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REVIEW
CVD risk factors

Targets for treatment and optimal strategies for managing hypertension in 2025: indications for clinical practice from recent hypertension guidelines

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Abstract

Recent hypertension guidelines differ in their recommendations on managing hypertension and associated cardiovascular risk. In this review, we highlight the key similarities and discrepancies among the recently published American College of Cardiology/American Heart Association (ACC/AHA), European Society of Cardiology (ESC), and European and International Society of Hypertension (ESH and ISH) hypertension guidelines. Despite differences in the definition of hypertension, all guidelines reflect a general trend towards earlier intervention and more stringent blood pressure (BP) targets, particularly for individuals at high cardiovascular risk. They align on lifestyle recommendations, such as dietary modification and physical activity, and advocate for combination therapy with a target BP of <130/80 mmHg if the risk is sufficiently high and treatment well tolerated. However, notable differences exist in treatment thresholds and BP targets for elderly individuals, as well as in the classification of hypertension phenotypes in younger patients. There are few discrepancies in recommended treatment classes, with all guidelines endorsing angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, calcium channel blockers, and thiazide-type diuretics as first-line therapy. Knowledge gaps remain regarding optimal BP thresholds and targets across sex, age, and ethnic groups. Additional uncertainties include the clinical utility of intermediate outcomes in cardiovascular risk assessment, the long-term impact of life-course approaches to prevention, and the role of novel therapeutic agents. Emerging concerns such as climate change and air pollution also warrant further investigation for their potential effects on hypertension and cardiovascular risk.

Lay summary

Guidelines are important tools to help clinicians make treatment decisions. For the management of hypertension, different guidelines have been released in recent years. Being the most important risk factor worldwide and with its burden still increasing, management of hypertension remains a challenge. This is especially true for low- and middle-income countries where hypertension awareness, treatment, and control rates are still low. To help clinicians make informed decisions, we have compared the most important hypertension guidelines that have appeared in the past 10 years and summarized their most important recommendations.

Key findings are that:

(1) All recent hypertension guidelines advocate earlier intervention and more stringent blood pressure targets and promote a healthy lifestyle

(2) Guidelines differ in their definitions of hypertension, treatment thresholds and blood pressure targets for elderly individuals.

Important knowledge gaps remain regarding optimal blood pressure thresholds and targets across sex, age, and ethnic groups.

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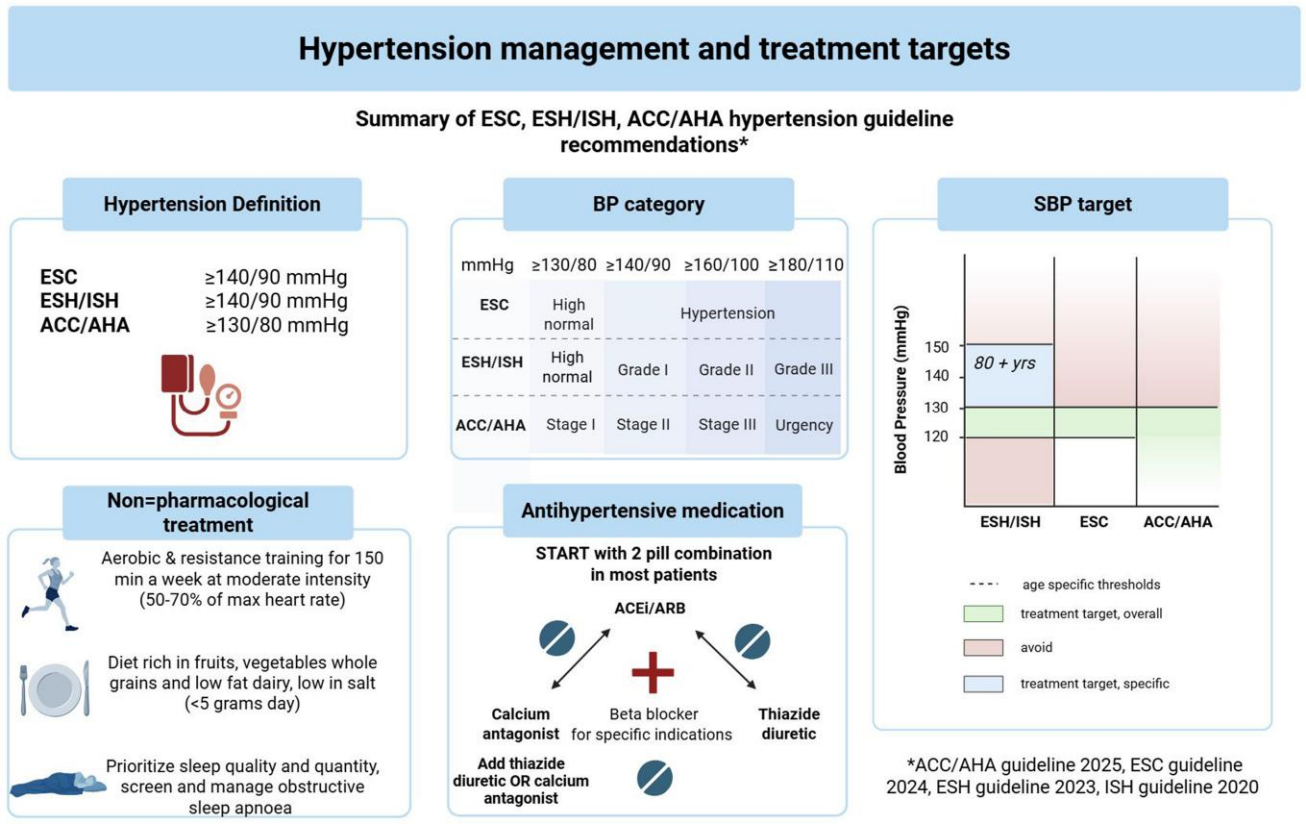
Graphical Abstract



Keywords Hypertension • Guideline • Preventive Care • Risk management

Introduction

Hypertension remains the single most important risk factor for cardiovascular disease (CVD) worldwide.[1,2] In 2015, an estimated 8.5 million deaths were attributable to high blood pressure (BP) with its burden still increasing in low- and middle-income countries accounting for an estimated 88% of hypertension-related deaths.[3] Worldwide, hypertension treatment is given to 47% of women and 38% of men, while control rates are 23% for women and 18% for men.[2] Treatment and control rates are especially poor in lower- and middle-income countries where the burden of hypertension and related complications is growing rapidly.[2,4] Reducing hypertension through lifestyle advice and pharmacological treatment is the cornerstone of hypertension management that should also be feasible in low- and middle-income countries. In recent years, different guidelines have been released for the management of hypertension. To help clinicians make informed decisions, we have compared the latest hypertension guidelines that have appeared in the past 5 years and summarized their most important recommendations.

Methods

We undertook a comparative analysis of the most recent international hypertension guidelines, with the objective of delineating their principal similarities and differences as well as the supporting evidence base. We focused on the recently published 2025 American College of Cardiology and American Heart Association (ACC/AHA), the 2024 European Society of Cardiology (ESC), the 2023 European Society of Hypertension (ESH), and the 2020 International Society of Hypertension (ISH) guidelines.[5–8] With respect to clinical practice, our synthesis concentrated on definitions and recommendations of greatest relevance, including treatment thresholds, criteria for the evaluation of secondary hypertension, and guidance on non-pharmacological and pharmacological management strategies. In addition, we identified research priorities by highlighting the knowledge gaps recurrently acknowledged across these guidelines. For an extensive review on the differences and similarities between the 2024 ESC guideline and 2023 ESH guideline on hypertension, we also refer to the recently published comparison on their key recommendations.[9]

Definition of hypertension and treatment thresholds

Lowering BP effectively prevents CVD, and aggregated data of randomized controlled trials show that the benefits of lowering BP is fairly consistent across BP levels.[10] Since pivotal trials have used office BP to guide treatment, all guidelines recommend its use in clinical practice. *Box 1* provides an overview of the definitions for hypertension, BP categories and treatment thresholds. For hypertension diagnosis, the ESH guideline recommends repeated office BP with out-of-office measurements for additional confirmation.[5,7] In contrast, both the recent ACC/AHA guideline and the ESC guideline give a Class 1 recommendation to

Box 1 Key guideline recommendations for blood pressure thresholds and definitions

Topic	Recommendation
Hypertension definition	≥140/90 mmHg, except the 2025 ACC/AHA guideline where the threshold is ≥130/80 mmHg
BP classification	Traditional categories in stages (2025 ACC/AHA) or grades (2023 ESH, 2020 ISH). ESC 2024 guideline proposes classification in non-elevated BP, elevated BP, and hypertension to facilitate communication to patients
Treatment threshold	≥140/90 mmHg; ≥130/80 mmHg for individuals at high CVD risk (2025 ACC/AHA and 2024 ESC) or coronary artery disease (2023 ESH)

confirm the diagnosis with out-of-office BP measurement (ABPM or validated home BP).[5,6] The question to how much BP should be lowered is a matter of debate and has fuelled discussions about both the definition of hypertension and its implications for the prevalence of hypertension and treatment target.[10,11] The justification for the definition of hypertension as BP ≥ 130/80 mmHg in the previous 2017 and recent 2025 ACC/AHA guideline is based on observational evidence showing increased CVD risk associated with BP levels between 130–140 and 80–90 mmHg.[5,12] The ESC and ESH and ISH guidelines have maintained a BP ≥ 140/90 mmHg to define hypertension, although both the ESC and ESH/ISH guidelines recognize an increase in CVD risk associated with 'high–normal'(ESH, 130–139/85–89 mmHg) or 'elevated' (ESC, 120–139/70–89 mmHg) BP.[6,7] Whether lowering BP to values below 120/70 mmHg or even 130/80 mmHg has universal benefit on CVD risk remains to be determined. Although BP is a continuous measure, it is traditionally divided into stages (2025 ACC/AHA) or grades (2023 ESH, 2020 ISH), approximating a doubling of CVD risk with every stage or grade, to guide treatment recommendation decisions. The ESC 2024 guideline has introduced a simpler classification, discriminating non-elevated BP, elevated BP, and hypertension to facilitate communication to patients.

Treatment in individuals according to cardiovascular disease risk

For predicting cardiovascular risk, the recent ACC/AHA guideline advocates the use of the predicting risk of cardiovascular disease EVENTs (PREVENT) equation as a more contemporary, broadly tested and comprehensive risk score compared with the pooled cohort equations (PCE) score. PREVENT estimates 10-year and 30-year risk (as a lifetime estimate) of fatal and non-fatal CVD that, next to stroke and coronary heart disease, also includes heart failure as a major outcome.[13,14] The ESC and ESH guidelines recommend using the updated Systematic Coronary Risk Evaluation 2 (SCORE2) tool for 10-year CVD risk stratification.[15] Given the shorter lifespan in elderly individuals, both the ESH and ESC guidelines use a separate risk assessment tool for adults aged ≥70 years, the Systematic Coronary Risk Evaluation 2–Older Persons (SCORE2-OP), to estimate the 5-year risk of CVD.[16] Within the broader context of the ISH guideline, general recommendations are given for the use of risk scores based on BP and additional risk factors.[8] *Figure 1* provides a graphical overview of the different treatment thresholds according to the guideline recommendations. Regardless of CVD risk, all guidelines recommend BP-lowering medication in individuals with confirmed BP ≥ 140/90 mmHg. This includes individuals with Type 2 diabetes, chronic kidney disease (CKD) (estimated glomerular filtration rate [eGFR] < 60 mL/min/1.73 m^2 or albumin-to-creatinine ratio ≥ 30 mg/g) and a history of CVD. Both the new ACC/AHA guideline and ESC guidelines also recommend BP-lowering medication in individuals with BP of 130–139/80–89 mmHg and history of CVD, Type 2 diabetes or CKD, or elevated CVD risk, defined as a 10-year CVD risk of 7.5% or higher according to the ACC/AHA guideline and ≥10% according to the ESC guideline. In contrast, the ESH and ISH advice to only consider pharmacological treatment in patients with a BP ≥ 130/80 mmHg and history of CVD, in particular coronary artery disease. In elderly patients, the ESC recommends to consider frailty rather than age alone and supports initiating treatment up to and beyond 85 years of age when BP ≥ 140/90 mmHg. In contrast, the ESH guideline advocates a more conservative approach in individuals aged ≥80 years, recommending treatment initiation at a systolic BP ≥ 160 mmHg and to consider starting at lower thresholds based on clinical judgement. In line with its broader objective, the ISH guideline discerns situations where treatment is essential and where treatment is optimal tailoring treatment to settings with limited availability of drug treatment. In situations where treatment is optimal, the ISH is similar to the ESH guideline, whereas in case of limited resources, immediate drug treatment is advised for those with BP ≥ 160/100 mmHg, while lifestyle interventions are recommended as the first step for those with a BP of 140–159/90–99 mmHg and low CVD risk. Next to BP-lowering treatment and focus on lifestyle, a multifactorial risk approach that also considers lipid-lowering therapy, glycaemic control, and antithrombotic therapy is recommended with reference to appropriate guidelines to further lower CVD risk.

Treatment of young individuals and different blood pressure phenotypes

All guidelines support initiating BP-lowering medication in young adults with persistent BP levels of 140/90 mmHg or higher, regardless of overall CVD risk,[5–7] while the recent ACC/AHA guideline takes a more proactive approach and recommends to start medication if BP remains 130/80 mmHg or higher despite 3–6 months of lifestyle intervention even when the risk of CVD is low (PREVENT risk < 7.5%).[8] Both the ESH and ESC guidelines give specific considerations for young adults under 40 years of age with isolated systolic hypertension, where additional assessments—such as central BP and arterial stiffness measurements—are advised for more accurate CVD risk stratification (*Table 1*). For isolated diastolic hypertension, watchful monitoring is generally recommended, although the ESH guideline suggests treatment can be considered because of the stronger association between isolated diastolic hypertension and future CVD.

Recommendations to initiate pharmacological BP-lowering treatment in individuals with low to intermediate cardiovascular risk are supported by evidence that elevated BP is independently associated with CVD and that the relative risk reduction is similar—or even greater—in younger compared with older adults.[17] The ESH guideline highlights that early BP-lowering treatment may have additional long-term benefits by delaying or preventing the transition to a high-risk CVD state later in life. Although no randomized trials have directly compared early vs. delayed initiation of treatment, so-called 'legacy effects' of early BP-lowering treatment—i.e. sustained benefits after discontinuation—have been suggested by post-trial follow-up data. They show that treatment

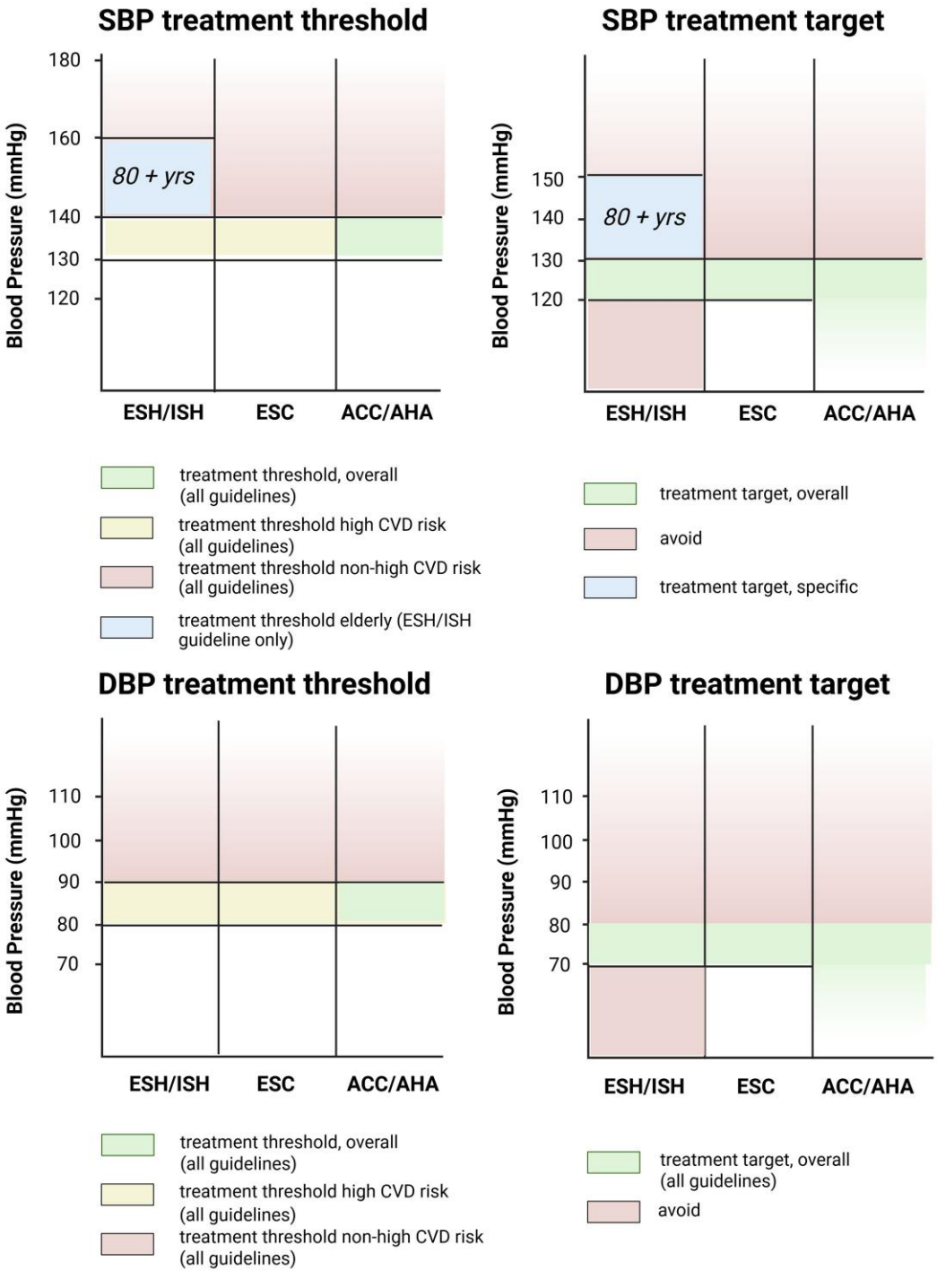


Figure 1 Recommended treatment thresholds and targets according to systolic and diastolic BP as well as to CVD risk level. In the ESH guideline, high CVD risk is defined as patients with a history of CVD, whereas the ESC and ACC/AHA guidelines also recommend treatment in those with elevated CVD risk (≥10% SCORE2 risk or ≥7.5% PREVENT risk in the next 10 years or higher). Lower thresholds and targets can be considered according to the ESH/ISH guidelines if treatment is well tolerated. BP, blood pressure; CVD, cardiovascular disease; ESC, European Society of Cardiology; ACC/AHA, American College of Cardiology and American Heart Association; SCORE2, Systematic Coronary Risk Evaluation 2; ESH/ISH, European and International Society of Hypertension.

effects, though attenuated, often persist despite a return to baseline BP levels.[18] Additionally, randomized trials have shown that BP-lowering therapy can reduce, but often not normalize, left ventricular hypertrophy (LVH)[19] and that many other consequences of hypertension, such as arterial stiffness, glomerulosclerosis, and white matter lesions, are irreversible.[20,21] This supports the rationale for early

Table 1 Guideline recommendations for specific hypertension phenotypes in the young (<40 years of age)

Guideline recommendation	2020 ISH guideline	2023 ESH guideline	2024 ESC guideline	2025 ACC/AHA guideline
Combined systolic diastolic hypertension	Lifestyle and pharmacologic treatment	Lifestyle and pharmacologic treatment	Lifestyle and pharmacologic treatment	Lifestyle and pharmacologic treatment
Isolated systolic hypertension of the young[a]	NR	Lifestyle advice	Lifestyle advice	NR
Isolated diastolic hypertension of the young[b]	NR	Lifestyle and pharmacologic treatment	Lifestyle advice	NR

NR, no specific recommendation given.
[a]Defined as a systolic BP of 140 mmHg or higher with a diastolic BP < 90 mmHg.
[b]Defined as a diastolic BP of 90 mmHg or higher and normal systolic BP (<140 mmHg).

BP-lowering therapy as a strategy to prevent irreversible subclinical organ damage and reduce long-term CVD risk. Consequently, the inclusion of additional evidence of hypertension-mediated organ damage—such as LVH, reduced eGFR, or albuminuria—may support the initiation of pharmacological treatment more promptly.[5–7]

Considerations for secondary hypertension

All guidelines emphasize the significance of potential diagnostic clues—such as recurrent episodes of sweating, anxiety, palpitations, or spontaneous hypokalaemia, as important clinical indicators for further testing. Basic diagnostics for screening of secondary hypertension including medical history, physical examination, blood analysis, urine status, and abdominal sonography usually allow for initial screening of the most common secondary forms of hypertension. Additionally, all guidelines highlight the importance of evaluating medication use and recreational substances, including alcohol, as potential contributors. The ESH and ISH guidelines recommend further screening in case hypertension rapidly progresses, while the ACC/AHA guideline also identifies disproportionate target organ damage and diastolic hypertension in older adults as additional indications to investigate secondary causes.

Both the ACC/AHA and ISH guidelines recommend screening for secondary hypertension in individuals with onset of hypertension before 30 years of age, while the ESH guideline recommends screening for secondary causes in individuals <40 years of age with Grade 2 or 3 hypertension. The ESC recommends screening for secondary hypertension in adults diagnosed with hypertension before 40 years of age except in obese individuals, where evaluation of obstructive sleep apnoea (OSA) is advised as a more likely cause of hypertension alongside obesity itself. Resistant hypertension has been reported in 10–20% of patients with hypertension.[22] In the ESC, ESH, and ISH guidelines, hypertension is considered resistant when office BP remains ≥140/90 mmHg despite adherence to appropriate lifestyle measures and treatment with the maximum tolerated doses of three antihypertensive agents of different classes, including a diuretic. In the ACC/AHA guidelines, resistant hypertension is more broadly defined as a BP that remains above the target despite the use of three antihypertensive agents of different classes at optimal doses, commonly including a long-acting calcium channel blocker (CCB), an angiotensin-converting enzyme inhibitor (ACEi) or angiotensin receptor blocker (ARB), and a diuretic. Before the diagnosis of resistant hypertension is confirmed, guidelines recommend to exclude pseudo-resistance caused by the white coat effect using out-of-office measurements, and non-adherence to BP-lowering medication and lifestyle modifications. While all guidelines recommend to consider secondary causes in patients with resistant hypertension, the 2025 ACC/AHA guidelines recommend screening for primary aldosteronism in all patients with resistant hypertension, regardless of the presence of hypokalaemia given the high prevalence in this group. *Box 2* shows the key considerations for secondary and resistant hypertension.

Box 2 Key considerations for secondary and resistant hypertension

Topic	Recommendation
Reasons for suspecting secondary hypertension	(1) Resistant hypertension (2) Young age (<40 years without alternative explanations or Grade II hypertension or higher) (3) Potential diagnostic clue
Considerations for patients with resistant hypertension	Exclude pseudo-resistance caused by the white coat effect (through out-of-office BP measurements) and by evaluating non-adherence to BP-lowering medication

Non-pharmacological approaches

Worldwide, there is a strong link between obesity and hypertension prevalence, especially in young and middle-aged men and women.[23] The ESC guideline highlights that even modest weight loss (5–10%) is associated with significant reductions in systolic and diastolic BP, LVH, and cardiovascular mortality. All guidelines state that weight loss reduces BP proportionally in overweight and obese individuals with on average 1 mmHg for every kilogram weight loss and are broadly aligned in their lifestyle recommendations (*Box 3*). The ACC/AHA and ISH guidelines use ethnicity-specific cut-offs to define weight-reducing strategies, whereas the ESH and ESC guidelines recommend weight reduction in all individuals with a BMI of 25 kg/m^2 or higher. All guidelines recommend dietary modification and physical activity as separate, key

components, for both the prevention and management of hypertension and for reducing excess body weight. Dietary recommendations are based on the Dietary Approaches to STOP Hypertension (DASH) programme and Mediterranean diet that both emphasize the consumption of whole grains, fruits, and vegetables with limited servings of fish (Mediterranean) or meat (DASH) in addition to weight management strategies. In clinical practice, the management of obesity is often complex and requires a multifaceted approach. These include goal setting, providing feedback, self-monitoring, follow-up, and promoting self-efficacy. In addition, the ACC/AHA guideline recommends behavioural and motivational strategies to achieve a healthy lifestyle. With the advent of glucagon-like peptide 1 (GLP-1) receptor agonists, these strategies are more and more combined with anti-obesity medication.[24,25]

Box 3 Lifestyle recommendations

Topic	Recommendation
Weight reduction	Strongly recommended for individuals with overweight and obesity
Exercise	Aerobic and resistance exercise for 150 min a week or more of moderate intensity (50–70% of max. heart rate)
Diet	Rich in fruits, vegetables, whole grains, low-fat dairy, low in salt (<5 g/day)
Sleep	Pay attention to sleep quality and duration. Screen and manage obstructive sleep apnoea
Smoking cessation	Strongly recommended regardless of cardiovascular risk

Beyond weight management, sodium restriction and salt substitution are the most important dietary considerations across all guidelines, which recommend that salt intake should be restricted to <5 g of salt/day (not more than a teaspoon) in adults with elevated BP or hypertension. Recommendations for increase in potassium are still much debated, but in clinical practice, an increase in potassium intake by 0.5–1.0 g/day can be recommended in patients without moderate-to-advanced chronic kidney disease and high daily sodium intake. Of note, salt substitutes such as potassium-enriched salt are not readily available in all European countries, which may represent a practical challenge to effectively reducing salt intake in this group of patients. An overview of the lifestyle recommendations in recent hypertension guidelines is listed in *Table 2*.

Exercise—either as a standalone intervention or in combination with antihypertensive medication—is among the most effective strategies for achieving BP targets and reducing CVD risk and mortality.[26] These include increasing physical activity to 150 min or more of moderate-intensity aerobic exercise per week (50–70% max. heart rate), complemented by resistance training, in combination with a heart-healthy dietary pattern such as the Mediterranean or DASH diet, reduced salt intake, and healthy body weight. Aerobic exercise is generally preferred over resistance training, with the option to reduce total exercise time to 75–90 min per week if performed at higher intensity. Exercise should be tailored to the individual's fitness level, age, comorbidities, and overall health status.[27] The hypertension guidelines acknowledge isometric exercise as a potential adjunctive strategy for BP reduction. However, existing trials are relatively small and heterogeneous, and further large-scale studies are warranted to better establish its efficacy, safety, and optimal implementation.[27,28] Next to dietary recommendations, exercise is an ideal first-line treatment option for overall CVD risk reduction.[29] This is particularly true for young hypertensive patients with low CVD risk. Finally, all guidelines strongly recommend smoking cessation as a core component of lifestyle

Table 2 Comparison of lifestyle recommendations in recent hypertension guidelines

Aspect	2020 ISH guideline	2023 ESH guideline	2024 ESC guideline	2025 ACC/AHA guideline
Weight reduction	Use ethnicity-specific cut-offs	BMI 25 kg/m^2 or higher	BMI 25 kg/m^2 or higher	Manage BMI ≥25.0 kg/m^2 (non-Asian) or ≥23.0 kg/m^2 (Asian)
Dietary pattern	DASH-like diet: fruits, vegetables, whole grains, low-fat dairy	DASH-like diet: fruits, vegetables, whole grains	Mediterranean-style diet: fruits, vegetables, whole grains, healthy fats	DASH diet: rich in fruits, vegetables, whole grains, low-fat dairy, low in sweets and red meats
Salt intake	<5 g of salt/day	<5 g of salt/day	Limiting to <6 g/day; ideal <4 g/day	<4 g/day ideal; <6 g/day acceptable
Potassium intake	Increase dietary intake (unless contraindicated)	Encourages intake through fruits and vegetables	Recommends rich diet via fruits and vegetables	Increase intake through diet (unless contraindicated)
Alcohol	Limit consumption	Limit consumption	Reduce intake to moderate levels	Abstinence as optimal goal
Exercise	Aerobic (and resistance) 150 min/week (moderate)	Aerobic (and resistance) 150 min/week (moderate) or 75 min/week (vigorous)	Aerobic (and resistance) 150 min/week (moderate) or 75 min/week (vigorous)	Aerobic or dynamic resistance 90–150 min/week (moderate)[a]
Sleep	Consider sleep apnoea as a cause of secondary hypertension	Consider sleep apnoea as a cause of secondary hypertension	Consider sleep apnoea as a cause of secondary hypertension	Lifestyle recommendations, focused on relaxation therapies
Other advices	Stress reduction, stop smoking	Stress management, stop smoking	Stress reduction, stop smoking	Smoking cessation

[a]ACC/AHA guideline also provides recommendations on isometric resistance exercise.

modification for all patients with hypertension as it is a major risk modifier for CVD and all-cause mortality. The ESH guideline highlights that, although the direct effect of smoking on BP may be inconsistent, it clearly contributes to increased arterial stiffness and the progression of atherosclerosis. Similarly, limiting alcohol consumption is advocated by all guidelines, with the recent ACC/AHA guideline recommending abstinence as the optimal goal for the best health outcomes.

Sleep quality and obstructive sleep apnoea treatment

Although epidemiological evidence suggests that short and long sleepers exhibit higher risk of developing CVD,[30] interventional studies demonstrating that restoring normal sleep patterns can improve cardiovascular outcomes are lacking. More evidence is available regarding the role of OSA in CVD development. The guidelines all recommend screening and appropriate management of OSA in patients with resistant or poorly controlled hypertension to improve BP control and overall cardiovascular health. While the ISH and ACC/AHA guidelines mention OSA as a potential cause of secondary hypertension, the ESC and ESH guidelines further expand on the evidence that OSA treatment induces a modest, but clinically meaningful, BP reduction. A recent individual data meta-analysis of more than 60 randomized controlled trials investigating the effect of OSA treatment confirmed that continuous positive airway pressure could be particularly relevant for young patients with uncontrolled BP.[31] Weight loss is often recommended as a first-line intervention in OSA patients as it can reduce the severity of OSA, improve sleep quality and reduce BP. Glucagon-like peptide 1 agonists are a class of drugs that are used for the treatment of Type 2 diabetes and have shown to lower both body weight and BP.[32,33] In patients with OSA, GLP-1 agonists may help to improve OSA severity.[34] In the ACC/AHA, ESH, and ESC guidelines, bariatric surgery is recommended as an effective and long-lasting strategy for managing BP and cardiovascular risk in patients with severe obesity with or without obesity-related complications. Bariatric surgery can lead to complete remission of hypertension and, in general, reduces the need for antihypertensive medications, particularly in patients with resistant hypertension.[35] The guidelines emphasize that bariatric surgery should be considered in patients with severe obesity who have not achieved adequate BP control through lifestyle modifications and pharmacological therapy.

Pharmacological treatment of hypertension

The primary goal of antihypertensive treatment is to reduce CVD risk through effective BP reduction. On average, pharmacological therapy with a single agent lowers BP with 7/4 mmHg at half the standard dose, 9/6 mmHg at the standard dose, and 11/7 mmHg at double the standard dose, compared with placebo.[36] This BP-lowering effect is consistent across drug classes, but depends on both the underlying pathophysiological mechanism of hypertension and baseline BP—roughly 1 mmHg greater reduction is seen for every 10 mmHg higher pre-treatment BP.

Although BP reduction is dose dependent, the therapeutic effect plateaus at higher doses, whereas adverse effects increase in a dose-linear fashion. Combining two or three drug classes at half-standard doses results in additive BP-lowering effects of ~13/7 and 20/11 mmHg, without a corresponding increase in adverse events.[36]

An overview of the recommended pharmacotherapy is shown in *Figure 2* and *Table 3*. All guidelines recommend combination therapy for most hypertensive patients with the ACC/AHA and ESC guidelines advising combination treatment in individuals with BP levels ≥ 140/90 mmHg and the ESH guideline propagating monotherapy in those with a BP < 150/95 mmHg or frail elderly. First-line agents are generally selected from the following classes: ACEi and ARBs, long-acting dihydropyridine CCB, and thiazide or thiazide-like diuretics. While the 2025 ACC/AHA and 2024 ESC guidelines do not specify a preferred combination, the 2023 ESH and 2020 ISH guidelines recommend including an ACEi or ARB in the initial regimen.

When combined with lifestyle modifications, up to 90% of patients can achieve BP control within 3 months by escalating to triple therapy and subsequently adjusting doses as needed. In case of resistant hypertension, early referral to specialized hypertension centres should be considered.

Beta-blockers as first-line therapy?

The ACC/AHA, ESC, and ESH guidelines do not recommend beta-blockers as first-line therapy unless specific clinical indications are present, including ischaemic heart disease, heart failure with reduced ejection fraction, atrial fibrillation, and pregnancy or women planning pregnancy. The ESH guideline also considers beta-blockers as a first-line option where monotherapy is appropriate. Although beta-blockers have demonstrated benefits in CVD outcomes in high-quality trials, meta-analyses suggest that older beta-blockers may be less effective at reducing stroke risk. Limited outcome data exist for newer beta1-selective agents (e.g. bisoprolol and nebivolol) and beta-blockers with vasodilatory properties (e.g. nebivolol, carvedilol, and labetalol) in hypertensive populations. Beta-blockers should be avoided in very old or frail elderly individuals due to the increased risk of bradycardia and orthostatic hypotension. However, they may still be useful in various non-cardiac conditions such as anxiety disorders, essential tremor, glaucoma, and postural orthostatic tachycardia syndrome.[37]

Management of resistant hypertension

For resistant hypertension, the preferred pharmacologic addition is a mineralocorticoid receptor antagonist (MRA), specifically spironolactone (25–50 mg).[38] If spironolactone is not tolerated, eplerenone (50–200 mg) may be used as an alternative. However, both agents are contraindicated in patients with hyperkalaemia or severe renal impairment. In such cases, beta- or alpha-blocking agents may be considered as alternatives. If BP remains uncontrolled despite the use of antihypertensive medication, renal denervation is considered a treatment option by most recent guidelines through shared decision-making and following evaluation in a multidisciplinary team at specialized centres with sufficient procedural experience. Both the 2025 ACC/AHA and 2023 ESH guidelines consider renal denervation a treatment option for patients with resistant hypertension or for those who experience significant side effects from drug therapy. In the 2024 ESC guideline, renal denervation is considered for patients with resistant hypertension or in those with high CVD risk and uncontrolled hypertension using fewer than three medications. Unlike the 2023 ESH guideline, the 2024 ESC guideline explicitly states that renal denervation should not be recommended as a first-line intervention due to the absence of

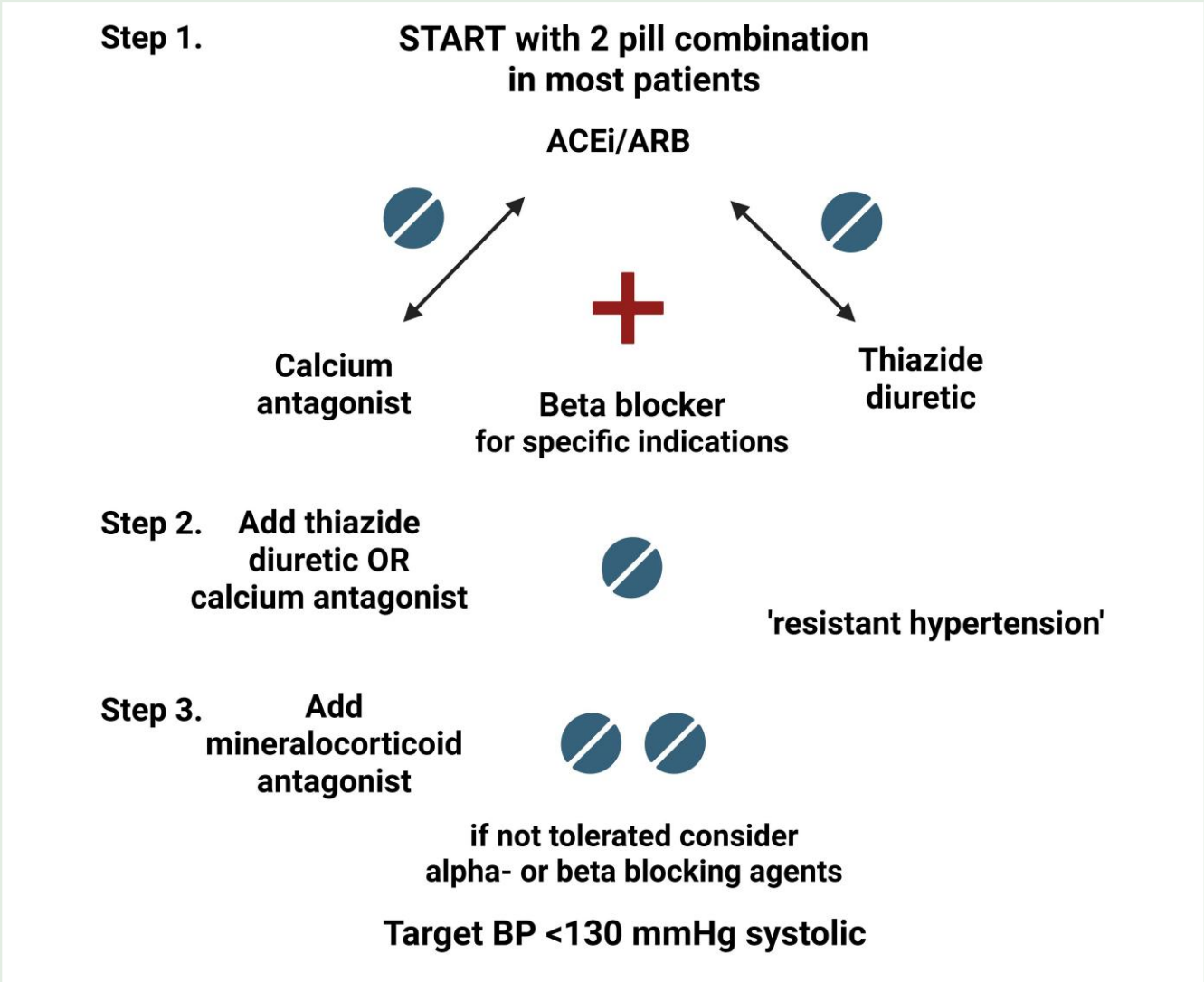


Figure 2 Recommended stepwise treatment approach for lowering BP in patients with hypertension by current guidelines. For most patients, it is recommended to start with ACE inhibitor or angiotensin receptor blocker (ACEi/ARB) combination with long-acting dihydropyridine calcium channel blockers (CCBs) or thiazide/thiazide-like diuretics on top of beta-blockers for specific indications (Step 1). Add thiazide diuretic or calcium antagonist if BP remains uncontrolled (Step 2). Consider pseudo-resistance and secondary causes if BP remains high ('resistant hypertension'), add a mineralocorticoid antagonist or alpha- or beta-blocking agent if mineralocorticoid receptor antagonists are not tolerated. BP, blood pressure.

cardiovascular outcome trials and advises against renal denervation in patients with an eGFR below 40 mL/min/1.73 m^2 or secondary hypertension.

Treatment targets and follow-up

The SPRINT and ACCORD trials have stimulated discussions about the optimal BP target for hypertensive patients and also fuelled the debate about the meaning of the J-curve in hypertension, where an increase in CVD events is observed in those with the lowest attained systolic and diastolic BP values.[39] The treatment targets for BP-lowering treatment according to the different guidelines are depicted in *Figure 1*. The ACC/AHA recommends to lower clinic BP to values <130/80 mmHg for most adults with confirmed hypertension, with encouragement to achieve systolic BP < 120 mmHg. The ESH guideline advices to lower BP to values <130/80 mmHg up to the age of 79 years if treatment is well tolerated and to avoid BP < 120/70 mmHg. For patients aged 80 years and older, the advice is to lower systolic BP < 150 mmHg and to further reduce BP if treatment is tolerated. The 2024 ESC guideline recommends to aim at a BP of 120–130/70–79 mmHg in all patients or as low as reasonably achievable in those where these targets cannot be met, while the ISH guideline recommends to lower BP to levels <130/80 mmHg in those <65 years and <140/90 mmHg in those who are older.

Recommendations that support intensive treatment are mainly based on aggregated evidence from trials that have shown that in individuals with high CVD risk, intensive treatment is superior to more conventional treatment targets.[40,41] These trials however had mixed treatment targets (some below 130 mmHg, but also below 140 mmHg). The SPRINT and ACCORD trials, which aimed to achieve even lower thresholds (<120 mmHg), showed different results:

Table 3 Guideline recommendations on pharmacotherapy

	2020 ISH guideline	2023 ESH guideline	2024 ESC guideline	2025 ACC/AHA guideline
Treatment thresholds	After 3–6 months of lifestyle measures if BP is 140–159/90–99 mmHg Immediate if BP ≥160/100 mmHg	Immediate if BP ≥ 140/90 mmHg in patients 18–79 years, ≥160 mmHg in patients ≥80 years, BP 130–139/80–89 mmHg in patients with CVD[a]	Immediate if BP ≥ 140/90 mmHg After 3 months of lifestyle if BP is 130–139/80–89 mmHg and high CVD risk[a]	Immediate if BP ≥ 140/90 mmHg Immediate if BP ≥ 130/80 mmHg and high CVD risk[b] After 3–6 months of lifestyle measures if BP is 130–139/80–89 mmHg and low CVD risk
Risk tool	Based on local guidelines	SCORE2	SCORE2	PREVENT
First-line drug classes	A/A—C—D—B	A/A—C—D—B	A/A—C—D	D[c]—C—A/A
First step	Two LD drugs, preferably A/A + C	Two drugs, preferably A/A + C or A/A + D One drug if BP ≥ 130/80 mmHg Morning dosing	Two LD drugs One drug if BP ≥ 130/80 mmHg Most convenient time of day	Two drugs if BP ≥ 140/90 mmHg and BP ≥ 20/10 mmHg above target One drug if BP is 130–139/80–89 mmHg
Further steps	Increase to full dose Three drugs	Increase dose Three drugs	Three LD drugs Increase dose	Increase dosage or sequential addition of other drugs
Treatment targets	BP < 130/80 mmHg	BP < 130/80 mmHg if well tolerated BP of 140–150/<80 mmHg for people aged 80 years and older	BP of 120–130/70–79 mmHg	BP < 130/80 mmHg, encourage goal < 120 mmHg
Timing of BP control	Within 3 months	Within 3 months	Within 3 months	No specific recommendation

A/A, ACE inhibitors/ARBs; B, beta-blockers; C, calcium channel blockers; D, diuretics thiazide or thiazide-like; LD, low-dose.
[a]High CVD risk defined as ≥10% SCORE2.
[b]High CVD risk defined as ≥7.5% PREVENT risk.
[c]Thiazide-type diuretics such as chlorthalidone preferred.

SPRINT was stopped early for reaching the primary endpoint, while the ACCORD trial in patients with Type 2 diabetes did not yield significant benefit. Both SPRINT and ACCORD had a similar design that allowed BP-lowering treatment to be stopped after randomization in case BP was below the intended target. Indeed, patients who had higher initial BP values benefited less than those with lower initial BP values, suggesting that patients who were already on target and were randomized to intensive therapy benefited more than patients who were randomized to conventional therapy and could have some of their BP-lowering medication stopped to attain higher BP levels.[42] Reasons for the more conservative approach in the ESH guideline are the decrease in incremental benefit following more intensive BP-lowering strategies and the higher level of side effects and treatment discontinuations observed with intensive treatment.[43] However, the existence of a so-called J-curve—where further reductions in BP are associated with increased CVD risk—is not supported by randomized trial evidence because the point estimates for risk remain largely unchanged even in individuals with achieved systolic BP below 120 mmHg or diastolic BP below 70 mmHg.[39] This is further supported by evidence from SPRINT and ACCORD demonstrating that the benefits of BP reduction extend both below and above the treatment target in those randomized to receive treatment aimed at systolic BP < 120 mmHg compared with treatment targeted at lowering systolic BP < 140 mmHg.[44]

The ESH, ESC, and ACC/AHA guidelines recommend that after initiating or adjusting antihypertensive treatment, patients should have their BP monitored at least monthly until target levels are achieved. Once BP targets are met, follow-up visits can be scheduled every 3–6 months and at least yearly in individuals with long-term stable BP control. More frequent visits may be necessary for patients with comorbidities or those requiring closer supervision. In all guidelines, patient education on BP self-monitoring and lifestyle modifications is emphasized to enhance adherence and long-term BP control. Moreover, self-monitoring enables patients to co-manage medications with their healthcare provider. Suitably validated and correctly used digital devices facilitate remote monitoring of BP during the diagnostic process while assessing the effect of non-pharmacological and pharmacological treatment. The ISH provides guidance adaptable to various healthcare settings. In low-resource settings, after initiating treatment, follow-up visits are recommended monthly until BP control is achieved and then every 3–6 months. In higher-resource settings, more frequent monitoring may be feasible and beneficial.

Evidence gaps and future perspectives

Overall, there is more consensus than disagreement across the major hypertension guidelines. All emphasize a trend towards earlier intervention and more stringent BP targets, particularly for individuals at high CVD risk. A key difference is the more stringent hypertension definition in the ACC/AHA guidelines. However, the recommendations for initiating BP-lowering therapy are largely aligned. The ESH and ESC guidelines, for example, also recommend treatment initiation at BP ≥ 130/80 mmHg in individuals at very high CVD risk. All guidelines endorse combination therapy as initial treatment in many cases and

Box 4 Key knowledge gaps identified in different guidelines

Topic	Knowledge gap
Hypertension definition	What is the effect of lowering BP in individuals with baseline 130–139/80–89 mmHg on CVD outcomes?
Population heterogeneity	Do optimal treatment strategies and target BP levels differ between men and women, and between different ethnic groups?
Long-term treatment benefits	What are the long-term treatment benefits for individuals with stage I hypertension and low CVD risk?
BP phenotypes	Should differentiation according to different BP phenotypes (isolated systolic hypertension, isolated diastolic hypertension, combined systolic diastolic hypertension) affect treatment decisions?
Salt substitution	What is the separate effect of sodium reduction compared with potassium supplementation on CVD outcomes?
Effect and place of novel compounds and interventions	What is the effect and place of novel compounds (e.g. GLP1 agonists, SGLT2 inhibitors, and neprilysin) and interventions influencing BP?
Environment	What is the effect of climate change and air pollution on hypertension prevalence, BP variability, and efficacy of BP-lowering medication?
BP variability	Should increased BP variability be considered as an additional CVD risk factor? How should we manage increased BP variability next to lowering average BP levels?
Optimal follow-up	What is the optimal timing and frequency of follow-up and what are the best tools for improving adherence and BP control?

support a BP target of <130/80 mmHg for most high-risk patients, provided treatment is well tolerated. While CVD risk scores remain valuable for patient communication, their role in treatment initiation is modest. In practice, all guidelines recommend pharmacological treatment for individuals with persistent BP ≥ 140/90 mmHg, with CVD risk assessment playing a greater role in guiding treatment decisions for those with BP between 120–139 mmHg systolic and 70–89 mmHg diastolic. Remaining differences between guidelines include treatment thresholds and target BP levels in elderly patients, as well as how hypertension phenotypes in younger individuals are defined and managed. A summary of the most important knowledge gaps identified in the different guidelines is provided in *Box 4*. One major area of uncertainty is the benefits of BP-lowering treatment in individuals with baseline BP 130–139/80–89 mmHg, except for meta-analysis suggesting that reducing BP lowers CVD risk even at normal or high–normal levels.[45] The optimal BP thresholds and BP targets between men and women and across different age categories and ethnic groups remain unclear,[5,6] as does the role of intermediate outcome measures next to existing risk scores.[6,7] Another knowledge gap concerns the long-term impact of early treatment and the efficacy of a life-course approach to hypertension management.[6,7] This may be especially relevant for distinct hypertension phenotypes, including isolated systolic hypertension, isolated diastolic hypertension, and combined systolic–diastolic hypertension. However, such evidence may only be obtained from trials with considerable follow-up duration. By contrast, the broad health benefits of lifestyle interventions arguably do not necessitate randomized controlled trial evidence, as their positive effects extend well beyond BP reduction. Exceptions may include salt substitutes and other non-pharmacological interventions, where controlled trials could guide product development and clinical recommendations. The role of novel drug classes in BP control and CVD prevention, including sodium-glucose co-transporter 2 (SGLT2) inhibitors, GLP-1 receptor agonists, and agents currently prescribed for other indications (e.g. finerenone and sacubitril–valsartan) also requires further study. In the context of medication simplification, evidence is needed to determine the optimal fixed-dose combinations ('polypills') and dosages across diverse populations.[6,7] For individuals with resistant hypertension, the optimal strategy to reduce CVD risk remains undefined, as there are no outcome trials comparing different pharmaceutical and intervention-based strategies, including renal denervation.[7] Another important knowledge gap is the effects of air pollution, noise exposure and climate change on BP and CVD risk, variations in BP, and efficacy of BP-lowering medication.[46,47] The guidelines do not provide graded recommendations to modify antihypertensive therapy based on pollution or climate, but recognize these exposures as relevant. Likewise, the influence of (occupational and environmental) noise exposure on BP is recognized by both the ESC and ESH guidelines,[46,48] recognizing it as a health risk that could be addressed in health promotion programmes. The same is true for the variation in BP itself and its association with CVD risk. Although increased BP variability is linked to target organ damage, CVD, and mortality, there is no interventional evidence that reducing variability improves outcomes. Nevertheless, specific pharmacological interventions that lower BP variability are also associated with improved outcomes, supporting suggestions to consider BP variability as an additional BP-related, potentially modifiable risk factor.[49] Finally, non-adherence to BP-lowering treatment remains a significant challenge, and the optimal methods to assess and address it as well as the ideal approach and frequency for follow-up visits have yet to be clearly defined.

Author contribution

G.P. contributed to the conception of the work. B.-J.H.v.d.B. contributed to the design and overview of the work. B.-J.H.v.d.B., T.B.-A., M.P., F.M., I.S., and H.H. drafted the manuscript. G.P., B.-J.H.v.d.B., T.B.-A., M.P., F.M., I.S., and H.H. provided critical feedback. All gave final approval and agree to be accountable for all aspects of work ensuring integrity and accuracy.

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Data availability

No new data were generated or analysed in support of this research.

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