## 2013 ESH/ESC Guidelines on the Treatment of Hypertension

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## **Classes of recommendations**

Classes of recommendations	Definition	Suggested wording to use
Class I	Evidence and/or general agreement that a given treatment or procedure is beneficial, useful, effective.	ls recommended/is indicated
Class II	<b>Conflicting evidence and/or a</b> divergence of opinion about the <b>usefulness/efficacy of the given</b> treatment or procedure.	
Class IIa	Weight of evidence/opinion is in favour of usefulness/efficacy.	Should be considered
Class IIb	<b>Usefulness/efficacy is less well</b> established by evidence/opinion.	May be considered
Class III	Evidence or general agreement that the given treatment or procedure is not useful/effective, and in some cases may be harmful.	ls not recommended

## **Levels of Evidence**

Level of evidence A	Data derived from multiple randomized trials or meta-analyses.
Level of evidence B	Data derived from a single randomized clinical trial or large non-randomized studies.
Level of evidence C	Consensus of opinion of the experts and/or small studies, retrospective studies, registries.

## **Blood pressure measurement**

### **Office blood pressure measurement (1)**

#### 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

### **Office blood pressure measurement (2)**

- 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 first visit BP 1 and 3 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

#### Clinical indications for out-of-office blood pressure measurement for diagnostic purposes (1)

#### **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

## Clinical indications for out-of-office blood pressure measurement for diagnostic purposes (2)

#### **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 apnea, CKD, or diabetes
- Assessment of BP variability

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

Category	SBP (mmHg)		DBP (mmHg)
Office BP	<u>&gt;</u> 140	and/or	<u>&gt;</u> 90
Ambulatory BP			
Daytime (or awake)	<u>&gt;</u> 135	and/or	<u>&gt;</u> 85
Nighttime (or asleep)	<u>&gt;</u> 120	and/or	<u>&gt;</u> 70
24-h	<u>&gt;</u> 130	and/or	<u>&gt;</u> 80
Home BP	<u>&gt;</u> 135	and/or	<u>&gt;</u> 85

## **Management of hypertension**

#### Definitions and classification of 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	<u>&gt;</u> 180	and/or	<u>&gt;</u> 110
Isolate systolic hypertension	<u>&gt;</u> 140	and	<90

When a patient's systolic and diastolic blood pressure fall into different categories, the higher category should apply.

# Factors other than office BP-influencing prognosis; used for stratification of total CV risk (1)

#### **Risk factors**

Male sex

Age (men <u>></u>55 yrs; women <u>></u>65 yrs)

Smoking

Dyslipidaemia

Total chol >4.9 mmol/L (190 mg/dL), and/or

LDL-C >3.0 mmol/L (115mg/dL), and/or

HDL-C: men <1.0 mmol/L (40 mg/dL), women <1.2 mmol/L (46 mg/dL), and/or

Triglycerides >1.7 mmol/L (150 mg/dL)

FPG 5.6-6.9 mmol/L (102-125 mg/dL)

Abnormal GTT

Obesity [BMI  $\geq$  30 kg/m<sup>2</sup> (height<sup>2</sup>)]

Abnormal obesity (waist cir.: men <a>102 cm; women <a>88 cm (in Caucasians)</a>

Family history of premature CVD (men aged <55 yrs; women aged <65 yrs)

#### Factors other than office BP-influencing prognosis; used for stratification of total CV risk (2)

#### Asymptomatic organ damage

Pulse pressure (in the elderly) >60 mmHg

Electrocardiographic LVH (Sokolow-Lyon index >3.5 mV; RaVL >1.1 mV;

Cornell voltage duration product >244 mV 125 pr

Echocardiographic LVH [LVM index:men >115 g/m<sup>2</sup>; women >95 g/m<sup>2</sup> (BSA)]<sup>a</sup>

Carotid wall thickening 12 >0.9 mm) or plaque

Carotid-femoral PWV >10 m/s

Ankle-brachial in <60 ).9

CKD with eGFR 30-60 ml/min/1.73 m<sup>2</sup> (BSA)

Microalbuminuria (30-300 mg/24 h), or albumin-creatinine ratio (30-300 mg/g;

3.4-34 mg/mmol) (preferentially on morning spot urine)  $\geq 22$  (M);  $\geq 31$  (F)

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# Factors other than office BP-influencing prognosis; used for stratification of total CV risk (3)

#### **Diabetes mellitus**

FPG  $\geq$ 7.0 mmol/L (126 mg/dL) on two repeated measurements, and/or

HbA<sub>1c</sub> >7% (53 mmol/mol), and/or

Post-load plasma glucose >11.0 mmol/L (198 mg/dL)

#### **Established CV or renal disease**

Cerebrovascular disease: ischaemic stroke; cerebral haemorrhage; TIA

CHD: MI; angina; myocardial revascularization with PCI or CABG

HF, including HF with preserved EF

Symptomatic lower extremities PAD

CKD with eGFR <30 mL/min/1.73 m<sup>2</sup> (BSA); proteinuria (>300 mg/24 h)

Advanced retinopathy: haemorrhages or exudates papilloedema

## Blood pressure management, history, and physical examination (1)

Recommendations	Class <sup>a</sup>	Level <sup>b</sup>
It is recommended to obtain a comprehensive medical history and PE in all patients with HT to verify the diagnosis, detect causes of 2° HT,	I	С
record CV risk factors, and to identify OD and other CVDs.		
Obtaining a family history is recommended to investigate familial predisposition to HT CVDs.	I	В
Office BP is recommended for screening and diagnosis of HT.	I	В
It is recommended that the diagnosis of HT be base on at least two BP measurements per visit and on at least two visits.	I	С

## **Blood pressure management, history, and physical examination (2)**

Recommendations	Class <sup>a</sup>	Level <sup>b</sup>
It is recommended that all hypertensive patients undergo palpation of the pulse at rest to determine HR and to search for arrhythmias, especially AF.	I	В
Out-of-office BP should be considered to confirm the diagnosis of HT identify the type of HT, detect hypotensive episodes, and maximize prediction of CV risk.	lla	В
For out-of-office BP measurement, ABPM or HBPM may be considered depending on indication, availability, ease, cost of use and, if appropriate, patient preference.	llb	С

### Laboratory investigations (1)

#### **Routine tests**

- Hb and/or Hct
- FPG
- Serum total cholesterol, LDL-C, HDL-C
- Fasting serum triglycerides
- Serum K and Na
- Serum uric acid
- Serum creatinine (with eGFR)
- Urine analysis:microscopic examination; urinary protein by dipstick test; test for microalbuminuria
- 12-lead ECG

### Laboratory investigations (2)

## Additional tests, based on history, physical examination, and findings from routine laboratory tests

- HbA<sub>1c</sub> (if FPG is >5.6 mmol/L (102 mg/dL) or previous diagnosis of diabetes)
- Quantitative proteinuria (if dipstick test if positive); urinary
   K and Na concentration and their ratio
- HBPM and 24-h ABPM
- ECG
- Holter monitoring in case of arrhythmias
- Carotid U/S
- Peripheral artery/abdominal U/S
- PWV
- ABI
- Fundoscopy

### Laboratory investigations (3)

#### **Extended evaluation (mostly domain of the specialist)**

- Further search for cerebral, cardiac, renal, and vascular damage, mandatory in resistant and complicated hypertension
- Search for secondary hypertension when suggested by history, physical examination, or routine and additional tests

# Stratification of total CV risk. Subjects with MH have a CV risk in the hypertension range

	Blood Pressure (mmHg)			
Other risk factors, asymptomatic organ damage or disease	High normal SBP 130–139 or DBP 85–89	Grade I 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
I–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.

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# Initiation of lifestyle changes and antihypertensive drug treatment

Other visit fraters	Blood Pressure (mmHg)					
Other risk factors, asymptomatic organ damage or disease	High normal SBP 130–139 or DBP 85–89	Grade   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	• No BP intervention	<ul> <li>Lifestyle changes for several months</li> <li>Then add BP drugs targeting &lt;140/90</li> </ul>	<ul> <li>Lifestyle changes for several weeks</li> <li>Then add BP drugs targeting &lt;140/90</li> </ul>	<ul> <li>Lifestyle changes</li> <li>Immediate BP drugs targeting &lt;140/90</li> </ul>		
I–2 RF	<ul> <li>Lifestyle changes</li> <li>No BP intervention</li> </ul>	<ul> <li>Lifestyle changes for several weeks</li> <li>Then add BP drugs targeting &lt;140/90</li> </ul>	<ul> <li>Lifestyle changes for several weeks</li> <li>Then add BP drugs targeting &lt;140/90</li> </ul>	<ul> <li>Lifestyle changes</li> <li>Immediate BP drugs targeting &lt;140/90</li> </ul>		
≥3 RF	<ul> <li>Lifestyle changes</li> <li>No BP intervention</li> </ul>	<ul> <li>Lifestyle changes for several weeks</li> <li>Then add BP drugs targeting &lt;140/90</li> </ul>	<ul> <li>Lifestyle changes</li> <li>BP drugs targeting &lt;140/90</li> </ul>	<ul> <li>Lifestyle changes</li> <li>Immediate BP drugs targeting &lt;140/90</li> </ul>		
OD, CKD stage 3 or diabetes	<ul> <li>Lifestyle changes</li> <li>No BP intervention</li> </ul>	<ul> <li>Lifestyle changes</li> <li>BP drugs targeting &lt;140/90</li> </ul>	<ul> <li>Lifestyle changes</li> <li>BP drugs targeting &lt;140/90</li> </ul>	<ul> <li>Lifestyle changes</li> <li>Immediate BP drugs targeting &lt;140/90</li> </ul>		
Symptomatic CVD, CKD stage ≥4 or diabetes with OD/RFs	<ul> <li>Lifestyle changes</li> <li>No BP intervention</li> </ul>	<ul> <li>Lifestyle changes</li> <li>BP drugs targeting &lt;140/90</li> </ul>	<ul> <li>Lifestyle changes</li> <li>BP drugs targeting &lt;140/90</li> </ul>	<ul> <li>Lifestyle changes</li> <li>Immediate BP drugs targeting &lt;140/90</li> </ul>		

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.

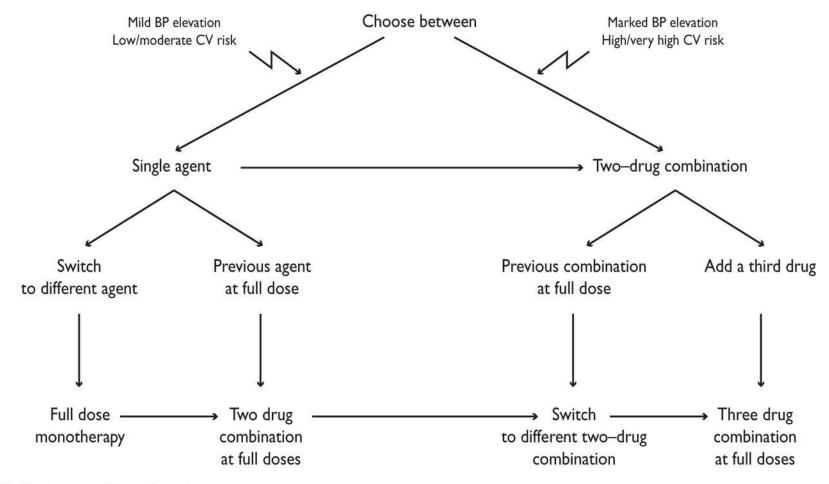
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## **Adoption of lifestyle changes**

Recommendations	Class <sup>a</sup>	Level <sup>b</sup>
Salt restriction to 5-6 g per day is recommended.	I	В
Moderation of alcohol consumption to no more than 20-30 g of ethanol per day in men and to no more than 10-20 g of ethanol per day in women is recommended.	I	В
Increased consumption of vegetables, fruits, and low-fat dairy products is recommended.	I	В
Reduction of weight to BMI of 25 kg/m <sup>2</sup> and of waist circumference to <102 cm in men and <88 cm in women is recommended, unless contraindicated.	I	В
Regular exercise, i.e. at least 30 min of moderate dynamic exercise on 5 to 7 days per week is recommended.	Ι	В
It is recommended to give all smokers advice to quit smoking and to offer assistance.	Ι	В

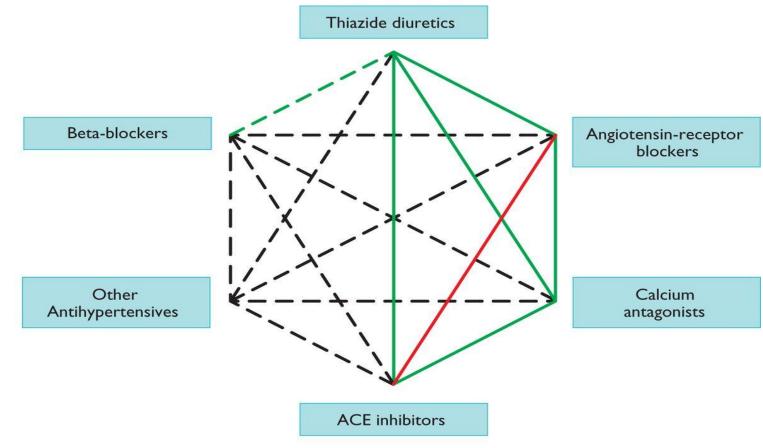
# Monotherapy vs. drug combination strategies to achieve target BP. Moving from a less intensive to a more intensive therapeutic strategy should be done whenever BP target is not achieved



BP = blood pressure; CV = cardiovascular.

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### Possible combinations of classes of antihypertensive drugs



ACE = angiotensin-converting enzyme.

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### **Treatment strategies and choice of drugs (1)**

Recommendations	Class <sup>a</sup>	Level <sup>b</sup>
Diuretics (thiazides, chlorthalidone and indapamide), BB, CA, ACEI, and ARB are all suitable and recommended for the initiation and maintenance of antihypertensive treatment, either as monotherapy or in some combinations with each other.		A
Some agents should be considered as the preferential choice in specific conditions because used in trials in those conditions or because of greater effectiveness in specific types of OD.	lla	С
Initiation of antihypertensive therapy with a two- drug combination may be considered in patients with markedly high baseline BP or at high CV risk.	llb	С

#### **Treatment strategies and choice of drugs (2)**

Recommendations	Class <sup>a</sup>	Level <sup>b</sup>
The combination of two antagonists of the RAS is not recommended and should be discouraged.	III	A
Other drug combinations are beneficial in BP reduction. However, combinations that have been successfully used in trials may b preferable.	lla	С
Fixed dose combination may be recommended and favoured, to improves adherence,	llb	В

### **Antihypertensive Treatment: Preferred Drugs (1)**

• General rules: lower SBP and DBP to goal. Use any effective agent at adequate doses, if useful in combination. Use long acting agents to lower BP throughout 24 hours. Avoid or minimize adverse effects.

#### <u>Condition</u>

ISH (elderly) Metabolic syndrome Diabetes mellitus Pregnancy Blacks

Diuretics, CCB ACE-I, ARB, CCB ACE-I, ARB CCB, methyldopa, β-blockers Diuretics, CCB

## • <u>Subclinical organ damage</u>

LVH

Asymptomatic atherosclerosis Microalbuminuria Renal dysfunction ACE-I, CCB, ARB CCB, ACE-I ACE-I, ARB ACE-I, ARB

#### **Antihypertensive Treatment: Preferred Drugs (2)**

#### <u>Clinical CV event</u>

Previous stroke Previous MI Angina pectoris Heart failure

#### Aortic aneurysm

Atrial filbrillation, prevention

Atrial fibrillation, ventricular rate control ESRD/proteinuria Peripheral artery disease Any agent effectively lowering BP BB, ACE-I, ARB

BB, calcium antagonist

Diuretic, BB, ACE -I, ARB, mineralocorticoid receptor antagonist

#### BB

Consider ARB, ACE-I, BB or mineralocorticoid receptor antagonist

BB, non-DHP calcium antagonist

ACE-I, ARB ACE-I, calcium antagonist

### **Blood pressure goals in hypertensive patients**

Recommendations	Class <sup>a</sup>	Level <sup>b</sup>
A SBP goal <140 mmHg;		
a) is recommended in patients at low-moderate CV risk;	I	В
b) is recommended in patients with diabetes;	I	А
c) should be considered in patients with previous stroke or TIA;	lla	В
d) should be considered in patients with CHD;	lla	В
e) should be considered in patients with DM or non-DM CKD	lla	В
In elderly <80 yrs old with SBP <u>&gt;</u> 160 mmHg reduces SBP to between 150-140 mmHg	I	А
In fit elderly patients <80 yrs old, target SBP <140 mmHg may be considered, whereas in the fragile elderly population SBP goals should be adapted to individual tolerability	llb	С
In individuals >80 yrs and with initial SBP $\geq$ 160 mmHg, reduces SBP to 150-140 mmHg provided they are in good physical and mental conditions		В
A DBP target of <90 mmHg is always recommended, except in diabetic patients, <85 mmHg are recommended. DBP 80-85 mmHg are safe and well tolerated	Ι	A

## **Treatment strategies in special conditions**

#### Therapeutic strategies in patients with resistant hypertension

Recommendations	Class <sup>a</sup>	Level <sup>b</sup>
In resistant hypertensive patients it is recommended that physicians check whether the drugs included in the existing multiple drug regimen have any BP lowering effect, and withdraw them if their effect is absent or minimal.	I	С
Mineralocorticoid receptor antagonists, amiloride, and the alpha-l- blocker doxazosin should be considered, if no contraindication exists.	lla	В
In case of ineffectiveness of drug treatment invasive procedures such as renal denervation and baroreceptor stimulation may be considered.	llb	С
Until more evidence is available on the long-term efficacy and safety of renal denervation and baroreceptor stimulation, it is recommended that these procedures remain in the hands of experienced operators and diagnosis and follow-up restricted to hypertension centers.	I	С
It is recommended that the invasive approaches are considered only for truly resistant hypertensive patients, with clinic values ≥160 mmHg SBP or ≥110 mmHg DBP and with BP elevation confirmed by ABPM.	Ι	С

