

Hypertension Review

MEDICINE COURSE 442: 2020 - 2021
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Outline

- Presentations
 - Introduction
 - Evidence
 - Definitions
 - Summary

Case 1

- 35-year-old woman was referred to your clinic after undergoing screening for employment. Her blood pressure was found to be high (149/93 mmHg). She has no complaints and is otherwise healthy.
- PMH: nil
- Meds: nil
- FHx: High BP in father and brother
- SHx: Single, works as a nurse, no illicit drug use.

Case 1

- On physical exam: BMI 29, looks well, not in distress
- BP: 145/93, HR: 78
- CVS: S1 + S2 + 0
- Chest: clear
- Abd: Soft, Lax, no bruit
- Rheum and Neuro: normal

Case 1

- What is your next step in management?
 - A. Advise for lifestyle modification and follow up in 3 months
 - B. Repeat blood pressure measurement in the office after 2 weeks
 - C. Perform a 24-hour ambulatory blood pressure monitor
 - D. Ask for home blood pressure readings over one week

How is blood pressure measured?

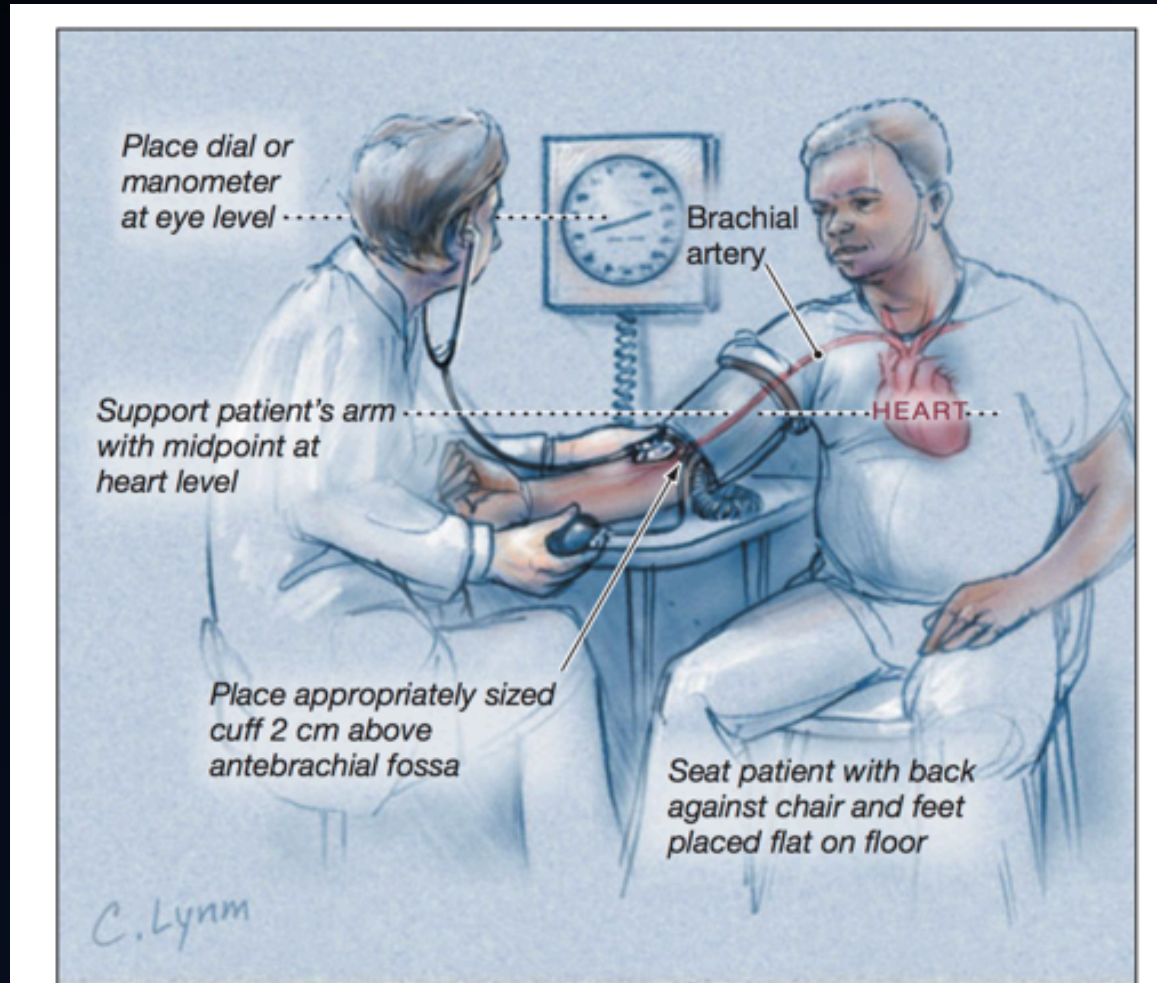


Figure 23-1 Clinical Measurement of Indirect Blood Pressure

See Table 23-2 for appropriate cuff sizing.

Other types blood pressure measurement devices :

- Mercury based manometer (phasing out)
- Oscillometer based measurements (most automated BP machines)

Epidemiology

- 1 in 3 adults (>20 years old) have high blood pressure
- Incidence increases with aging
- 5 – 10% of all hypertension is secondary
- Searching for secondary hypertension is expensive and cumbersome
- Need better selection of who to screen and offer specific treatments

Effects of Treatment on Morbidity in Hypertension

Results in Patients With Diastolic Blood Pressures
Averaging 115 Through 129 mm Hg

Veterans Administration Cooperative Study Group on Antihypertensive Agents

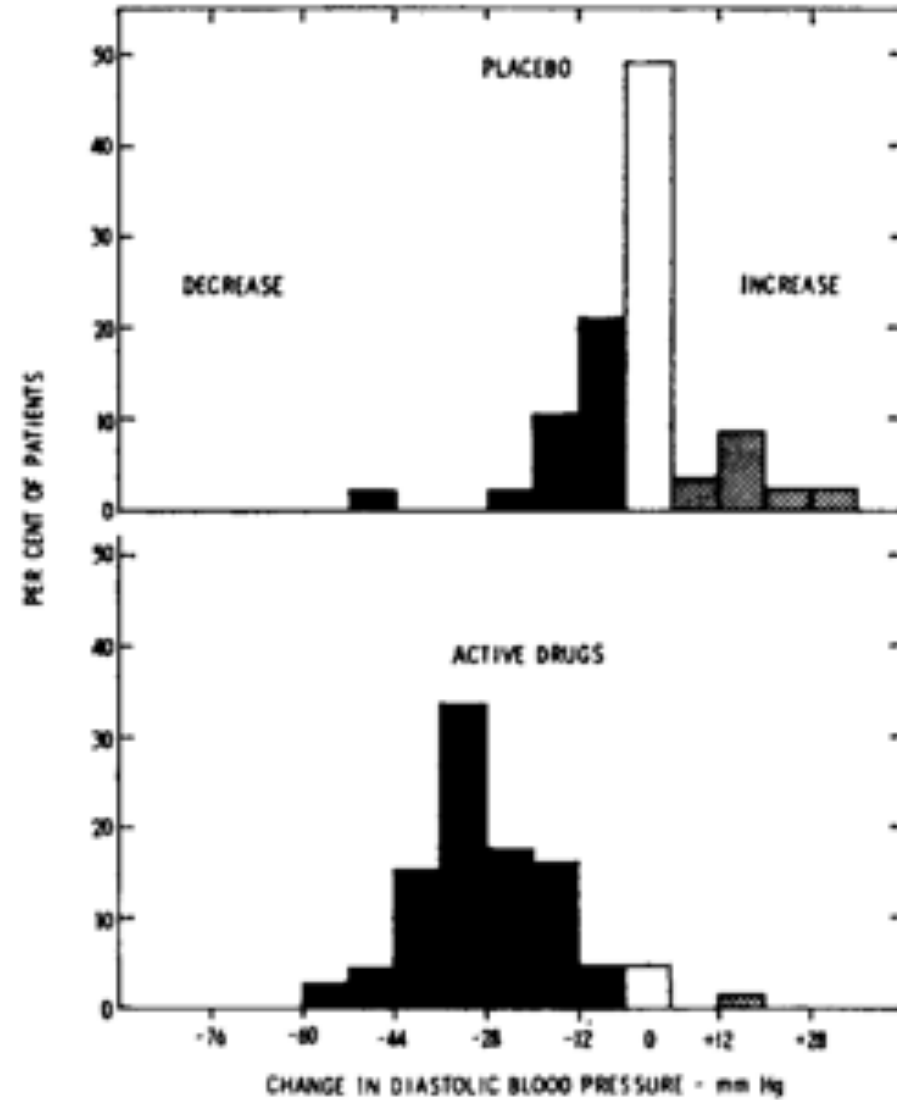
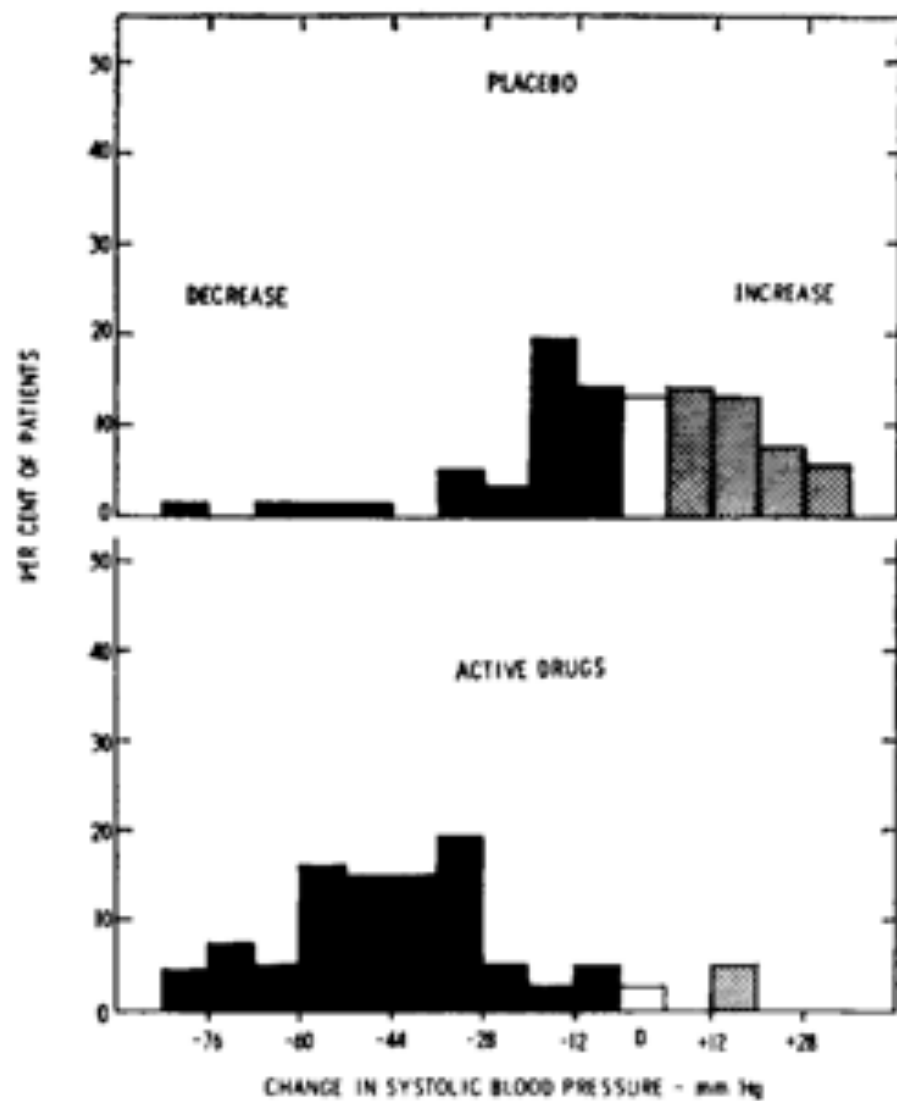
A group of 143 male hypertensive patients with diastolic blood pressures (at the clinic) averaging between 115 and 129 mm Hg were randomly assigned to either active (hydrochlorothiazide plus reserpine plus hydralazine hydrochloride) or placebo treatment. Twenty-seven severe, complicating events developed in the placebo-treated patients as compared to two in the active group. Four deaths occurred in the placebo-treated group and none in the actively treated patients. Other complications in the placebo group included grade 3 or 4 hypertensive retinopathy, congestive heart failure, increasing azotemia, cerebrovascular thrombosis, transient ischemic attacks, cerebral hemorrhage, myocardial infarction, and severely elevated blood pressure. Severe complications in the active-treatment group were one cerebrovascular thrombosis and one case of multiple drug toxicity. Male patients with diastolic blood pressures averaging 115 mm Hg or above represent a high-risk group in which antihypertensive therapy exerts a significant beneficial effect.

without signs of accelerated hypertension at admission whose diastolic blood pressures prior to treatment averaged 115 through 129 mm Hg.

Plan of Investigation

All patients were hospitalized for the initial work-up. Male patients whose diastolic blood pressures from the fourth through the sixth day of hospitalization averaged 90 through 129 mm Hg without treatment were considered for admission to the prerandomization trial period.

Severity was evaluated in five categories. These were the average diastolic blood pressure during hospitalization and the degree of clinically detectable hypertensive damage in the following four target organs: the optic fundi, the brain, heart, and kidneys. Severity of damage in each category was graded on a scale from 0 (no detectable abnormality) to 4 (most severe changes). The criteria used



Changes in systolic (*left*) and diastolic blood pressure (*right*) after four months of treatment in 57 patients given placebos (*above*) and 68 patients treated with hydrochlorothiazide plus reserpine plus hydralazine (*below*).

Modification in Treatment Regimens.—Of the 73

Table 4.—Incidence of Mortality and Morbidity

	Placebo-Treated Patients	Actively Treated Patients
Deaths	4	0
Class A events	10	0
Subtotal	14	0
Other treatment failures	7	1
Total terminating events	21	1
Class B events (nonterminating)	6	1
Total	27	2

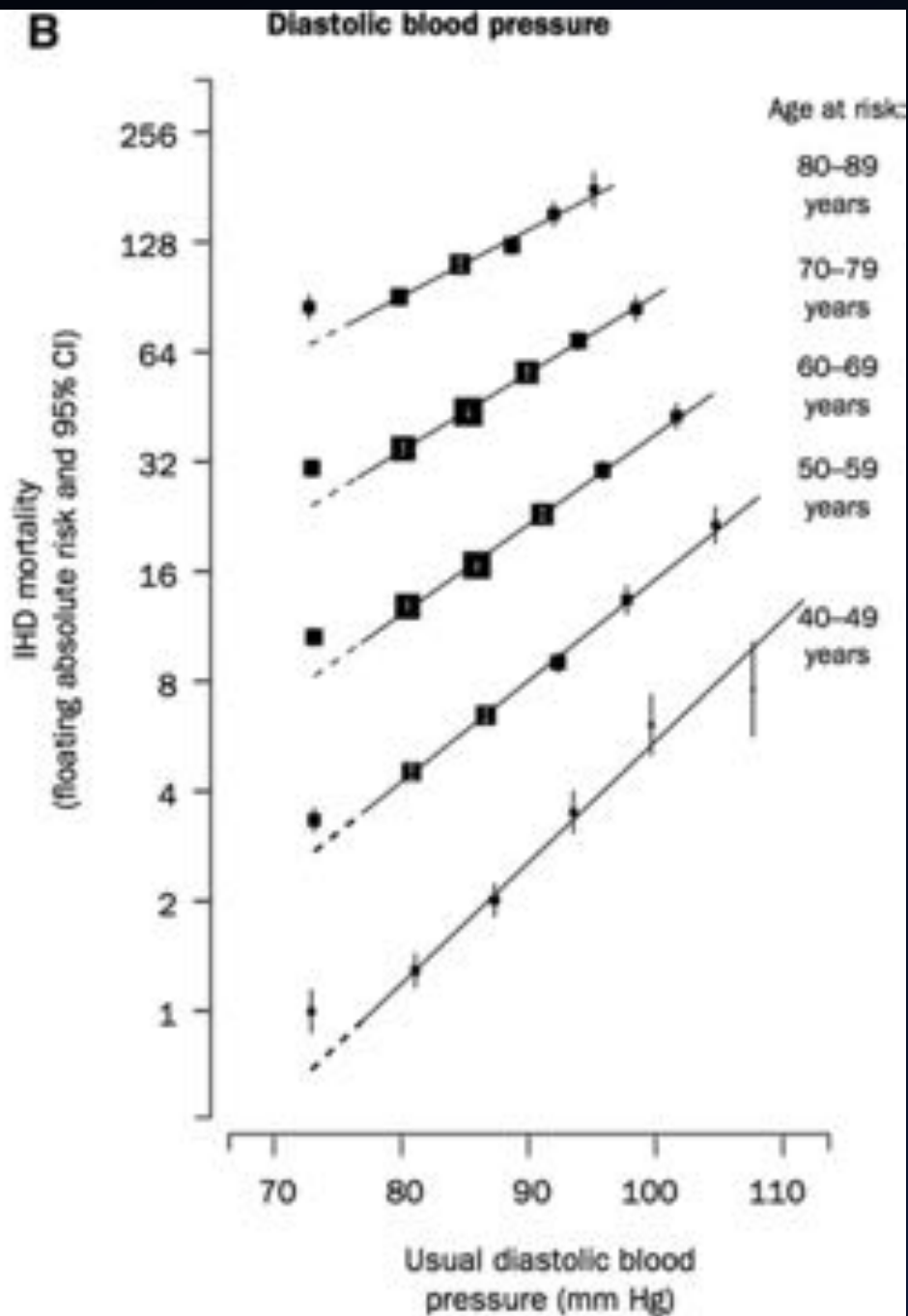
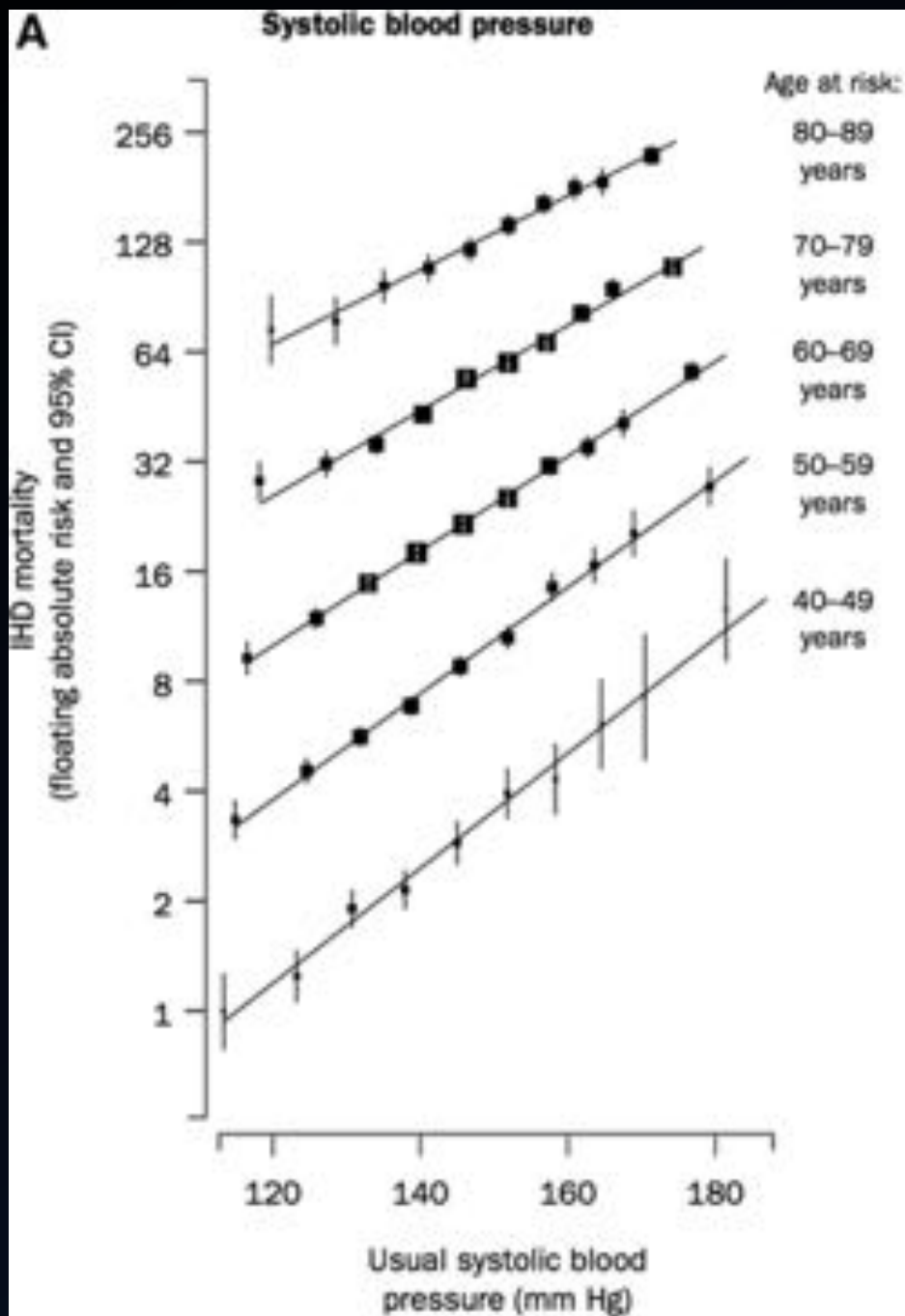
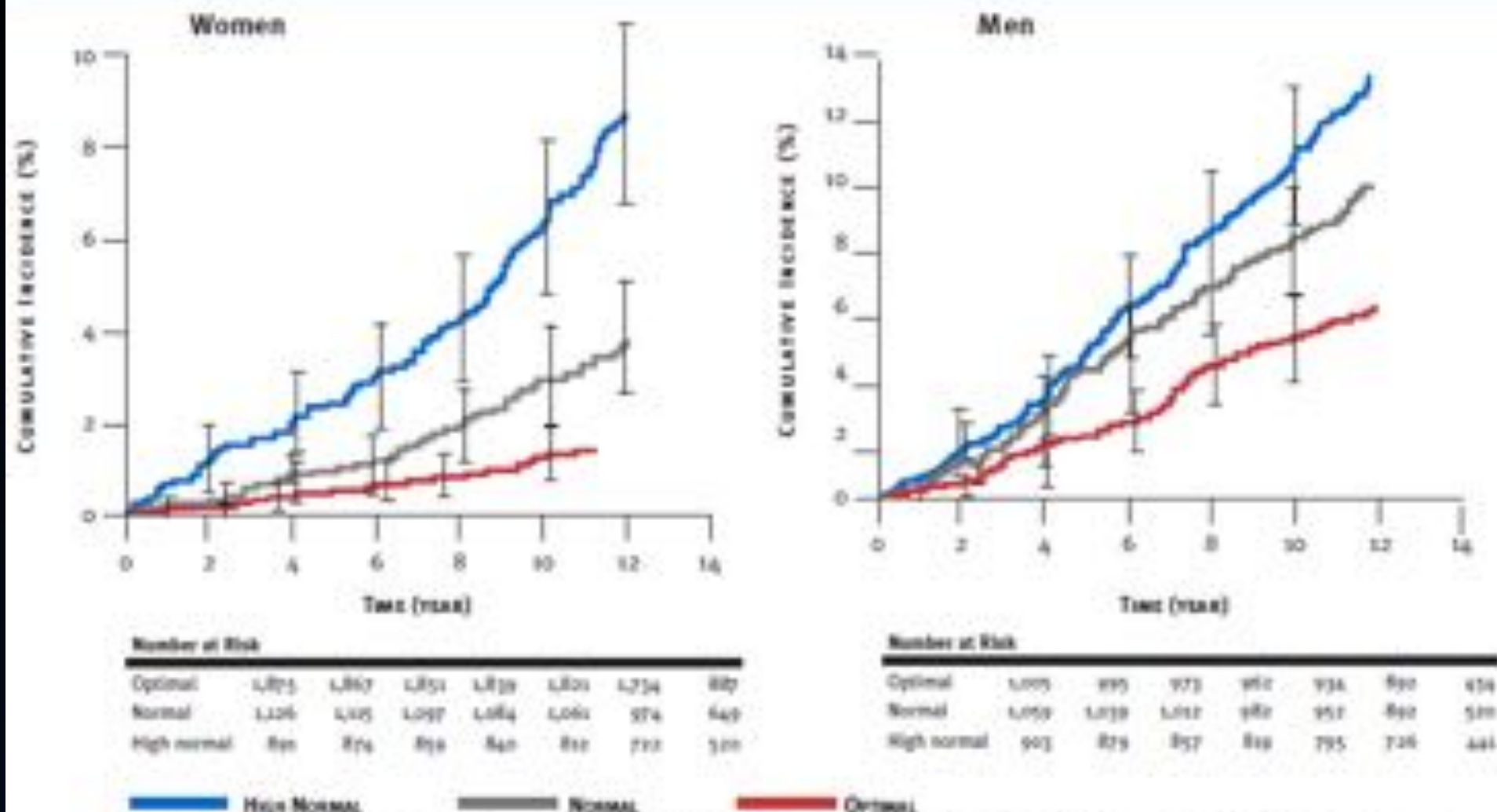


Figure 11. Impact of high normal blood pressure on the risk of cardiovascular disease

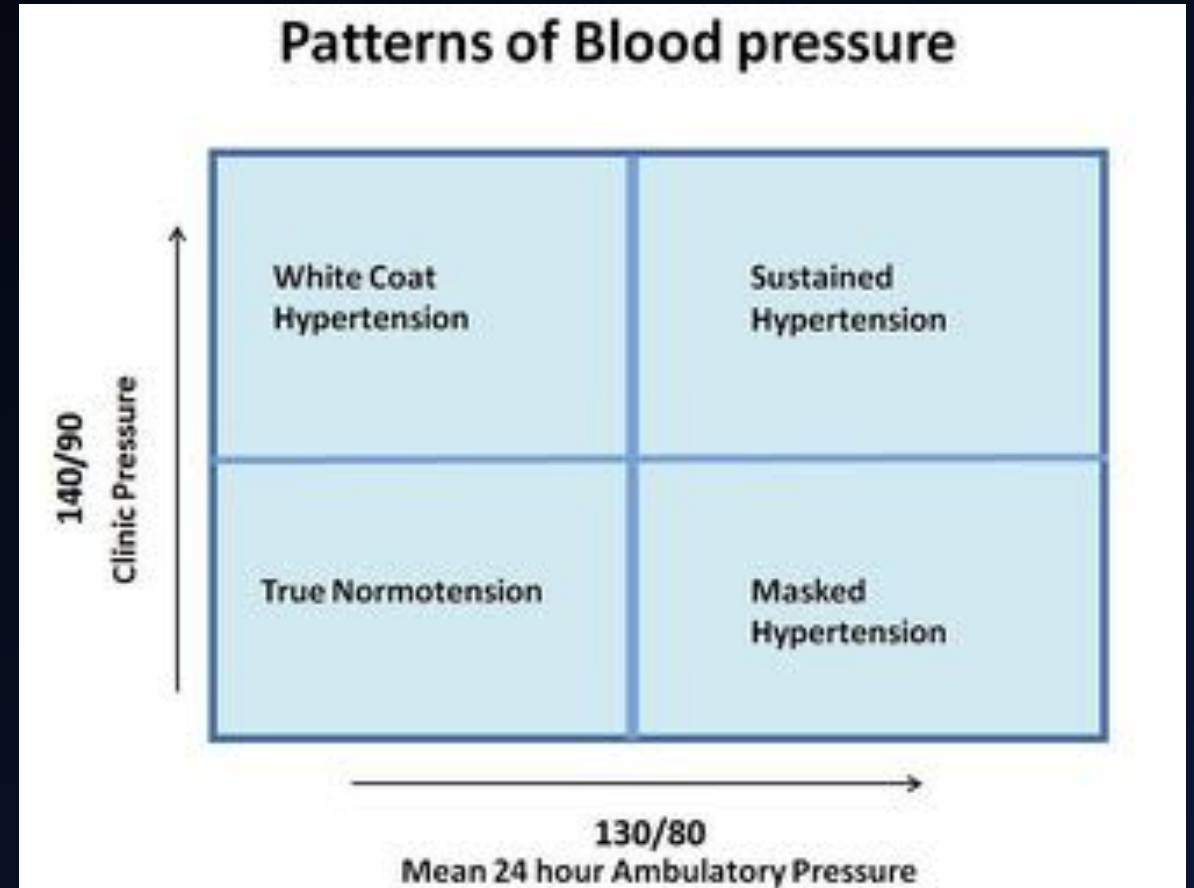


Cumulative incidence of cardiovascular events in women (panel A) and men (panel B) without hypertension, according to blood pressure category at the base-line examination. Vertical bars indicate 95 percent confidence intervals. Optimal BP is defined here as a systolic pressure of <120 mmHg and a diastolic pressure of <80 mmHg. Normal BP is a systolic pressure of 120-129 mmHg or a diastolic pressure of 80-84 mmHg. High-normal BP is a systolic pressure of 130-139 mmHg or a diastolic pressure of 85-89 mmHg. If the systolic and diastolic pressure readings for a subject were in different categories, the higher of the two categories was used.

Source: Vasan RS, et al. Impact of high-normal blood pressure on risk of cardiovascular disease. *N Engl J Med* 2001;345:1297-7. Copyright 2001, Massachusetts Medical Society. All rights reserved.

Hypertension definitions

- Prehypertension
- Hypertension
 - Stages
 - Urgency
 - Emergency
- White Coat syndrome
- Masked Hypertension



Criteria for HTN diagnosis

Table 3

Thresholds values for office, home and ambulatory blood pressure measurement

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

Ambulatory BP measurement

1.2.2 If blood pressure measured in the clinic is 140/90 mmHg or higher:

- Take a second measurement during the consultation.
- If the second measurement is substantially different from the first, take a third measurement.

Record the lower of the last two measurements as the clinic blood pressure.
[2011]

1.2.3 If the clinic blood pressure is 140/90 mmHg or higher, offer ambulatory blood pressure monitoring (ABPM) to confirm the diagnosis of hypertension. [2011]

1.2.4 If a person is unable to tolerate ABPM, home blood pressure monitoring (HBPM) is a suitable alternative to confirm the diagnosis of hypertension. [2011]

Ambulatory BP measurement

Table 4.4 Recommendations on methods of blood pressure measurement

Methods of measuring blood pressure	Grade of recommendation	Level of evidence
a. If clinic blood pressure is $\geq 140/90$ mmHg, or hypertension is suspected, ambulatory and/or home monitoring should be offered to confirm the blood pressure level.	Strong	I
b. Clinic blood pressure measures are recommended for use in absolute CVD risk calculators. If home or ambulatory blood pressure measures are used in absolute CVD risk calculators, risk may be inappropriately underestimated.	Strong	–
c. Procedures for ambulatory blood pressure monitoring should be adequately explained to patients. Those undertaking home measurements require appropriate training under qualified supervision.	Strong	I
d. Finger and/or wrist blood pressure measuring devices are not recommended.	Strong	–

Ambulatory BP

Table 4.2 Clinical indications for out-of-clinic blood pressure measurements

Clinical indications for out-of-clinic blood pressure measurements

Suspicion of white-coat hypertension

Suspicion of masked hypertension

Identified white-coat hypertension

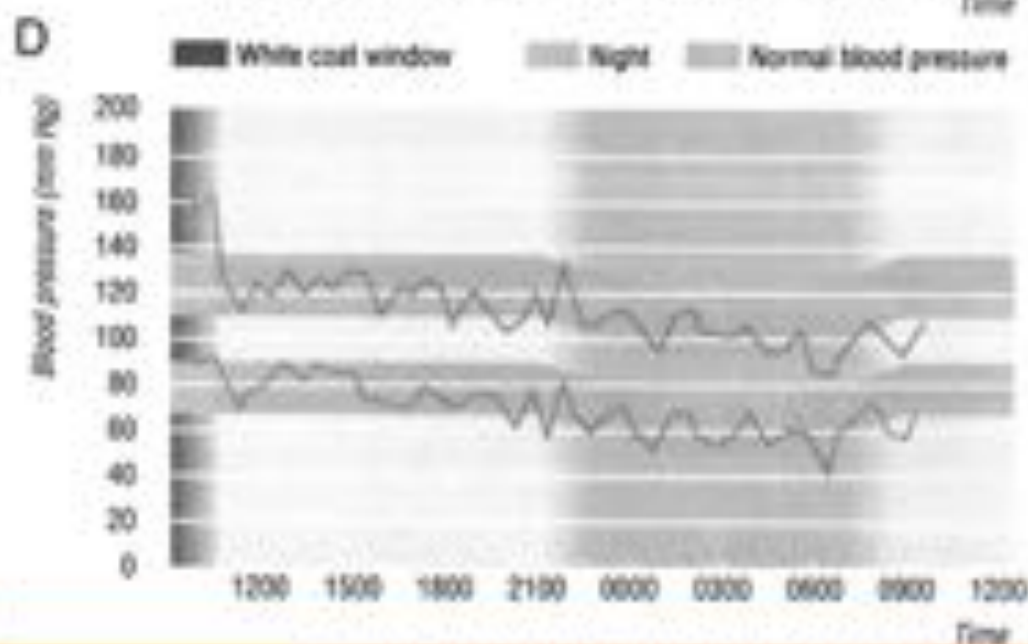
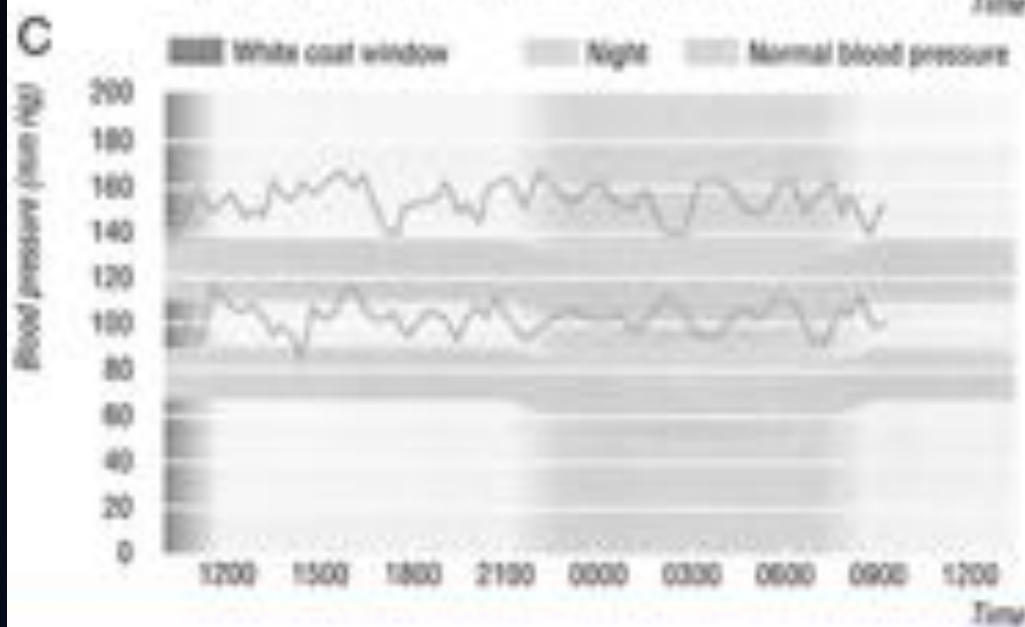
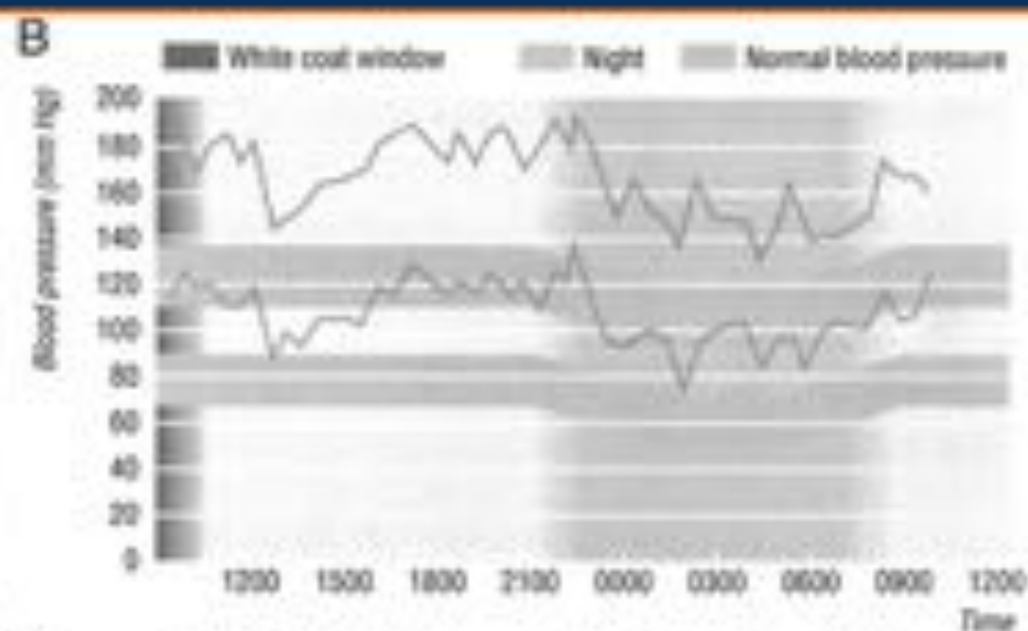
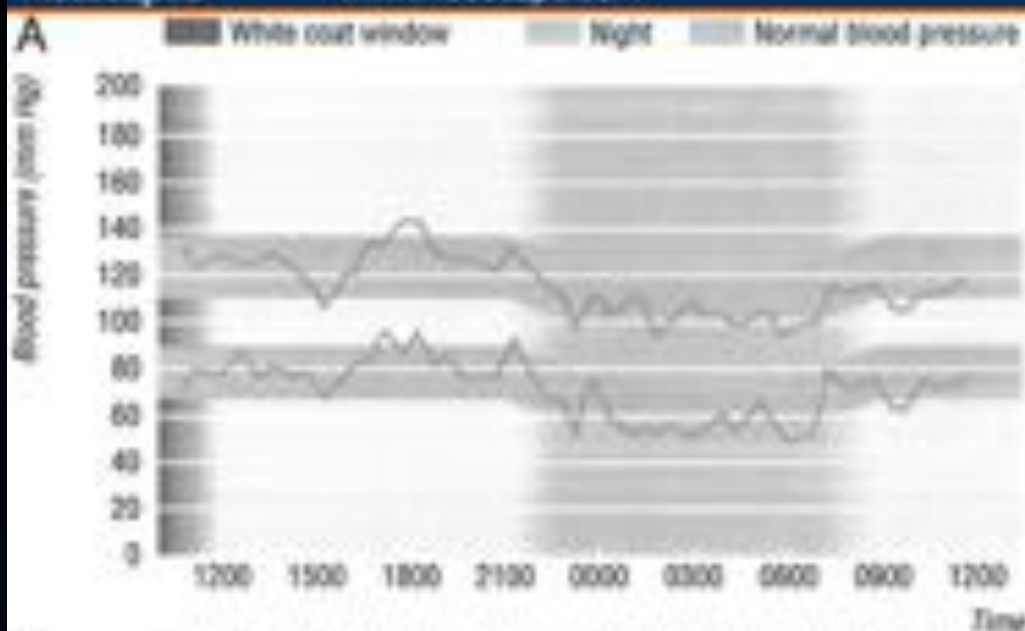
Marked variability of clinic or clinic and home blood pressure measurements

Autonomic, postural, post-prandial and drug-induced hypotension

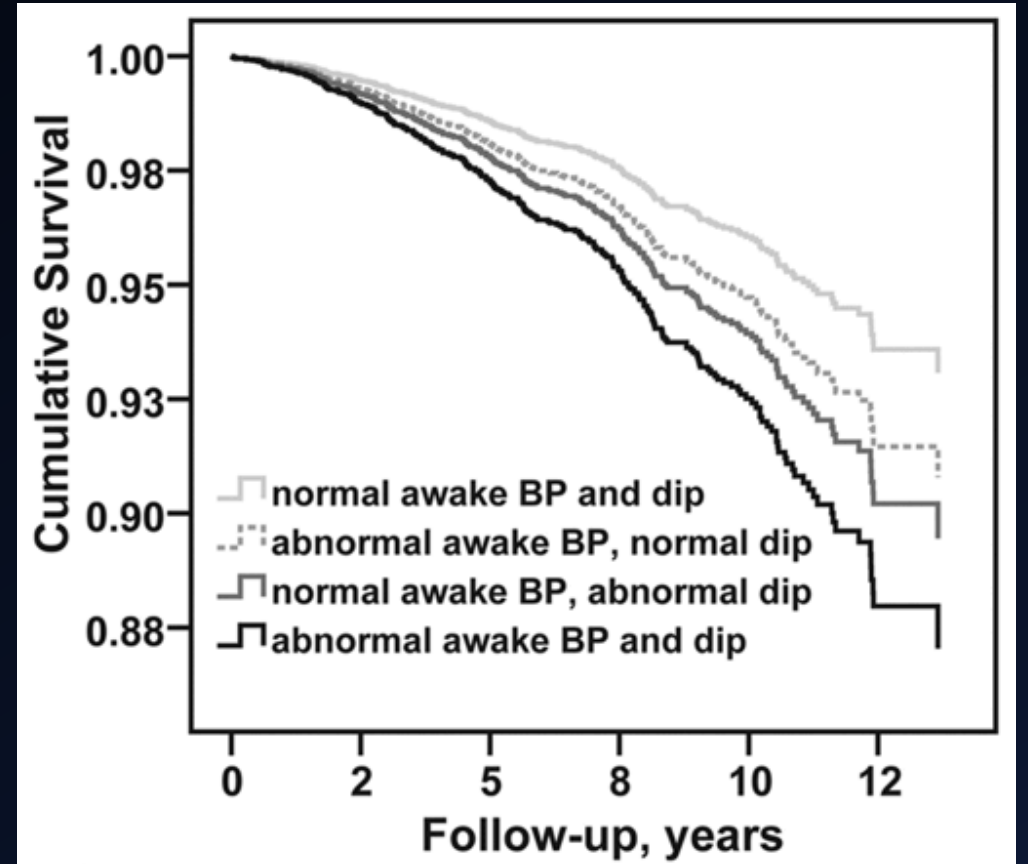
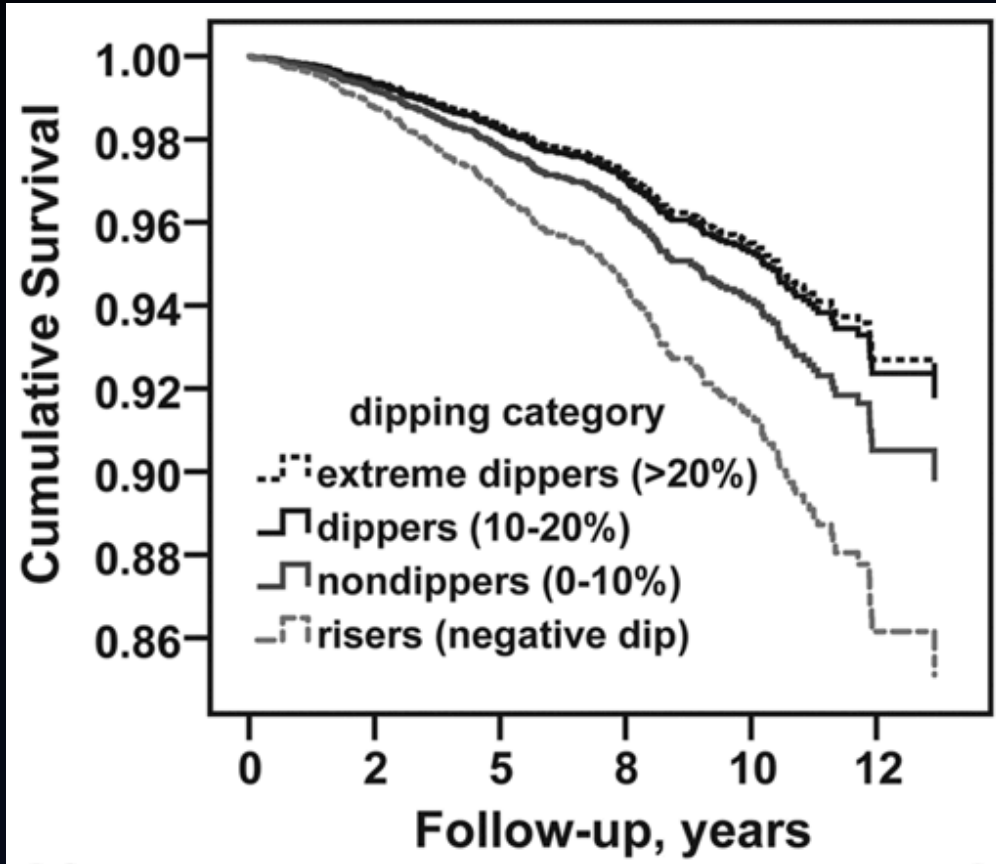
Identification of true resistant hypertension

Suspicion of nocturnal hypertension or absence of nocturnal dipping, for example in patients with sleep apnoea, chronic kidney disease or diabetes

Table adapted with permission from European Society of Hypertension guidelines²⁵ and Ambulatory blood pressure monitoring in Australia: 2011 consensus position statement.²³



Nocturnal Blood pressure

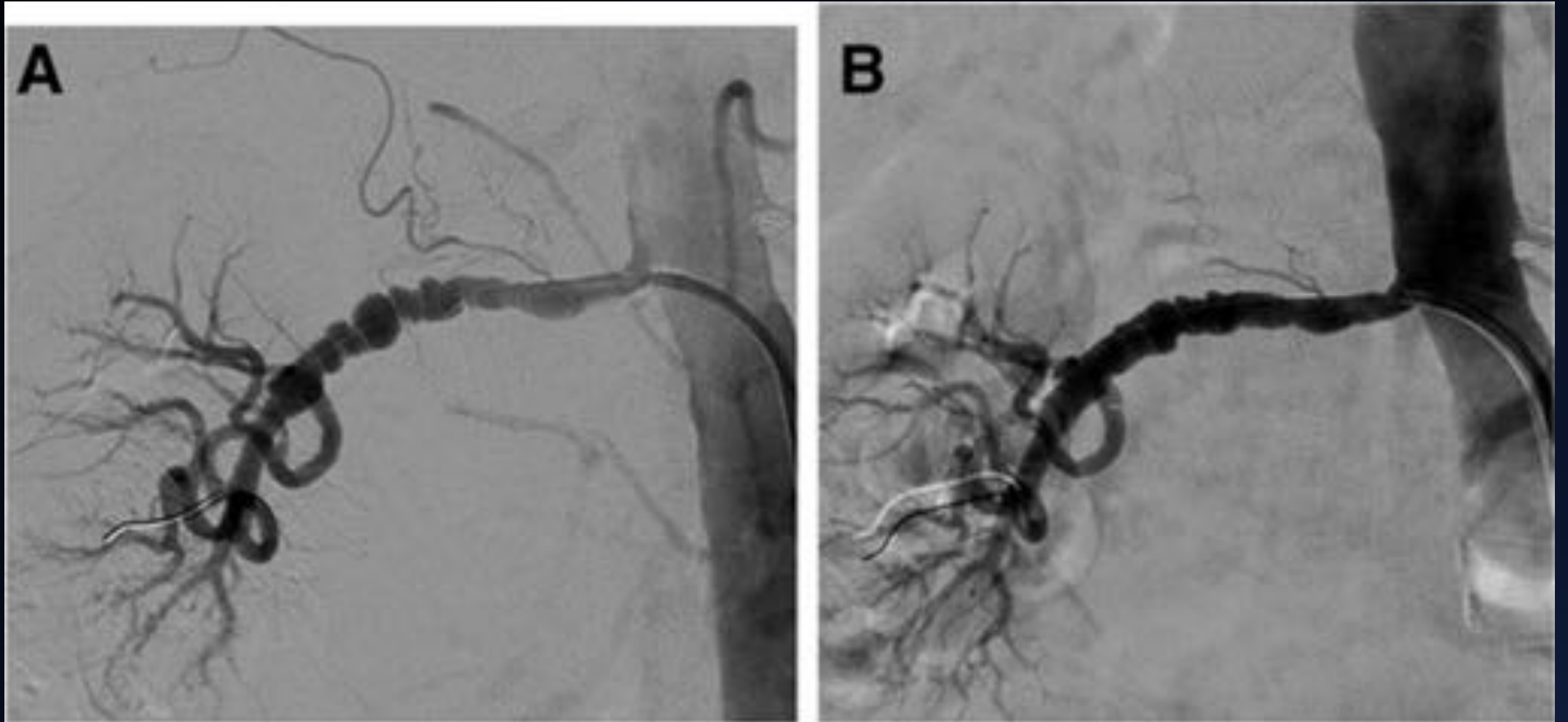


Secondary HTN

Table 1 Overview of the most common causes for secondary hypertension

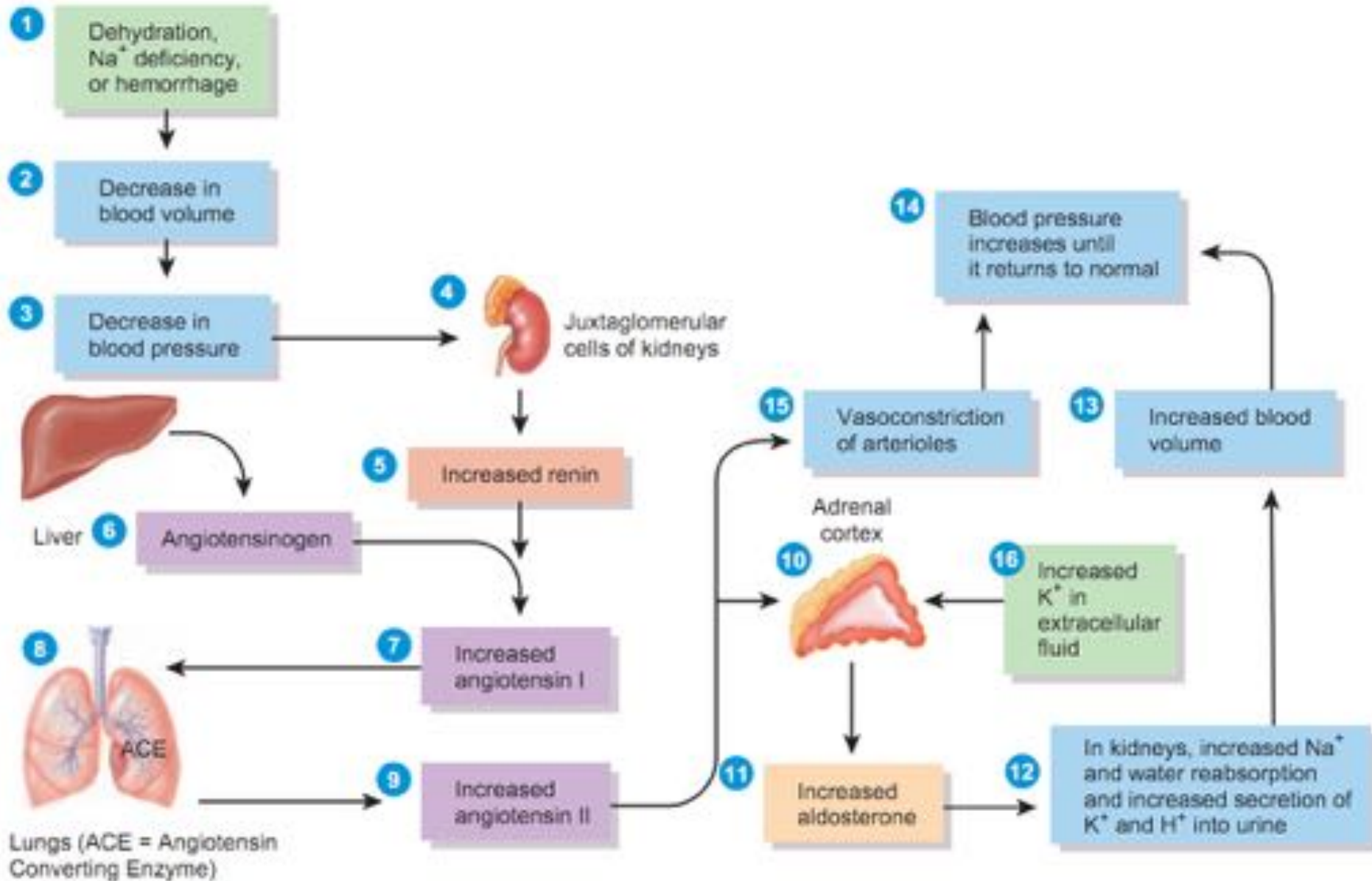
Secondary cause	Prevalence ^a	Prevalence ^b	History	Screening	Clinical findings	Laboratory findings
Obstructive sleep apnoea	>5–15%	>30%	Snoring, daytime sleepiness, morning headache, irritability	Screening questionnaire; polysomnography	↑ neck circumference; obesity; peripheral oedema	Not specific
Renal parenchymal disease	1.6–8.0%	2–10%	Loss of good BP-control; diabetes; smoking; generalized atherosclerosis; previous renal failure; nocturia	Creatinine, ultrasound of the kidney	Peripheral oedema; pallor; loss of muscle mass	↑ Creatinine, proteinuria; ↓ Ca ²⁺ , ↑ K ⁺ , ↑ PO ₄
Renal artery stenosis	1.0–8.0%	2.5–20%	Generalized atherosclerosis; diabetes; smoking; recurrent flush pulmonary oedema	Duplex, or CT, or MRI, or angiography (drive by)	Abdominal bruits; peripheral vascular disease;	Secondary aldosteronism: ARR →; ↓ K ⁺ ; ↓ Na ⁺
Primary aldosteronism	1.4–10%	6–23%	Fatigue; constipation; polyuria, polydipsia	Aldosterone–renin ratio (ARR)	Muscle weakness	↓ K ⁺ ; ARR ↑
Thyroid disease	1–2%	1–3%	Hyperthyroidism: palpitations, weight loss, anxiety, heat intolerance; Hypothyroidism: weight gain, fatigue, obstipation	TSH	Hyperthyroidism: tachycardia, AF; accentuated heart sounds; exophthalmus; Hypothyroidism: Bradycardia; muscle weakness; myxoedema	Hyperthyroidism: TSH ↓; FT4 and/or FT3 ↑; Hypothyroidism: TSH ↑; FT4 ↓; cholesterol ↑
Cushing's Syndrome	0.5%	<1.0%	Weight gain; impotence; fatigue; psychological changes; polydipsia and polyuria	24 h urinary cortisol; dexamethasone testing	Obesity, hirsutism, skin atrophy, Striae rubrae, muscle weakness, osteopenia	24 h urinary: cortisol ↑; Glucose ↑; Cholesterol ↑; K ⁺ ↓
Pheochromocytoma	0.2–0.5%	<1%	Headache; palpitations; flushing; anxiety	Plasma-metanephrines; 24 h urinary catecholamine	The 5 P's ^c : paroxysmal hypertension; pounding headache; perspiration; palpitations; pallor	metanephrines ↑
Coarctation of the aorta	<1%	<1%	Headache; nose bleeding; leg weakness or claudicatio	Cardiac ultrasound	Different BP (≥20/10 mmHg) between upper–lower extremities and/or between right–left arm; ↓ and delayed femoral pulsations; interscapular ejection murmur; rib notching on chest Rx	Not specific

This is not her image



Regulation of aldosterone secretion by the renin–angiotensin–aldosterone (RAA) pathway.

Aldosterone helps regulate blood volume, blood pressure, and levels of Na^+ , K^+ , and H^+ in the blood.



Case 1

- 35 F, BP 149/98 mmHg, FHx father, brother. No significant PMHx
- Labs: CBC normal, Urea 4, Cr 56, Na 143, K 3.1, Cl 89, HCO₃ 30
- LFT Normal, TSH Normal
- US Kidneys: R kidney 11.2 cm, L kidney 12 cm, Dopplers Normal renal artery flow

ARR

Table 2. Conditions That May Affect the Aldosterone-Renin Ratio (ARR)^a

Condition	Effect on PAC	Effect on PRA	Overall Effect on the ARR
Hypokalemia	Decreased	May be increased	Decreased
Potassium loading	Increased	May be decreased	Increased
Sodium restriction	Increased	Increased	Increased
Sodium loading	Decreased	Decreased	Decreased
Advanced age	Decreased	Decreased	Decreased
Renal impairment	Unchanged	Decreased	Increased
Pregnancy	Increased	Increased	Decreased
Luteal phase of menstrual cycle	Increased	Unchanged	Increased

ARR

Table. Impact of Medications on the Aldosterone/Renin Ratio (ARR)¹

False-positive ARR	False-negative ARR
β -Adrenergic blockers	Potassium-wasting or -sparing diuretics
Central α 2 agonists (eg, clonidine, α -methyldopa)	ACE inhibitors
NSAIDs	Angiotensin II type 1 receptor blockers
Renin inhibitors	Calcium blockers (eg, dihydropyridine)

NSAIDs, nonsteroidal anti-inflammatory drugs; ACE, angiotensin-converting enzyme.

ARR results should be interpreted in light of the patient's age, sample collection conditions (eg, time of day, posture and length of time in that posture, sodium and potassium status, and medications being taken), as well as the patient's clinical history.

PA Confirmatory tests

- Try to inhibit Aldosterone (demonstrate that it is regulated)
 - Oral salt loading (1 g po od x3days)
 - NS infusion (500 ml)
 - Captopril challenge
 - Fludrocortisone + Na

PA testing

- Imaging
- Venous sampling

Case 1

- Results:
 - High Aldosterone
 - Low Renin
- CT Abdomen: No adenoma, normal adrenal glands
- 24-hour K excretion: high
- What to do next?

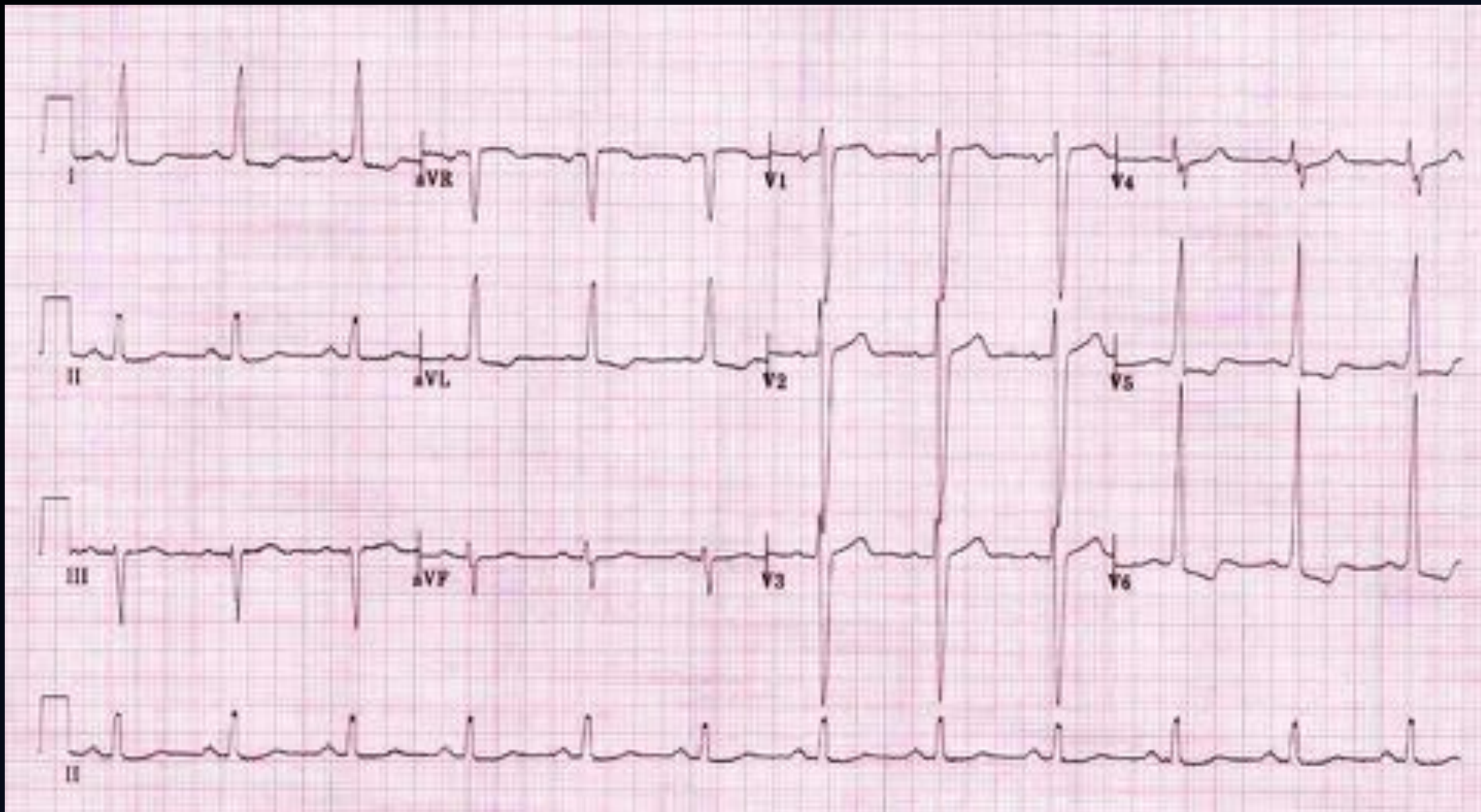
Case 2

- A 67-year-old man presents to the emergency department with headache. He has a history of uncontrolled hypertension as he is not compliant on medications.
- On physical examination: He is conscious, tired but oriented.
- BP is 230/120 mmHg, HR 89 bpm, O2 saturation is 95% on RA. CVS reveals S1+S2+S4, Chest is clear.
- Remaining exam is unremarkable.

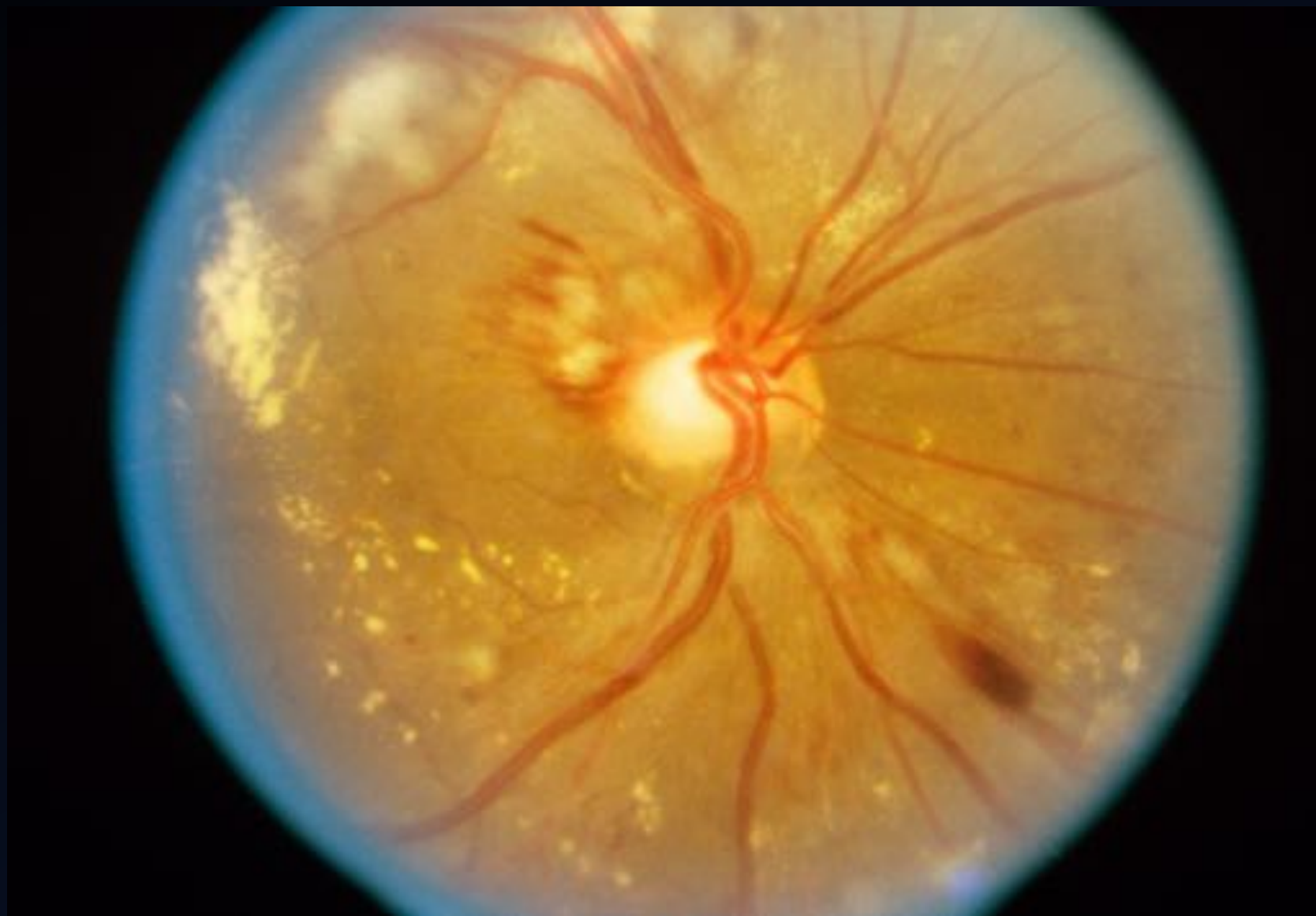
Case 2

- Which one of the following is the most appropriate next step in management?
 - A. ECG
 - B. Fundoscopy
 - C. Urinalysis
 - D. CT Scan of the head
 - E. None of the above
 - F. All the above

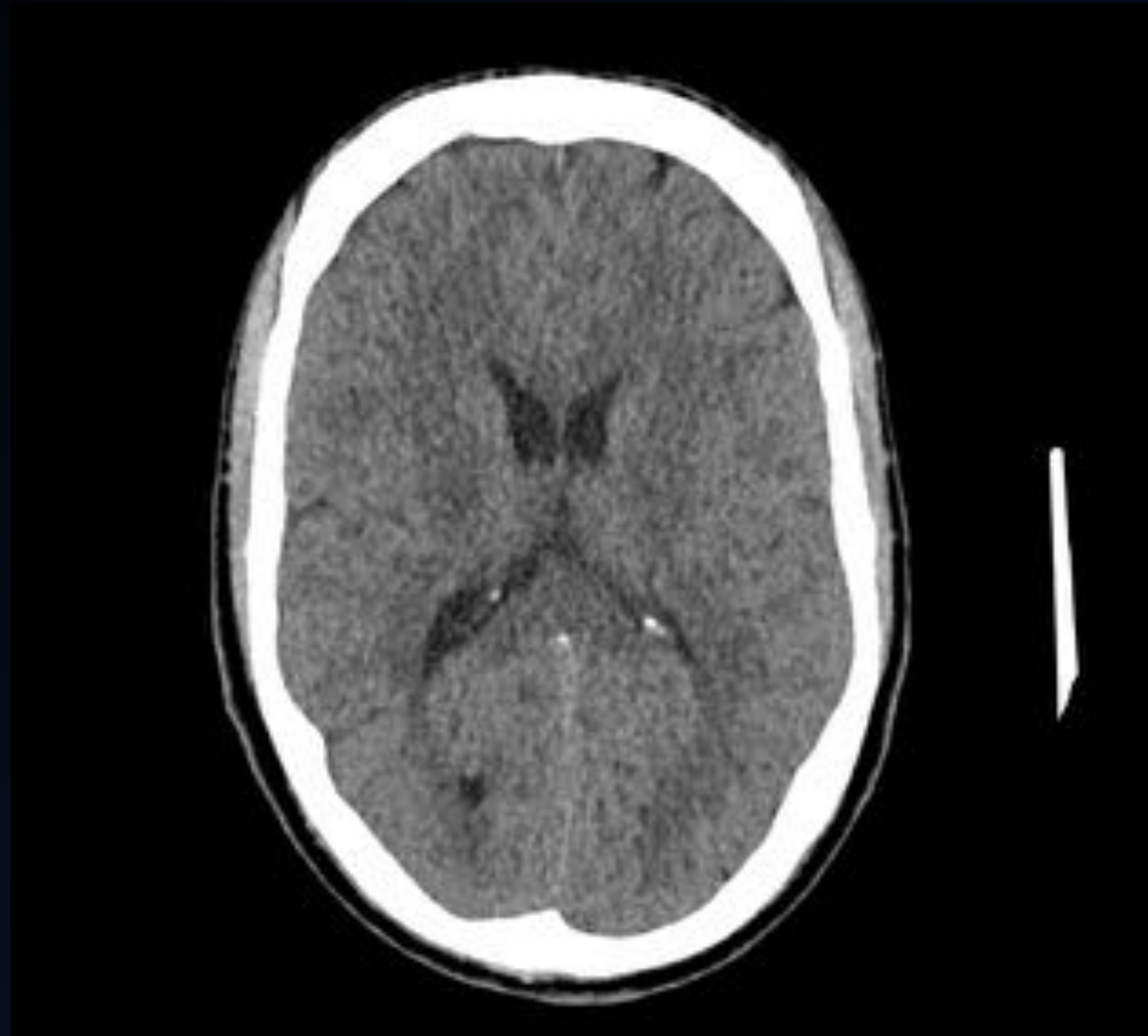
Case 2 - ECG



Case 2 - Fundoscopy



Case 2 – CT Scan - Brain



Hypertensive Crisis

	Definition	BP values
Hypertensive Emergencies	Severe and acute elevation of blood pressure associated to a new onset or worsening organ damage*	SBP>180 mmHg and/or DBP>120 mmHg
Hypertensive Urgencies	Elevation of blood pressure values without clinical, laboratory or instrumental evidence of acute hypertensive organ damage*	

* Organ damage: hypertensive encephalopathy, acute stroke, intracranial hemorrhage, acute coronary syndromes, pulmonary edema, aortic dissection, acute or rapidly progressing renal failure, sympathetic crises (i.e. cocaine toxicity/pheochromocytoma), eclampsia or severe pre-eclampsia

Which one of the following treatments is given for Hypertensive Emergencies

- A. Metoprolol IV infusion
- B. Labetalol IV infusion
- C. Nifedipine IV infusion

Drugs for hypertensive emergencies and urgencies

Agent	Action	Dosage	Onset	Duration	Adverse Effects	Comments
Hypertensive Emergencies						
Nicardipine (Cardene)	Calcium channel blocker	5 mg/h intravenously; may increase by 1-2.5 mg/h every 15 minutes to 15 mg/h	1-5 minutes	3-6 hours	Hypotension, tachycardia, headache.	May precipitate myocardial ischemia.
Clevidipine (Cleviprex)	Calcium channel blocker	1-2 mg/h intravenously initially; double rate every 90 seconds until near goal, then by smaller amounts every 5-10 minutes to a maximum of 32 mg/h	2-4 minutes	5-15 minutes	Headache, nausea, vomiting.	Lipid emulsion; contraindicated in patients with allergy to soy or egg.
Labetalol (Trandate)	Beta- and alpha-blocker	20-40 mg intravenously every 10 minutes to 300 mg; 2 mg/min infusion	5-10 minutes	1-6 hours	GI, hypotension, bronchospasm, bradycardia, heart block.	Avoid in acute LV systolic dysfunction, asthma. May be continued orally.
Esmolol (Brevibloc)	Beta-blocker	Loading dose 500 mcg/kg intravenously over 1 minute; maintenance, 25-200 mcg/kg/min	1-2 minutes	10-30 minutes	Bradycardia, nausea.	Avoid in acute LV systolic dysfunction, asthma. Weak antihypertensive.
Fenoldopam (Corlopam)	Dopamine receptor agonist	0.1-1.6 mcg/kg/min intravenously	4-5 minutes	< 10 minutes	Reflex tachycardia, hypotension, increased intraocular pressure.	May protect kidney function.
Enalaprilat (Vasotec)	ACE inhibitor	1.25 mg intravenously every 6 hours	15 minutes	6 hours or more	Excessive hypotension.	Additive with diuretics; may be continued orally.
Furosemide (Lasix)	Diuretic	10-80 mg orally	15 minutes	4 hours	Hypokalemia, hypotension.	Adjunct to vasodilator.
Hydralazine (Apresoline)	Vasodilator	5-20 mg intravenously; may repeat after 20 minutes	10-30 minutes	2-6 hours	Tachycardia, headache, GI.	Avoid in coronary artery disease, dissection. Rarely used except in pregnancy.
Nitroglycerin	Vasodilator	0.25-5 mcg/kg/min intravenously	2-5 minutes	3-5 minutes	Headache, nausea, hypotension, bradycardia.	Tolerance may develop. Useful primarily with myocardial ischemia.
Nitroprusside (Nitroprussil)	Vasodilator	0.25-10 mcg/kg/min intravenously	Seconds	3-5 minutes	GI, CNS; thiocyanate and cyanide toxicity, especially with renal and hepatic insufficiency; hypotension. Coronary steal, decreased cerebral blood flow, increased intracranial pressure.	No longer the first-line agent.
Hypertensive Urgencies						
Clonidine (Catapres)	Central sympatholytic	0.1-0.2 mg orally initially; then 0.1 mg every hour to 0.8 mg orally	30-60 minutes	6-8 hours	Sedation.	Rebound may occur.
Captopril (Capoten)	ACE inhibitor	12.5-25 mg orally	15-30 minutes	4-6 hours	Excessive hypotension.	
Nifedipine (Adalat, Procardia)	Calcium channel blocker	10 mg orally initially; may be repeated after 30 minutes	15 minutes	2-6 hours	Excessive hypotension, tachycardia, headache, angina, myocardial infarction, stroke.	Response unpredictable.

ACE, angiotensin-converting enzyme; CNS, central nervous system; GI, gastrointestinal; LV, left ventricular.

Source : Current Medical Diagnosis and Treatment 2018

Summary

General clinical clues

- Age, Habitus
- Resistant/severe hypertension
- Target organ damage



24h ABPM

- Exclude white coat hypertension
- Exclude pseudo-resistance
- Dipping status, heart rate



Exclude other factors

- Exclude drug-related hypertension
- Confirm therapy adherence



Screening for secondary forms

- Obstructive sleep apnoea
- Renal parenchymal/vascular disease
- Primary aldosteronism
- Other endocrine causes
- Aortic coarctatio

Summary

General clinical characteristics suggestive of secondary hypertension

Early onset of hypertension (i.e. <30 years) in patients without other risk factors (i.e. family history, obesity, etc.); increased BP in prepubertal children

Resistant hypertension (>140/90 mmHg despite three antihypertensive drugs including a diuretic)

Severe hypertension (>180/110 mmHg) or hypertensive emergencies

Sudden increase of BP in a previously stable patient

Non-dipping or reverse dipping during 24 h ambulatory BP monitoring

Presence of target organ damage (i.e. LVH, hypertensive retinopathy, etc.)
