

## 2013 Practice guidelines for the management of arterial hypertension of the European Society of Hypertension (ESH) and the European Society of Cardiology (ESC)

### *ESH/ESC Task Force for the Management of Arterial Hypertension*

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## 1. INTRODUCTION

### 1.1 Principles

The 2013 European Society of Hypertension/European Society of Cardiology (ESH/ESC) guidelines continue to adhere to some fundamental principles that inspired the 2003 and 2007 guidelines, namely to base recommendations on properly conducted studies identified from an extensive review of the literature; to consider, as the highest priority, data from randomized, controlled trials and their meta-analyses, but not to disregard the results of observational and other studies of appropriate scientific calibre; and to grade the level of scientific evidence and the strength of recommendations in order to more effectively alert physicians on recommendations that are based on the opinions of the experts rather than on evidence (Tables 1 and 2). When appropriately recognized, this can avoid guidelines being perceived as prescriptive and favour the performance of studies wherein opinion prevails and evidence is lacking.

This shortened version of the ESH/ESC guidelines is for the practicing physician who often requires simplified information. However, whenever the physicians would like to know the source of the data upon which the recommendations are based, they are encouraged to consult the extensive version of the ESH/ESC guidelines wherein adequate references are given. These guidelines, however, do not override the individual responsibility of healthcare professionals to make appropriate decisions in the circumstances of the individual patient.

### 1.2 New aspects

Because of new evidence on several diagnostic and therapeutic aspects of hypertension, the present guidelines differ from the 2007 ones in several points:

1. Re-emphasis on integration of blood pressure (BP), cardiovascular risk factors, asymptomatic organ damage and clinical complications for total cardiovascular risk assessment.
2. Update of the prognostic significance of out-of-office BP (both ambulatory and home BP), white-coat hypertension and masked hypertension.
3. Initiation of antihypertensive drug treatment only in patients with SBP or DBP values at least 140 or 90 mmHg, independent of level of total cardiovascular risk.

4. Unified target SBP (<140 mmHg) in both higher and lower cardiovascular risk patients.
5. Revised recommendations on treatment of hypertension in young people and in the elderly.
6. Liberal approach to initial monotherapy, without any all-ranking purpose scheme.
7. Revised therapeutic algorithm for achieving target BP.
8. Revised attention to resistant hypertension.

## 2. DEFINITIONS AND CLASSIFICATIONS

The continuous relationship between BP and cardiovascular and renal events make the distinction between normotension and hypertension difficult. In practice, however, cut-off BP values are universally used to facilitate the decision about treatment (Table 3).

In order to help prognosis, total cardiovascular risk should be stratified in different categories (low, moderate, high and very high risk referred to the 10-year risk of cardiovascular mortality), based on BP category, cardiovascular risk factors, asymptomatic organ damage and presence of diabetes, and symptomatic cardiovascular disease or chronic kidney disease (CKD), as summarized in Fig. 1.

## 3. DIAGNOSTIC EVALUATION

The initial evaluation of a patient with hypertension should confirm the diagnosis of hypertension; detect causes of secondary hypertension; and assess cardiovascular risk, organ damage and concomitant clinical conditions. This calls for BP measurement, medical history including family history, physical examination, laboratory investigation and further diagnostic tests. Some of the investigations are needed in all patients; others only in specific patient groups.

### 3.1 Blood pressure measurement

#### 3.1.1 Office and out-of-office blood pressure

Although conventional office BP measurement currently remains the 'gold standard' for screening, diagnosis and management of hypertension, it is generally accepted that out-of-office BP provides important adjunct information.

TABLE 1. 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 and effective.	Is recommended/is indicated
Class II Class II a Class II b	Conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of the given treatment or procedure. Weight of evidence/opinion is in favour of usefulness/efficacy. Usefulness/efficacy is less well established by evidence/opinion.	Should be considered 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.	Is not recommended

**TABLE 2. Levels of evidence**

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

**TABLE 3. Definitions and classification of office blood pressure levels (mmHg)**

Category	SBP		DBP
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

The blood pressure (BP) category is defined by the highest BP level, whether systolic blood pressure (SBP) or diastolic blood pressure (DBP). Isolated systolic hypertension should be graded 1, 2 or 3 according to SBP values in the ranges indicated.

At present, BP can no longer be estimated using a mercury manometer in many – although not all – European countries. Auscultatory or oscillometric semiautomatic sphygmomanometers are used instead, but these devices should be validated according to standardized protocols and their accuracy checked periodically. Table 4 gives instructions for correct office BP measurements, and Table 5 provides clinical indications for out-of-office BP measurement, namely measurements at home or over the 24 h.

Office BP is usually higher than ambulatory and home BP and the difference increases as office BP increases. Cut-off values for the definition of hypertension by home and ambulatory BP are reported in Table 6.

### 3.1.2 White-coat and masked hypertension

The term ‘white-coat’ or ‘isolated office’ hypertension refers to a condition in which BP is elevated in the office

at repeated visits and normal out of the office either on ambulatory blood pressure monitoring or on home blood pressure monitoring. Conversely, BP may be normal in the office and abnormally high out of the medical environment, which is termed ‘masked’ or ‘isolated ambulatory’ hypertension. Cut-off values to be used are those in Table 6.

### 3.1.3 Central blood pressure

Owing to the variable superposition of incoming and reflected pressure waves along the arterial tree, aortic BP (central BP) may be different from brachial BP. Central BP can be estimated indirectly by various methods. The current guidelines consider that, despite the growing interest in these methods, more investigation is needed before recommending the routine measurement of central BP for clinical use.

### 3.2 Medical history

The information to be obtained at the time of the first diagnosis of hypertension is indicated in Table 7.

### 3.3 Physical examination

Physical examination aims to establish or verify the diagnosis of hypertension, establish current BP, screen for secondary causes of hypertension and refine global cardiovascular risk. Procedures for BP measurement are indicated in Tables 4 and 5. Other information to be obtained by physical examination is in Table 8.

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

**FIGURE 1** Stratification of total cardiovascular risk in categories of low, moderate, high and very high risk according to SBP and DBP and presence of risk factors (RFs), asymptomatic organ damage (OD), diabetes, chronic kidney disease (CKD) stage or symptomatic cardiovascular disease (CVD). Individuals with a high normal office but a raised out-of-office BP (masked hypertension) have a cardiovascular risk in the hypertension range. Individuals with a high office BP but normal out-of-office BP (white-coat hypertension), particularly if there is no diabetes, OD, CVD or CKD, have lower risk than sustained hypertension for the same office BP. BP, blood pressure; CV, cardiovascular; DBP, diastolic blood pressure; HT, hypertension; SBP, systolic blood pressure.

**TABLE 4. Office blood pressure measurement**

When measuring BP in the office, care should be taken:

- To allow the patients to sit for 3–5 min 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 SBP and DBP, 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 min after assumption of the standing position in elderly participants, 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.

BP, blood pressure; DBP, diastolic blood pressure; SBP, systolic blood pressure.

**TABLE 5. Clinical indications for out-of-office blood pressure measurement for diagnostic purposes**

Clinical indications for HBPM or ABPM

- Suspicion of white-coat hypertension
- Grade 1 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, postprandial, siesta-induced and drug-induced hypotension
- Elevated office BP or suspected preeclampsia 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

ABPM, ambulatory blood pressure monitoring; BP, blood pressure; CKD, chronic kidney disease; CV, cardiovascular; HBPM, home blood pressure monitoring.

### 3.4 Laboratory investigations

Laboratory investigations are directed at providing evidence for additional risk factors, searching for secondary hypertension and looking for organ damage. Investigations should proceed from the most simple to the more complicated ones, as summarized in Table 9.

**TABLE 6. Definitions of hypertension by office and out-of-office blood pressure levels**

Category	SBP (mmHg)	and/or	DBP (mmHg)
Office BP	≥140	and/or	≥90
Ambulatory BP			
Daytime (or awake)	≥135	and/or	≥85
Night-time (or asleep)	≥120	and/or	≥70
24-h	≥130	and/or	≥80
Home BP	≥135	and/or	≥85

BP, blood pressure; DBP, diastolic blood pressure; SBP, systolic blood pressure.

**TABLE 7. Personal and family medical history**

- Duration and previous level of high BP, including measurements at home
- Secondary hypertension
  - Family history of CKD (polycystic kidney)
  - History of renal disease, urinary tract infection, haematuria, analgesic abuse (parenchymal renal disease)
  - Drug/substance intake, for example oral contraceptives, liquorice, carbenoxolone, vasoconstrictive nasal drops, cocaine, amphetamines, glucocorticosteroids and mineralocorticosteroids, NSAIDs, erythropoietin, cyclosporine
  - Repetitive episodes of sweating, headache, anxiety, palpitations (pheochromocytoma)
  - Episodes of muscle weakness and tetany (hyperaldosteronism)
  - Symptoms suggestive of thyroid disease
- Risk factors
  - Family and personal history of hypertension and CVD
  - Family and personal history of dyslipidaemia
  - Family and personal history of diabetes mellitus (medications, blood glucose levels, polyuria).
  - Smoking habits
  - Dietary habits
  - Recent weight changes; obesity
  - Amount of physical exercise
  - Snoring; sleep apnoea (information also from partner)
  - Low birth weight.
- History and symptoms of organ damage and CVD
  - Brain and eyes: headache, vertigo, impaired vision, TIA, sensory or motor deficit, stroke, carotid revascularization
  - Heart: chest pain, shortness of breath, swollen ankles, myocardial infarction, revascularization, syncope, history of palpitations, arrhythmias, especially atrial fibrillation
  - Kidney: thirst, polyuria, nocturia, haematuria
  - Peripheral arteries: cold extremities, intermittent claudication, pain-free walking distance, peripheral revascularization
  - History of snoring/chronic lung disease/sleep apnoea
  - Cognitive dysfunction
- Hypertension management
  - Current antihypertensive medication
  - Past antihypertensive medication
  - Evidence of adherence or lack of adherence to therapy
  - Efficacy and adverse effects of drugs

BP, blood pressure; CKD, chronic kidney disease; CVD, cardiovascular disease; TIA, transient ischaemic attack.

### 3.5 Searching for asymptomatic organ damage

Owing to the importance of asymptomatic organ damage as an intermediate stage in the continuum of cardiovascular disease, and as a determinant of overall cardiovascular disease, signs of organ involvement should be sought carefully by appropriate techniques as indicated below.

### Search for asymptomatic organ damage, cardiovascular disease, and chronic kidney disease

Recommendations	Class	Level
<b>Heart</b>		
An ECG is recommended in all hypertensive patients to detect LVH, left atrial dilatation, arrhythmias, or concomitant heart disease.	I	B
In all patients with a history or physical examination suggestive of major arrhythmias, long-term ECG monitoring, and, in case of suspected exercise-induced arrhythmias, a stress ECG test should be considered.	IIa	C
An echocardiogram should be considered to refine CV risk, and confirm ECG diagnosis of LVH, left atrial dilatation or suspected concomitant heart disease, when these are suspected.	IIa	B
Whenever history suggests myocardial ischaemia, a stress ECG test is recommended, and, if positive or ambiguous, an imaging stress test (stress echocardiography, stress cardiac magnetic resonance or nuclear scintigraphy) is recommended.	I	C
<b>Arteries</b>		
Ultrasound scanning of carotid arteries should be considered to detect vascular hypertrophy or asymptomatic atherosclerosis, particularly in the elderly.	IIa	B
Carotid–femoral PWV should be considered to detect large artery stiffening.	IIa	B
Ankle–brachial index should be considered to detect PAD.	IIa	B
<b>Kidney</b>		
Measurement of serum creatinine and estimation of GFR is recommended in all hypertensive patients.	I	B
Assessment of urinary protein is recommended in all hypertensive patients by dipstick.	I	B
Assessment of microalbuminuria is recommended in spot urine and related to urinary creatinine excretion.	I	B
<b>Fundoscopy</b>		
Examination of the retina should be considered in difficult to control or resistant hypertensive patients to detect haemorrhages, exudates, and papilloedema, which are associated with increased CV risk.	IIa	C
Examination of the retina is not recommended in mild-to-moderate hypertensive patients without diabetes, except in young patients.	III	C
<b>Brain</b>		
In hypertensive patients with cognitive decline, brain magnetic resonance imaging or computed tomography may be considered for detecting silent brain infarctions, lacunar infarctions, microbleeds, and white matter lesions.	IIb	C

CV, cardiovascular; ECG, electrocardiogram; GFR, glomerular filtration rate; LVH, left ventricular hypertrophy; MRI, magnetic resonance imaging; PAD, peripheral artery disease; PWV, pulse wave velocity.

**TABLE 8. Physical examination for secondary hypertension, organ damage and obesity**

Signs suggesting secondary hypertension
Features of Cushing syndrome
Skin stigmata of neurofibromatosis (pheochromocytoma)
Palpation of enlarged kidneys (polycystic kidney)
Auscultation of abdominal murmurs (renovascular hypertension)
Auscultation of precordial or chest murmurs (aortic coarctation; aortic disease: upper extremity artery disease)
Diminished and delayed femoral pulses and reduced femoral BP compared to simultaneous arm BP (aortic coarctation; aortic disease; lower extremity artery disease)
Left–right arm BP difference (aortic coarctation; subclavian artery stenosis)
Signs of organ damage
Brain: motor or sensory defects
Retina: fundoscopic abnormalities
Heart: heart rate, 3rd or 4th heart sound, heart murmurs, arrhythmias, location of apical impulse, pulmonary rales, peripheral oedema
Peripheral arteries: absence, reduction or asymmetry of pulses cold extremities, ischaemic skin lesions
Carotid arteries: systolic murmurs
Evidence of obesity
Weight and height
Calculate BMI: $\text{body weight}/\text{height}^2$ ( $\text{kg}/\text{m}^2$ )
Waist circumference measured in the standing position, at a level midway between the lower border of the costal margin (the lowest rib) and uppermost border of the iliac crest

BP, blood pressure; BMI, body mass index.

**TABLE 9. Laboratory investigations**

Routine tests
Haemoglobin and/or haematocrit
Fasting plasma glucose
Serum total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol
Fasting serum triglycerides
Serum potassium and sodium
Serum uric acid
Serum creatinine (with estimation of GFR),
Urine analysis: microscopic examination; urinary protein by dipstick test; test for microalbuminuria
12-lead EGG.
Additional tests, based on history, physical examination and findings from routine laboratory tests
Haemoglobin A <sub>1c</sub> [if fasting plasma glucose is >5.6 mmol/l (102 mg/dl) or previous diagnosis of diabetes]
Quantitative proteinuria (if dipstick test is positive); urinary potassium and sodium concentration and their ratio
Home and 24-h ABPM
Echocardiogram
Holter monitoring in case of arrhythmias
Carotid ultrasound
Peripheral artery/abdominal ultrasound
Pulse wave velocity
Ankle–brachial index
Fundoscopy
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

ABPM, ambulatory blood pressure monitoring; ECG, electrocardiogram; GFR, glomerular filtration rate.

### 3.6 Searching for secondary forms of hypertension

A specific, potentially reversible cause of BP elevation can be identified in a relatively small number of adult patients with hypertension. However if basal work-up leads to the suspicion of a secondary form of hypertension, the patient should be referred to a specialized centre where specific diagnostic procedures may be performed.

## 4. TREATMENT APPROACH

### 4.1 Recommendations of previous guidelines revised

The 2007 ESH/ESC Guidelines, like many other scientific guidelines, recommended the use of antihypertensive drugs in patients with Grade 1 hypertension even in the absence of other risk factors or organ damage after nonpharmacological treatment had proved unsuccessful. This recommendation also specifically included the

elderly hypertensive patient. The 2007 Guidelines also suggested drug treatment of patients with diabetes, previous cardiovascular disease (CVD) or CKD even when their BP was in the high normal range (130–139/85–89 mmHg). Furthermore, a lower BP target was recommended for these high or very high risk patients (<130/80 mmHg) than in patients at low–moderate risk (<140/90 mmHg). These recommendations were reappraised in a 2009 ESH Task Force document on the basis of an extensive critical review of the evidence. The following now summarizes the conclusions for the current guidelines: attention should be directed to the Class of recommendation and the Level of evidence, in order to distinguish what is considered compelling and what simply prudent.

Figure 2 also summarizes recommendations and suggestions for treatment initiation and BP targets in the context of total risk stratification of hypertensive individuals.

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	• No BP intervention	• Lifestyle changes for several months • Then add BP drugs targeting <140/90	• Lifestyle changes for several weeks • Then add BP drugs targeting <140/90	• Lifestyle changes • Immediate BP drugs targeting <140/90
1–2 RF	• Lifestyle changes • No BP intervention	• Lifestyle changes for several weeks • Then add BP drugs targeting <140/90	• Lifestyle changes for several weeks • Then add BP drugs targeting <140/90	• Lifestyle changes • Immediate BP drugs targeting <140/90
≥3 RF	• Lifestyle changes • No BP intervention	• Lifestyle changes for several weeks • Then add BP drugs targeting <140/90	• Lifestyle changes • BP drugs targeting <140/90	• Lifestyle changes • Immediate BP drugs targeting <140/90
OD, CKD stage 3 or diabetes	• Lifestyle changes • No BP intervention	• Lifestyle changes • BP drugs targeting <140/90	• Lifestyle changes • BP drugs targeting <140/90	• Lifestyle changes • Immediate BP drugs targeting <140/90
Symptomatic CVD, CKD stage ≥4 or diabetes with OD/RFs	• Lifestyle changes • No BP intervention	• Lifestyle changes • BP drugs targeting <140/90	• Lifestyle changes • BP drugs targeting <140/90	• Lifestyle changes • Immediate BP drugs targeting <140/90

**FIGURE 2** Initiation of lifestyle changes and antihypertensive drug treatment. Targets of treatment are also indicated. Colours are as in Fig. 1. See 4.3 and 6.5 for evidence that, in patients with diabetes, the optimal DBP target is between 80 and 85 mmHg. In the high normal blood pressure (BP) range, drug treatment should be considered in the presence of a raised out-of-office BP (masked hypertension). See 4.2 and 6.3 for lack of evidence in favour of drug treatment in young individuals with isolated systolic hypertension. CKD, chronic kidney disease; CVD, cardiovascular disease; DBP, diastolic blood pressure; HT, hypertension; OD, organ damage; RF, risk factor; SBP, systolic blood pressure.

## 4.2 When to initiate antihypertensive drug treatment

### Initiation of antihypertensive drug treatment

Recommendations	Class	Level
Prompt initiation of drug treatment is recommended in individuals with grade 2 and 3 hypertension with any level of CV risk, a few weeks after or simultaneously with initiation of lifestyle changes.	I	A
Lowering BP with drugs is also recommended when total CV risk is high because of OD, diabetes, CVD or CKD, even when hypertension is in the grade 1 range.	I	B
Initiation of antihypertensive drug treatment should also be considered in grade 1 hypertensive patients at low to moderate risk, when BP is within this range at several repeated visits or elevated by ambulatory BP criteria, and remains within this range despite a reasonable period of time with lifestyle measures.	IIa	B
In elderly hypertensive patients drug treatment is recommended when SBP is $\geq 160$ mmHg.	I	A
Antihypertensive drug treatment may also be considered in the elderly (at least when younger than 80 years) when SBP is in the 140–159 mmHg range, provided that antihypertensive treatment is well tolerated.	IIb	C
Unless the necessary evidence is obtained it is not recommended to initiate antihypertensive drug therapy at high normal BP.	III	A
Lack of evidence does also not allow recommending to initiate antihypertensive drug therapy in young individuals with isolated elevation of brachial SBP, but these individuals should be followed closely with lifestyle recommendations.	III	A

BP, blood pressure; CKD, chronic kidney disease; CV, cardiovascular; CVD cardiovascular disease; OD, organ damage, SBP, systolic blood pressure.

## 4.3 Blood pressure treatment targets

### Blood pressure goals in hypertensive patients

Recommendations	Class	Level
A SBP goal <140 mmHg:		
a) is recommended in patients at low–moderate CV risk;	I	B
b) is recommended in patients with diabetes;	I	A
c) should be considered in patients with previous stroke or TIA;	IIa	B
d) should be considered in patients with CHD;	IIa	B
e) should be considered in patients with diabetic or non-diabetic CKD.	IIa	B
In elderly hypertensives less than 80 years old with SBP $\geq 160$ mmHg there is solid evidence to recommend reducing SBP to between 150 and 140 mmHg.	I	A
In fit elderly patients less than 80 years old SBP values <140 mmHg may be considered, whereas in the fragile elderly population SBP goals should be adapted to individual tolerability.	IIb	C
In individuals older than 80 years and with initial SBP $\geq 160$ mmHg, it is recommended to reduce SBP to between 150 and 140 mmHg provided they are in good physical and mental conditions.	I	B
A DBP target of <90 mmHg is always recommended, except in patients with diabetes, in whom values <85 mmHg are recommended. It should nevertheless be considered that DBP values between 80 and 85 mmHg are safe and well tolerated.	I	A

CHD, coronary heart disease; CKD, chronic kidney disease; CV, cardiovascular; DBP, diastolic blood pressure; SBP, systolic blood pressure; TIA, transient ischaemic attack.

## 5. TREATMENT STRATEGIES

### 5.1 Lifestyle changes

Appropriate lifestyle changes are the cornerstone for the prevention of hypertension. They are also important for its treatment, although they should never delay the initiation of drug therapy in patients at high level of risk. In addition to the BP-lowering effect, lifestyle changes contribute to the control of other cardiovascular risk factors and clinical conditions.

The lifestyle measures that have been shown to be capable of reducing BP and therefore recommended are as follows:

1. salt restriction to 5–6 g/day;

2. moderation of alcohol consumption to no more than 20–30 g of ethanol per day in men and 10–20 g/day in women;
3. high consumption of vegetables and fruits and low-fat dairy products;
4. reduction of weight to a BMI of 25 kg/m<sup>2</sup> and waist circumference to less than 102 cm in men and less than 88 cm in women;
5. at least 30 min of moderate dynamic exercise on 5 to 7 days per week.

### 5.2 Pharmacological therapy

#### 5.2.1 Choice of antihypertensive drugs

The current guidelines reconfirm that all major classes of antihypertensive agents are suitable for the initiation and

**TABLE 10. Compelling and possible contraindications to the use of antihypertensive drugs**

Drug	Compelling	Possible
Diuretics	Gout	Metabolic syndrome; glucose intolerance; pregnancy; hypercalcaemia; hypokalaemia
β-Blockers	Asthma; A-V block (Grade 2 or 3)	Metabolic syndrome; glucose intolerance; athletes and physically active patients; chronic obstructive pulmonary disease (except for vasodilator β-blockers)
Calcium antagonists (dihydropyridines)		Tachyarrhythmia; heart failure
Calcium antagonists (verapamil, diltiazem)	A-V block (Grade 2 or 3, trifascicular block); severe left ventricular dysfunction; heart failure	
ACE inhibitors	Pregnancy; angioneurotic oedema; hyperkalaemia; bilateral renal artery stenosis	Women with childbearing potential
ARBs	Pregnancy; hyperkalaemia; bilateral renal artery stenosis	Women with childbearing potential
Mineralocorticoid receptor antagonists	Acute or severe renal failure (eGFR <30 ml/min); hyperkalaemia	

ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; A-V, atrio-ventricular; eGFR, estimated glomerular filtration rate.

**TABLE 11. Drugs to be preferred in specific conditions**

Condition	Drug
Asymptomatic organ damage	
Left ventricular hypertrophy	ACE inhibitor, calcium antagonist, ARB
Asymptomatic atherosclerosis	Calcium antagonist, ACE inhibitor
Microalbuminuria	ACE inhibitor, ARB
Renal dysfunction	ACE inhibitor, ARB
Clinical CV event	
Previous stroke	Any agent effectively lowering BP
Previous myocardial infarction	BB, ACE inhibitor, ARB
Angina pectoris	BB, calcium antagonist
Heart failure	Diuretic, BB, ACE inhibitor, ARB, mineralocorticoid receptor antagonists
Aortic aneurysm	BB
Atrial fibrillation, prevention	Consider ARB, ACE inhibitor, BB or mineralocorticoid receptor antagonist
Atrial fibrillation, ventricular rate control	BB, non-dihydropyridine calcium antagonist
ESRD/proteinuria	ACE inhibitor, ARB
Peripheral artery disease	ACE inhibitor, calcium antagonist
Other	
Isolated systolic hypertension (elderly)	Diuretic, calcium antagonist
Metabolic syndrome	ACE inhibitor, ARB, calcium antagonist
Diabetes mellitus	ACE inhibitor, ARB
Pregnancy	Methyldopa, BB, calcium antagonist
Blacks	Diuretic, calcium antagonist

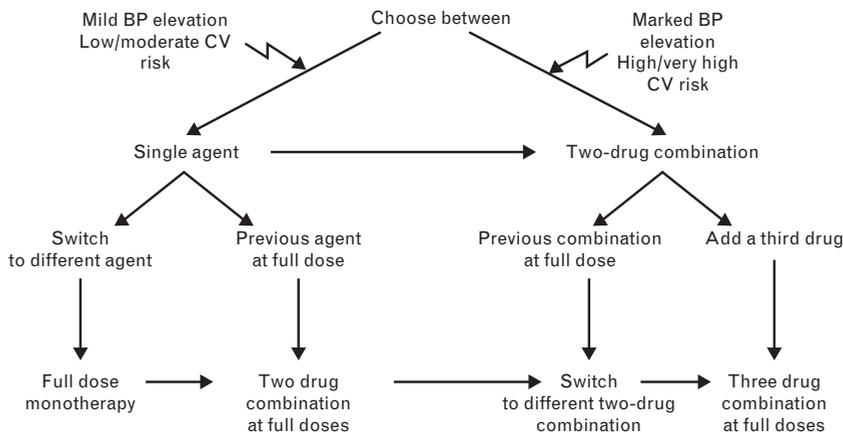
ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; BB, β-blocker; BP, blood pressure; CV, cardiovascular; ESRD, end-stage renal disease.

maintenance of antihypertensive treatment either in monotherapy or in some combinations, and that no all-purpose ranking of drugs for general antihypertensive usage is evidence based. All classes have their advantages but also contraindications, and may be preferentially used or avoided in specific conditions. Contraindications and preferred indications are listed in Tables 10 and 11.

### 5.2.2 Monotherapy and combination therapy

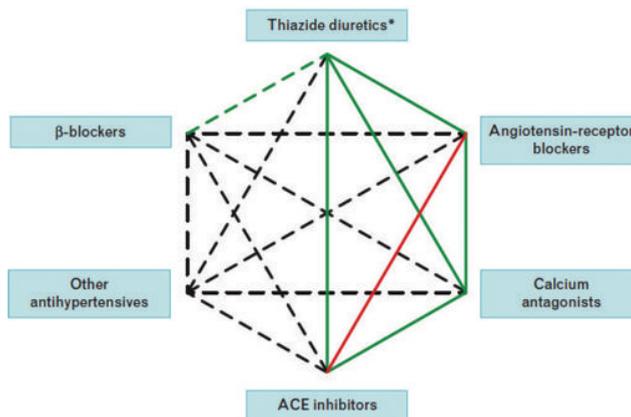
The current guidelines share the 2007 Guidelines' opinion that monotherapy can reduce BP to target only

in a limited number of patients and that most patients require the combination of at least two drugs, and they reconfirm that initiation with a drug combination can be considered in patients at high cardiovascular risk or with markedly high BP. The algorithm of Fig. 3, however, is a modification of the 2007 one, to emphasize that adding drugs to drugs should be done with attention to results and any compound overtly ineffective or minimally effective should be replaced, rather than retained in an automatic step-up multiple-drug approach. Combinations to be preferred or avoided are illustrated in Fig. 4.



**Moving from a less intensive to a more intensive therapeutic strategy should be done whenever BP target is not achieved.**

**FIGURE 3** Monotherapy vs. drug combination strategies to achieve target blood pressure (BP). CV, cardiovascular.



**FIGURE 4** Possible combinations of classes of antihypertensive drugs. Green continuous lines: preferred combinations; green dashed line: useful combination (with some limitations); black dashed lines: possible but less well tested combinations; red continuous line: not recommended combination. Although verapamil and diltiazem are sometimes used with a  $\beta$ -blocker to improve ventricular rate control in permanent atrial fibrillation, only dihydropyridine calcium antagonists should normally be combined

Strengths of recommendations about choice of drugs and combinations of antihypertensive agents are given in the summary table below.

**Treatment strategies and choice of drugs**

Recommendations	Class	Level
Diuretics (thiazides, chlorthalidone and indapamide), beta-blockers, calcium antagonists, ACE inhibitors, and angiotensin receptor blockers are all suitable and recommended for the initiation and maintenance of antihypertensive treatment, either as monotherapy or in some combinations with each other.	I	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.	IIa	C
Initiation of antihypertensive therapy with a two-drug combination may be considered in patients with markedly high baseline BP or at high CV risk.	IIb	C
The combination of two antagonists of the RAS is not recommended and should be discouraged.	III	A
Other drug combinations should be considered and probably are beneficial in proportion to the extent of BP reduction. However, combinations that have been successfully used in trials may be preferable.	IIa	C
Combinations of two antihypertensive drugs at fixed doses in a single tablet may be recommended and favoured, because reducing the number of daily pills improves adherence, which is low in patients with hypertension.	IIb	B

ACE, angiotensin-converting enzyme; BP, blood pressure, CV, cardiovascular; OD, organ damage; RAS, renin-angiotensin system.

## 6. TREATMENT STRATEGIES IN SPECIAL CONDITIONS

Summary recommendations for antihypertensive treatment strategies in various conditions are listed below.

### 6.1 White-coat and masked hypertension

#### Treatment strategies in white-coat and masked hypertension

Recommendations	Class	Level
In white-coat hypertensives without additional risk factors, therapeutic intervention should be considered to be limited to lifestyle changes only, but this decision should be accompanied by a close follow-up.	IIa	C
In white-coat hypertensives with a higher CV risk because of metabolic derangements or asymptomatic OD, drug treatment may be considered in addition to lifestyle changes.	IIb	C
In masked hypertension, both lifestyle measures and antihypertensive drug treatment should be considered, because this type of hypertension has been consistently found to have a CV risk very close to that of in- and out-of-office hypertension.	IIa	C

CV, cardiovascular; OD, organ damage.

### 6.2 Elderly

#### Antihypertensive treatment strategies in the elderly

Recommendations	Class	Level
In elderly hypertensives with SBP $\geq 160$ mmHg there is solid evidence to recommend reducing SBP to between 150 and 140 mmHg.	I	A
In fit elderly patients <80 years old antihypertensive treatment may be considered at SBP values $\geq 140$ mmHg with a target SBP <140 mmHg if treatment is well tolerated.	IIb	C
In individuals older than 80 years with an initial SBP $\geq 160$ mmHg it is recommended to reduce SBP to between 150 and 140 mmHg, provided they are in good physical and mental conditions.	I	B
In frail elderly patients, it is recommended to leave decisions on antihypertensive therapy to the treating physician, and based on monitoring of the clinical effects of treatment.	I	C
Continuation of well-tolerated antihypertensive treatment should be considered when a treated individual becomes octogenarian.	IIa	C
All hypertensive agents are recommended and can be used in the elderly, although diuretics and calcium antagonists may be preferred in isolated systolic hypertension.	I	A

SBP, systolic blood pressure.

### 6.3 Young adults

Recommendations	Class	Level
Antihypertensive drug treatment, in addition to lifestyle measures, may be considered prudent in young adults with DBP > 90 mmHg and, especially when other risk factors are present, BP should be reduced to < 140/90 mmHg	IIb	B
Antihypertensive drug therapy is not recommended in young individuals with isolated elevation of brachial SBP, but these individuals should be followed closely with lifestyle recommendations	III	A

BP, blood pressure; DBP, diastolic blood pressure; SBP, systolic blood pressure.

### 6.4 Women

#### Treatment strategies in hypertensive women

Recommendations	Class	Level
Hormone therapy and selective oestrogen receptor modulators are not recommended and should not be used for primary or secondary prevention of CVD. If treatment of younger perimenopausal women is considered for severe menopausal symptoms, the benefits should be weighed against potential risks.	III	A
Drug treatment of severe hypertension in pregnancy (SBP >160 mmHg or DBP >110 mmHg) is recommended.	I	C
Drug treatment may also be considered in pregnant women with persistent elevation of BP $\geq 150/95$ mmHg, and in those with BP $\geq 140/90$ mmHg in the presence of gestational hypertension, subclinical OD or symptoms.	IIb	C
In women at high risk of pre-eclampsia, provided they are at low risk of gastrointestinal haemorrhage, treatment with low dose aspirin from 12 weeks until delivery may be considered.	IIb	B
In women with child-bearing potential RAS blockers are not recommended and should be avoided.	III	C
Methyldopa, labetalol and nifedipine should be considered preferential antihypertensive drugs in pregnancy. Intravenous labetalol or infusion of nitroprusside should be considered in case of emergency (pre-eclampsia).	IIa	B

BP, blood pressure; CVD, cardiovascular disease; DBP, diastolic blood pressure; OD, organ damage; RAS, renin-angiotensin system; SBP, systolic blood pressure.

## 6.5 Diabetes mellitus

Treatment strategies in patients with diabetes

Recommendations	Class	Level
While initiation of antihypertensive drug treatment in diabetic patients whose SBP is $\geq 160$ mmHg is mandatory, it is strongly recommended to start drug treatment also when SBP is $\geq 140$ mmHg.	I	A
A SBP goal $<140$ mmHg is recommended in patients with diabetes.	I	A
The DBP target in patients with diabetes is recommended to be $<85$ mmHg.	I	A
All classes of antihypertensive agents are recommended and can be used in patients with diabetes; RAS blockers may be preferred, especially in the presence of proteinuria or microalbuminuria.	I	A
It is recommended that individual drug choice takes comorbidities into account.	I	C
Simultaneous administration of two blockers of the RAS is not recommended and should be avoided in patients with diabetes.	III	B

DBP, diastolic blood pressure; RAS, renin-angiotensin system; SBP, systolic blood pressure.

## 6.6 Metabolic syndrome

Treatment strategies in hypertensive patients with metabolic syndrome

Recommendations	Class	Level
Lifestyle changes, particularly weight loss and physical exercise, are to be recommended to all individuals with the metabolic syndrome. These interventions improve not only BP, but the metabolic components of the syndrome and delay diabetes onset.	I	B
As the metabolic syndrome can be considered a 'pre-diabetic' state, antihypertensive agents potentially improving or at least not worsening insulin sensitivity, such as RAS blockers and calcium antagonists, should be considered as the preferred drugs. Beta-blockers (with the exception of vasodilating beta-blockers) and diuretics should be considered only as additional drugs, preferably in association with a potassium-sparing agent.	IIa	C
It is recommended to prescribe antihypertensive drugs with particular care in hypertensive patients with metabolic disturbances when BP is $\geq 140/90$ mmHg after a suitable period of lifestyle changes, and to maintain BP $<140/90$ mmHg.	I	B
BP lowering drugs are not recommended in individuals with metabolic syndrome and high normal BP.	III	A

BP, blood pressure; RAS, renin-angiotensin system.

## 6.7 Diabetic and nondiabetic nephropathy

Therapeutic strategies in hypertensive patients with nephropathy

Recommendations	Class	Level
Lowering SBP to $<140$ mmHg should be considered.	IIa	B
When overt proteinuria is present, SBP values $<130$ mmHg may be considered, provided that changes in eGFR are monitored.	IIb	B
RAS blockers are more effective in reducing albuminuria than other antihypertensive agents, and are indicated in hypertensive patients in the presence of microalbuminuria or overt proteinuria.	I	A
Reaching BP goals usually requires combination therapy, and it is recommended to combine RAS blockers with other antihypertensive agents.	I	A
Combination of two RAS blockers, though potentially more effective in reducing proteinuria, is not recommended.	III	A
Aldosterone antagonists cannot be recommended in CKD, especially in combination with a RAS blocker, because of the risk of excessive reduction in renal function and of hyperkalaemia.	III	C

BP, blood pressure; CKD, chronic kidney disease; GFR, glomerular filtration rate; RAS, renin-angiotensin system; SBP, systolic blood pressure.

## 6.8 Cerebrovascular disease

Therapeutic strategies in hypertensive patients with cerebrovascular disease

Recommendations	Class	Level
It is not recommended to intervene with BP-lowering therapy during the first week after acute stroke irrespective of BP level, although clinical judgement should be used in the face of very high SBP values.	III	B
Antihypertensive treatment is recommended in hypertensive patients with a history of stroke or TIA, even when initial SBP is in the 140–159 mmHg range.	I	B
In hypertensive patients with a history of stroke or TIA, a SBP goal of $<140$ mmHg should be considered.	IIa	B
In elderly hypertensives with previous stroke or TIA, SBP values for intervention and goal may be considered to be somewhat higher.	IIb	B
All drug regimens are recommended for stroke prevention, provided that BP is effectively reduced.	I	A

BP, blood pressure; SBP, systolic blood pressure; TIA, transient ischaemic attack.

## 6.9 Heart disease

### Therapeutic strategies in hypertensive patients with heart disease

Recommendations	Class	Level
In hypertensive patients with CHD, a SBP goal <140 mmHg should be considered.	IIa	B
In hypertensive patients with a recent myocardial infarction beta-blockers are recommended. In case of other CHD all antihypertensive agents can be used, but beta-blockers and calcium antagonists are to be preferred, for symptomatic reasons (angina).	I	A
Diuretics, beta-blockers, ACE inhibitors, angiotensin receptor blockers, and/or mineralocorticoid receptor antagonists are recommended in patients with heart failure or severe LV dysfunction to reduce mortality and hospitalization.	I	A
In patients with heart failure and preserved EF, there is no evidence that antihypertensive therapy per se or any particular drug, is beneficial. However, in these patients, as well as in patients with hypertension and systolic dysfunction, lowering SBP to around 140 mmHg should be considered. Treatment guided by relief of symptoms (congestion with diuretics, high heart rate with beta-blockers, etc.) should also be considered.	IIa	C
ACE inhibitors and angiotensin receptor blockers (and beta-blockers and mineralocorticoid receptor antagonists if heart failure coexists) should be considered as antihypertensive agents in patients at risk of new or recurrent atrial fibrillation.	IIa	C
It is recommended that all patients with LVH receive antihypertensive agents.	I	B
In patients with LVH, initiation of treatment with one of the agents that have shown a greater ability to regress LVH should be considered, i.e. ACE inhibitors, angiotensin receptor blockers and calcium antagonists.	IIa	B

ACE, angiotensin-converting enzyme; CHD, coronary heart disease; EF, ejection fraction; LV, left ventricular; LVH, left ventricular hypertrophy; SBP, systolic blood pressure.

## 6.10 Atherosclerosis, arteriosclerosis and peripheral artery disease

### Therapeutic strategies in hypertensive patients with atherosclerosis, arteriosclerosis, and peripheral artery disease

Recommendations	Class	Level
In the presence of carotid atherosclerosis, prescription of calcium antagonists and ACE inhibitors should be considered as these agents have shown a greater efficacy in delaying atherosclerosis progression than diuretics and beta-blockers.	IIa	B
In hypertensive patients with a PWV above 10 m/s all antihypertensive drugs should be considered provided that a BP reduction to <140/90 mmHg is consistently achieved.	IIa	B
Antihypertensive therapy is recommended in hypertensive patients with PAD to achieve a goal of <140/90 mmHg, because of their high risk of myocardial infarction, stroke, heart failure, and CV death.	I	A
Though a careful follow up is necessary, beta-blockers may be considered for the treatment of arterial hypertension in patients with PAD, since their use does not appear to be associated with exacerbation of PAD symptoms.	IIb	A

ACE, angiotensin-converting enzyme; BP, blood pressure; CV, cardiovascular; PAD, peripheral artery disease; PWV, pulse wave velocity.

## 6.11 Resistant hypertension

### Therapeutic strategies in patients with resistant hypertension

Recommendations	Class	Level
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	C
Mineralocorticoid receptor antagonists, amiloride, and the alpha-1-blocker doxazosin should be considered, if no contraindication exists.	IIa	B
In case of ineffectiveness of drug treatment invasive procedures such as renal denervation and baroreceptor stimulation may be considered.	IIb	C
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	C
It is recommended that the invasive approaches are considered only for truly resistant hypertensive patients, with clinic values $\geq 160$ mmHg SBP or $\geq 110$ mmHg DBP and with BP elevation confirmed by ABPM.	I	C

ABPM, ambulatory blood pressure monitoring; BP, blood pressure; DBP, diastolic blood pressure; SBP, systolic blood pressure.

## 7. TREATMENT OF ASSOCIATED RISK FACTORS

### Treatment of risk factors associated with hypertension

Recommendations	Class	Level
It is recommended to use statin therapy in hypertensive patients at moderate to high CV risk, targeting a low-density lipoprotein cholesterol value $< 3.0$ mmol/l (115 mg/dl).	I	A
When overt CHD is present, it is recommended to administer statin therapy to achieve low-density lipoprotein cholesterol levels $< 1.8$ mmol/l (70 mg/dl).	I	A
Antiplatelet therapy, in particular low-dose aspirin, is recommended in hypertensive patients with previous CV events.	I	A
Aspirin should also be considered in hypertensive patients with reduced renal function or a high CV risk, provided that BP is well controlled.	IIa	B
Aspirin is not recommended for CV prevention in low-moderate risk hypertensive patients, in whom absolute benefit and harm are equivalent.	III	A
In hypertensive patients with diabetes, a HbA <sub>1c</sub> target of $< 7.0\%$ is recommended with antidiabetic treatment.	I	B
In more fragile elderly patients with a longer diabetes duration, more comorbidities and at high risk, treatment to a HbA <sub>1c</sub> target of $< 7.5\text{--}8.0\%$ should be considered.	IIa	C

BP, blood pressure; CHD, coronary heart disease; CV, cardiovascular.

## 8. FOLLOW-UP

### 8.1 Follow-up visits

After initiation of antihypertensive drug therapy, it is important to see the patient at 2-week to 4-week intervals to evaluate the effects on BP and to assess possible side-effects. Some medications will have an effect within days or weeks but a continued delayed response may occur during the first 2 months. Once the target is reached, a visit interval of a few months is reasonable.

### 8.2 Elevated blood pressure at control visits

Patients and physicians have a tendency to interpret an uncontrolled BP at a given visit as due to occasional factors and thus to downplay its clinical significance. Due attention should be given to poor adherence or irregular consumption of drugs (sometimes because of adverse effects), to the white-coat effect and to substances or drugs opposing the antihypertensive effect of treatment.

### 8.3 Can antihypertensive medication be stopped?

In some patients, in whom treatment is accompanied by an effective BP control for an extended period, it may be possible to reduce the number and dosage of drugs. This may be particularly the case if BP control is accompanied by

healthy lifestyle changes. Reduction of medications should be made gradually and the patient should frequently be checked because of the risk of reappearance of hypertension.

## 9. IMPROVEMENT OF BLOOD PRESSURE CONTROL IN HYPERTENSION

Despite overwhelming evidence that hypertension is a major cardiovascular risk factor and that BP-lowering substantially reduce the risk, there is evidence that all over the world a noticeable proportion of hypertensive individuals are unaware of this condition or, if aware, do not undergo treatment; target BP values are seldom achieved; failure to achieve BP control is associated with persistence of an elevated cardiovascular risk; and the rate of awareness of hypertension and BP control is improving slowly or not at all. As a consequence, high BP remains a leading cause of death and cardiovascular morbidity in Europe, as elsewhere in the world. Overall, three main causes of the low rate of BP control in real life have been identified: physician inertia; patient low adherence to treatment; and deficiencies of healthcare systems in their approach to chronic diseases. Methods to improve adherence to physicians' recommendations are listed in Table 12.

**TABLE 12. Methods to improve adherence to physicians' recommendations**

Patient level
Information combined with motivational strategies
Group sessions
Self-monitoring of BP
Self-management with simple patient-guided systems
Complex interventions <sup>a</sup>
Drug treatment level
Simplification of the drug regimen
Reminder packaging
Healthcare 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

BP, blood pressure.

<sup>a</sup>Almost all of the interventions that were effective for long-term care were complex, including combinations of more convenient care, information, reminders, self-monitoring, reinforcement, counselling, family therapy, psychological therapy, crisis intervention, manual telephone follow-up, supportive care, worksite and pharmacy-based programmes.