2018 Practice Guidelines for the management of arterial hypertension of the European Society of Hypertension and the European Society of Cardiology: ESH/ESC Task Force for the Management of Arterial Hypertension

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2018 Practice Guidelines for the management of arterial hypertension of the European Society of Cardiology and the European Society of Hypertension

ESC/ESH Task Force for the Management of Arterial Hypertension

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Keywords: adherence, blood pressure measurement, blood pressure treatment thresholds and targets, blood pressure, combination therapy, device therapy, drug therapy, hypertension-mediated organ damage, lifestyle interventions, secondary hypertension, special conditions

Abbreviations: ABI, ankle–brachial index; ABPM, ambulatory blood pressure monitoring; ACE, angiotensin-converting enzyme; ACEI, angiotensin-converting enzyme inhibitor; ACR, albumin:creatinine ratio; ARB, angiotensin receptor blocker; BP, blood pressure; bpm, beats per minute; BSA, body surface area; CAD, coronary artery disease; CKD, chronic kidney disease; CVD, cardiovascular disease; DHP, dihydropyridine; eGFR, estimated glomerular filtration rate; ESC, European Society of Cardiology; ESH, European Society of Hypertension; HbA1c, Haemoglobin A1c; HBPM, home blood pressure monitoring; HDL-C, HDL-cholesterol; HfPEF, heart failure with preserved ejection fraction; HfPEF, heart failure with reduced ejection fraction; HMOD, hypertension-mediated organ damage; IMT, intima–media thickness; LDLC, LDL cholesterol; LEAD, lower extremity artery disease; LVH, left ventricular hypertrophy; MAP, mean arterial pressure; MI, myocardial infarction; MR, magnetic resonance; MRA, mineralocorticoid receptor antagonist; MUCH, masked uncontrolled hypertension; NTproBNP, N-terminal pro-B natriuretic peptide; o.d., omni die (every day); PAC, plasma aldosterone concentration; RAD, peripheral artery disease; PRA, plasma renin activity; PRC, plasma renin concentration; PWV, pulse wave velocity; RAS, renin–angiotensin system; RCT, randomized controlled trial; RWT, relative wall thickness; SPC, single-pill combination; SUCH, sustained uncontrolled hypertension; TIA, transient ischaemic attack; WUCH, white-coat uncontrolled hypertension

Summary

The key messages in 20 points

1. Blood pressure, epidemiology and risk. Globally, over 1 billion people have hypertension. As populations age and adopt more sedentary lifestyles, the worldwide prevalence of hypertension will continue to rise towards 1.5 billion by 2025. Elevated blood pressure (BP) is the leading global contributor to premature death, accounting for almost 10 million deaths in 2015, 4.9 million due to ischaemic heart disease and 3.5 million due to stroke. Hypertension is also a major risk factor for heart failure, atrial fibrillation, chronic kidney disease (CKD), peripheral artery disease (PAD) and cognitive decline.

2. Definition of hypertension. The classification of BP and the definition of hypertension is unchanged from previous European guidelines, and is defined as an office SBP at least 140 mmHg and/or DBP at...
least 90 mmHg, which is equivalent to a 24-h ABPM average of at least 130/80 mmHg, or a home blood pressure monitoring (HBPM) average at least 135/85 mmHg.

3. Screening and diagnosis of hypertension. Hypertension is usually asymptomatic (hence the term ‘silent killer’). Because of its high prevalence, screening programmes should be established to ensure that BP is measured in all adults, at least every 5 years and more frequently in people with a high-normal BP. When hypertension is suspected because of an elevated screening BP, the diagnosis of hypertension should be confirmed either by repeated office BP measurements, over a number of visits, or by out-of-office BP measurement using 24-h ABPM or by HBPM.

4. The importance of cardiovascular risk assessment and detection of HMOD. Other cardiovascular risk factors such as dyslipidaemia and metabolic syndrome frequently cluster with hypertension. Thus, unless the patient is already at high or very high risk due to established CVD, formal cardiovascular risk assessment is recommended using the SCORE system. It is important to recognize, however, that the presence of HMOD, especially left ventricular hypertrophy (LVH), chronic kidney disease (CKD) or advanced retinopathy, further increases the risk of cardiovascular morbidity and mortality, and should be screened for as part of risk assessment in hypertensive patients because the SCORE system alone may underestimate their risk.

5. Think – could this patient have secondary hypertension? For most people with hypertension, no underlying cause will be detected. Secondary (and potentially remediable) causes of hypertension are more likely to be present in people with young onset of hypertension (<40 years), people with severe or treatment-resistant hypertension, or people who suddenly develop significant hypertension in midlife on a background of previously normal BP. Such patients should be referred for specialist evaluation.

6. Treatment of hypertension – importance of lifestyle interventions. The treatment of hypertension involves lifestyle interventions and drug therapy. Many patients with hypertension will require drug therapy, but lifestyle interventions are important because they can delay the need for drug treatment or complement the BP-lowering effect of drug treatment. Moreover, lifestyle interventions such as sodium restriction, alcohol moderation, healthy eating, regular exercise, weight control and smoking cessation, all have health benefits beyond their impact on BP.

7. When to consider drug treatment of hypertension. The treatment thresholds for hypertension are now less conservative than they were in previous guidelines. We now recommend that patients with low–moderate risk grade 1 hypertension (office BP 140–159/90–99 mmHg), even if they do not have HMOD, should now receive drug treatment if their BP is not controlled after a period of lifestyle intervention alone. For higher risk patients with grade 1 hypertension, including those with HMOD, or patients with higher grades of hypertension (e.g. grade 2 hypertension, ≥160/100 mmHg), we recommend initiating drug treatment alongside lifestyle interventions. These recommendations apply to all adults up to the age of 80 years.

8. Special considerations in frail and older patients. It is increasingly recognized that biological rather than chronological age, as well as consideration of frailty and independence, are important determinants of the tolerability of and likely benefit from BP-lowering medications. It is important to note that even in the very old (i.e. >80 years), BP-lowering therapy reduces mortality, stroke and heart failure. Thus, these patients should not be denied treatment, or have treatment withdrawn simply on the basis of age. For people more than 80 years of age who have not yet received treatment for their BP, treatment is recommended when their office SBP is at least 160 mmHg, provided that the treatment is well tolerated.

9. How low should SBP be lowered? This has been a hotly debated topic. A key discussion point is the balance of potential benefits versus potential harm or adverse effects. This is especially important whenever BP targets are lowered, as there is a greater potential for harm to exceed benefit. Thus, in this guideline, we recommend a target range. The evidence strongly suggests that lowering office SBP to less than 140 mmHg is beneficial for all patient groups, including independent older patients. There is also evidence to support targeting SBP to 130 mmHg for most patients, if tolerated. Even lower SBP levels (<130 mmHg) will be tolerated and potentially beneficial for some patients, especially to further reduce the risk of stroke. SBP should not be targeted to below 120 mmHg because the balance of benefit versus harm becomes concerning at these levels of treated SBP.

10. Blood pressure targets in old and very old patient. As discussed above, independence, frailty and comorbidities will all influence treatment decisions, especially in older (>65 years) and very old (>80 years) patients. The desired SBP target range for all patients aged more than 65 years is less than 140 mmHg but not less than 130 mmHg. This is lower than in previous guidelines and may not be achievable in all older patients, but any BP lowering towards this target is likely to be beneficial provided that the treatment is well tolerated.

11. Blood pressure targets in patients with diabetes and/or chronic kidney disease. The BP-treatment targets for patients with diabetes or kidney disease have been a moving target in previous guidelines because of seemingly contradictory results from major outcome trials and meta-analyses. For diabetes, targeting the SBP to less than 140 mmHg and towards 130 mmHg, as recommended for all other patient groups, is beneficial
on major outcomes. Moreover, targeting SBP to less than 130 mmHg, for those who will tolerate it, may further reduce the risk of stroke but not other major outcomes. SBP should not be lowered below 120 mmHg. For patients with CKD, the evidence suggests that the target BP range should be less than 140 mmHg but not less than 130 mmHg.

12. **How low should DBP be lowered?** The optimal DBP target has been less well defined, but a DBP target of less than 80 mmHg is recommended. Some patients with stiff arteries and isolated systolic hypertension will already have DBP levels below this target. These are high-risk patients and the low DBP should not discourage treatment of their elevated SBP to the recommended target, provided that treatment is well tolerated.

13. **The need to do better on blood pressure control.** A key message in this guideline is the need to do better at improving BP control rates. Despite the overwhelming evidence of treatment benefit, on average, less than 50% of patients with treated hypertension achieve a SBP target of less than 140 mmHg. Physician inertia (inadequate up-titration of treatment, especially from monotherapy) and poor patient adherence to treatment (especially when based on multiple pills) are now recognized as the major factors contributing to poor BP control.

14. **Start treatment in most patients with two drugs, not one.** Monotherapy is usually inadequate therapy for most people with hypertension; this will be especially true now that the BP-treatment targets for many patients are lower than in previous guidelines. This guideline sets out to normalize the concept that initial therapy for the majority of patients with hypertension should be with a combination of two drugs, not a single drug. The only exception would be in a limited number of patients with a lower baseline BP close to their recommended target, who might achieve that target with a single drug, or in some frailer old or very old patients, in whom more gentle reduction of BP may be desirable. Evidence suggests that this approach will improve the speed, efficiency and consistency of initial BP lowering and BP control, and is well tolerated by patients.

15. **A single pill strategy to treat hypertension.** Poor adherence to longer-term BP lowering medication is now recognized as a major factor contributing to poor BP control rates. Research has shown a direct correlation between the number of BP-lowering pills and poor adherence to medications. Moreover, SPC therapy has been shown to improve adherence to treatment. SPC therapy is now the preferred strategy for initial two-drug combination treatment of hypertension and for three-drug combination therapy when required. This will control the BP in most patients with a single pill and could transform BP control rates.

16. **A simplified drug-treatment algorithm.** We have simplified the treatment strategy so that patients with uncomplicated hypertension and many patients with a variety of comorbidities (e.g. HMOD, diabetes, PAD or cerebrovascular disease) receive similar medication. We recommend a combination of an angiotensin-converting enzyme (ACE) inhibitor or angiotensin receptor blocker (ARB) with a CCB or thiazide/thiazide-like diuretic as initial therapy for most patients. For those requiring three drugs, we recommend a combination of an ACE inhibitor or ARB with a CCB and a thiazide/thiazide-like diuretic. We recommend beta-blockers be used when there is a specific indication for their use (e.g. angina, postmyocardial infarction, HFREF or when heart-rate control is required).

17. **Hypertension in women and in pregnancy.** In women with hypertension who are planning pregnancy, ACE inhibitors or ARBs and diuretics should be avoided and the preferred medications to lower BP, if required, include alpha-methyl dopa, labetalol or CCBs. The same drugs are suitable if BP lowering is required in pregnant women. ACE inhibitors or ARBs should not be used in pregnant women.

18. **Is there a role for device-based therapy for the treatment of hypertension?** A number of device-based interventions have been developed and studied for the treatment of hypertension. To date, the results from these studies have not provided sufficient evidence to recommend their routine use. Consequently, the use of device-based therapies is not recommended for the treatment of hypertension, unless in the context of clinical studies and randomized controlled trials, until further evidence regarding their safety and efficacy becomes available.

19. **Managing cardiovascular disease risk in hypertensive patients, beyond BP—statins.** For hypertensive patients at moderate CVD risk or higher, or those with established CVD, BP lowering alone will not optimally reduce their risk. These patients would also benefit from statin therapy, which further reduces the risk of a myocardial infarction by approximately one-third and stroke by approximately one-quarter, even when BP is controlled. Similar benefits have been seen in hypertensive patients at the border between low and moderate risk. Thus, many more hypertensive patients would benefit from statin therapy than are currently receiving this treatment.

20. **Managing cardiovascular disease risk in hypertensive patients, beyond BP—antiplatelet therapy.** Antiplatelet therapy, especially low-dose aspirin, is recommended for secondary prevention in hypertensive patients, but is not recommended for primary prevention (i.e. in patients without CVD).

**INTRODUCTION**

These 2018 European Society of Cardiology/European Society of Hypertension (ESC/ESH) guidelines for the management of arterial hypertension are designed for adults with hypertension, that is aged at least 18 years. The purpose of the review and update of these guidelines was to evaluate and incorporate new evidence into the
guideline recommendations. The specific aims of these guidelines were to produce pragmatic recommendations to improve the detection and treatment of hypertension, and to improve the poor rates of BP control by promoting simple and effective treatment strategies.

**Principles**
These fundamental principles are to base recommendations on properly conducted studies, identified from an extensive review of the literature; to give the highest priority to data from randomized controlled trials (RCTs); and to also consider well conducted meta-analyses of RCTs as strong evidence. This contrasts with network meta-analyses, which we do not consider to have the same level of evidence because many of the comparisons are nonrandomized; to recognize that RCTs cannot address many important questions related to the diagnosis, risk stratification and treatment of hypertension, which can be addressed by observational or registry-based studies of appropriate scientific calibre; to grade the level of scientific evidence and the strength of recommendations according to ESC recommendations; to recognize that opinions may differ on key recommendations, which are resolved by voting; and to recognize that there are circumstances in which there is inadequate or no evidence, but the question is important for clinical practice and cannot be ignored. In these circumstances, we resort to pragmatic expert opinion and endeavour to explain its rationale.

**What is new and what is changed in the 2018 European Society of Cardiology/European Society of Hypertension hypertension guidelines?**
Because of new evidence on several diagnostic and therapeutic aspects of hypertension, the present guidelines differ from the 2013 ones in several points indicated as follows (Fig. 1).

**New concepts**

**Blood pressure measurement**
1. Wider use of out-of-office BP measurement with ABPM and/or HBPM, especially HBPM, as an option to confirm the diagnosis of hypertension, detect white coat and masked hypertension and monitor BP control.

**Less conservative treatment of blood pressure in older and very old patients**
1. Lower BP thresholds and treatment targets for older patients, with an emphasis on considerations of biological rather than chronological age (i.e. the importance of frailty, independence and the tolerability of treatment).
2. Recommendation that treatment should never be denied or withdrawn on the basis of age, provided that treatment is tolerated.

**A SPC treatment strategy to improve blood pressure control**
1. Preferred use of two-drug combination therapy for the initial treatment of most people with hypertension.

**2018 Practice Guidelines for the management of hypertension**

2. A single-pill treatment strategy for hypertension with the preferred use SPC therapy for most patients.
3. Simplified drug-treatment algorithms with the preferred use of an ACE inhibitor or ARB combined with a CCB or/and a thiazide/thiazide-like diuretic as the core treatment strategy for most patients, with beta-blockers used for specific indications.

**New target ranges for blood pressure in treated patients**
1. Target BP ranges for treated patients to better identify the recommended BP target and lower safety boundaries for treated BP, according to a patient’s age and specific comorbidities.

**Detecting poor adherence to drug therapy**
1. A strong emphasis on the importance of evaluating treatment adherence as a major cause of poor BP control.

**A key role for nurses, pharmacists in the longer-term management of hypertension**
1. The important role of nurses and pharmacists in the education, support and follow-up of
2. Treated hypertensive patients are emphasized as part of the overall strategy to improve BP control.

**DEFINITIONS AND CLASSIFICATIONS**
The relationship between BP and cardiovascular and renal events is continuous, making the distinction between normotension and hypertension—based on cut-off BP values—somewhat arbitrary. ‘Hypertension’ is defined as the level of BP at which the benefits of treatment (either with lifestyle interventions or drugs), unequivocally outweigh the risks of treatment, as documented by clinical trials. This evidence has been reviewed and provides the basis for the recommendation that the classification of BP and definition of hypertension remain unchanged from previous ESH/ESC guidelines (Fig. 2).

**DIAGNOSTIC EVALUATION**

**Evaluation of the cardiovascular risk**
Quantification of total cardiovascular risk (i.e. the likelihood of a person developing a cardiovascular event over a defined period) is an important part of the risk-stratification process for patients with hypertension. Many cardiovascular risk-assessment systems are available and most project 10-year risk. Since 2003, the European guidelines on CVD prevention have recommended use of the Systematic Coronary Risk Evaluation (SCORE) system (Figs. 3–5) because it is based on large, representative European cohort datasets (http://www.escardio.org/Guidelines-&-Education/Practice-tools/CVD-prevention-toolbox/SCORE-Risk-Charts). The SCORE system only estimates the risk of fatal cardiovascular events.

**Measurement of blood pressure**
Auscultatory or oscillometric semiautomatic or automatic sphygmomanometers are the preferred method for
measuring BP in the doctor’s office. These devices should be validated according to standardized conditions and protocols.

BP can be highly variable, thus the diagnosis of hypertension should not be based on a single set of BP readings at a single office visit, unless the BP is substantially increased (e.g. grade 3 hypertension) and there is clear evidence of HMOD (e.g. hypertensive retinopathy with exudates and haemorrhages, or LVH, or vascular or renal damage). For all others (i.e. almost all patients), repeat BP measurements at

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<th>Changes in recommendations</th>
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<td><strong>Diagnosis</strong></td>
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<td>Office BP is recommended</td>
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<th><strong>Treatment thresholds</strong></th>
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<td><strong>High-normal BP (130–139/85–89 mmHg):</strong></td>
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<td>Unless the necessary evidence is obtained it is not recommended to initiate antihypertensive drug therapy at high-normal BP.</td>
<td>Drug treatment may be considered when CV risk is very high due to established CVD, especially CAD.</td>
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<th><strong>Treatment thresholds</strong></th>
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<td><strong>Treatment of low-risk grade 1 hypertension:</strong></td>
<td><strong>Treatment of low-risk grade 1 hypertension:</strong></td>
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<tr>
<td>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.</td>
<td>In patients with grade 1 hypertension at low–moderate risk and without evidence of HMOD, BP-lowering drug treatment is recommended if the patient remains hypertensive, after a period of lifestyle intervention.</td>
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<th><strong>Treatment thresholds</strong></th>
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<td><strong>Older patients</strong></td>
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<td>Antihypertensive drug treatment may 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.</td>
<td>BP-lowering drug treatment and lifestyle intervention is recommended in fit older patients (&gt; 65 years but not &gt; 80 years) when SBP is in the grade 1 range (140–159 mmHg), provided that treatment is well tolerated.</td>
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FIGURE 1 Changes in ESC/ESH recommendations between 2013 and 2018. The codes used for the classes of recommendations and level of evidence are found in supplementary Figure 1, http://links.lww.com/HJH/B29.
repeat office visits have been a long-standing strategy to confirm a persistent elevation in BP, as well as for the classification of the hypertension status in clinical practice and RCTs.

White-coat hypertension refers to the untreated condition in which BP is elevated in the office, but is normal when measured by ABPM, HBPM, or both. Conversely, ‘masked hypertension’ refers to untreated patients in whom the BP is normal in the office, but is elevated when measured by HBPM or ABPM. The term ‘true normotension’ is used when both office and out-of-office BP measurements are normal, and ‘sustained hypertension’ is used when both are abnormal. In white-coat hypertension, the difference between the higher office and the lower out-of-office BP is referred to as the ‘white-coat effect’ and is believed to mainly reflect the pressor response to an alerting reaction elicited by office BP measurements by a doctor or a nurse, although other factors are probably also involved (Fig. 6).

These guidelines also support the use of out-of-office BP (i.e. HBPM and/or ABPM) (Figs. 7–10) as an alternative strategy to repeated office BP measurements, to confirm the diagnosis of hypertension, when these measurements are

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<th>2013</th>
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<td><strong>BP treatment targets</strong></td>
<td><strong>BP treatment targets</strong></td>
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<td>A SBP goal of &lt; 140 mmHg is recommended.</td>
<td>It is recommended that the first objective of treatment should be to lower BP to &lt; 140/90 mmHg in all patients and provided that the treatment is well tolerated, treated BP values should be targeted to 130/80 mmHg or lower, in most patients.</td>
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<td>In patients &lt; 65 years it is recommended that SBP should be lowered to a BP range of 120 to &lt; 130 mmHg in most patients.</td>
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<th>BP treatment targets in older patients (65–80 years)</th>
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<tr>
<td>A SBP target between of 140 and 150 mmHg is recommended for older patients (65–80 years).</td>
<td>In older patients (≥ 65 years), it is recommended that SBP should be targeted to a BP range of 130 to &lt; 140 mmHg.</td>
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<th>BP treatment targets in patients aged over 80 years</th>
<th>BP treatment targets in patients aged over 80 years</th>
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<tr>
<td>A SBP target between 140 and 150 mmHg should be considered in people older than 80 years, with an initial SBP ≥ 160 mmHg, provided that they are in good physical and mental condition.</td>
<td>A SBP target range of 130 to &lt; 140 mmHg is recommended for people older than 80 years, if tolerated.</td>
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<th>DBP targets</th>
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<td>A DBP target of &lt; 90 mmHg is always recommended, except in patients with diabetes, in whom values &lt; 85 mmHg are recommended.</td>
<td>A DBP target of &lt; 80 mmHg should be considered for all hypertensive patients, independent of the level of risk and comorbidities.</td>
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logistically and economically feasible. This approach can provide important supplementary clinical information, for example detecting white-coat hypertension, which should be suspected, especially in people with grade 1 hypertension on office BP measurement and in whom there is no evidence of HMOD or CVD. A particular challenge is the detection of masked hypertension. Masked hypertension is more likely in people with a BP in the high-normal range in whom out-of-office BP should be considered to exclude masked hypertension. Out-of-office BP measurements are also indicated in other specific circumstances (Figs. 7–9).

All adults should have their BP recorded in their medical record and be aware of their BP, and further screening should be undertaken at regular intervals with the frequency dependent on the BP level as illustrated in Fig. 10.

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<th>2013</th>
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<td><strong>Initiation of drug treatment</strong></td>
<td><strong>Initiation of drug treatment</strong></td>
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<td>Initiation of antihypertensive therapy with a two-drug combination may be considered in patients with markedly high baseline BP or at high CV risk.</td>
<td>It is recommended to initiate an antihypertensive treatment with a two-drug combination, preferably in a SPC. The exceptions are frail older patients and those at low risk and with grade 1 hypertension (particularly if SBP is &lt; 150 mmHg).</td>
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**Resistant hypertension**
Mineralocorticoid receptor antagonists, amiloride, and the alpha-1 blocker doxazosin should be considered if no contraindication exists.

**Resistant hypertension**
Recommended treatment of resistant hypertension is the addition of low-dose spironolactone to existing treatment, or the addition of further diuretic therapy if intolerant to spironolactone, with either eplerenone, amiloride, higher-dose thiazide/thiazide-like diuretic or a loop diuretic, or the addition of bisoprolol or doxazosin.

**Device-based therapy for hypertension**
In case of ineffectiveness of drug treatment, invasive procedures such as renal denervation and baroreceptor stimulation may be considered.

**Device-based therapy for hypertension**
Use of device-based therapies is not recommended for the routine treatment of hypertension, unless in the context of clinical studies and RCTs, until further evidence regarding their safety and efficacy becomes available.

**Recommendation Grading**

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<th>Grade I</th>
<th>Grade IIa</th>
<th>Grade IIb</th>
<th>Grade III</th>
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ABPM = ambulatory blood pressure monitoring; BP = blood pressure; CAD = coronary artery disease; CV = cardiovascular; CVD = cardiovascular disease; DBP = diastolic blood pressure; HBPM = home blood pressure monitoring; HMOD = hypertension-mediated organ damage; RCT = randomized controlled trial; SBP = systolic blood pressure; SPC = single-pill combination.
Clinical evaluation
The information to be obtained at the time of the first diagnosis of hypertension is indicated in Figs. 11–14.

TREATMENT OF HYPERTENSION
The routine treatment of hypertension involves lifestyle interventions for all patients (including those with high normal BP) and drug therapy for most patients.

All guidelines agree that patients with grade 2 or 3 hypertension should receive antihypertensive drug treatment alongside lifestyle interventions. Guidelines are also consistent in recommending that patients with grade 1 hypertension and high cardiovascular risk or HMOD should be treated with BP-lowering drugs. There has been less consistency about whether BP-lowering drugs should be offered to patients with grade 1 hypertension and low-to-moderate cardiovascular risk or grade 1 hypertension in older patients (> 60 years), or the need for BP-lowering drug treatment in patients with high-normal BP levels. This uncertainty relates to the fact that low-risk patients with high-normal BP or grade 1 hypertension have rarely been included in RCTs, and that in older patients, RCTs have invariably recruited patients with at least grade 2 hypertension.

Drug treatment strategy and blood pressure targets (Figs 15–20)
The level to which BP should be lowered with drug treatment will depend on the patients’ age, comorbidities and tolerability of treatment. Corresponding BP targets for home and ambulatory BP are less well established, but an office BP less than 130 mmHg probably corresponds to a

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<th>Categorya</th>
<th>Systolic (mmHg)</th>
<th>Diastolic (mmHg)</th>
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<tr>
<td>Optimal</td>
<td>&lt; 120</td>
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<td>Normal</td>
<td>120–129</td>
<td>and/or</td>
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<td>High normal</td>
<td>130–139</td>
<td>and/or</td>
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<td>Grade 1 hypertension</td>
<td>140–159</td>
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<td>Grade 2 hypertension</td>
<td>160–179</td>
<td>and/or</td>
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<td>Grade 3 hypertension</td>
<td>≥ 180</td>
<td>and/or</td>
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<tr>
<td>Isolated systolic hypertensionb</td>
<td>≥ 140</td>
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a BP category is defined according to seated clinic BP and by the highest level of BP, whether systolic or diastolic.

b Isolated systolic hypertension is graded 1, 2, or 3 according to SBP values in the ranges indicated.

FIGURE 2 Classification of office blood pressure and definitions of hypertension grades.

FIGURE 3 Evaluation of the cardiovascular risk: 10-year cardiovascular risk categories SCORE. CKD, chronic kidney disease; CVD cardiovascular disease; eGFR, estimated glomerular filtration rate; LVH, left ventricular hypertrophy; PAD, peripheral artery disease; TIA, transient ischaemic attack.
Social deprivation – the origin of many causes of CVD

Obesity (measured by BMI) and central obesity (measured by waist circumference)

Physical inactivity

Psychosocial stress, including vital exhaustion

Family history of premature CVD (occurring at age < 55 years in men and < 60 years in women)

Autoimmune and other inflammatory disorders

Major psychiatric disorders

Treatment for infection with human immunodeficiency virus

Atrial fibrillation

LV hypertrophy

CKD

Obstructive sleep apnoea syndrome

**FIGURE 4** Risk modifiers increasing cardiovascular risk estimated by the SCORE system. CKD, chronic kidney disease; CVD cardiovascular disease.

<table>
<thead>
<tr>
<th>Hypertension disease staging</th>
<th>Other risk factors, HMOD, or disease</th>
<th>BP (mmHg) grading</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 1 (uncomplicated)</td>
<td>No other risk factors</td>
<td>Low risk</td>
</tr>
<tr>
<td></td>
<td>1 or 2 risk factors</td>
<td>Low risk</td>
</tr>
<tr>
<td></td>
<td>≥ 3 risk factors</td>
<td>Low to moderate risk</td>
</tr>
<tr>
<td>Stage 2 (asymptomatic disease)</td>
<td>HMOD, CKD grade 3, or diabetes mellitus without organ damage</td>
<td>Moderate to high risk</td>
</tr>
<tr>
<td>Stage 3 (established disease)</td>
<td>Established CVD, CKD grade ≥ 4, or diabetes mellitus with organ damage</td>
<td>Very high risk</td>
</tr>
</tbody>
</table>

BP = blood pressure; CKD = chronic kidney disease; CV = cardiovascular; DBP = diastolic blood pressure; HMOD = hypertension-mediated organ damage; SBP = systolic blood pressure; SCORE = Systematic Coronary Risk Evaluation. CV risk is illustrated for a middle-aged male. The CV risk does not necessarily correspond to the actual risk at different ages. The use of the SCORE system is recommended for formal estimation of CV risk for treatment decisions.

**FIGURE 5** Classification of hypertension stages according to blood pressure levels, presence of risk factors, hypertension-mediated organ damage or comorbidities.

**FIGURE 6** Office blood pressure measurements. AF, atrial fibrillation.
FIGURE 7 Definitions of hypertension according to office, ambulatory and home blood pressure levels.

<table>
<thead>
<tr>
<th>Category</th>
<th>Systolic (mmHg)</th>
<th>Diastolic (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Office BP(^a)</td>
<td>≥ 140 and/or</td>
<td>≥ 90</td>
</tr>
<tr>
<td>Ambulatory BP</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Daytime (or awake) mean</td>
<td>≥ 135 and/or</td>
<td>≥ 85</td>
</tr>
<tr>
<td>Night-time (or asleep) mean</td>
<td>≥ 120 and/or</td>
<td>≥ 70</td>
</tr>
<tr>
<td>24-h mean</td>
<td>≥ 130 and/or</td>
<td>≥ 80</td>
</tr>
<tr>
<td>Home BP mean</td>
<td>≥ 135 and/or</td>
<td>≥ 85</td>
</tr>
</tbody>
</table>

BP, blood pressure; \(^a\)Refers to conventional office BP rather than unattended office BP.

FIGURE 8 Advantages and disadvantages of ambulatory blood pressure monitoring and home blood pressure monitoring.

<table>
<thead>
<tr>
<th>ABPM</th>
<th>HBPM</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Advantages</strong></td>
<td><strong>Advantages</strong></td>
</tr>
<tr>
<td>Can identify white-coat and masked hypertension</td>
<td>Can identify white-coat and masked hypertension</td>
</tr>
<tr>
<td>Stronger prognostic evidence</td>
<td>Cheap and widely available</td>
</tr>
<tr>
<td>Night-time readings</td>
<td>Measurement in a home setting, which may be more relaxed than the doctor’s office</td>
</tr>
<tr>
<td>Measurement in real-life settings</td>
<td>Patient engagement in BP measurement</td>
</tr>
<tr>
<td>Additional prognostic BP phenotypes</td>
<td>Easily repeated and used over longer periods to assess day-to-day BP variability</td>
</tr>
<tr>
<td>Abundant information from a single measurement session, including short-term BP variability</td>
<td></td>
</tr>
<tr>
<td><strong>Disadvantages</strong></td>
<td><strong>Disadvantages</strong></td>
</tr>
<tr>
<td>Expensive and sometimes limited availability</td>
<td>Only static BP is available</td>
</tr>
<tr>
<td>Can be uncomfortable</td>
<td>Potential for measurement error</td>
</tr>
<tr>
<td></td>
<td>No nocturnal readings</td>
</tr>
</tbody>
</table>

BP, blood pressure. \(^a\)Techniques are being developed to enable nocturnal BP measurement with home BP devices.

FIGURE 9 Clinical indications for home blood pressure monitoring (HBPM) or ambulatory blood pressure monitoring (ABPM). CKD, chronic kidney disease; HMOD, hypertension-mediated organ damage.

Conditions in which white-coat hypertension is more common, e.g.
- Grade I hypertension on office BP measurement
- Marked office BP elevation without HMOD

Conditions in which masked hypertension is more common, e.g.
- High-normal office BP
- Normal office BP in individuals with HMOD or at high total CV risk

Postural and post-prandial hypotension in untreated and treated patients
Evaluation of resistant hypertension
Evaluation of BP control, especially in treated higher-risk patients
Exaggerated BP response to exercise
When there is considerable variability in the office BP
Evaluating symptoms consistent with hypotension during treatment

Specific indications for ABPM rather than HBPM:
- Assessment of nocturnal BP values and dipping status (e.g. suspicion of nocturnal hypertension, such as in sleep apnoea, CKD, diabetes, endocrine hypertension, or autonomic dysfunction)
### Risk factors
- Family and personal history of hypertension, CVD, stroke, or renal disease
- Family and personal history of associated risk factors (e.g., familial hypercholesterolaemia)
- Smoking history
- Dietary history and salt intake
- Alcohol consumption
- Lack of physical exercise/sedentary lifestyle
- History of erectile dysfunction
- Sleep history, snoring, sleep apnoea (information also from partner)
- Previous hypertension in pregnancy/pre-eclampsia

### History and symptoms of HMOD, CVD, stroke, and renal disease
- Brain and eyes: headache, vertigo, syncope, impaired vision, TIA, sensory or motor deficit, stroke, carotid revascularization, cognitive impairment, or dementia (in the elderly)
- Heart: chest pain, shortness of breath, oedema, myocardial infarction, coronary revascularization, syncope, history of palpitations, arrhythmias (especially AF), heart failure
- Kidney: thirst, polyuria, nocturia, haematuria, urinary tract infections
- Peripheral arteries: cold extremities, intermittent claudication, pain-free walking distance, pain at rest, peripheral revascularization
- Patient or family history of CKD (e.g., polycystic kidney disease)

### History of possible secondary hypertension
- Young onset of grade 2 or 3 hypertension (< 40 years), or sudden development of hypertension or rapidly worsening BP in older patients
- History of renal/urinary tract disease
- Recreational drug/substance abuse/concurrent therapies: corticosteroids, nasal vasoconstrictor, chemotherapy, yohimbine, liquorice
- Repetitive episodes of sweating, headache, anxiety, palpitations, suggestive of pheochromocytoma
- History of spontaneous or diuretic-provoked hypokalaemia, episodes of muscle weakness, and tetany (hyperaldosteronism)
- Symptoms suggestive of thyroid disease or hyperparathyroidism
- History of or current pregnancy and oral contraceptive use
- History of sleep apnoea

### Hypertension treatment
- Current/past antihypertensive medication including effectiveness and intolerance to previous medications
- Adherence to therapy

---

**FIGURE 10** Screening for hypertension.

**FIGURE 11** Key information to be collected in personal and family medical history (1). AF, atrial fibrillation; CKD, chronic kidney disease; CVD cardiovascular disease; HMOD, hypertension-mediated organ damage; TIA, transient ischaemic attack.

**FIGURE 12** Key information to be collected in personal and family medical history (2).
**Routine laboratory tests**

<table>
<thead>
<tr>
<th>Test</th>
<th>Indication and interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haemoglobin and/or haematocrit</td>
<td></td>
</tr>
<tr>
<td>Fasting blood glucose and glycated HbA₁c</td>
<td></td>
</tr>
<tr>
<td>Blood lipids: total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol</td>
<td></td>
</tr>
<tr>
<td>Blood triglycerides</td>
<td></td>
</tr>
<tr>
<td>Blood potassium and sodium</td>
<td></td>
</tr>
<tr>
<td>Blood uric acid</td>
<td></td>
</tr>
<tr>
<td>Blood creatinine and eGFR</td>
<td></td>
</tr>
<tr>
<td>Blood liver function tests</td>
<td></td>
</tr>
<tr>
<td>Urine analysis: microscopic examination; urinary protein by dipstick test or, ideally, albumin:creatinine ratio</td>
<td></td>
</tr>
<tr>
<td>12-lead ECG</td>
<td></td>
</tr>
</tbody>
</table>

**FIGURE 13** Routine work-up for evaluation of hypertensive patients.

**Figures and Table Legend**

- **HB A₁c**: Glycosylated hemoglobin; **eGFR**: estimated glomerular filtration rate; **ECG**: electrocardiogram
- **HMOD**: Hypertension-mediated organ damage
- **ABI**: Ankle Brachial Index

<table>
<thead>
<tr>
<th>Basic screening tests for HMOD</th>
<th>Indication and interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>12-lead ECG</td>
<td>Screen for LVH and other possible cardiac abnormalities and to document heart rate and cardiac rhythm</td>
</tr>
<tr>
<td>Urine albumin:creatinine ratio</td>
<td>To detect elevations in albumin excretion indicative of possible renal disease</td>
</tr>
<tr>
<td>Blood creatinine and eGFR</td>
<td>To detect possible renal disease</td>
</tr>
<tr>
<td>Fundoscopy</td>
<td>To detect hypertensive retinopathy, especially in patients with grade 2 or 3 hypertension</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>More detailed screening for HMOD</th>
<th>Indication and interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Echocardiography</td>
<td>To evaluate cardiac structure and function, when this information will influence treatment decisions</td>
</tr>
<tr>
<td>Carotid ultrasound</td>
<td>To determine the presence of carotid plaque or stenosis, particularly in patients with cerebrovascular disease or vascular disease elsewhere</td>
</tr>
<tr>
<td>Abdominal ultrasound and Doppler studies</td>
<td>To evaluate renal size and structure (e.g. scarring) and exclude renal tract obstruction as possible underlying causes of CKD and hypertension Evaluate abdominal aorta for evidence of aneurysmal dilatation and vascular disease Examine adrenal glands for evidence of adenoma or pheochromocytoma (CT or MRI preferred for detailed examination) Renal artery Doppler studies to screen for the presence of renovascular disease, especially in the presence of asymmetric renal size</td>
</tr>
<tr>
<td>PWV</td>
<td>An index of aortic stiffness and underlying arteriosclerosis</td>
</tr>
<tr>
<td>ABI</td>
<td>Screen for evidence of PAD</td>
</tr>
<tr>
<td>Cognitive function testing</td>
<td>To evaluate cognition in patients with symptoms suggestive of cognitive impairment</td>
</tr>
<tr>
<td>Brain imaging</td>
<td>To evaluate the presence of ischaemic or haemorrhagic brain injury, especially in patients with a history of cerebrovascular disease or cognitive decline</td>
</tr>
</tbody>
</table>

**FIGURE 14** Assessments of hypertension-mediated organ damage (HMOD).
24-h ABPM SBP of less than 125 mmHg and a home average SBP of less than 130 mmHg.

The core algorithm is also appropriate for most patients with HMOD, cerebrovascular disease, diabetes or peripheral artery disease.

Drug treatment strategy for specific clinical situations: coronary heart disease, chronic kidney disease, heart failure, atrial fibrillation (Figures 21–25)

Device-based therapy for hypertension

The actual recommendation is the following: ‘Use of device-based therapies is not recommended for the routine treatment of hypertension, unless in the context of clinical studies and RCTs, until further evidence regarding their safety and efficacy becomes available’.

Resistant hypertension

Hypertension is defined as resistant to treatment when the recommended treatment strategy fails to lower office SBP and DBP values to below 140 and/or 90 mmHg, respectively, and the inadequate control of BP is confirmed by ABPM or HBPM, in patients whose adherence to therapy has been confirmed (Figs. 26 and 27). The recommended treatment strategy should include appropriate lifestyle measures and treatment with optimal or best-tolerated doses of three or more drugs that should include a diuretic and typically an ACE inhibitor or ARB, and a CCB.
**Recommendations**

It is recommended that the first objective of treatment should be to lower BP to < 140/90 mmHg in all patients, and provided that the treatment is well tolerated, treated BP values should be targeted to 130/80 mmHg or lower, in most patients.

In patients < 65 years receiving BP-lowering drugs, it is recommended that SBP should be lowered to a BP range of 120 to < 130 mmHg in most patients.

In older patients (aged ≥ 65 years) receiving BP-lowering drugs:
- It is recommended that SBP should be targeted to a BP range of 130 to < 140 mmHg.
- Close monitoring of adverse effects is recommended.
- These BP targets are recommended for patients at any level of CV risk and in patients with and without established CVD.

In patients with diabetes receiving BP-lowering drugs:
- An SBP target range of 120–130 mmHg should be considered.
- In older patients (aged ≥ 65 years) an SBP target range of 130 to < 140 mmHg is recommended.

A DBP target of < 80 mmHg should be considered for all hypertensive patients, independent of the level of risk and comorbidities.

---

**Recommendations**

Salt restriction to < 5 g per day is recommended.

It is recommended to restrict alcohol consumption to:
- Less than 14 units per week for men.
- Less than 8 units per week for women.

It is recommended to avoid binge drinking.

Increased consumption of vegetables, fresh fruits, fish, nuts, 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 (BMI > 30 kg/m² or WC > 102 cm in men and > 88 cm in women) and aim at a healthy BMI (about 20–25 kg/m²) and WC values (< 94 cm in men and < 80 cm in women) to reduce BP and CV risk.

Regular aerobic exercise (e.g. at least 30 min of moderate dynamic exercise on 5–7 days per week) is recommended.

Smoking cessation and supportive care and referral to smoking cessation programs are recommended.
FIGURE 19 Core drug-treatment strategy for uncomplicated hypertension. ACEI, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blockers; CCB, calcium channel blockers.

FIGURE 20 Compelling and possible contraindications to the use of specific antihypertensive drugs. ACE, angiotensin-converting enzyme; ARBs, angiotensin receptor blockers; LV EF, left ventricular ejection fraction.

FIGURE 21 Drug-treatment strategy for hypertension and coronary artery disease. ACEI, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blockers; CCB, calcium channel blockers; CVD, cardiovascular disease.
FIGURE 22 Drug-treatment strategy for chronic kidney disease. ACEI, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blockers; CCB, calcium channel blockers; CVD, cardiovascular disease. ACEI, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blockers; CCB, calcium channel blockers; CKD, chronic kidney disease.

FIGURE 23 Drug-treatment strategy for hypertension and heart failure with reduced ejection fraction. ACEI, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blockers.

FIGURE 24 Drug-treatment strategy for hypertension and atrial fibrillation. ACEI, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blockers; CCB, calcium channel blockers; DHP, dihydropyridine.
Secondary hypertension
Secondary hypertension is hypertension due to an identifiable cause, which may be treatable with an intervention specific to the cause (Figs. 28–31). A high index of suspicion and early detection of secondary hypertension is important because interventions may be curative, especially in younger patients.

Hypertension emergency
Hypertension emergencies are situations in which severe hypertension (grade 3) is associated with acute HMOD, which is often life-threatening and requires immediate but careful intervention to lower BP, usually with intravenous (i.v.) therapy (Figs. 32 and 33). The rate and magnitude of increase in BP may be at least as important as the absolute level of BP in determining the magnitude of organ injury.

Treatment recommendations in special situations (Figs. 34–42)

FOLLOW-UP OF PATIENTS

Frequency of visits
After the initiation of antihypertensive drug therapy, it is important to review the patient at least once within the first 2 months to evaluate the effects on BP and assess possible side effects until BP is under control. The frequency of review will

<table>
<thead>
<tr>
<th>Characteristics of patients with resistant hypertension</th>
<th>Causes of secondary resistant hypertension</th>
<th>Drugs and substances that may cause raised BP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographics</td>
<td>More common causes</td>
<td>Prescribed drugs</td>
</tr>
<tr>
<td>• Older age (especially &gt; 75 years)</td>
<td>• Primary hyperaldosteronism</td>
<td>• Oral contraceptives</td>
</tr>
<tr>
<td>• Obesity</td>
<td>• Atherosclerotic renovascular disease</td>
<td>• Sympathomimetic agents (e.g. decongestants in proprietary cold remedies)</td>
</tr>
<tr>
<td>• More common in black people</td>
<td>• Sleep apnoea</td>
<td>• Non-steroidal anti-inflammatory drugs</td>
</tr>
<tr>
<td>• Excess dietary sodium intake</td>
<td>• CKD</td>
<td>• Cyclosporin</td>
</tr>
<tr>
<td>• High baseline BP and chronicity of uncontrolled hypertension</td>
<td></td>
<td>• Erythropoetin</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Steroids (e.g. prednisolone, hydrocortisone)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Some cancer therapies</td>
</tr>
<tr>
<td>Concomitant disease</td>
<td>Uncommon causes</td>
<td>Non-prescription drugs</td>
</tr>
<tr>
<td>• HMOD: LVH and/or CKD</td>
<td>• Phaeochromocytoma</td>
<td>• Recreational drugs (e.g. cocaine, amphetamines, anabolic steroids)</td>
</tr>
<tr>
<td>• Diabetes</td>
<td>• Fibromuscular dysplasia</td>
<td>• Excess liquorice ingestion</td>
</tr>
<tr>
<td>• Atherosclerotic vascular disease</td>
<td>• Aortic coarctation</td>
<td>• Herbal remedies (e.g. ephedra, ma huang)</td>
</tr>
<tr>
<td>• Aortic stiffening and isolated systolic hypertension</td>
<td>• Cushing’s disease</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Hyperparathyroidism</td>
<td></td>
</tr>
</tbody>
</table>
### Recommendations

It is recommended that hypertension be defined as resistant to treatment (i.e., resistant hypertension) when:

- Optimal doses (or best-tolerated doses) of an appropriate therapeutic strategy, which should include a diuretic (typically an ACE inhibitor or an ARB with a CCB and a thiazide/thiazide-type diuretic), fails to lower clinic SBP and DBP values to < 140 mmHg and/or 90 mmHg, respectively; and
- The inadequate control of BP has been confirmed by ABPM or HBPM; and
- After exclusion of various causes of pseudo-resistant hypertension (especially poor medication adherence) and secondary hypertension.

Recommended treatment of resistant hypertension is:

- Reinforcement of lifestyle measures, especially sodium restriction.
- Addition of low-dose spironolactone to existing treatment.
- Or the addition of further diuretic therapy if intolerant to spironolactone, with either eplerenone, amiloride, higher dose thiazide/thiazide-like diuretic, or a loop diuretic.
- Or the addition of bisoprolol or doxazosin.

### Characteristic

| Younger patients (< 40 years) with grade 2 hypertension or onset of any grade of hypertension in childhood |
| Acute worsening hypertension in patients with previously documented chronically stable normotension |
| Resistant hypertension |
| Severe (grade 3) hypertension or a hypertension emergency |
| Presence of extensive HMOD |
| Clinical or biochemical features suggestive of endocrine causes of hypertension or CKD |
| Clinical features suggestive of obstructive sleep apnoea |
| Symptoms suggestive of phaeochromocytoma or family history of phaeochromocytoma |

**FIGURE 27** Resistant hypertension: recommendations. ABPM, ambulatory blood pressure monitoring; ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blockers; CCB, calcium channel blockers; HBPM, home blood pressure monitoring.

**FIGURE 28** Patients characteristics that should raise the suspicion of secondary hypertension. CKD, chronic kidney disease; HMOD, hypertension-mediated organ damage.
depend on the severity of hypertension, the urgency to achieve BP control and the patient’s comorbidities. Patients with high-normal BP or white-coat hypertension frequently have additional risk factors, including HMOD, and have a higher risk of developing sustained hypertension. Thus, even when untreated, they should be scheduled for regular follow-up (at least annual visits) to measure office and out-of-office BP, as well as to check the cardiovascular risk profile.

Adherence to therapy (Fig. 43)
There is growing evidence that poor adherence to treatment—in addition to physician inertia (i.e. lack of therapeutic action when the patient’s BP is uncontrolled)—is the most important cause of poor BP control. Nonadherence to antihypertensive therapy correlates with higher risk of cardiovascular events.

Note: The levels of evidence for each of the recommendations presented in the figures can be found in the original
### Medication/Substance

<table>
<thead>
<tr>
<th>Medication/Substance</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral contraceptive pill</td>
<td>Especially oestrogen containing – cause hypertension in ~5% of women,</td>
</tr>
<tr>
<td>Diet pills</td>
<td>usually mild but can be severe</td>
</tr>
<tr>
<td>Nasal decongestants</td>
<td>For example, phenylephrine hydrochloride and naphazoline hydrochloride</td>
</tr>
<tr>
<td>Stimulant drugs</td>
<td>Amphetamine, cocaine, and ecstasy – these substances usually cause acute</td>
</tr>
<tr>
<td></td>
<td>rather than chronic hypertension</td>
</tr>
<tr>
<td>Liquorice</td>
<td>Chronic excessive liquorice use mimics hyperaldosteronism by stimulating</td>
</tr>
<tr>
<td></td>
<td>the mineralocorticoid receptor and inhibiting cortisol metabolism</td>
</tr>
<tr>
<td>Immunosuppressive medications</td>
<td>For example, cyclosporin A (tacrolimus has less effect on BP and rapamycin</td>
</tr>
<tr>
<td></td>
<td>has almost no effect on BP), and steroids (e.g. corticosteroids,</td>
</tr>
<tr>
<td></td>
<td>hydrocortisone)</td>
</tr>
<tr>
<td>Antiangiogenic cancer therapies</td>
<td>Antiangiogenic drugs, such as VEGF inhibitors (e.g. bevacizumab), tyrosine</td>
</tr>
<tr>
<td></td>
<td>kinase inhibitors (e.g. sunitinib), and sorafenib, have been reported to</td>
</tr>
<tr>
<td></td>
<td>increase BP</td>
</tr>
<tr>
<td>Other drugs and substances that may raise</td>
<td>Anabolic steroids, erythropoietin, non-steroidal anti-inflammatory drugs,</td>
</tr>
<tr>
<td>BP</td>
<td>herbal remedies (e.g. ephedra, ma huang)</td>
</tr>
</tbody>
</table>

**FIGURE 31** Medications and substances that may increase blood pressure.

### 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
- Urine albumin:creatinine ratio, urine microscopy for red cells, leucocytes, and 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)

**FIGURE 32** Diagnostic work-up for patients with a suspected hypertension emergency. eGFR, estimated glomerular filtration rate; LDH, lactate dehydrogenase.
<table>
<thead>
<tr>
<th>Clinical presentation</th>
<th>Time line and target for BP reduction</th>
<th>First-line treatment</th>
<th>Alternative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malignant hypertension with or without acute renal failure</td>
<td>Several hours Reduce MAP by 20–25%</td>
<td>Labetalol Nicardipine</td>
<td>Nitroprusside Urapidil</td>
</tr>
<tr>
<td>Hypertensive encephalopathy</td>
<td>Immediately reduce MAP by 20–25%</td>
<td>Labetalol Nicardipine</td>
<td>Nitroprusside</td>
</tr>
<tr>
<td>Acute coronary event</td>
<td>Immediate reduce SBP to &lt; 140 mmHg</td>
<td>Nitroglycerine Labetalol</td>
<td>Urapidil</td>
</tr>
<tr>
<td>Acute cardiogenic pulmonary oedema</td>
<td>Immediately reduce SBP to &lt; 140 mmHg</td>
<td>Nitroprusside OR nitroglycerine (with loop diuretic)</td>
<td>Urapidil (with loop diuretic)</td>
</tr>
<tr>
<td>Acute aortic dissection</td>
<td>Immediately reduce SBP to &lt; 120 mmHg AND heart rate to &lt; 60 bpm</td>
<td>Esmolol AND nitroprusside OR nitroglycerine OR nicardipine</td>
<td>Labetalol OR metoprolol</td>
</tr>
<tr>
<td>Eclampsia and severe pre-eclampsia/HELLP</td>
<td>Immediately reduce SBP to &lt; 160 mmHg AND DBP to &lt; 105 mmHg</td>
<td>Labetalol OR nicardipine AND magnesium sulphate</td>
<td>Consider delivery</td>
</tr>
</tbody>
</table>

**FIGURE 33** Hypertensive emergencies requiring immediate blood pressure lowering with intravenous drug therapy. MAP, mean arterial pressure.

**Management of white-coat hypertension**

**Recommendations**

In white-coat hypertensive patients, it is recommended to implement lifestyle changes aimed at reducing CV risk as well as a regular follow-up with periodic out-of-office BP monitoring.

In patients with white-coat hypertension:

- Drug treatment may be considered in people with evidence of HMOD or in whom CV risk is high or very high.
- Routine drug treatment is not indicated.

**Management of masked hypertension**

**Recommendations**

In masked hypertension, lifestyle changes are recommended to reduce CV risk, with regular follow-up, including periodic out-of-office BP monitoring.

Antihypertensive drug treatment should be considered in masked hypertension to normalize the out-of-office BP based on the prognostic importance of out-of-office BP elevation.

Antihypertensive drug up-titration should be considered in treated patients whose out-of-office BP is not controlled (i.e. masked uncontrolled hypertension), because of the high CV risk of these patients.

**FIGURE 34** White-coat and masked hypertension. CV, cardiovascular; HMOD, hypertension-mediated organ damage.
### Recommendations

In women with gestational hypertension or pre-existing hypertension superimposed by gestational hypertension, or with hypertension and subclinical organ damage or symptoms, initiation of drug treatment is recommended when SBP is \( \geq 140 \) or DBP \( \geq 90 \) mmHg.

In all other cases, initiation of drug treatment is recommended when SBP is \( \geq 150 \) mmHg or DBP is \( \geq 95 \) mmHg.

Methyldopa, labetalol, and CCBs are recommended as the drugs of choice for the treatment of hypertension in pregnancy.

ACE inhibitors, ARBs, or direct renin inhibitors are not recommended during pregnancy.

SBP \( \geq 170 \) mmHg or DBP \( \geq 110 \) mmHg in a pregnant woman is an emergency, and admission to hospital is recommended.

In severe hypertension, drug treatment with i.v. labetalol or oral methyldopa or nifedipine is recommended.

The recommended treatment for hypertensive crisis is i.v. labetalol or nicardipine and magnesium.

In pre-eclampsia associated with pulmonary oedema, nitroglycerin given as an i.v. infusion is recommended.

In women with gestational hypertension or mild pre-eclampsia, delivery is recommended at 37 weeks.

It is recommended to expedite delivery in pre-eclampsia with adverse conditions such as visual disturbances or haemostatic disorders.

**FIGURE 35** Hypertension in pregnancy. ACEI, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blockers; CCB, calcium channel blockers.

### Recommendations

Antihypertensive drug treatment is recommended for people with diabetes when office BP is \( \geq 140/90 \) mmHg.

In people with diabetes receiving BP-lowering drugs it is recommended:
- To target SBP to 130 mmHg and lower, if tolerated, but not lower than 120 mmHg.
- In older people (aged \( \geq 65 \) years), to target to an SBP range of 130 to \( < 140 \) mmHg.
- To target the DBP to \( < 80 \) mmHg, but not lower than 70 mmHg.

It is recommended to initiate treatment with a combination of a RAS blocker with a CCB or thiazide/thiazide-like diuretic.

Simultaneous administration of two RAS blockers, e.g. and ACE inhibitor and ARB, is not indicated.

**FIGURE 36** Hypertension in diabetes. ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blockers; CCB, calcium channel blockers; RAS, renin-angiotensin system.
**Recommendations**

In patients with diabetic or non-diabetic CKD, it is recommended that an office BP of ≥ 140/90 mmHg be treated with lifestyle advice and BP-lowering medication.

In patients with diabetic or non-diabetic CKD:
- It is recommended to lower SBP to a range of 130-139 mmHg.
- Individualized treatment should be considered according to its tolerability and impact on renal function and electrolytes.

RAS blockers are more effective at reducing albuminuria than other antihypertensive agents, and are recommended as part of the treatment strategy in hypertensive patients in the presence of microalbuminuria or proteinuria.

A combination of a RAS blocker with a CCB or a diuretic is recommended as initial therapy.

A combination of two RAS blockers is not recommended.

**FIGURE 37** Hypertension in chronic kidney disease. CCB, calcium channel blockers; CKD, chronic kidney disease; RAS, renin–angiotensin system.

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**Recommendations**

In patients with CAD receiving BP-lowering drugs, it is recommended:
- To target SBP to 130 mmHg and lower, if tolerated, but not lower than 120 mmHg.
- In older patients (aged ≥ 65 years), to target to a SBP range of 130–140 mmHg.
- To target DBP to < 80 mmHg, but not lower than 70 mmHg.

In hypertensive patients with a history of myocardial infarction, beta-blockers and RAS blockers are recommended as part of treatment.

In patients with symptomatic angina, beta-blockers and/or CCBs are recommended.

**FIGURE 38** Hypertension in coronary artery disease. CAD, coronary artery disease; CCB, calcium channel blockers.

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**Recommendations**

In hypertensive patients with heart failure (with reduced or preserved ejection fraction), BP-lowering treatment should be considered if BP is ≥ 140/90 mmHg.

In patients with HFrEF, it is recommended that BP-lowering treatment comprises an ACE inhibitor or ARB and a beta-blocker and diuretic and/or mineralocorticoid receptor antagonist if required.

Dihydropyridine CCBs may be added if BP control is not achieved.

In patients with HFrEF, BP-treatment threshold and target values should be the same as for HFrEF.

Because no specific drug has proven its superiority, all major agents can be used.

In all patients with LVH:
- It is recommended to treat with a RAS blocker in combination with a CCB or diuretic.
- SBP should be lowered to a range of 120–130 mmHg.

**FIGURE 39** Hypertension in left ventricular hypertrophy and heart failure. ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blockers; CCB, calcium channel blockers; LVH, left ventricular hypertrophy; RAS, renin–angiotensin system.
### Recommendations

**In patients with acute intracerebral haemorrhage:**
- Immediate BP lowering is not recommended for patients with SBP < 220 mmHg.
- In patients with SBP ≥ 220 mmHg, careful acute BP lowering with i.v. therapy, to < 180 mmHg should be considered.

**In acute ischaemic stroke, routine BP lowering with antihypertensive therapy is not recommended, with the exceptions:**
- In patients with acute ischaemic stroke who are eligible for i.v. thrombolysis, BP should be carefully lowered and maintained to < 180/105 mmHg for at least the first 24 h after thrombolysis.
- In patients with markedly elevated BP who do not receive fibrinolysis, drug therapy may be considered, based on clinical judgement, to reduce BP by 15% during the first 24 h after the stroke onset.

**In hypertensive patients with an acute cerebrovascular event, antihypertensive treatment is recommended:**
- Immediately for TIA.
- After several days in ischaemic stroke.

**In all hypertensive patients with ischaemic stroke or TIA, a SBP target range of 120–130 mmHg should be considered.**

The recommended antihypertensive drug treatment strategy for stroke prevention is a RAS blocker plus a CCB or a thiazide-like diuretic.

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**FIGURE 40** Hypertension and cerebrovascular diseases. CCB, calcium channel blocker; RAS, renin–angiotensin system; TIA, transient ischaemic attack.

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### Recommendations

**In patients with AF, screening for hypertension is recommended.**

A beta-blocker or non-dihydropyridine CCB should be considered as part of the treatment of hypertension if rate control is needed.

**Stroke prevention with oral anticoagulation is recommended in patients with AF and hypertension and a CHA2DS2-VASc score of ≥ 2 in men and ≥ 3 in women.**

**Stroke prevention with oral anticoagulants should be considered in AF patients with hypertension, even when hypertension is the single additional risk factor (CHA2DS2-VASc score of 1).**

Oral anticoagulants should be used with caution in patients with marked BP elevation (SBP ≥ 180 mmHg and/or DBP ≥ 100 mmHg) and the aim should be to lower SBP to at least < 140 mmHg and SBP lowering to < 130 should be considered. If this is not possible, then patients should make an informed decision that they accept that the stroke protection provided by the anticoagulant will be associated with higher bleeding risk.

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**FIGURE 41** Hypertension and atrial fibrillation. AF, atrial fibrillation; CCB, calcium channel blocker.
### Recommendations

It is recommended that newly diagnosed hypertensive patients who are scheduled for elective surgery should be preoperatively screened for HMOD and CV risk.

It is recommended to avoid large perioperative BP fluctuations during the perioperative period.

Non-cardiac surgery may not be deferred in patients with grade 1 or 2 hypertension (SBP < 180 mmHg; DBP < 110 mmHg).

Perioperative continuation of beta-blockers is recommended in hypertensive patients on chronic treatment with these drugs.

Abrupt discontinuation of beta-blockers or centrally acting agents (e.g., clonidine) is potentially harmful and is not recommended.

Transient preoperative discontinuation of RAS blockers should be considered in patients with hypertension undergoing non-cardiac surgery.

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**FIGURE 42** Hypertension in perioperative diseases. CV, cardiovascular; HMOD, hypertension-mediated organ damage.

**Physician level**
- Provide information on the risks of hypertension and the benefits of treatment, as well as agreeing a treatment strategy to achieve and maintain BP control using lifestyle measures and a single-pill-based treatment strategy when possible (information material, programmed learning, computer-aided counselling)
- Empowerment of the patient
- Feedback on behavioural and clinical improvements
- Assessment and resolution of individual barriers to adherence
- Collaboration with other healthcare providers, especially nurses and pharmacists

**Patient level**
- Self-monitoring of BP (including telemonitoring)
- Group sessions
- Instruction combined with motivational strategies
- Self-management with simple patient-guided systems
- Use of reminders
- Obtain family, social, or nurse support
- Provision of drugs at worksite

**Drug-treatment level**
- Simplification of the drug regimen favouring the use of SPC therapy
- Reminder packaging

**Health-system level**
- Support the development of monitoring systems (telephone follow-up, home visits, telemonitoring of home BP)
- Support financially the collaboration between healthcare providers (pharmacists, nurses)
- Reimbursement of SPC pills
- Development of national databases, including prescription data, available for physicians and pharmacists
- Accessibility to drugs

**FIGURE 43** Interventions that may improve drug adherence in hypertension.
publications cited below. Additional figures can also be found in the printed versions of the guidelines. The grading scale can be found as supplementary material (Supplementary Figure 1, http://links.lww.com/HJH/B29).

REFERENCES
