

Hypertension Treatment



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Step 1 Facility and equipment	• Quiet room with a comfortable temperature. • Clinically validated BP measurement device; an automated device measuring BP at the brachial artery is recommended. • A range of cuff sizes to fit a range of upper-arm circumferences.
Step 2 Personnel performing BP measurement	• Trained healthcare professional should perform the BP measurement. Annual re-training is recommended.
Step 3 Prepare the patient	• The patient should be provided with instructions to abstain from caffeine, alcohol, nicotine, and exercise for at least 30 minutes prior to the BP measurement. • Eliminate discomfort such as a full bladder. • Prior to the BP measurement, there should be a short rest period (3–5 minutes) without provocation (including talking, or being talked to in-person or on the phone).
Step 4 The measurement procedure [see figure below]	• The healthcare professional should explain the procedure, including the number of BP measurements to be obtained. • Use the arm with the higher SBP readings during an initial visit, unless a new medical condition (e.g., arm ischemia) has developed in the interim in that arm. • ≥ 2 measurements should be obtained at least 30 seconds apart; the values should be averaged and recorded.

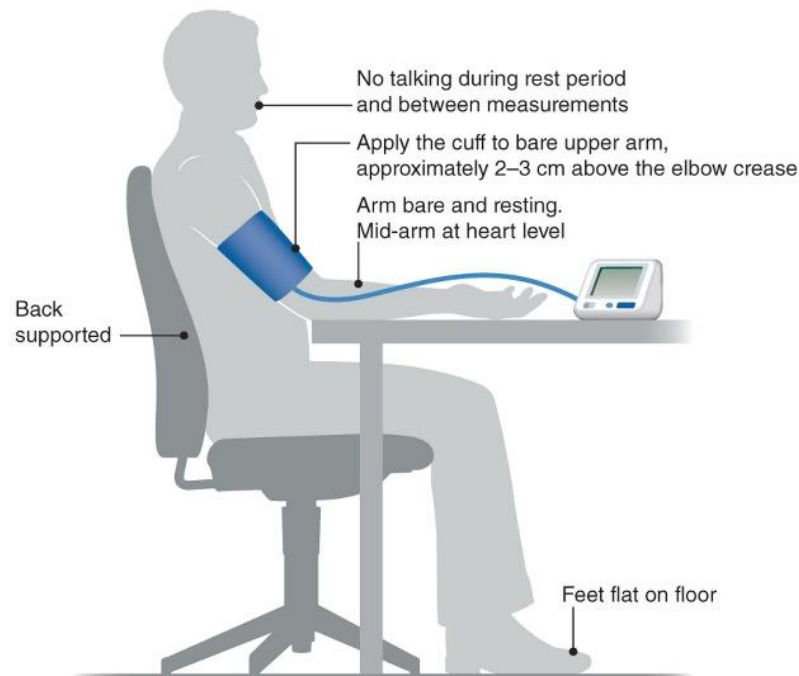


Figure 1

Pathophysiology of elevated blood pressure and hypertension

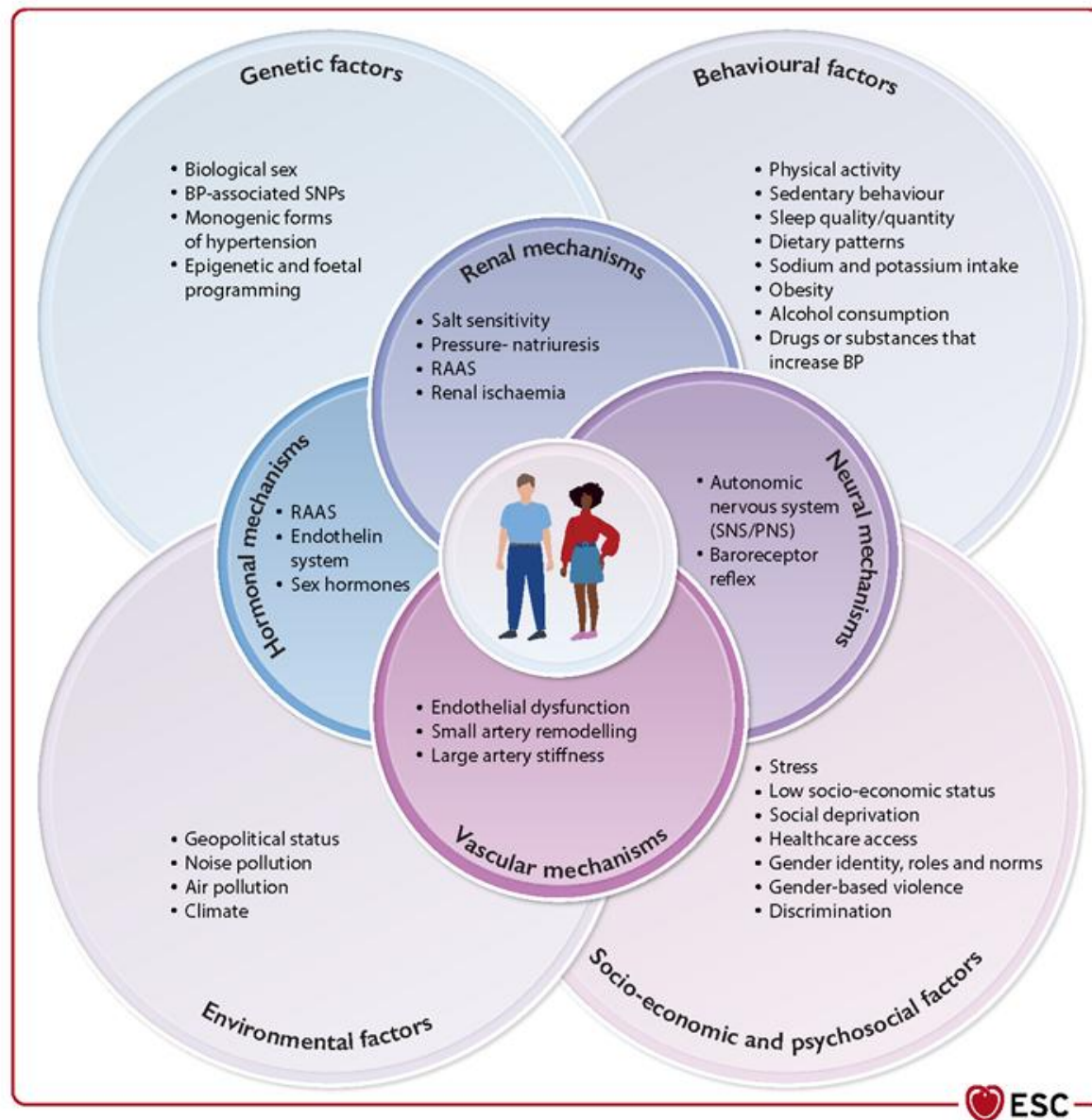


Figure 3

Summary of office blood pressure measurement

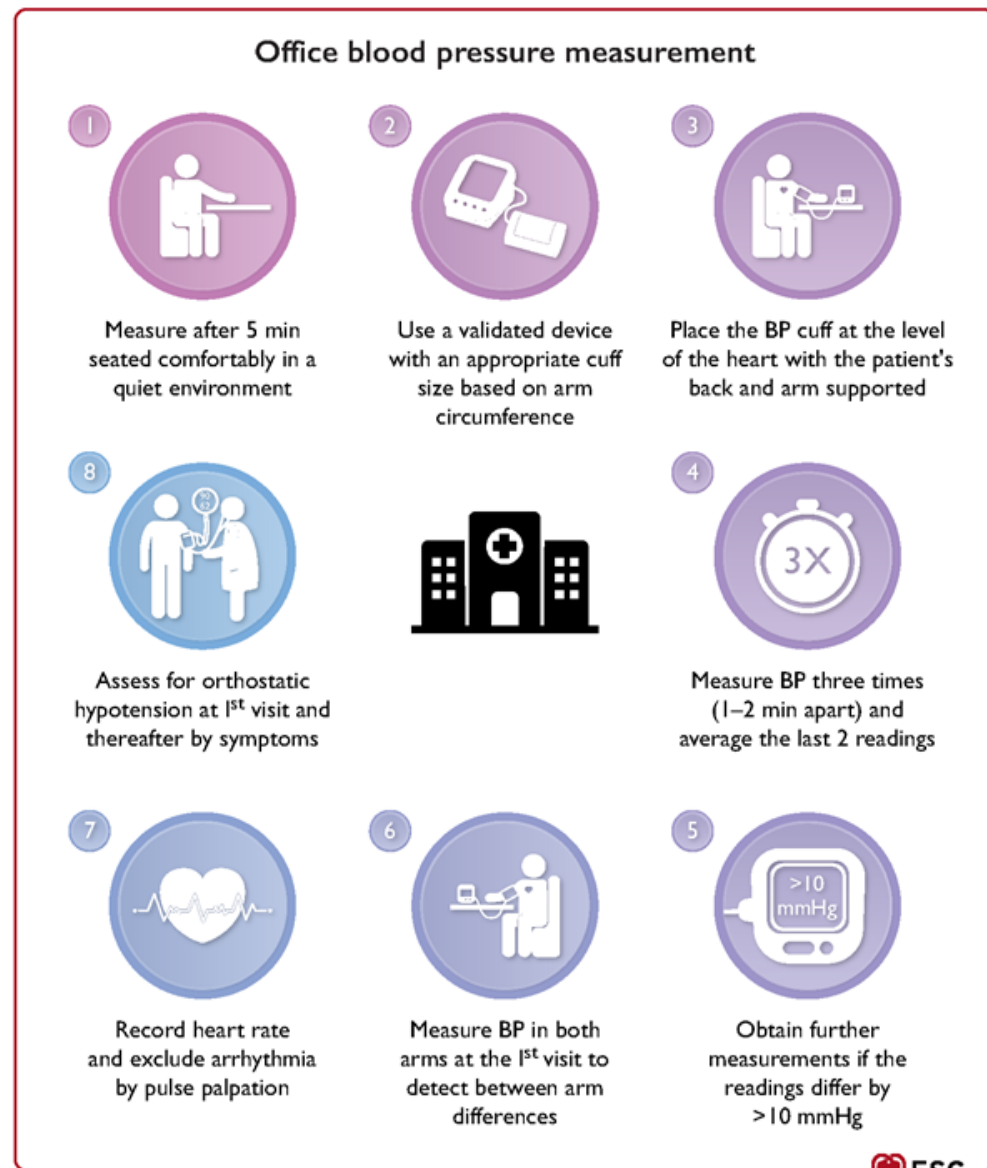


Figure 4

Summary of home blood pressure measurement



Figure 5

Summary of ambulatory blood pressure measurement

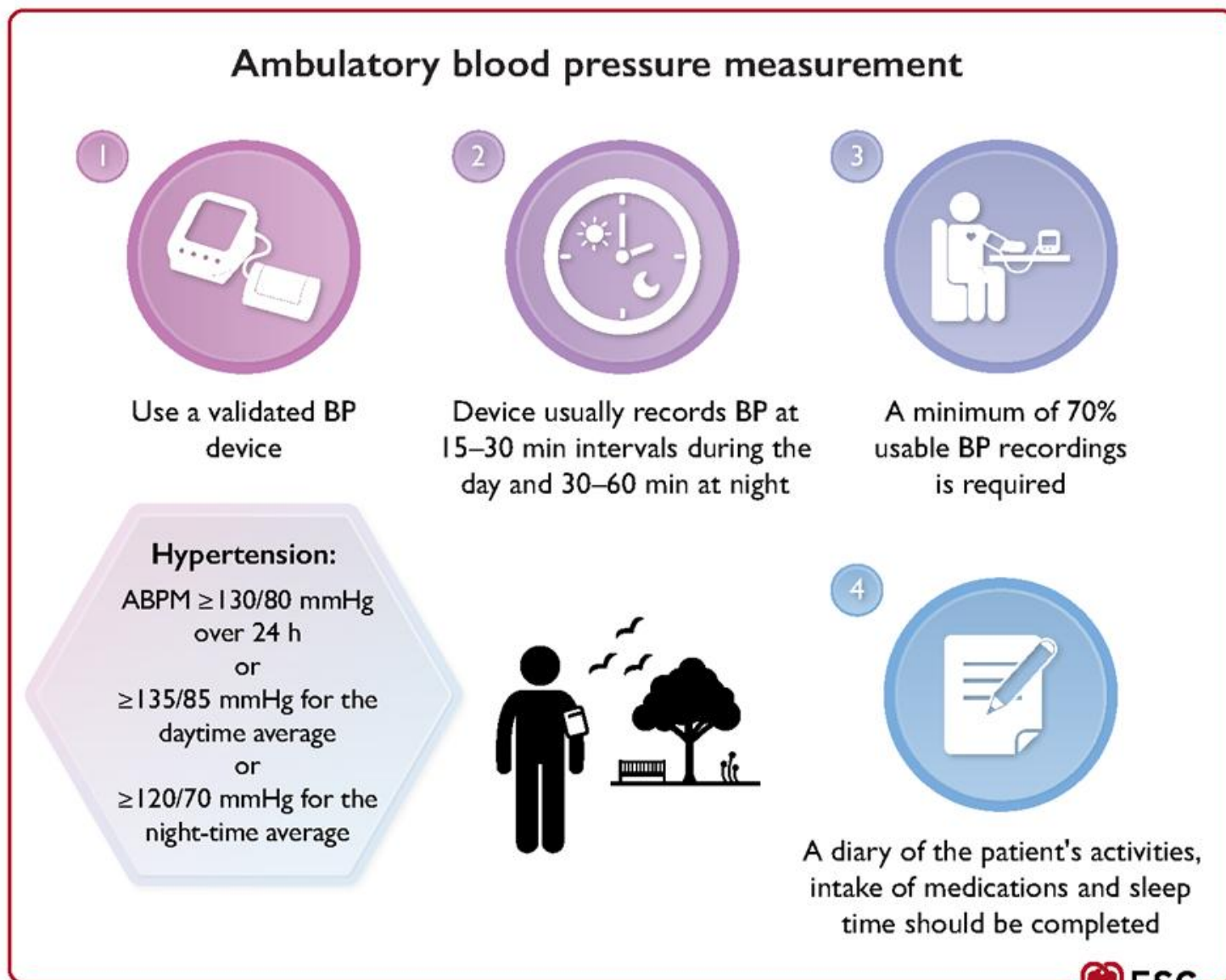


Figure 6

Blood pressure categories

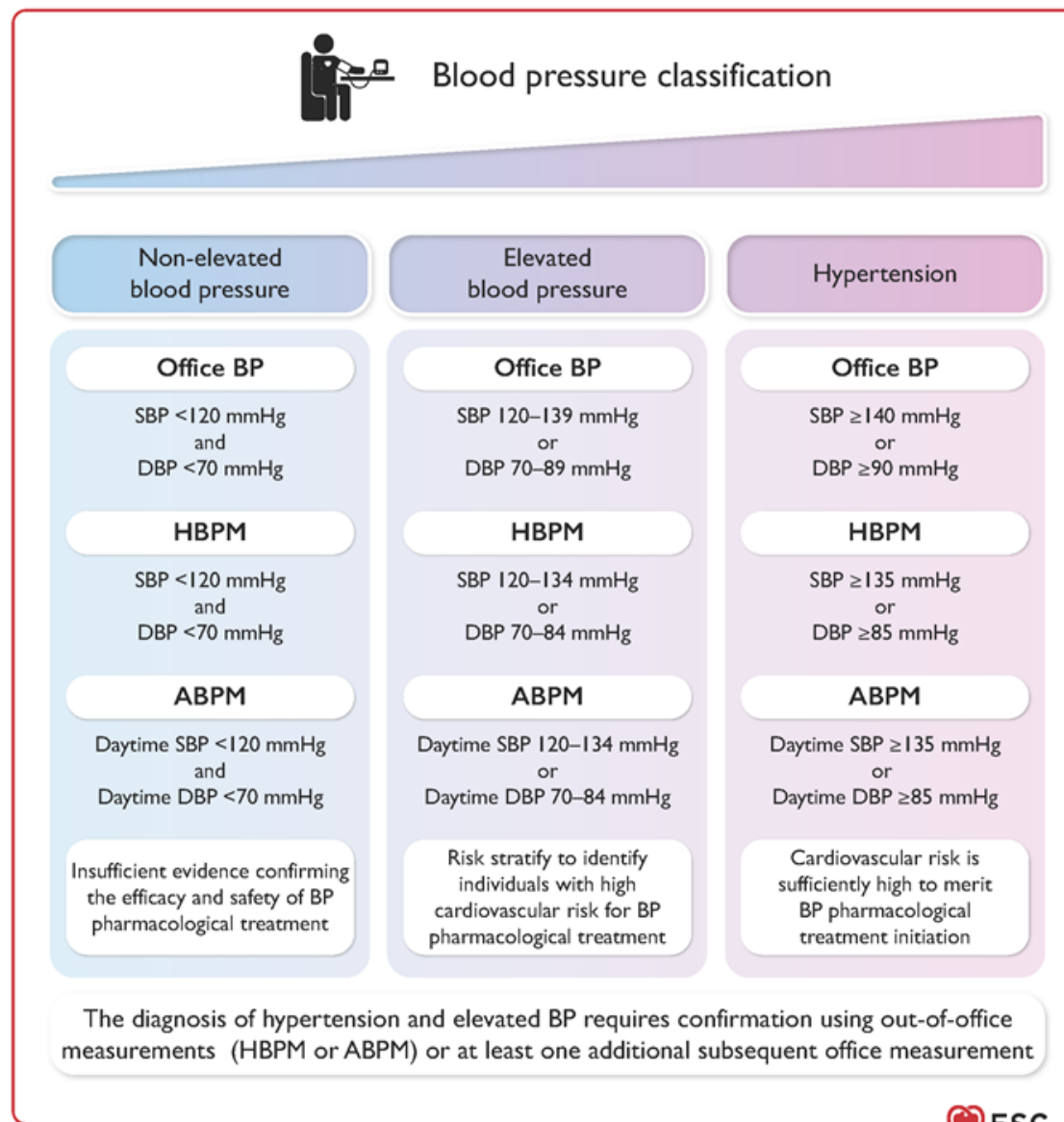


Table 5 Comparison of office, home, and ambulatory blood pressure measurement thresholds for elevated blood pressure and hypertension

	Office BP (mmHg) ^a	Home BP (mmHg)	Daytime ABPM (mmHg)	24 h ABPM (mmHg)	Night-time ABPM (mmHg)
Reference					
Non-elevated BP	<120/70	<120/70	<120/70	<115/65	<110/60
Elevated BP	120/70–<140/90	120/70–<135/85	120/70–<135/85	115/65–<130/80	110/60–<120/70
Hypertension	≥140/90	≥135/85	≥135/85	≥130/80	≥120/70

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Figure 10

Protocol for confirming hypertension diagnosis

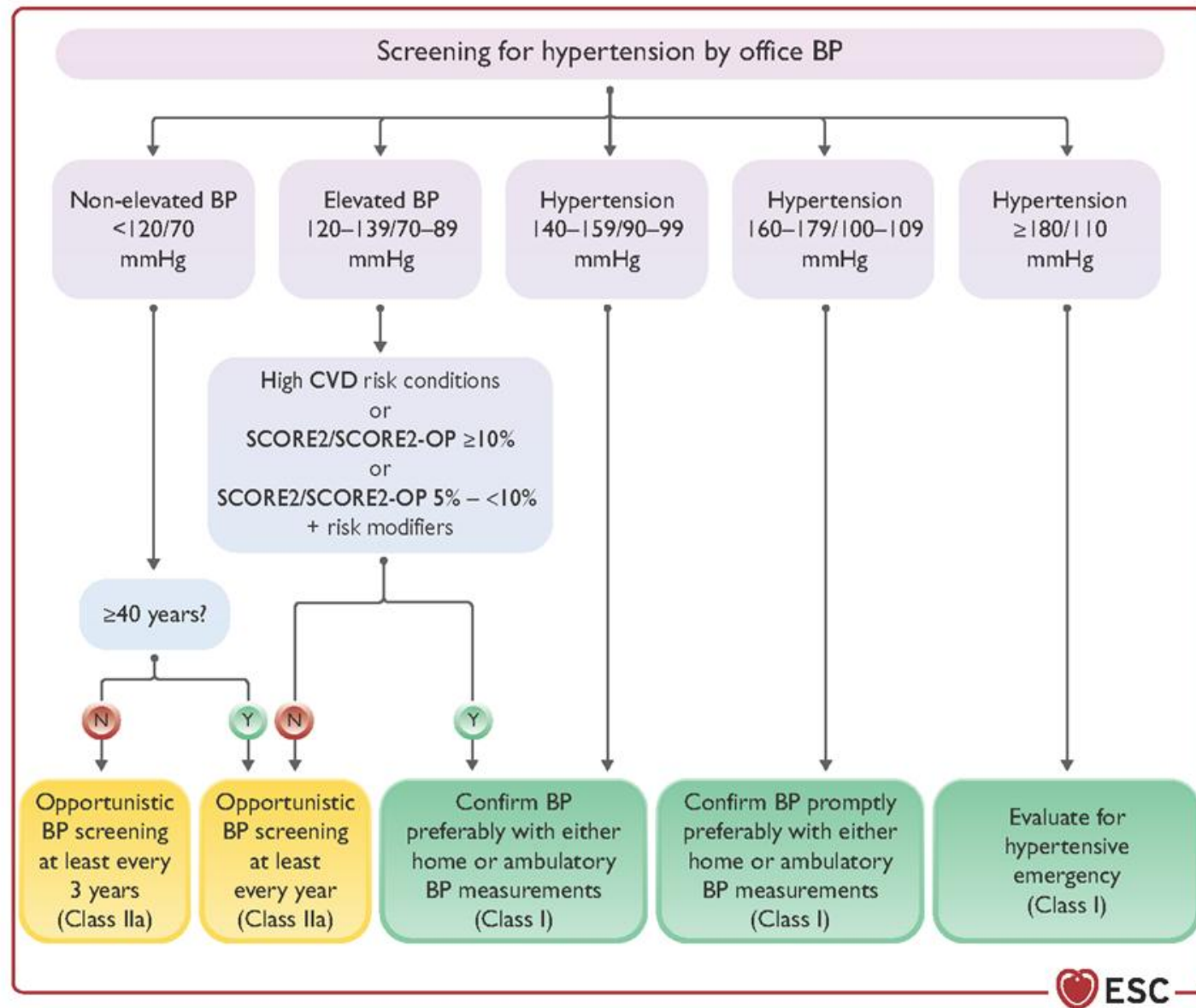


Table 8 Routine tests recommended in the initial work-up of a patient with elevated blood pressure or hypertension

Routine test	Clinical utility
Fasting blood glucose (and HbA1c if fasting blood glucose is elevated)	Assessing CVD risk and comorbidities
Serum lipids: total cholesterol, LDL cholesterol, HDL and non-HDL cholesterol, triglycerides	Assessing CVD risk
Blood sodium and potassium, haemoglobin and/or haematocrit, calcium, and TSH	Screening secondary hypertension (primary aldosteronism, Cushing's disease, polycythaemia, hyperparathyroidism, and hyperthyroidism)
Blood creatinine and eGFR; urinalysis and urinary albumin-to-creatinine ratio	Assessing CVD risk and HMOD Guiding treatment choice Screening secondary hypertension (renoparenchymal and renovascular)
12-lead ECG	Assessing HMOD (left atrial enlargement, left ventricular hypertrophy) Assessing irregular pulse and other comorbidities (AF, previous acute myocardial infarction)



Figure 2

Persistently elevated blood pressure and hypertension lead to hypertension-mediated organ damage and cardiovascular disease

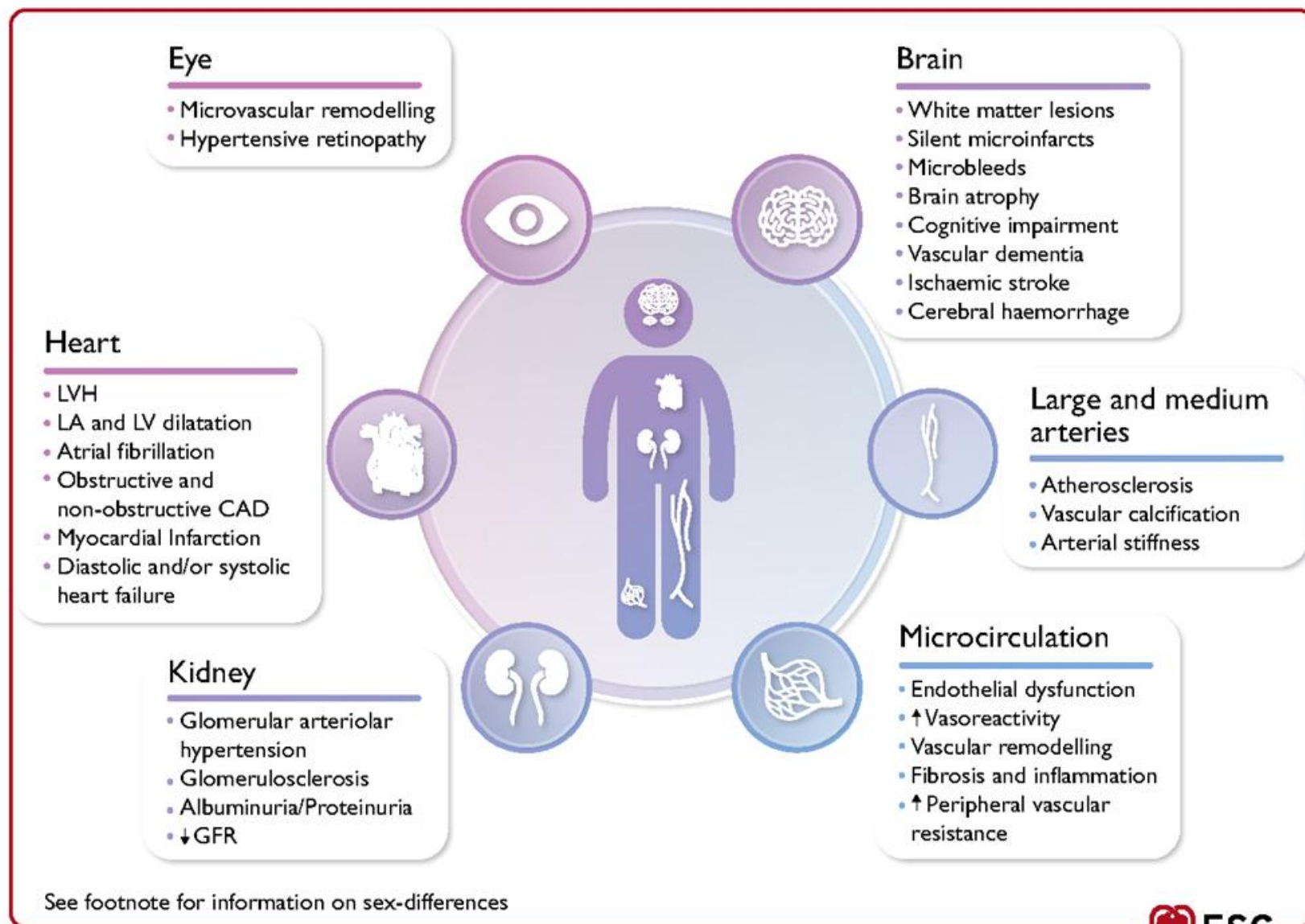


Figure 12

Tests and criteria for defining hypertension-mediated target organ damage and considerations for their use in clinical practice

Why measure?	Which organ?	What to measure?	How to diagnose HMOD?
 Support decision to start or intensify BP-lowering treatment for: - Individuals with elevated BP with SCORE2/SCORE2-OP risk of 5–<10% - Uncertain situations (i.e. BP or risk close to thresholds, masked or white-coat hypertension, non-traditional CVD risk factors) - Individuals <40 years old with elevated blood pressure - Assistance overcoming patient and physician inertia	Kidney	 eGFR ACR	Moderate-to-severe kidney disease - eGFR <60 mL/min/1.73 m² irrespective of albuminuria - Albuminuria ≥30 mg/g irrespective of eGFR
	Heart	ECG	LVH - Sokolow-Lyon: SV1+RV5 >35 mm - RaVL ≥11 mm - Cornell voltage: SV3+RaVL >28 mm (men) SV3+RaVL >20 mm (women)
		Echocardiography	LVH - LV mass/height^{2.7} (g/m^{2.7}): >50 (men) >47 (women) - LV mass/BSA (g/m²): >115 (men) >95 (women) - LV concentric geometry: RWT ≥0.43 Diastolic dysfunction - LA volume/height² (mL/m²): >18.5 (men) >16.5 (women) - LA volume index (mL/m²): 34 - e' <7cm; E/e' >14
		Cardiac biomarkers	- hs-cTnT or I >99th percentile upper reference limit - NT-proBNP >125 pg/mL if age <75 years or >450 pg/mL if ≥75 years
	Arteries	Carotid or femoral ultrasound	Plaque (focal wall thickening >1.5 mm)
		Pulse wave velocity	- Carotid-femoral PWV >10 m/s - Brachial-ankle PWV >14 m/s
		Cardiac CT	Coronary artery calcium score >100 Agatston units

Figure 16

Physical activity according to different types of exercise and reduction of blood pressure and overall CVD risk

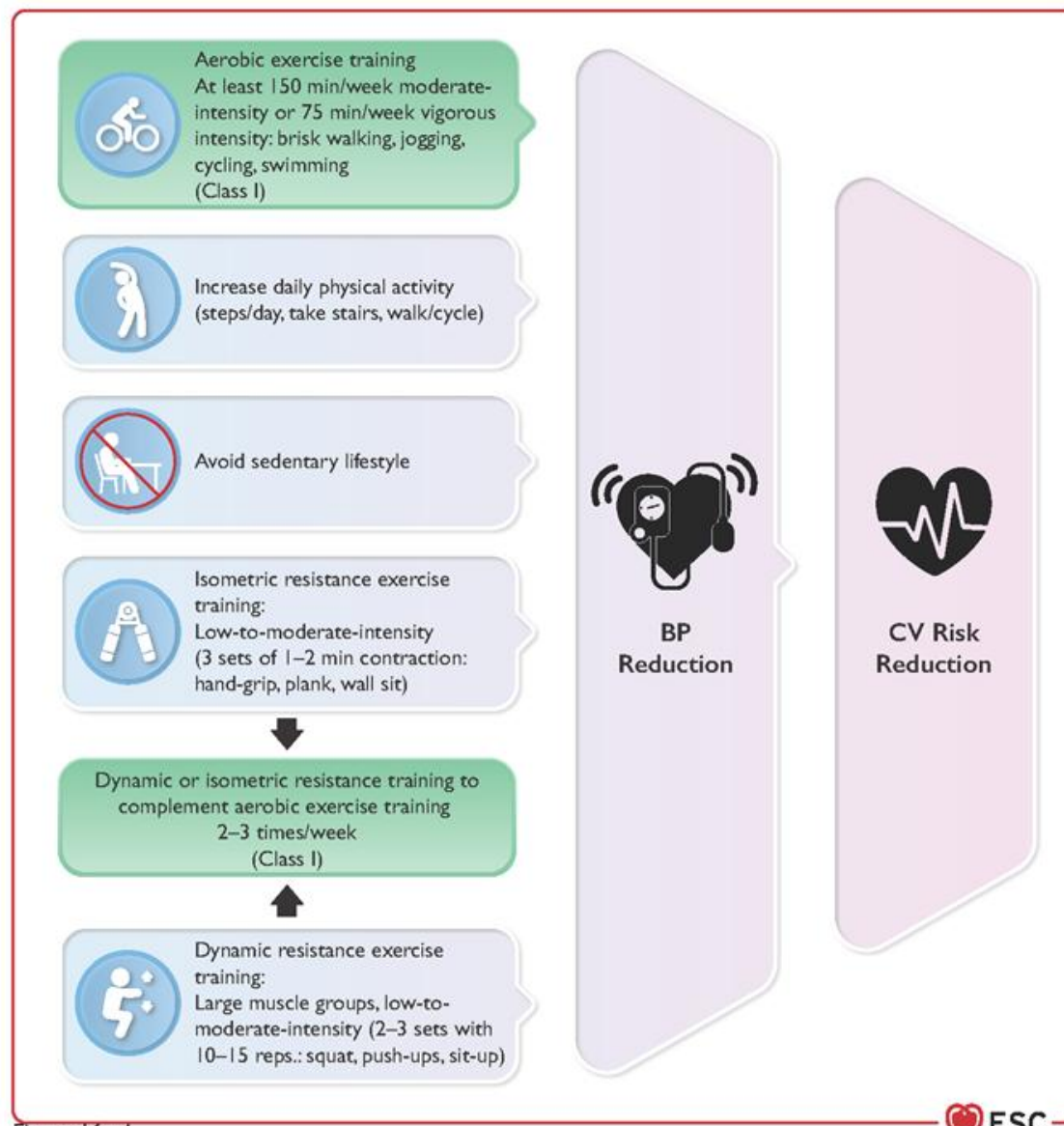
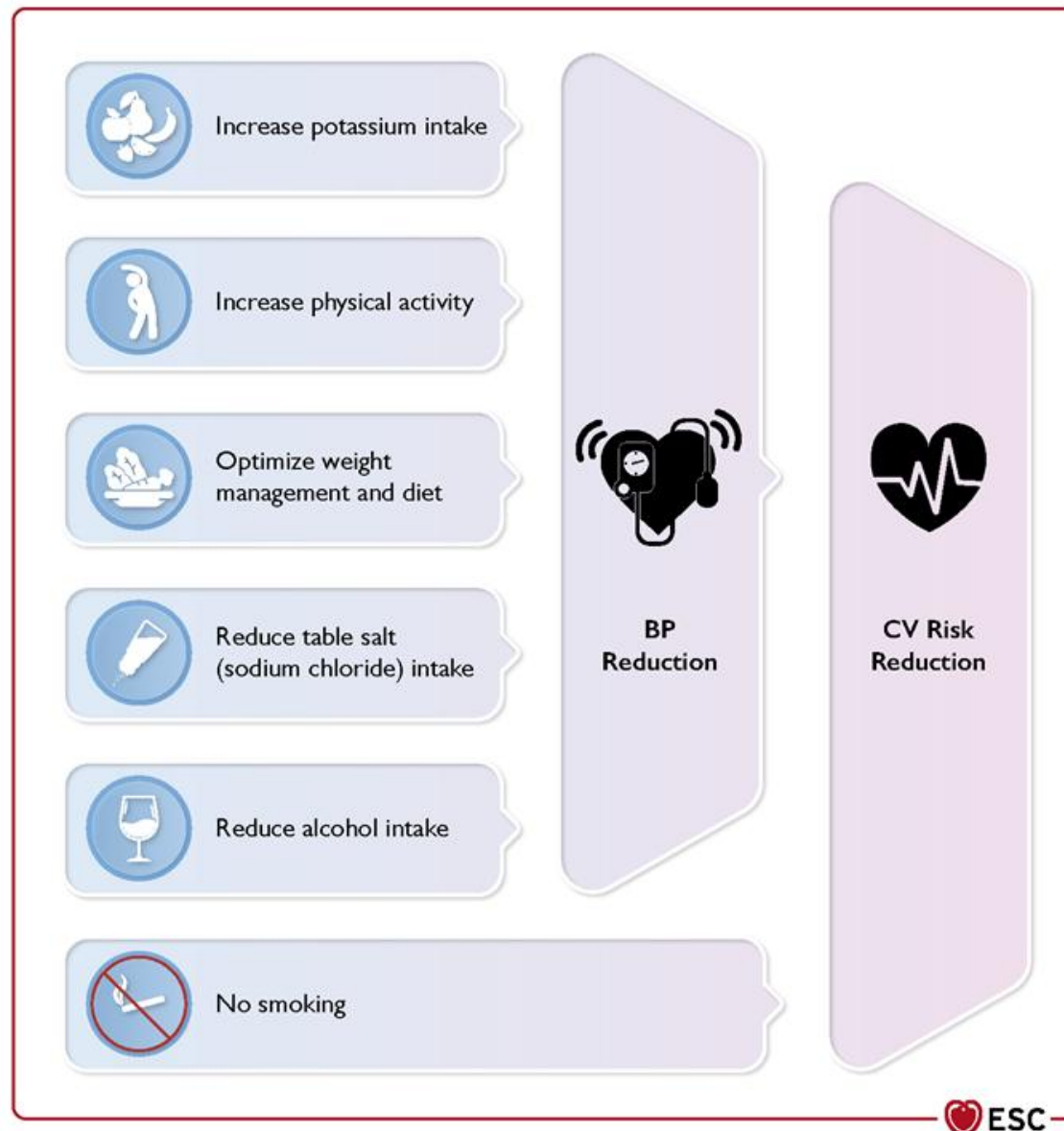


Figure 16 v4

Figure 17

Effects of main lifestyle factors on blood pressure and cardiovascular risk reduction



Lifestyle interventions

- Salt restriction to <5 g per day is recommended
- Recommended to restrict alcohol consumption
- Increased consumption of vegetables, fresh fruits, fish, nuts, and unsaturated fatty acids (olive oil); low consumption of red meat; and consumption of low-fat dairy products are recommended



- Body-weight control is indicated to avoid obesity
- Regular aerobic exercise (e.g. at least 30 min of moderate dynamic exercise on 5-7 days per week) is recommended
- Smoking cessation, supportive care, and referral to smoking cessation programs are recommended



Figure 18

Practical algorithm for pharmacological blood pressure lowering

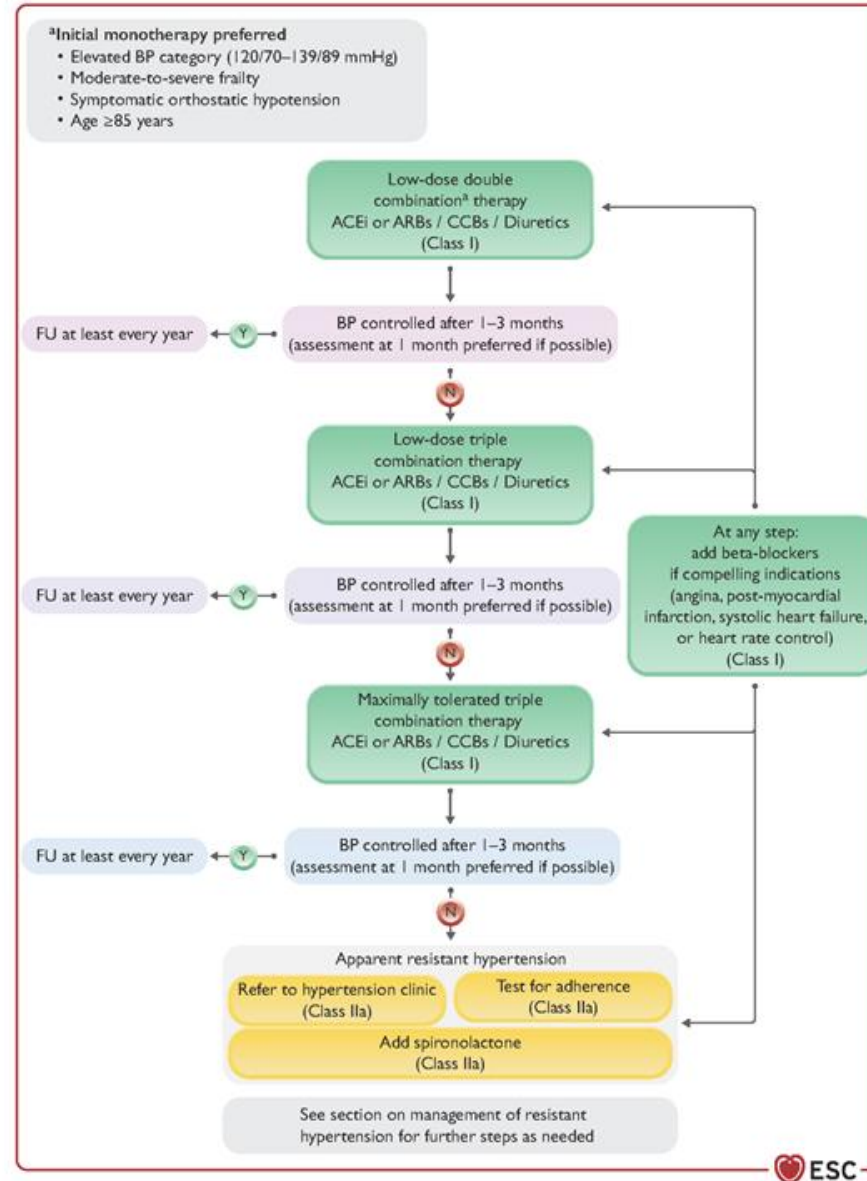
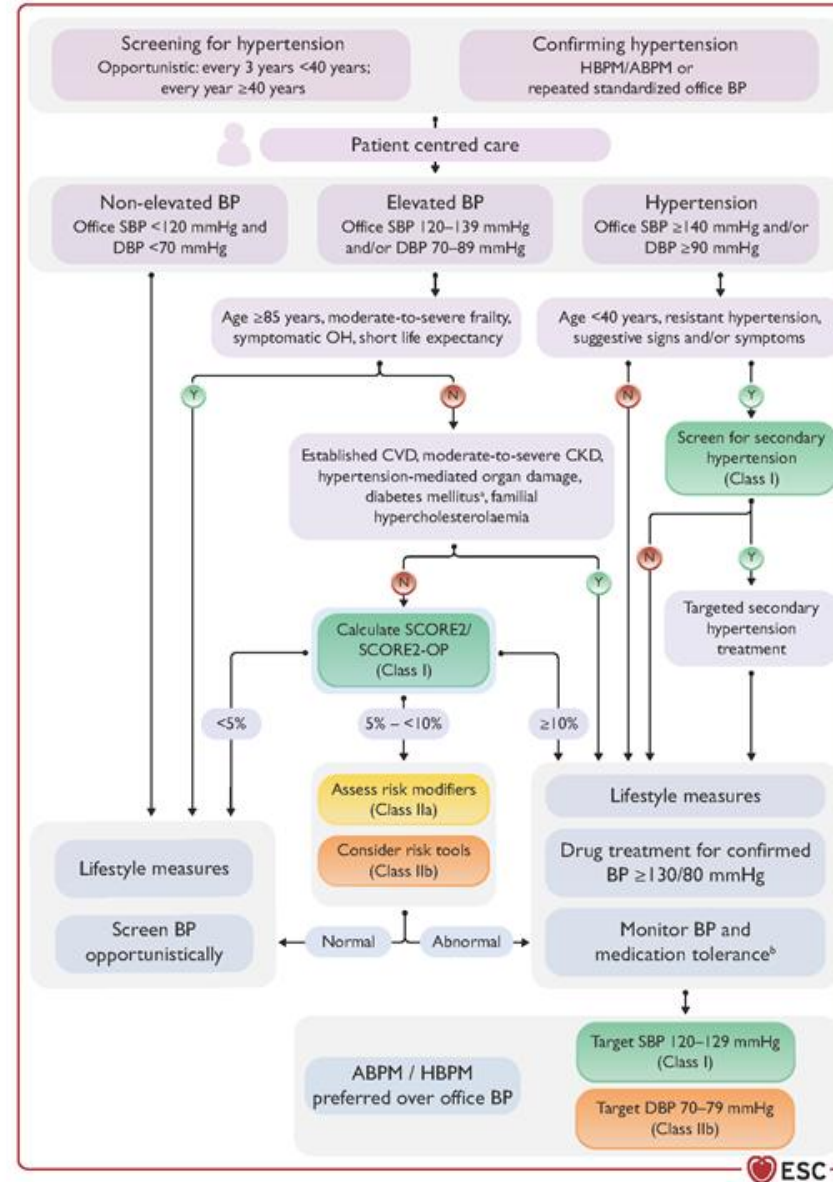


Figure 19

Central Illustration



Case No. 1

- A 75 year old man with Hx of CKD
- Cr: 1.4
- BP: 135/75
- Plan?



Case No. 2

- A 64 year old woman with Hx of Diabetic nephropathy
- BP: 130/90
- Plan?



Case No. 3

- A 35 year old with no PMH
- BP: 170/95
- Plan?



Case No. 4

- A 48 year old man without prominent PMH
- BP: 145/90
- Plan?



Figure 21

Frailty assessment in the management of blood pressure

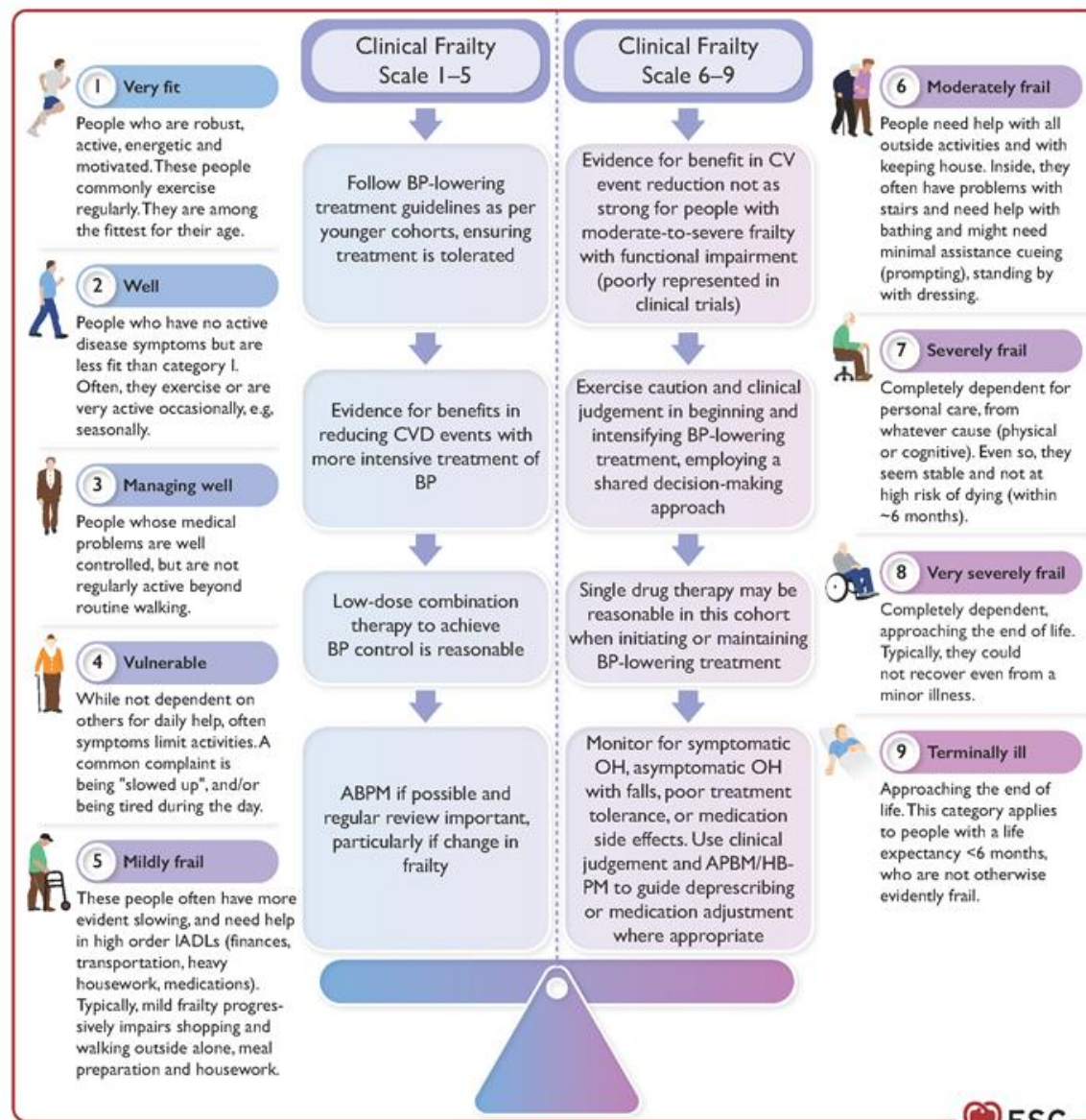


Figure 22

Management of resistant hypertension

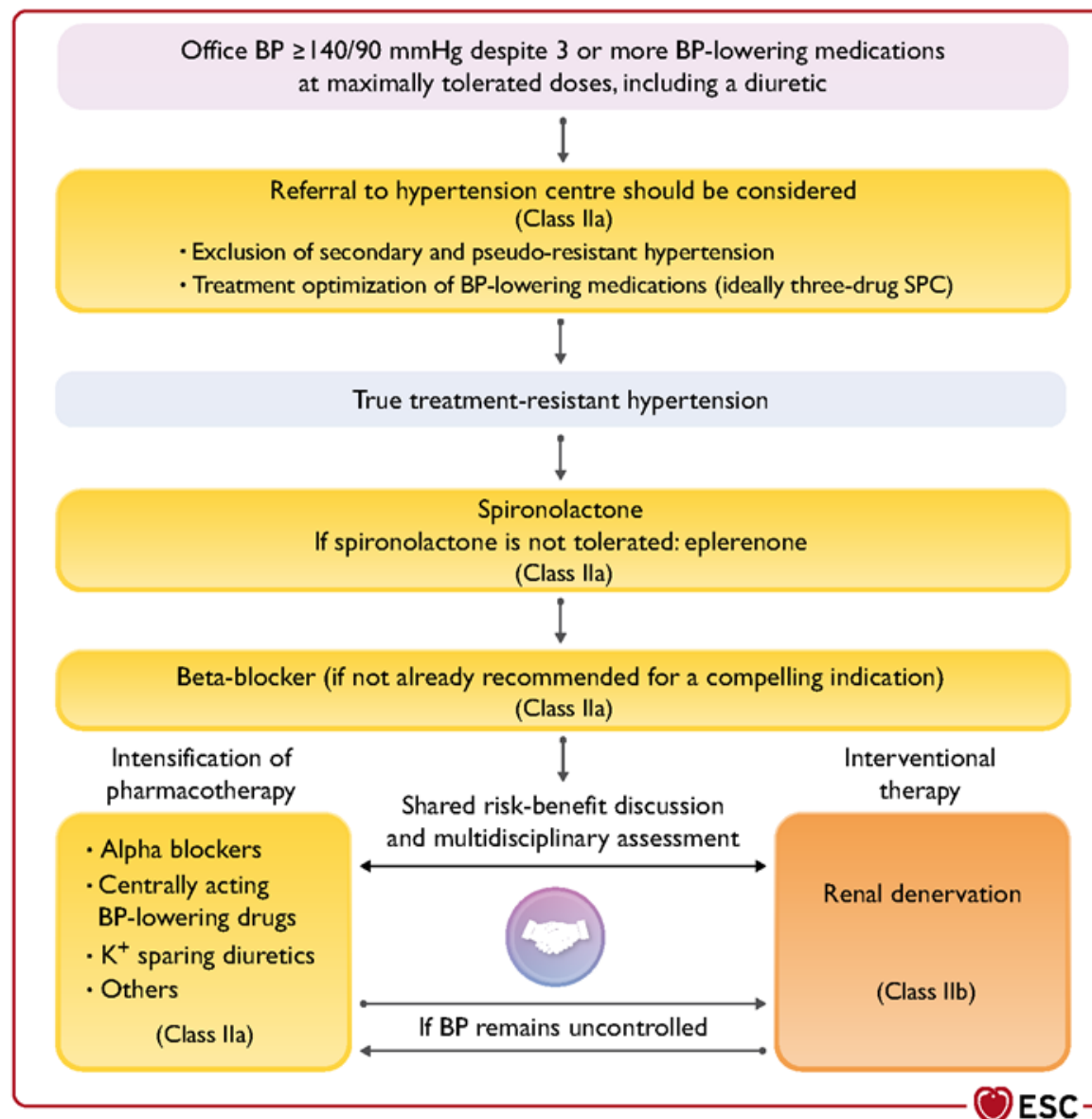


Figure 23

Patient-centred care



Antihypertensive Drugs



1st Line

ACEI

Captopril
Enalapril
Lisinopril

ARB

Losartan
Valsartan
Telmisartan

CCB

DHP
Amlodipine
Nifedipine
NDHP
Diltiazem
Verapamil

Thiazide

Hydrochlorothiazide
Indapamide
Metolazone

2nd Line

MRA

Spironolactone
Eplerenone

3rd Line

B-Blocker

Metoprolol
Bisoprolol
Carvedilol -
Atenolol
Propranolol
Esmolol
Labetalol

Alpha-Blocker

Prazosin
Terazosin

Which one?

4th Line

**Central alpha2
Agonist**

Clonidine
Methyldopa

Vasodilators

Minoxidil
Hydralazine

Loop diuretic

Furosemide

It depends on
the Patient

1st Line

ACEI

Captopril
Enalapril
Lisinopril

ARB

Losartan
Valsartan
Telmisartan

CCB

DHP
Amlodipine
Nifedipine
NDHP
Diltiazem
Verapamil

Thiazide

Hydrochlorothiazide
Indapamide
Metolazone

2nd Line

MRA

Spironolactone
Eplerenone

3rd Line

B-Blocker

Metoprolol
Bisoprolol
Carvedilol -
Atenolol
Propranolol
Esmolol
Labetalol

Alpha-Blocker

Prazosin
Terazosin

Which one?

4th Line

Central alpha2 Agonist

Clonidine
Methyldopa

Vasodilators

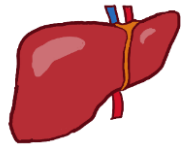
Minoxidil
Hydralazine

Loop diuretic

Furosemide

It depends on
the Patient

↓BP
↓Body fluid vol



ACEI
Captopril
Enalapril
Lisinopril

ARB
Losartan
Valsartan
Telmisartan



Renin

Angiotensin

Angiotensin 1

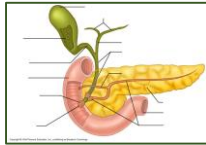
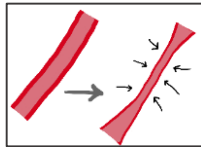
Do not use ACEI + ARB
For HTN
ACEI + MRA
ARB + MRA

Angiotensin converting
enzyme

ACEI

ARB

Angiotensin 2



MRA

Aldosterone



ACEI

Captopril
Enalapril
Lisinopril

Nephroprotective,
Cardioprotective

Adverse Effects

Increase Serum Li



AKI

Hyper K

Cough 15% (Bradykinin)

Angioedema (Bradykinin)



Contraindications::

- Pregnancy
- Bilateral Renal artery stenosis

ARB

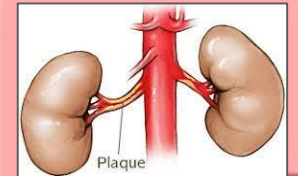
Losartan
Valsartan
Telmisartan

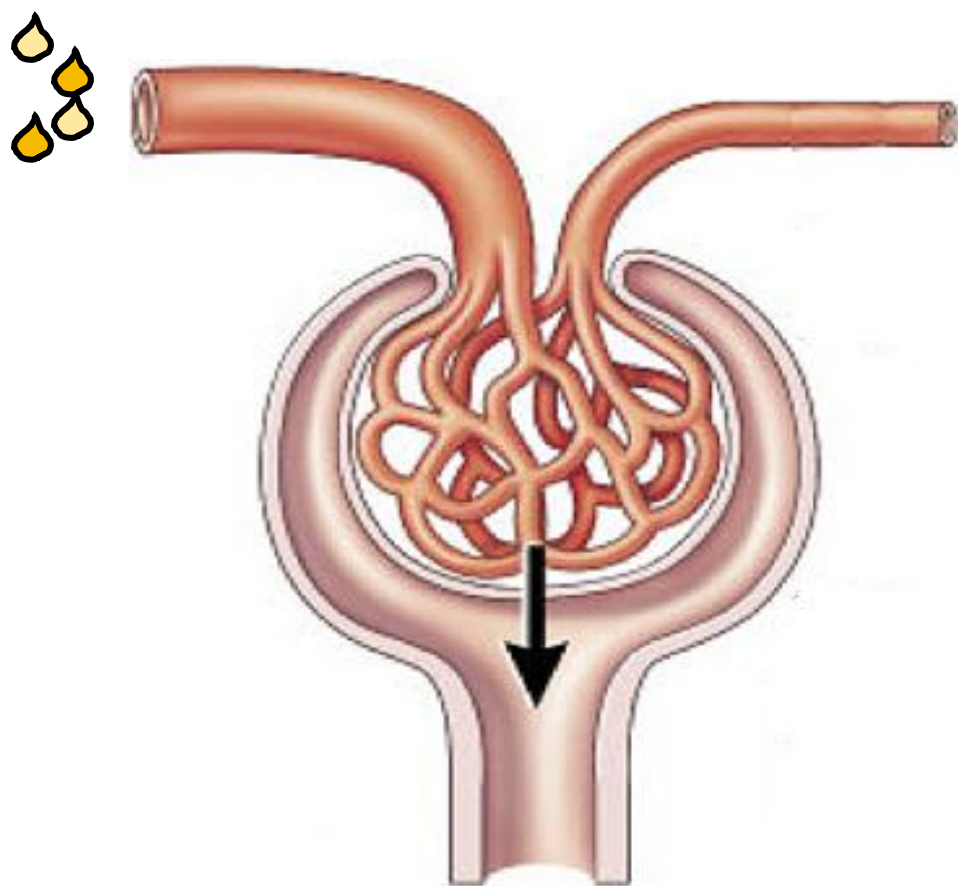
Nephroprotective,
Cardioprotective

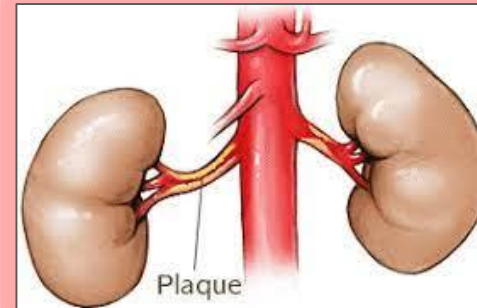
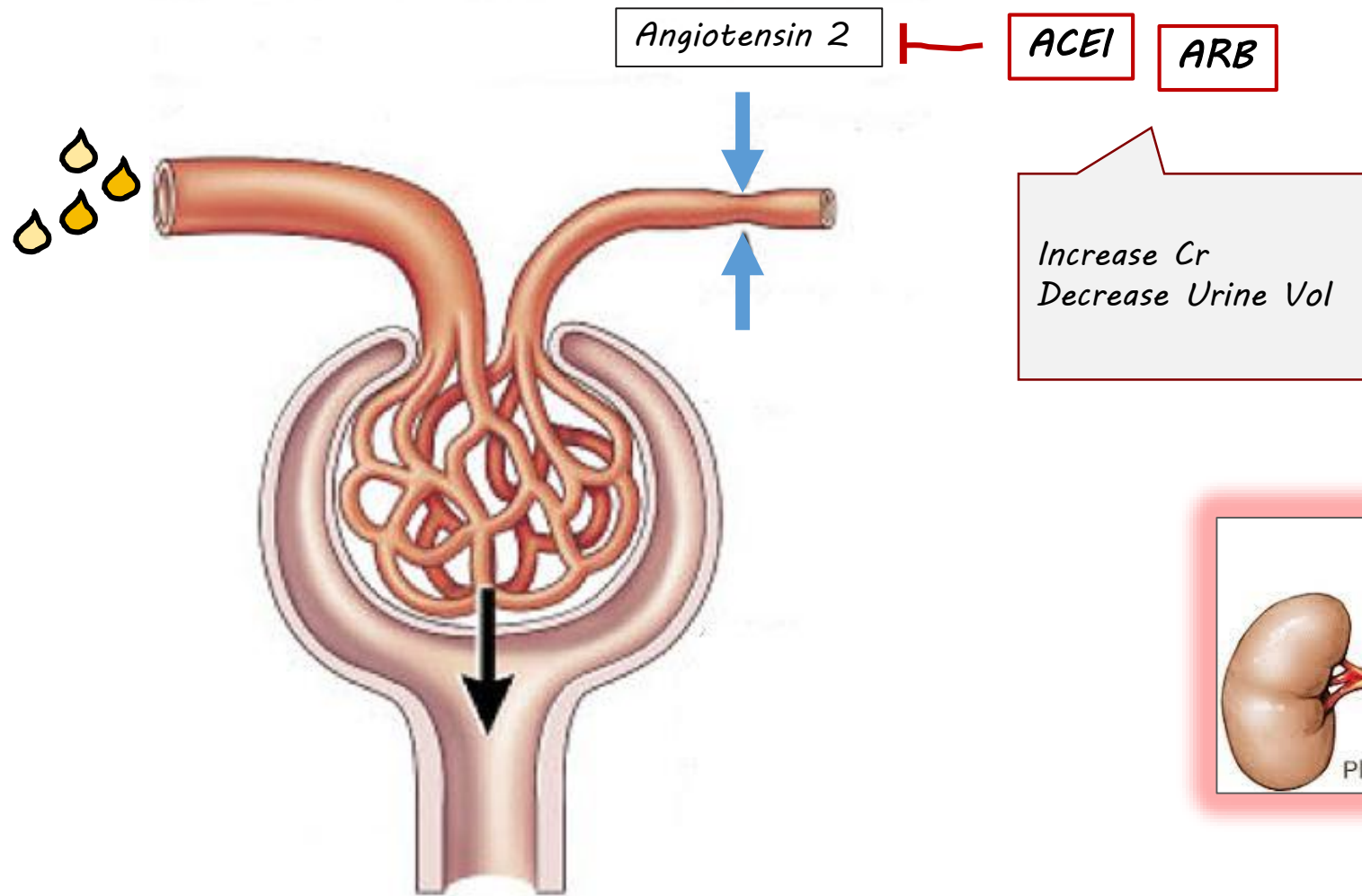
Adverse Effects

AKI

Hyper K







ACEI

Captopril
Enalapril
Lisinopril

Captopril (TDS to BD)
25, 50 mg, (6-25-25 BD/TDS), (Max 50 TDS)
Empty stomach



Enalapril (BD to D)
5, 20 mg, (5-10 D), (Max 40D or 20BD)



Lisinopril (D)
5, 20 mg, (5-10 D), (Max 40D)



ARB

Losartan
Valsartan
Telmisartan

Valsartan (D to BD)
40, 80, 160 mg, (80-160 D), (Max 320 D)



Losartan (D to BD)
25, 50 mg, (25-50 D), (Max 100D or 50BD)



Telmisartan (D)
20, 40, 80 mg, (20-40 D), (Max 80D)



1st Line

ACEI

Captopril
Enalapril
Lisinopril

ARB

Losartan
Valsartan
Telmisartan

CCB

DHP
Amlodipine
Nifedipine
NDHP
Diltiazem
Verapamil

Thiazide

Hydrochlorothiazide
Indapamide
Metolazone

2nd Line

MRA

Spironolactone
Eplerenone

3rd Line

B-Blocker

Metoprolol
Bisoprolol
Carvedilol -
Atenolol
Propranolol
Esmolol
Labetalol

Alpha-Blocker

Prazosin
Terazosin

4th Line

Central alpha2 Agonist

Clonidine
Methyldopa

Vasodilators

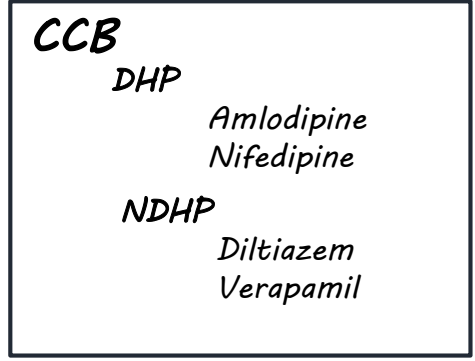
Minoxidil
Hydralazine

Loop diuretic

Furosemide

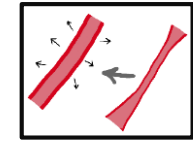
Which one?

It depends on
the Patient

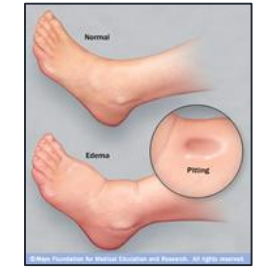


DHP
Amlodipine
Nifedipine

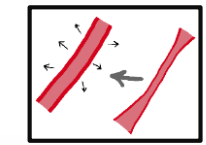
Ca blocking effects



Adverse effects:
-Ankle Edema
 (+ACEI/ARB)
-Flushing
-Headache



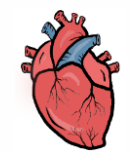
Arteries



Ca blocking effects

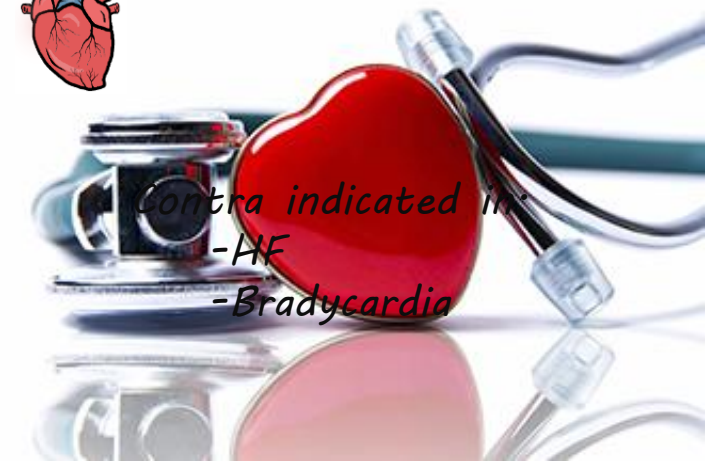
NDHP
Diltiazem
Verapamil

Myocardium



Adverse effects
-Bradycardia, Negative inotrope
-Constipation
 (More with Verapamil)

Contra indicated in:
-HF
-Bradycardia



CCB_{DHP}

Amlodipine

NDHP Nifedipine

Diltiazem
Verapamil

Amlodipine (D)

5mg, (2.5-5 D), (Max 10 D)



Nifedipine (D)

10mg

30mg SR

Diltiazem (D, BD, TDS)

60 ,SR 120 mg, (60-120 BD, SR 120-240D), (Max 240-360 BD or D)



Verapamil (TDS)

40, 80 mg, (40-80 TDS), (Max 160 TDS)



1st Line

ACEI

Captopril
Enalapril
Lisinopril

ARB

Losartan
Valsartan
Telmisartan

CCB

DHP
Amlodipine
Nifedipine
NDHP
Diltiazem
Verapamil

Thiazide

Hydrochlorothiazide
Indapamide
Metolazone

2nd Line

MRA

Spironolactone
Eplerenone

3rd Line

B-Blocker

Metoprolol
Bisoprolol
Carvedilol -
Atenolol
Propranolol
Esmolol
Labetalol

Alpha-Blocker

Prazosin
Terazosin

4th Line

Central alpha2 Agonist

Clonidine
Methyldopa

Vasodilators

Minoxidil
Hydralazine

Loop diuretic

Furosemide

Which one?

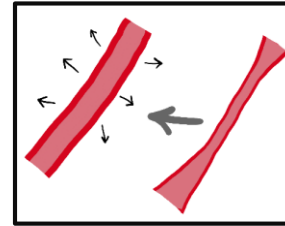
It depends on
the Patient

Thiazide

Hydrochlorothiazide
Indapamide
Metolazone

With Chronic use:

- Diuresis disappears
- PVR



Decrease Ca^{2+} urea (Good for osteoporosis)

Adverse
Effects

Hyper uricemia

Hyper G

Hyper chol

Hypo Na

Hypo Mg

Hypo K

-Reaching a nadir within the first month of therapy and remaining stable thereafter



Thiazide

Hydrochlorothiazide

Indapamide

Metolazone

Hydrochlorothiazide (D)

50, 25, 12.5 mg

(+Triamteren)

(12.5-25 D)

(Max 50 D)



Indapamide (D)

(NatriliX)

SR 1.5 mg

(1.25-2.5 D)

(Max 2.5 D)



Metolazone (D)

5 mg

(+ Lasix for edema not HT)



1st Line

ACEI

Captopril
Enalapril
Lisinopril

ARB

Losartan
Valsartan
Telmisartan

CCB

DHP
Amlodipine
Nifedipine
NDHP
Diltiazem
Verapamil

Thiazide

Hydrochlorothiazide
Indapamide
Metolazone

2nd Line

MRA

Spironolactone
Eplerenone

3rd Line

B-Blocker

Metoprolol
Bisoprolol
Carvedilol -
Atenolol
Propranolol
Esmolol
Labetalol

Alpha-Blocker

Prazosin
Terazosin

4th Line

Central alpha2 Agonist

Clonidine
Methyldopa

Vasodilators

Minoxidil
Hydralazine

Loop diuretic

Furosemide

Which one?

It depends on
the Patient



MRA

Spironolactone
Eplerenone

Spironolactone

*Adverse
Effects*

Hyper K

*Gynecomastia, Erectile
dysfunction*



Eplerenone

*Adverse
Effects*

Hyper K



MRA

*Spironolactone
Eplerenone*

*Spironolactone (D)
(Aldactone)
(12.5 to 25 D)
(Max 50 D)
25, 100 mg*



*Eplerenone (D)
25, 50 mg
(25-50 D)
(Max 50 BD)*



1st Line

ACEI

Captopril
Enalapril
Lisinopril

ARB

Losartan
Valsartan
Telmisartan

CCB

DHP
Amlodipine
Nifedipine
NDHP
Diltiazem
Verapamil

Thiazide

Hydrochlorothiazide
Indapamide
Metolazone

2nd Line

MRA

Spironolactone
Eplerenone

3rd Line

B-Blocker

Metoprolol
Bisoprolol
Carvedilol -
Atenolol
Propranolol
Esmolol
Labetalol

Alpha-Blocker

Prazosin
Terazosin

4th Line

Central alpha2 Agonist

Clonidine
Methyldopa

Vasodilators

Minoxidil
Hydralazine

Loop diuretic

Furosemide

Which one?

It depends on
the Patient

B-Blocker

B1 Metoprolol
Tartarated
Succinate

B1 Bisoprolol

B1 Atenolol

B1, B2, a Carvedilol

B1, B2 Propranolol

B1, B2, a Labetalol

More BP lowering
Effect

More BP lowering
Effect

Adverse
Effects

Bronchospasm

Brady cardia

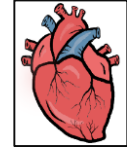
Depression

Erectile dysfunction

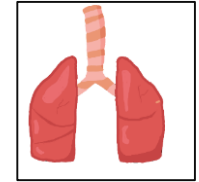
Insomnia (Propranolol)

Covering hypoglycemic
symptoms (Tremors,
Tachycardia BUT not the
Sweating)

B1



B2



B-Blocker

Metoprolol
Tartarated
Succinate

Bisoprolol

Atenolol

Carvedilol -

Propranolol

Esmolol

Labetalol

-Metoprolol tartrate (BD)

Tab 50 mg (50 BD to Max 100/200BD) Administer with food

-Metoprolol succinate (Long act) (D)

Metohexal

23.75, 47.5, 95



Bisoprolol (Concor) (D)

2.5, 5, 10 mg (starting dose 2.5-5D, Max 20D)



Carvedilol (BD)

6.25, 12.5, 25 mg, Administer with food (6.25BD-25BD)



Atenolol (D)

50, 100 mg



Propranolol (BD, TDS)(Inderal)

10, 20, 40 mg Empty Stomach



Short act

Labetalol (Inj)

5 mg/ml

HTN Crise



1st Line

ACEI

Captopril
Enalapril
Lisinopril

ARB

Losartan
Valsartan
Telmisartan

CCB

DHP
Amlodipine
Nifedipine
NDHP
Diltiazem
Verapamil

Thiazide

Hydrochlorothiazide
Indapamide
Metolazone

2nd Line

MRA

Spironolactone
Eplerenone

3rd Line

B-Blocker

Metoprolol
Bisoprolol
Carvedilol -
Atenolol
Propranolol
Esmolol
Labetalol

Alpha-Blocker

Prazosin
Terazosin

4th Line

Central alpha2 Agonist

Clonidine
Methyldopa

Vasodilators

Minoxidil
Hydralazine

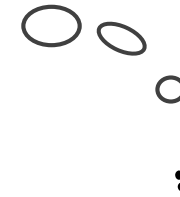
Loop diuretic

Furosemide

Which one?

It depends on
the Patient

Orthostatic
hypotension



..

:

Alpha-Blocker
Prazosin
Terazosin

Adverse
Effects

First dose and with postural
changes

Reflex Tachycardia and Edema
+ diuretic (Thiazide)

+ Heart rate lowering agent (BB, CCB
(NDHP)

BPH

Prazosin 1mg Qhs

Terazosin 2mg

Qhs

Alpha1 blocker:

-Relaxation
of Urethra
and
prostate



Alpha-Blocker
Prazosin
Terazosin

Prazosin (BD, TDS)

1, 5mg



Trazocin (D, BD)

2, 5mg



1st Line

ACEI

Captopril
Enalapril
Lisinopril

ARB

Losartan
Valsartan
Telmisartan

CCB

DHP
Amlodipine
Nifedipine
NDHP
Diltiazem
Verapamil

Thiazide

Hydrochlorothiazide
Indapamide
Metolazone

2nd Line

MRA

Spironolactone
Eplerenone

3rd Line

B-Blocker

Metoprolol
Bisoprolol
Carvedilol -
Atenolol
Propranolol
Esmolol
Labetalol

Alpha-Blocker

Prazosin
Terazosin

4th Line

Central alpha2 Agonist

Clonidine
Methyldopa

Vasodilators

Minoxidil
Hydralazine

Loop diuretic

Furosemide

Which one?

It depends on
the Patient

*Loop diuretic
Furosemide*

*Reserved for patients with heart failure or severe
CKD (in whom the overload of the fluid is the main
cause of the HTN)*

*Adverse
Effects*

Hyper uricemia

Hypo Na

Hypo Mg

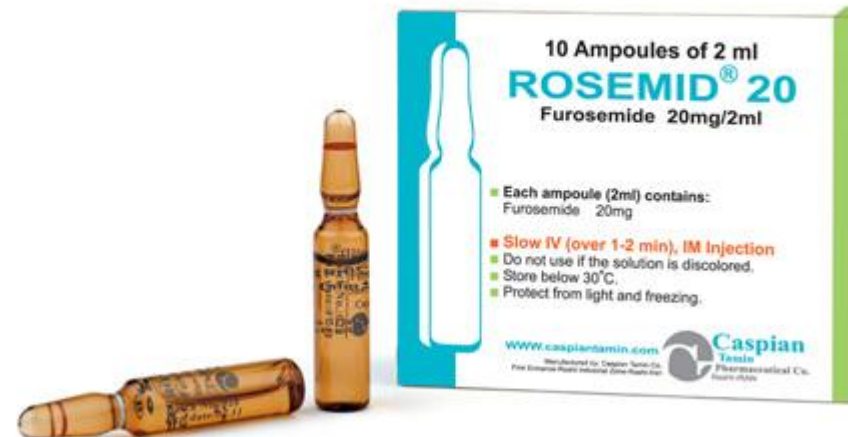
Hypo K

*-Reaching a nadir within the
first week*



Loop diuretic
Furosemide

Frusemide (BD, TDS)
(Lasix)
Tab 40 mg, Inj 40 mg



1st Line

ACEI

Captopril
Enalapril
Lisinopril

ARB

Losartan
Valsartan
Telmisartan

CCB

DHP
Amlodipine
Nifedipine
NDHP
Diltiazem
Verapamil

Thiazide

Hydrochlorothiazide
Indapamide
Metolazone

2nd Line

MRA

Spironolactone
Eplerenone

3rd Line

B-Blocker

Metoprolol
Bisoprolol
Carvedilol -
Atenolol
Propranolol
Esmolol
Labetalol

Alpha-Blocker

Prazosin
Terazosin

4th Line

Central alpha2 Agonist

Clonidine
Methyldopa

Vasodilators

Minoxidil
Hydralazine

Loop diuretic

Furosemide

Which one?

It depends on
the Patient

Vasodilators

Minoxidil

Hydralazine

Reserved for patients with high resistant HTN

*Adverse
Effects*

Reflex Tachycardia and Edema

+ diuretic (Thiazide or lasix)

+ Heart rate lowering agent(BB, or NDHP CCB)

Hydralazine

*Dose dependent lupus-like syndrome (risk is reduce
when the dose is less than 200 mg Daily)*

Minoxidil

Hypertrichosis



Vasodilators
Minoxidil
Hydralazine

Hydralazine
(Qid)

Tab 10, 25 mg
INJ 20/ml



Minoxidil (D, BD, TDS)
2.5 mg



1st Line

ACEI

Captopril
Enalapril
Lisinopril

ARB

Losartan
Valsartan
Telmisartan

CCB

DHP
Amlodipine
Nifedipine
NDHP
Diltiazem
Verapamil

Thiazide

Hydrochlorothiazide
Indapamide
Metolazone

2nd Line

MRA

Spironolactone
Eplerenone

3rd Line

B-Blocker

Metoprolol
Bisoprolol
Carvedilol -
Atenolol
Propranolol
Esmolol
Labetalol

Alpha-Blocker

Prazosin
Terazosin

4th Line

Central alpha2 Agonist

Clonidine
Methyldopa

Vasodilators

Minoxidil
Hydralazine

Loop diuretic

Furosemide

Which one?

It depends on
the Patient



Central alpha2

Agonist

Clonidine

Methyldopa

Reserved for patients with high resistant HTN

Decrease sympathetic outflow from the CNS

*-Decrease in PVR, HR and CO
lowers BP*

**Adverse
Effects**

Edema

**+ diuretic (Thiazide or
lasix)**

Anticholinergic side effects:

*Sedation, dry mouth, urinary
retention, constipation) and possibly
sexual dysfunction.*

Methyldopa:

Choice in Pregnancy

HT

Adverse effects:

Hemolytic anemia

hepatitis

Clonidine

*Can cause rebound hypertension when abruptly
stopped.*



Central alpha2 Agonist
Clonidine
Methyldopa

Clonidine
(BD)

0.2 mg



Methyldopa (BD, T.
250 mg



1st Line

ACEI

Captopril
Enalapril
Lisinopril

ARB

Losartan
Valsartan
Telmisartan

CCB

DHP
Amlodipine
Nifedipine
NDHP
Diltiazem
Verapamil

Thiazide

Hydrochlorothiazide
Indapamide
Metolazone

2nd Line

MRA

Spironolactone
Eplerenone

3rd Line

B-Blocker

Metoprolol
Bisoprolol
Carvedilol -
Atenolol
Propranolol
Esmolol
Labetalol

Alpha-Blocker

Prazosin
Terazosin

4th Line

Central alpha2 Agonist

Clonidine
Methyldopa

Vasodilators

Minoxidil
Hydralazine

Loop diuretic

Furosemide

Which one?

It depends on
the Patient

1st Line

ACEI

Captopril
Enalapril
Lisinopril

ARB

Losartan
Valsartan
Telmisartan

CCB

DHP

Amlodipine
Nifedipine

NDHP

Diltiazem
Verapamil

Thiazide

Hydrochlorothiazide
Indapamide
Metolazone



ARB

*Losartan
Valsartan*



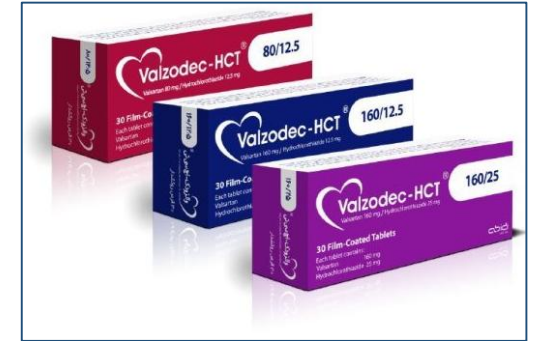
CCB

Amlodipine



Thiazide

Hydrochlorothiazide



*-Valsartan +
Amlodipine*

-Daily

-80/5

-160/5

-160/10

*-Losartan +
HCT*

-Daily

-50/12.5

*Valsartan + Amlodipine
+ HCT*

-Daily

-160/10/25

-160/10/12.5

-160/5/12.5

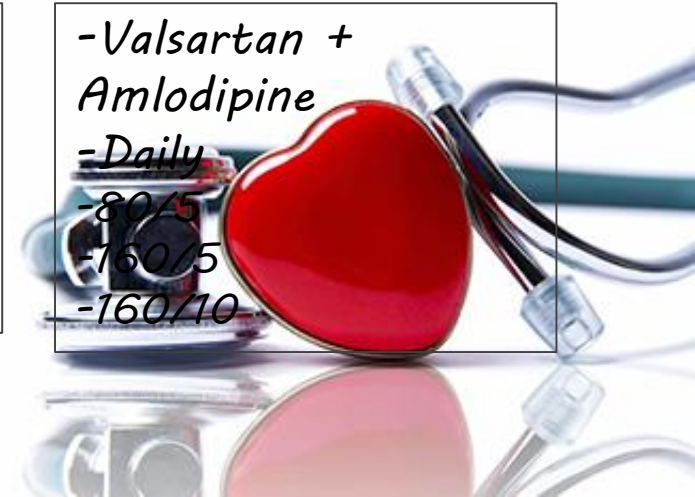
*-Valsartan +
Amlodipine*

-Daily

-80/5

-160/5

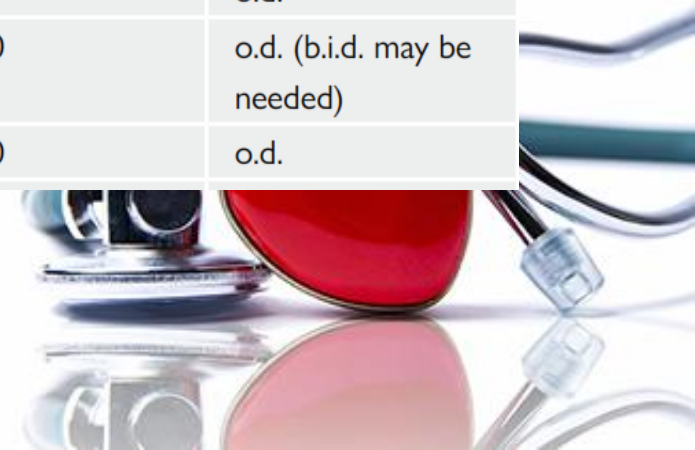
-160/10



Drug class	Drug name	Low dose (mg/day)	Standard dose (mg/day)	High dose (mg/day)	Recommended dosing regimen
ACE inhibitors					
	Captopril	12.5	50	100	b.i.d.
	Enalapril	5	10	40	o.d.
	Lisinopril	5	10–20	40	o.d.
	Perindopril	2.5	5	10	o.d.
	Ramipril	2.5	5–10	10	o.d.
ARBs					
	Candesartan	4	8–16	32	o.d.
	Irbesartan	75	150	300	o.d.
	Losartan	25	50–100	100	o.d.
	Olmesartan	10	20	40	o.d.
	Telmisartan	40	40–80	80	o.d.
	Valsartan	80	16	320	o.d.
	Azilsartan	40	40–80	80	o.d.



Drug class	Drug name	Low dose (mg/day)	Standard dose (mg/day)	High dose (mg/day)	Recommended dosing regimen
Calcium channel blockers					
Dihydropyridines	Amlodipine	5	5–10	10	o.d.
	Felodipine	5	5–10	10	o.d.
	Lercanidipine	10	10–20	20	o.d.
	Nifedipine	30	30–60	90	o.d.
	Manidipine	10	10–20	40	o.d.
Diuretics					
Thiazide and thiazide-like diuretics	Chlorthalidone	12.5	12.5–25	25	o.d.
	Hydrochlorothiazide	12.5	25	50	o.d.
	Indapamide	1.25	2.5	2.5	o.d.
Potassium-sparing diuretics	Amiloride	5	10	20	o.d.
	Eplerenone	25	50	200	o.d. (b.i.d. may be needed)
	Spironolactone	12.5	25	100	o.d.



Drug class	Drug name	Low dose (mg/day)	Standard dose (mg/day)	High dose (mg/day)	Recommended dosing regimen
Beta-blockers^a					
	Atenolol	25	50	100	o.d.
	Bisoprolol	2.5	5	10–20	o.d.
	Carvedilol ^b	6.25	25	50	b.i.d.
	Labetalol ^b	100	200	400	b.i.d.
	Metoprolol succinate	25	50	100	o.d.
	Metoprolol tartrate	25	50	100–200	b.i.d.
	Nebivolol ^b	2.5	5	10	o.d.
	Propranolol	40	80	160	b.i.d.



Drug class	Absolute contraindication	Special precautions
ACE inhibitors	Pregnancy Previous angioneurotic oedema Hyperkalaemia ($K^+ > 5.5$ mmol/L) Bilateral severe renal artery stenosis Severe renal artery stenosis in a single functioning kidney	Women of childbearing potential without reliable contraception
ARBs	Pregnancy Hyperkalaemia ($K^+ > 5.5$ mmol/L) Bilateral severe renal artery stenosis Severe renal artery stenosis in a single functioning kidney	Women of childbearing potential without reliable contraception
CCBs		
Dihydropyridines		Tachyarrhythmia Heart failure (HFrEF, class III or IV) Pre-existing severe leg oedema
Non-dihydropyridines	Any high-grade sinoatrial or atrioventricular block Severe LV dysfunction (LVEF $< 40\%$) Bradycardia (heart rate < 50 b.p.m.)	Severe constipation
Diuretics		
Thiazide and thiazide-like diuretics	Active gout	Metabolic syndrome Glucose intolerance Pregnancy Hypercalcaemia Hypokalaemia Gout history Urinary incontinence
Beta-blockers	Acute asthma exacerbation Any high-grade sinoatrial or atrioventricular block Bradycardia (heart rate < 50 b.p.m.)	Asthma ^a Metabolic syndrome Glucose intolerance Athletes and physically active patients



Comorbidity	Initial drug class
Diabetes mellitus Metabolic syndrome	ACE inhibitor ARB CCB
Chronic kidney disease Proteinuria/albuminuria	ACE inhibitor ARB Diuretic CCB SGLT2 inhibitors
Post-myocardial infarction	Beta-blocker ACE inhibitor ARB MRA
AF	Beta-blocker ACE inhibitor ARB
Heart failure	ACE inhibitor ARB MRA Beta-blocker SGLT2 inhibitor Diuretic



Uncomplicated Hypertension





Initial therapy
Dual combination

ACEi or ARB + CCB or diuretic

Consider monotherapy in
low risk grade 1 hypertension
(systolic BP <150mmHg), or in
very old (≥ 80 years) or frailer patients



Step 2
Triple combination

ACEi or ARB + CCB + diuretic



Step 3
Triple combination +
spironolactone or
other drug

Resistant hypertension
Add spironolactone (25-50 mg o.d.)
or other diuretic, alpha-blocker or beta-blocker

Consider referral to a specialist centre
for further investigation

Beta-blockers

Consider beta-blockers at any treatment step, when there is a specific indication for their use, e.g. heart failure, angina, post-MI, atrial fibrillation, or younger women with, or planning, pregnancy

- a)** Consider monotherapy in low risk grade 1 hypertension or in very old (≥ 80 yrs) or frailer patients.
- b)** Consider A + D in post-stroke, very elderly, incipient HF or CCB intolerance.
- c)** Consider A + C or C + D in black patients.
- d)** Caution with spironolactone or other potassium sparing diuretics when estimated GFR < 45 ml/min/1.73m² or K⁺ > 4.5 mmol/L.

A = ACE-Inhibitor or ARB (Angiotensin Receptor Blocker)

C = DHP-CCB (Dihydropyridine -Calcium Channel Blocker)

D = Thiazide-like diuretic

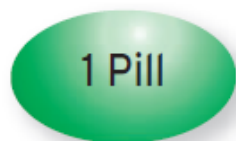


- For initiation of RAS inhibitor or diuretic therapy, assess blood tests for electrolytes and renal function 2 to 4 weeks after initiating therapy



Hypertension and coronary artery disease





Initial therapy
Dual combination

**ACEi or ARB + beta-blocker or CCB
or CCB + diuretic or beta-blocker
or beta-blocker + diuretic**

Consider monotherapy in low risk
grade 1 hypertension
(systolic BP <150mmHg), or in
very old (≥ 80 years) or frailer patients



Step 2
Triple combination

Triple combination of above

Consider initiating therapy
when systolic BP is
 ≥ 130 mmHg in these very
high risk patients with
established CVD



Step 3
Triple combination +
spironolactone or
other drug

Resistant hypertension
Add spironolactone (25-50 mg o.d.)
or other diuretic, alpha-blocker or beta-blocker

Consider referral to a specialist centre
for further investigation

Hypertension and chronic kidney disease





1 Pill

Initial therapy
Dual combination

**ACEi or ARB + CCB
or ACEi or ARB + diuretic (or loop
diuretic)^b**



1 Pill

Step 2
Triple combination

**ACEi or ARB + CCB + diuretic (or
loop diuretic)^b**



2 Pills

Step 3
Triple combination +
spironolactone^c or
other drug

Resistant hypertension
Add spironolactone (25-50 mg o.d.)
or other diuretic, alpha-blocker or beta-blocker

Beta-blockers

Consider beta-blockers at any treatment step, when there is a specific indication for their use, e.g. heart failure, angina, post-MI, atrial fibrillation, or younger women with, or planning, pregnancy

A reduction in eGFR and rise in serum creatinine is expected in patients with CKD^a who receive BP-lowering therapy, especially in those treated with an ACEi or ARB but a rise in serum creatinine of >30% should prompt evaluation of the patient for possible renovascular disease.

- Use loop diuretics when eGFR is $<30 \text{ mL/min/1.72 m}^2$, because thiazide/thiazide-like diuretics are much less effective/ineffective when eGFR is reduced to this level



Hypertension and heart failure with reduced ejection fraction



Initial therapy

**ACEi or ARB^a + diuretic^b (or loop diuretic) +
beta-blocker**



Step 2

**ACEi or ARB^a + diuretic^b (or loop diuretic) +
beta-blocker + MRA^c**

When antihypertensive therapy is not required in HFrEF, treatment should be prescribed according to the ESC Heart Failure Guidelines.¹³⁶

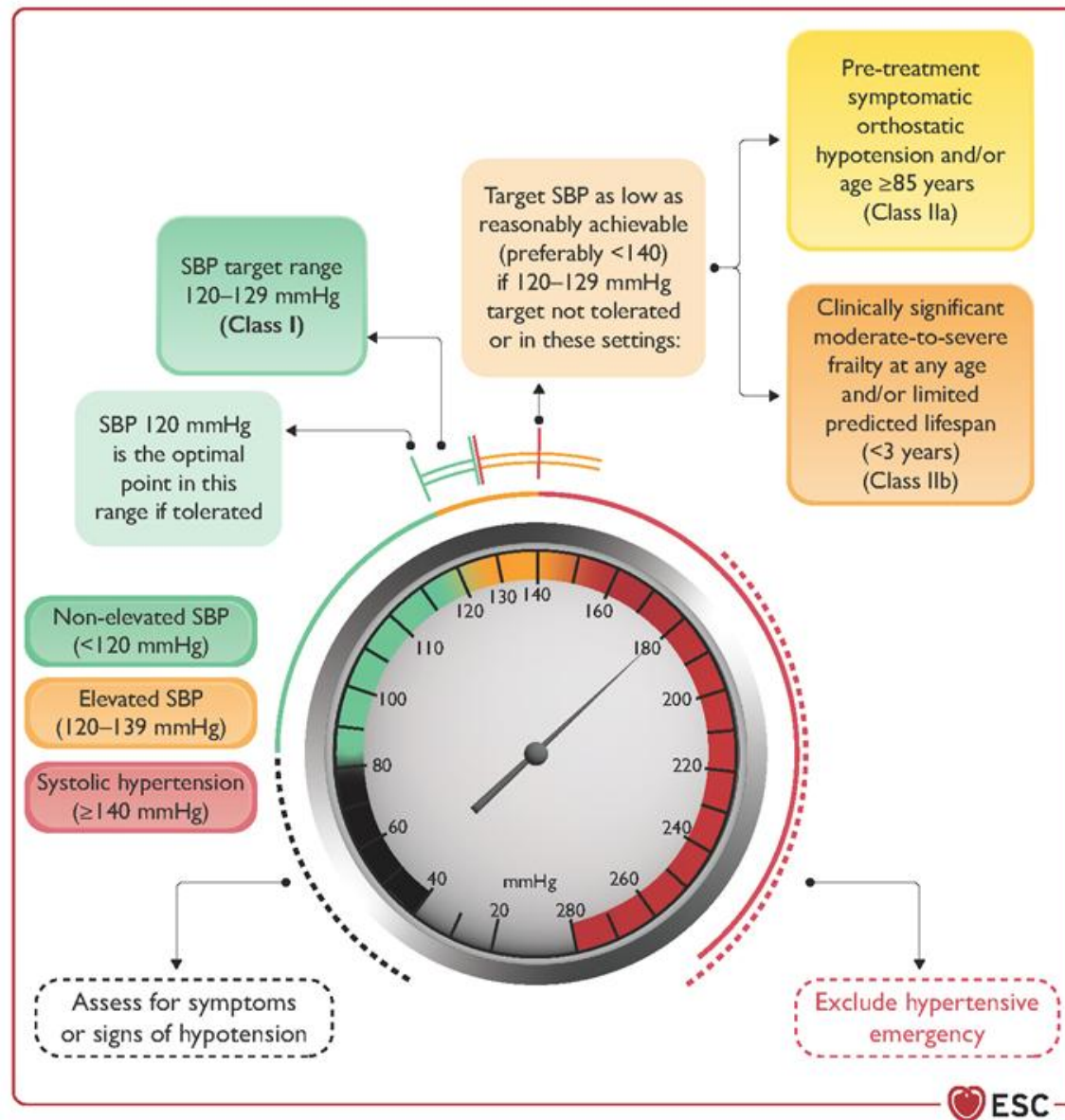


Blood pressure target range



Figure 20

Systolic blood pressure categories and treatment target range



Acute and short-term lowering of blood pressure



HTN Urgency

- Severe hypertension in patients **without** clinical evidence of acute organ damage.
- require BP reduction, they do not usually require admission to hospital, and BP reduction is best achieved with oral medication



HTN Emergency

- BP $\geq 180/110$ mmHg associated with acute **HMOD**, often in the presence of symptoms.
- Hypertensive emergencies are potentially life-threatening and require immediate and careful intervention to reduce BP, often with i.v. therapy.
- Symptoms:
 - headache
 - visual disturbances
 - chest pain
 - shortness of breath
 - dizziness and other neurological deficit



Table S12 Diagnostic work-up for patients with a suspected hypertensive emergency

Common tests for all potential causes
Fundoscopy is a critical part of the diagnostic work-up
12-Lead ECG
Haemoglobin, platelet count, fibrinogen
Creatinine, eGFR, electrolytes, LDH, haptoglobin
Urinary albumin:creatinine ratio, urine microscopy for red cells, leucocytes, casts
Pregnancy test in women of child-bearing age
Specific tests by indication
Troponin, CK-MB (in suspected cardiac involvement, e.g. acute chest pain or acute heart failure), and NT-proBNP
Chest X-ray (fluid overload)
Echocardiography (aortic dissection, heart failure, or ischaemia)
CT angiography of thorax and/or abdomen in suspected acute aortic disease (e.g. aortic dissection)
CT or MRI brain (nervous system involvement)
Renal ultrasound (renal impairment or suspected renal artery stenosis)
Urine drug screen (suspected methamphetamine or cocaine use)



Table S13 Most common drugs used for the treatment of hypertensive emergencies

Drug	Onset of action	Duration of action	Dose	Contraindications	Adverse effects
Esmolol	1–2 min	10–30 min	0.5–1 mg/kg as i.v. bolus; 50–300 µg/kg/min as i.v. infusion	Second or third-degree AV block, systolic heart failure, asthma, bradycardia	Bradycardia
Metoprolol	1–2 min	5–8 h	2.5–5 mg i.v. bolus over 2 min – may be repeated every 5 min to a maximum dose of 15 mg	Second or third-degree AV block, systolic heart failure, asthma, bradycardia	Bradycardia
Labetalol	5–10 min	3–6 h	0.25–0.5 mg/kg i.v. bolus; 2–4 mg/min infusion until goal BP is reached, thereafter 5–20 mg/h	Second or third-degree AV block, systolic heart failure, asthma, bradycardia	Bronchoconstriction, foetal bradycardia
Fenoldopam	5–15 min	30–60 min	0.1 µg/kg/min i.v. infusion, increase every 5 min with 0.05–0.1 µg/kg/min increments until goal BP is reached	Caution in glaucoma	
Clevidipine	2–3 min	5–15 min	2 mg/h i.v. infusion, increase every 2 min with 2 mg/h until goal BP		Headache, reflex tachycardia
Nicardipine	5–15 min	30–40 min	5–15 mg/h i.v. infusion, starting dose 5 mg/h, increase every 15–30 min with 2.5 mg until goal BP, thereafter decrease to 3 mg/h	Liver failure	Headache, reflex tachycardia
Nitroglycerin	1–5 min	3–5 min	5–200 µg/min i.v. infusion, 5 µg/min increase every 5 min		Headache, reflex tachycardia
Nitroprusside	Immediate	1–2 min	0.3–10 µg/kg/min i.v. infusion, increase by 0.5 µg/kg/min every 5 min until goal BP	Liver/kidney failure (relative)	Cyanide intoxication
Enalaprilat	5–15 min	4–6 h	0.625–1.25 mg i.v. bolus	History of angioedema	
Urapidil	3–5 min	4–6 h	12.5–25 mg as bolus injection; 5–40 mg/h as continuous infusion		
Clonidine	30 min	4–6 h	150–300 µg i.v. bolus over 5–10 min		Sedation, rebound hypertension
Phentolamine	1–2 min	10–30 min	0.5–1 mg/kg i.v. bolus OR 50–300 µg/kg/min as i.v. infusion		Tachyarrhythmias, chest pain



In patients with acute ischaemic stroke, early BP lowering with BP-lowering therapy should be considered in the first 24 h in the following settings:

- In patients who are eligible for re-perfusion therapy with intravenous thrombolysis or mechanical thrombectomy, BP should be carefully lowered and maintained at $<180/105$ mmHg for at least the first 24 h after treatment.^{956–960}

IIa

B

- In patients with ischaemic stroke not receiving re-perfusion treatment and BP of $\geq 220/110$ mmHg, BP should be carefully lowered by approximately 15% during the first 24 h after stroke onset.^{956–960}

IIa

C

In patients with intracerebral haemorrhage, immediate BP lowering (within 6 h of symptom onset) should be considered to a systolic target 140–160 mmHg to prevent haematoma expansion and improve functional outcome.^{948,949}

IIa

A

In patients with intracerebral haemorrhage presenting with systolic BP ≥ 220 mmHg, acute reduction in systolic BP >70 mmHg from initial levels within 1 h of commencing treatment is not recommended.^{950,951,960–963}

III

B

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WHO Guideline



Drug therapy initiation



R1: BP threshold for starting drug treatment

Those with diagnosis of HTN and BP of $\geq 140/\geq 90$ mmHg

Those with CVD and SBP $\geq 130-139$ mmHg

Recommendation: strong

Evidence: moderate–high certainty

Those without CVD but with high CVD risk, diabetes, CKD and

SBP $\geq 130-139$ mmHg

Recommendation: conditional

Evidence: moderate–high certainty



R2 & 3: Whether screening and assessment are needed before treatment is started

Obtain tests to screen for comorbidities and conduct CV risk assessment

but only if it doesn't delay treatment

Recommendation: conditional

Evidence: low certainty



R4: Which drug(s) to prescribe

Any of these drug classes:

diuretics/ACEi, ARB/CCBs

Recommendation: strong

Evidence: high certainty

R5: Combination therapy

To improve adherence and persistence **combination therapy recommended** preferably in a **single pill**

Recommendation: conditional

Evidence: moderate certainty



Targets and follow-up



R6: BP target for control of HTN

140/90 mmHg

in those without comorbidities

SBP 130 mmHg

in those with CVD

Recommendation: strong

Evidence: moderate certainty

SBP <130 mmHg

in those with high CVD risk, diabetes and CKD

Recommendation: conditional

Evidence: moderate certainty



R7: Follow-up intervals

Monthly follow up

until patient reaches target BP

Recommendation: conditional

Evidence: low certainty

3–6 month follow up

once target BP is reached

Recommendation: conditional

Evidence: low certainty



R8: Use of nonphysician HCWs in further management of HTN

Treatment can be provided by

nonphysician professionals

as long as they are given training, prescribing authority, management protocols and physician oversight

Recommendation: conditional

Evidence: low certainty



HTN in Pregnancy



Definition

- SBP $\geq$ 140 mmHg and/or DBP $\geq$ 90 mmHg on two measurement at least 4 hours apart
 - Mild: 140-159 / 90-109 mmHg
 - Severe: $\geq$ 160-110 mmHg
- The second measurement can obtained within 15 minutes if the BP is severely elevated



Measurement

- Office BP measurement following general guidelines
- Gold standard: **Manual auscultation**
- Automated: Under-record the BP, unreliable in severe pre-eclampsia
- ABPM or HBPM:
 - to evaluate white coat hypertension (avoid unnecessary treatment)
 - High risk patients including DM or nephropathy



Investigation

- **Essential:**

- U/A, CBC, LFT, Hct, Cr, S-UA
- Proteinuria:
 - Early pregnancy: preexisting renal disease
 - Second half of pregnancy: Pre-eclampsia
- Dipstick test $\geq 1+$ should follow with ACR in single spot urine sample (ACR < 30 mg/mmol exclude proteinuria)



Prevention of pre-eclampsia

- **Indication**

- **High risk of pre-eclampsia:**

1. Hypertensive disease during a previous pregnancy
2. Chronic kidney disease
3. Autoimmune disease (SLE, APS)
4. Type 1 or 2 Diabetes
5. Chronic HTN

- **Moderate risk with more than one of the following:**

1. First pregnancy
2. Age ≥ 40 years
3. Pregnancy interval ≥ 10 years
4. BMI ≥ 35 kg/m² at first visit
5. Multiple pregnancy



Prevention of pre-eclampsia (Cont.)

- **ASA**
 - 100-150 mg, daily, at weeks 12-36
- **Oral calcium supplementation**
 - 1.5-2 gr/day in women with low dietary intake (< 600 mg/day)
- **Vit C or E**
 - does not decrease the risk of pre-eclampsia



Management of Mild HTN

- BP > 140/90 mmHg in women with:
 - Gestational HTN
 - Preexisting HTN superimposed with Gestational HTN
 - HTN with subclinical HMOD at any time of pregnancy
- Target: No data for optimal BP target
 - European < 140/90 mmHg
 - Canadian, DBP < 85 mmHg
 - United States : 140-150 / 90-100 mmHg
- Tight (DBP < 85 mmHg) vs. less Tight Control:
 - Showed no differences in risk of adverse perinatal outcomes
 - Reduce the risk of severe HTN and pre-eclampsia



Management of Mild HTN (Cont.)

- **First Line**

- Methyldopa
- β -blocker (Labetalol): may induce fetal bradycardia, IUGR or hypoglycemia/
Atenolol best avoided
- DHP-CCB (Non-capsular Nifedipine or Nicardipine)

- **Second Line**

- Diuretics: generally avoided due to volume depletion in pre-eclampsia

- **Contraindicated**

- ACE-I, ARB, Direct Renin Inhibitors



Management of Mild HTN (Cont.)

Drug	Dosage	Maternal side effect
Labetalol	200-400 mg per day in 2-3 divided doses	Dizziness, fatigue, orthostatic hypotension, nausea
Nifedipine	30-120 mg per day of a slow-release preparation	Headache, flushing, peripheral edema, orthostatic hypotension
Amlodipine	5-10 mg per day	Same as nifedipine
methyldopa	0.5 - 3 gr per day in 2-3 divided doses	Maternal sedation, elevated LFT, depression
Hydralazine	50-300 mg per day in 2- divided doses	Use with methyldopa or labetalol to prevent reflex tachycardia; risk of neonatal thrombocytopenia

Management of Severe HTN

- **Definition:**

- SBP $\geq$ 170 mmHg or DBP $\geq$ 110 mmHg

- **Management:**

- Immediate hospitalization and start IV labetalol or oral Methyldopa/ DHP-CCB

- **Goal:**

- To reduce BP < 160/105 mmHg
- To reduce risk of heart failure, stroke or renal disease



Management of Severe HTN (Cont.)

- **IV drugs:**

- Labetalol:
 - Cumulative dose < 800 mg/24 h (Bradycardia)
- Nicardipine
- Esmolol
- Hydralazine:
 - No longer the drug of choice
 - Perinatal adverse outcomes more than other drugs
- Urapidil

- **Fetal HR monitoring with labetalol or nicardipine**

- **Magnesium sulfate:**

- Prevent of pre-eclampsia/Tx of seizure in eclampsia
- Potential synergy with CCB
- 4 gr over 20 min, followed with 2-3 gr/h
- Toxic level reverse by IV Ca



Management of Severe HTN (Cont.)

- **TNG:**

- In cases of pre-eclampsia presented with pulmonary edema
- 5 mcg/min , gradually increased every 3-5 min
- Max dose: 100 mcg/min

- **Sodium nitropruside:**

- No use due to the risk of fetal cyanide poisoning prolong treatment

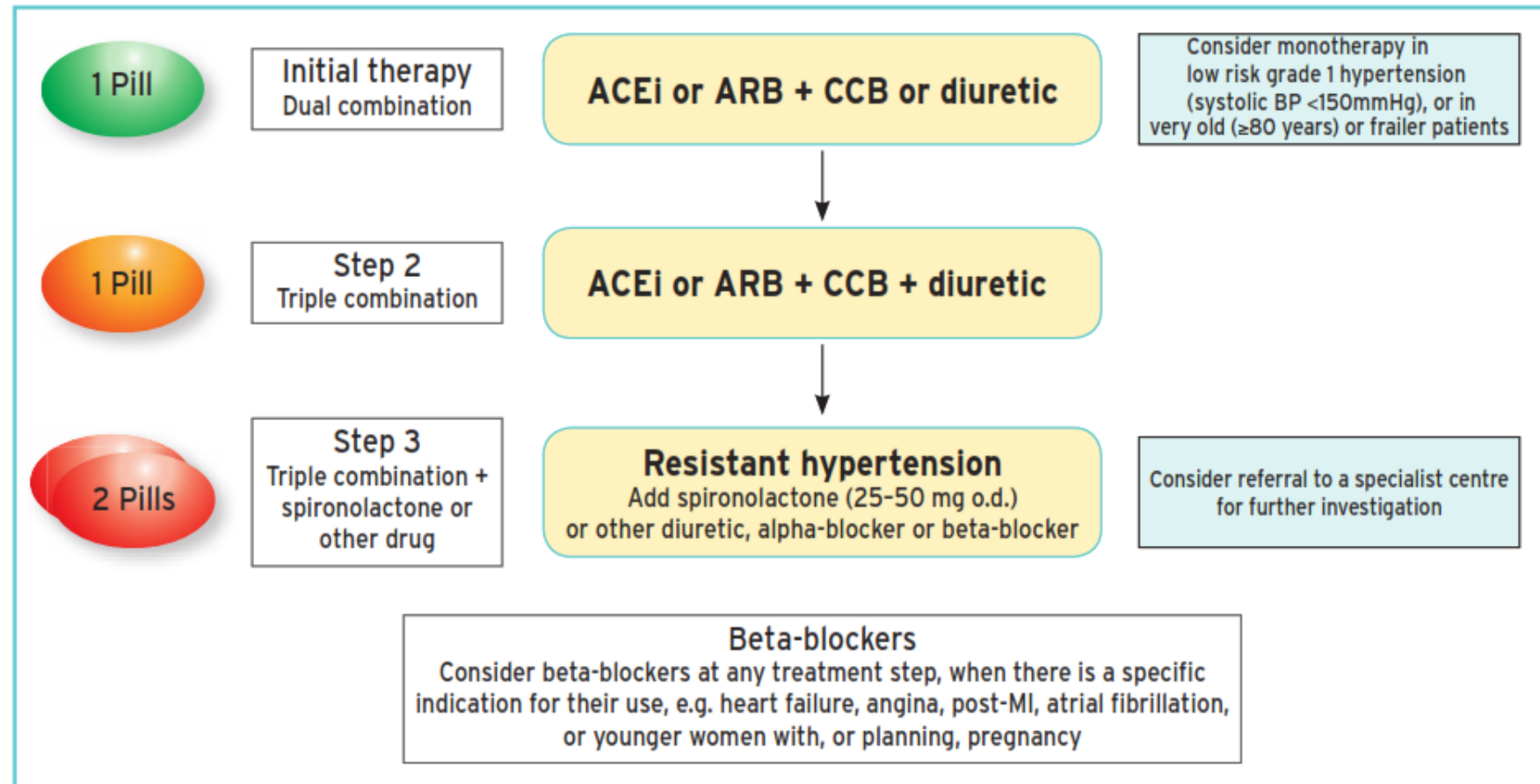
- **Delivery:**

- At week 37 in **asymptomatic** women with Gestational HTN or pre-eclampsia
- Expedite delivery in women with visual disturbances of hemostatic disorders



Management of Post partum HTN

- If BP persist $\geq 150/90$ mmHg
- Any of recommended drugs except methyldopa (PPD)
- Early ambulatory in the 1st to 2nd after delivery



Management of HTN in breast feeding

- All anti-HTN drug excreted into breast milk at low concentration
- Avoid:
 - Atenolol, and nifedipine (as high concentration as mothers' plasma)
 - Captopril and enalapril in mother with pre-term neonate (Seizure)
 - HCT < 50 mg per day is safe in nursing mother



Table S11 Blood pressure-lowering medications that are considered safe with breastfeeding^{367,390}

Drug class	Drug
ACE inhibitors	Benazepril
	Captopril
	Enalapril
	Quinapril
Calcium channel blockers	Diltiazem
	Nifedipine
	Verapamil
Beta-blockers	Labetalol
	Metoprolol
	Nadolol
	Oxprenolol
	Propranolol
	Timolol
Diuretics	Furosemide
	Hydrochlorothiazide
	Spirolactone
Other	Clonidine
	Hydralazine
	Methyldopa
	Minoxidil



THANK YOU
FOR YOUR ATTENTION