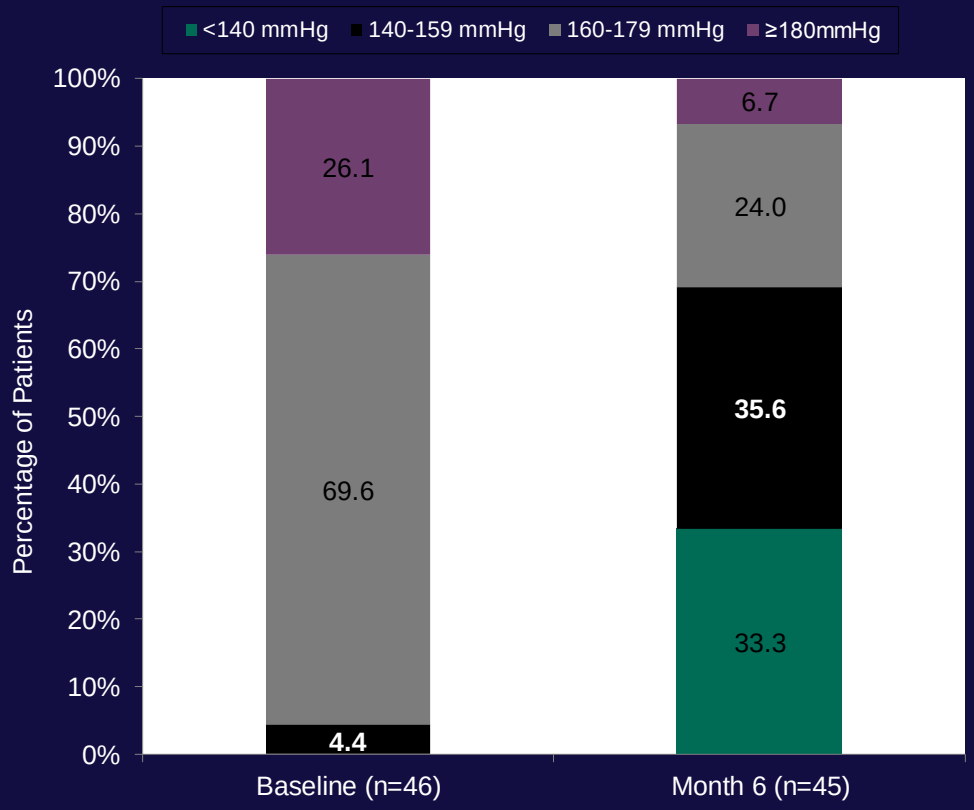
24 hr Ambulatory BP Reduction from Baseline



P values are <0.0001, except
Diastolic 1 mo p-value 0.0003
Diastolic 3 mo p-value 0.0002

EnligHTN therapy delivers a rapid and significant reduction in Ambulatory BP that is sustained through the 6M timeframe

Responder & Goal Blood Pressure Parameters



2/3 of patients will have a great enough reduction in their BP to move to a lower stage of HTN classification / treatment and approximately 1/3 of patients treated with EnligHTN no longer meet HTN classification

- % Responders (>10 mmHg Reduction from baseline) = 76% (n=34)
- At Goal SBP:

Future

Clinical Trials

- Does it work reliably in resistant hypertension?
- Is it durable?
- Is it cost effective?
- What is the best way to deliver this therapy?
  - More rapid ablation
  - Trans-radial route

Novel Clinical Research

- Resistant hypertension
- Moderate hypertension?
- Heart failure?
- Moderate renal failure?
- Dialysis dependent renal failure?
- Obstructive sleep apnoea?
- Type 2 diabetes?


SAPERE·AUDE

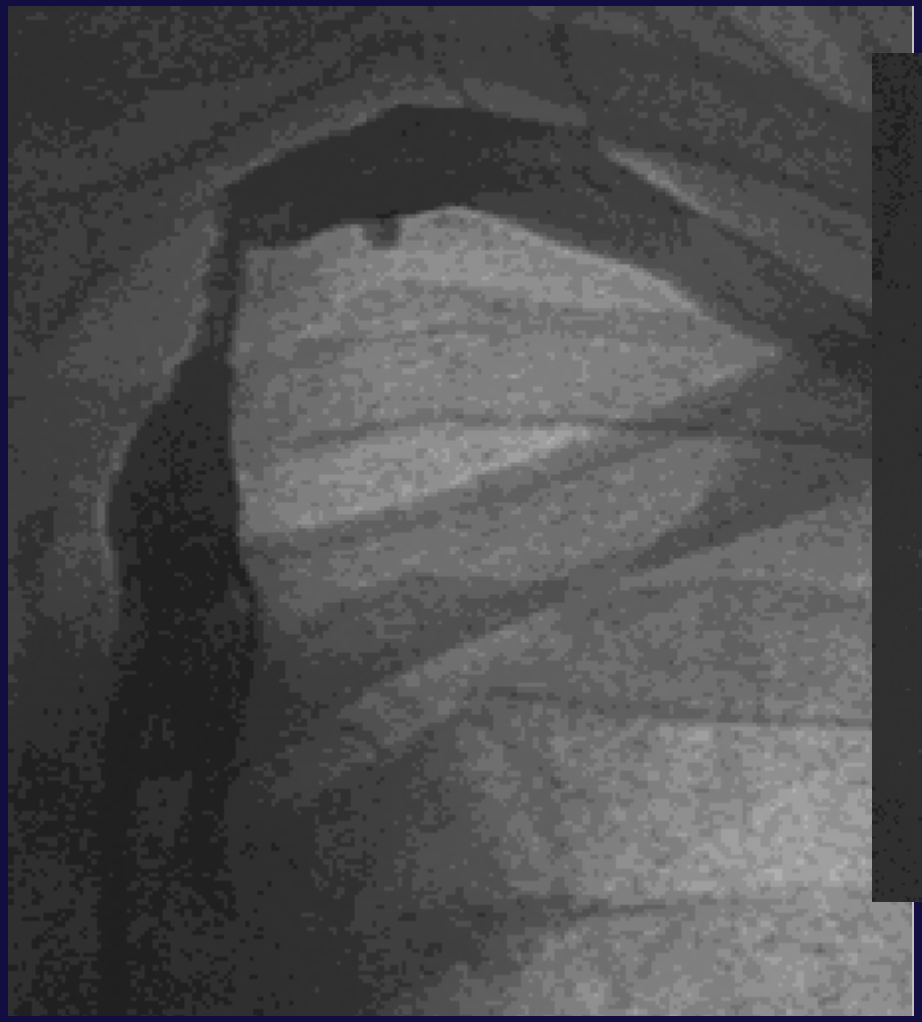
Case E

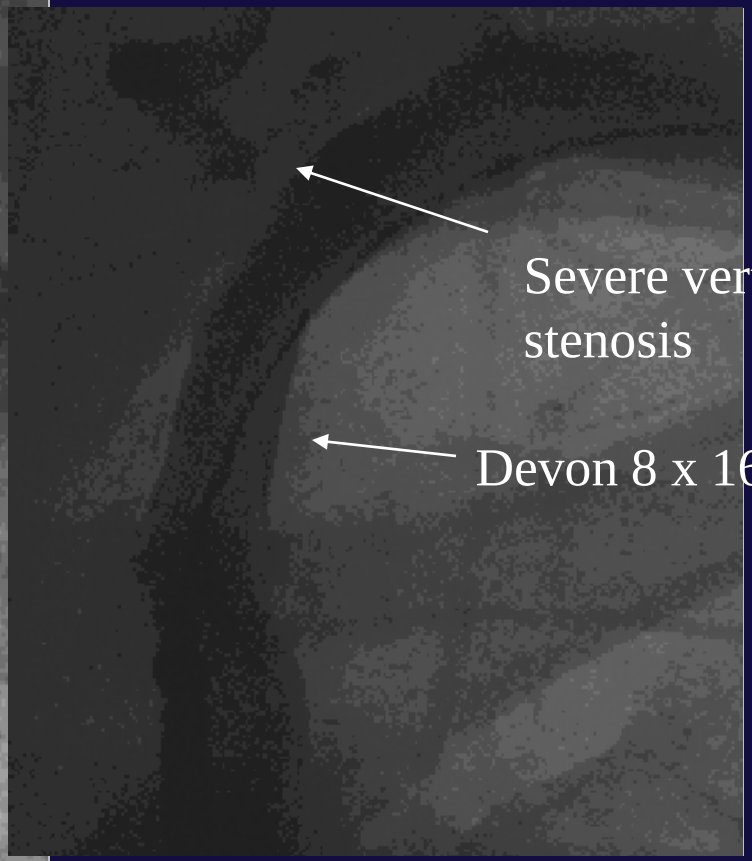
- An 84 year old woman presents for assessment. She has recently had a fall with bruising and no boney injury. She appears to have tripped on the edge of a mat in her hallway. There was no LOC, She presents infrequently and is independent at home. Her previous GP has retired and this is her first visit to you. On closer questioning she presents a story some dizziness when hanging up washing. When you take her BP she suggests you use her right arm “because her last Doctor said it was easier there” BP is 180/60 right arm. Left arm pulse seems lower volume. The BP is 130/70.
- Which BP is a true reflection of central BP
- What is the mechanism of her dizziness?
- What investigations may be helpful?
- Do you treat her BP under these circumstances?

Subclavian Stenosis

- Common condition easily diagnosed by BP difference between arms
- Diagnosis confirmed by carotid and vertebral duplex: reverse flow in vertebral
- Cause of subclavian steal (vertibrobasilar)
- Can be managed conservatively if no neurological symptoms
- Can be stented if vertebreobasilar symptoms are troublesome

Left Subclavian Stenosis





Hypertension in Older Persons

- More than two-thirds of people over 65 have HTN.
- This population has the lowest rates of BP control.
- Treatment, including those who with isolated systolic HTN, should follow same principles outlined for general care of HTN.
- There is convincing evidence for treatment benefit across all age groups
- Lower initial drug doses may be indicated to avoid symptoms; standard doses and m[illegible]will be needed to reach BP targets.

JNC VII GUIDELINES

HYVET study

- Randomised, double blind, placebo controlled
- 3845 patients all > 80 years age all SBP>160
- Step Rx Indapamide then Perindopril target <150/80
- After 2 yrs prematurely terminated: significant benefit in stroke and death
  - Death all cause 21% relative risk reduction
  - Death from Stroke 39%
  - Reduction in heart 64%

Postural Hypotension

- Decrease in standing SBP >10 mmHg, when associated with dizziness/fainting, more frequent in older SBP patients with diabetes, taking diuretics, venodilators, and some psychotropic drugs.
- BP in these individuals should be monitored in the upright position.
- Avoid volume depletion and excessively rapid dose titration of drugs.

JNC VII GUIDELINES

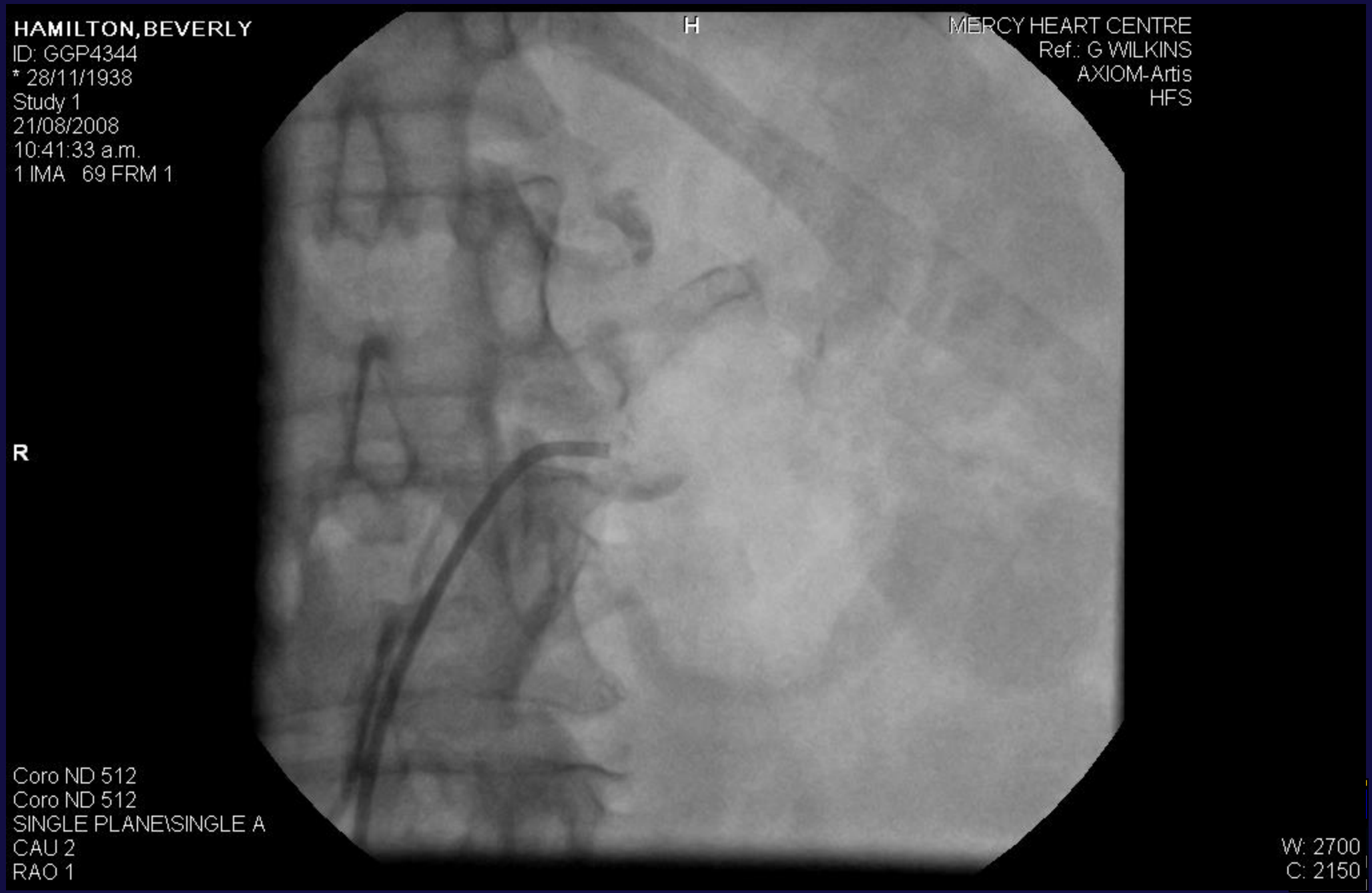
Case D

- A young man with type one diabetes presents for review. He is 34 and developed insulin dependent diabetes aged 7 years. He has early retinopathy and mild early peripheral neuropathy. There is a history of type one diabetes in his family and early vascular death in those involved. He is reluctant to take “pills” but is very fastidious about blood sugar management and insulin. BP is 130-140/90 range. There is microproteinuria.
- Treat hypertension?
- What investigations are reasonable?
- What are the treatment options?

Case A

- 65 year old male. BP recordings have been high for some years. He seeks medical review infrequently.
- There is a past history of claudication resulting in left leg below knee amputation for an ischemic foot. He has continued to smoke. No diabetes. No other vascular history
- Serial BPs are in the range 170/95
- He is already a low dose thiazide (bendrofluazide 2.5mg daily) and felodipine 5mg daily partly to combat his claudicant symptoms. Routine bloods show Urea 10.3, Creatinine 130. You start a third agent. He returns in two weeks feeling miserable. You cannot find much but repeat bloods show renal failure (urea 25, Creatinine 316). What's the problem?

- What agent was used?
- What assessment was reasonable here prior to additional therapy?
- What management options do you have?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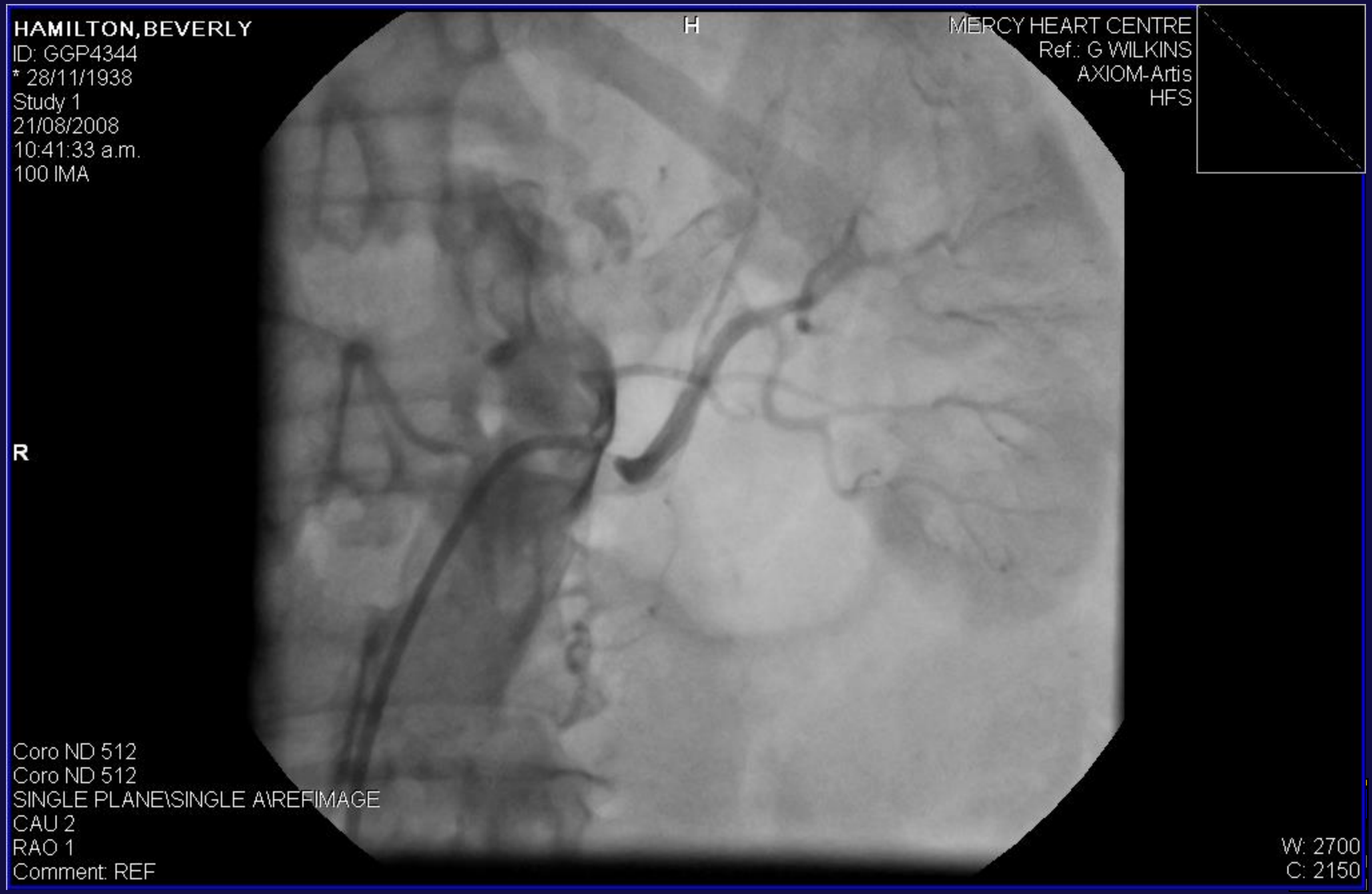
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Diagnosis of Renal Artery Stenosis

- Suspect in older age group, smokers and with PAD or aortic pathology
- Bruits
- Ultrasound small and or assymetrical size
- Doppler vs MRI (MRA)
- CT angio - excellent but contrast
- Selective angio ⟶ renal stent