APPENDIX 1: SUPPLEMENTARY TABLES

Supplementary Table 1: Routine screening tests suggested upon hypertension diagnosis

Blood chemistry (potassium, sodium, and creatinine)
Urinalysis and urinary albumin excretion
Hemoglobin A1c and/or fasting blood glucose
Fasting lipid panel
Standard 12-lead electrocardiography

Supplementary Table 2: Adaptation process for recommendation "*BP assessment with a validated automated device and using a standardized method is recommended (Strong recommendation; Moderate-certainty evidence).*"

Source Guideline	Recommendation	Strength of Recommendation	Certainty of Evidence
ESC[1]	*"It is recommended to measure BP using a validated and calibrated device, to enforce the correct measurement technique, and to apply a consistent approach to BP measurement for each patient."*	Strong	Moderate
AHA[2]	*"For diagnosis and management of high BP, proper methods are recommended for accurate measurement and documentation of BP."*	Strong	Low
WHO[3]	Not addressed.	N/A	N/A
Adaptation Process	The committee evaluated the evidence tables listed below from the 2024 ESC guidelines which were relevant to this recommendation. The evidence tables provide data from systematic reviews and meta-analyses on device validation status, sources of bias in BP measurements, the sensitivity and specificity of office, home, and ambulatory BP monitoring as diagnostic tests, and their use for long-term management. They show conclusive evidence arguing for the use of validated BP devices and a standardized BP measurement method. The committee endorsed the 2024 ESC assessment of the strength of recommendation and certainty of evidence on this topic.		
Values and Preferences	This recommendation places a high value on using proper BP measurement technique and equipment to ensure accurate readings. As such, it prioritizes precision in BP assessment to ensure appropriate diagnosis and management. While recognizing that access to validated devices and standardized methods may be limited in some settings, this recommendation underscores the importance of maintaining measurement quality to reduce errors and improve clinical decision-making.		

Links to evidence syntheses:

1. ESC: Evidence tables 1-8 at https://oup.silverchair-cdn.com/oup/backfile/Content_public/Journal/eurheartj/45/38/10.1093_eurheartj_ehae178/1/2024_hypertension_guidelines_evidence_tables.pdf?Expires=1740736053&Signature=gG9t6zeidOyXkx2yKAvow1R~A1Dj7y1UKs0XGTEtrS31QYV8GU9prHNEiLRANUehQaWnRG97RW3IVgpVxrgi1WUeZ30BY291UWcYaC~17bPBVNOziDzmpF8NwfEP65UmJ5Nvvm8gNUiRh6vc69QZlmyW2vq5zKv7ayV0AaXB2Z06jFu5qislJw4VyxsD8QxLkW-j3~s23YNvC42rLzKhdxlEAEz4-~SD1Fd6thXy3qAAYQOzE5u7kQD1CKPzUaOzuQM3Fhl~FC~cWQn3iPQe~XVsNlqtwWNZp3Ya4-575mlWAmkzLSyawm7CVl~mYGD0Ma98zTuyce7C3TMJozMRMA__&Key-Pair-Id=APKAIE5G5CRDK6RD3PGA

2. AHA: Not provided. Labeled as “expert opinion”.

3. WHO: Not addressed.

Abbreviations:

AHA, American Heart Association; BP, blood pressure; ESC, European Society of Cardiology; WHO, World Health Organization.

Supplementary Table 3: Adaptation process for recommendation "*Out-of-office BP assessment is recommended to confirm the diagnosis of hypertension and/or to detect white coat hypertension and masked hypertension (Strong recommendation; Moderate-certainty evidence).*"

Source Guideline	Recommendation	Strength of Recommendation	Certainty of Evidence
ESC[1]	*"Out-of-office BP measurement is recommended for diagnostic purposes, particularly because it can detect both white-coat hypertension and masked hypertension. Where out-of-office measurements are not logistically and/or economically feasible, then it is recommended that the diagnosis can be confirmed with a repeat office BP measurement using the correct standardized measurement technique."*	Strong	Moderate
AHA[2]	*"Out-of-office BP measurements are recommended to confirm the diagnosis of hypertension and for titration of BP-lowering medication, in conjunction with telehealth counseling or clinical interventions."*	Strong	High
WHO[3]	Not addressed.	N/A	N/A
Adaptation Process	The committee evaluated the evidence syntheses listed below from ESC and AHA. The evidence tables provided data from systematic reviews and meta-analysis demonstrating strong data against the reliance on a single office-based BP measurement to diagnose hypertension. They show evidence of the benefit in the use of out-of-office BP measurement for confirming the diagnosis of hypertension and detecting white coat and masked hypertension phenotypes. After reviewing the evidence syntheses from both ESC and AHA, the committee agreed with both that the strength of evidence was strong but felt the certainty of evidence was moderate, consistent with ESC.		
Values and Preferences	This recommendation prioritizes the importance of accurate hypertension diagnosis by emphasizing out-of-office BP assessment. It places a high value on minimizing misdiagnosis due to white coat hypertension or masked hypertension, which could lead to unnecessary treatment or missed cases of		

	hypertension. While accessibility and feasibility of out-of-office BP monitoring may vary across different settings, this recommendation places greater importance on diagnostic precision over potential challenges in implementation.

Links to evidence syntheses:

1. ESC: Evidence tables 1-8 available at: https://oup.silverchair-cdn.com/oup/backfile/Content_public/Journal/eurheartj/45/38/10.1093_eurheartj_ehae178/1/2024_hypertension_guidelines_evidence_tables.pdf?Expires=1740736053&Signature=gG9t6zeidOyXkx2yKAvow1R~A1Dj7y1UKs0XGTEtrS31QYV8GU9prHNEiLRANUehQaWnRG97RW3IVgpVxrgi1WUeZ30BY291UWcYaC~17bPBVNOziDzmpF8NwfEP65UmJ5Nvvm8gNUiRh6vc69QZlmyW2vg5zKv7ayV0AaXB2Z06jFu5qislJw4VyxsD8QxLkW-j3~s23YNvC42rLzKhdxlEAEz4-~SD1Fd6thXy3qAAYQOzE5u7kQD1CKPzUaOzuQM3Fhl~FC~cWQn3iPQe~XVsNlqtwWNZp3Ya4-575mlWAmkzLSyawm7CVl~mYGD0Ma98zTuyce7C3TMJozMRMA__&Key-Pair-Id=APKAIE5G5CRDK6RD3PGA.

2. AHA: Online data supplement 3 available for download at: https://www.ahajournals.org/doi/10.1161/hyp.0000000000000065#supplementary-materials.

3. WHO: Not addressed.

Abbreviations:

AHA, American Heart Association; BP, blood pressure; ESC, European Society of Cardiology; WHO, World Health Organization.

Supplementary Table 4: Adaptation process for recommendation "*The definition of hypertension in adults is recommended as BP ≥130/80 mmHg when measured with a validated device under optimal conditions. (Strong recommendation; Moderate-certainty evidence).*"

Source Guideline	Recommendation	Strength of Recommendation	Certainty of Evidence
ESC[1]	*"It is recommended that BP be categorized as non-elevated BP, elevated BP, and hypertension to aid treatment decisions."*	Strong	Moderate
AHA[2]	*"BP should be categorized as normal, elevated, or stage 1 or 2 hypertension to prevent and treat high BP."*	Strong	Moderate
WHO[3]	Not addressed.	N/A	N/A
Adaptation Process	The committee evaluated the evidence syntheses listed below from ESC and AHA. The evidence tables provided data from systematic reviews and meta-analysis demonstrating cardiovascular and mortality risks based on different levels of BP. ESC and AHA vary in their definitions of hypertension. Also worth noting is that both ESC and AHA do no simply list a BP threshold for hypertension but also an intermediate category for "elevated blood pressure". First, the committee discussed whether this primary care-focused guideline should have separate categories for normal BP, elevated BP, and hypertension. Given the overarching goal of this primary care-specific guideline to provide streamlined and pragmatic recommendations for primary care, the committee collectively decided to establish a single threshold of hypertension vs. no hypertension. This relates to the committee wanting to avoid what was felt to be a "gray zone" with an "elevated BP" category that may lead to confusion on how to manage these patients. Second, the committee reviewed the evidence syntheses from ESC and AHA to determine what level of BP would be considered the optimal threshold to define hypertension. ESC defines hypertension as office BP ≥140/90 mmHg or HBPM/daytime ABPM ≥135/85 mmHg. In contrast, AHA defines hypertension at a lower threshold as BP ≥130/80 mmHg. On review of the evidence, the committee felt the existing evidence (as summarized in the guideline manuscript) favored the AHA definition of a BP ≥130/80 mmHg as hypertension though not necessarily as the threshold to start pharmacotherapy (as discussed in later in the "Treatment" recommendations). The committee felt it also important for the BP		

	threshold for defining hypertension to align with the treatment target which is later set in the guideline as systolic BP <130 mmHg. The committee endorsed the AHA assessment of the strength of recommendation as strong and the certainty of evidence as moderate.
Values and Preferences	This recommendation places high value on early detection and intervention by defining hypertension at a lower threshold (BP 130/80 mmHg) compared to previous Hypertension Canada guidelines. It reflects a high value on aligning with emerging evidence that associates cardiovascular risk with lower BP levels. While this lower threshold will increase the number of individuals labelled as having hypertension, the recommendation emphasizes the benefits of earlier management in preventing long-term complications.

Links to evidence syntheses:

1. ESC: Evidence table 9 available at: https://oup.silverchair-cdn.com/oup/backfile/Content_public/Journal/eurheartj/45/38/10.1093_eurheartj_ehae178/1/2024_hypertension_guidelines_evidence_tables.pdf?Expires=1740736053&Signature=gG9t6zeidOyXkx2yKAvow1R~A1Dj7y1UKs0XGTEtrS31QYV8GU9prHNEiLRANUehQaWnRG97RW3IVgpVxrgi1WUeZ30BY291UWcYaC~17bPBVNOziDzmpF8NwfEP65UmJ5Nvvm8gNUiRh6vc69QZlmyW2vg5zKv7ayV0AaXB2Z06jFu5qislJw4VyxsD8QxLkW-j3~s23YNvC42rLzKhdxlEAEz4-~SD1Fd6thXy3qAAYQOzE5u7kQD1CKPzUaOzuQM3Fhl~FC~cWQn3iPQe~XVsNlqtwWNZp3Ya4-575mlWAmkzLSyawm7CVl~mYGD0Ma98zTuyce7C3TMJozMRMA__&Key-Pair-Id=APKAIE5G5CRDK6RD3PGA.

2. AHA: Online data supplement 2 available for download at: https://www.ahajournals.org/doi/10.1161/hyp.0000000000000065#supplementary-materials.

3. WHO: Not addressed.

Abbreviations:

ABPM, ambulatory blood pressure monitor; AHA, American Heart Association; BP, blood pressure; ESC, European Society of Cardiology; HBPM, home blood pressure monitor; WHO, World Health Organization.

Supplementary Table 5: Adaptation process for recommendation "*Healthy lifestyle changes are recommended for all adults with hypertension. (Strong recommendation; High-certainty evidence)*."

Source Guideline	Recommendation	Strength of Recommendation	Certainty of Evidence
ESC[1]	*"Restriction of sodium to approximately 2 g per day is recommended where possible in all adults with elevated BP and hypertension [this is equivalent to about 5 g of salt (sodium chloride) per day or about a teaspoon or less]."*	Strong	High
	"Moderate intensity aerobic exercise of ≥150 min/ week (≥30 min, 5–7 days/week) or alternatively 75 min of vigorous intensity aerobic exercise per week over 3 days are recommended and should be complemented with low- or moderate-intensity dynamic or isometric resistance training (2–3 times/ week) to reduce BP and CVD risk."	Strong	High
	"It is recommended to aim for a stable and healthy BMI (e.g. 20–25 kg/m^2) and waist circumference values (e.g. <94 cm in men and <80 cm in women) to reduce BP and CVD risk."	Strong	High
	"Men and women are recommended to drink less alcohol than the upper limit, which is about 100 g/week of pure alcohol. How this translates into number of drinks depends on portion size (the standards of which differ per country), but most drinks contain 8–14 g of alcohol per drink. Preferably, it is recommended to avoid alcohol to achieve the best health outcomes."	Strong	Moderate
	"It is recommended to stop tobacco smoking, initiate supportive care and refer to smoking cessation programmes, as tobacco use strongly and independently causes CVD, CVD events, and all-cause mortality."	Strong	High

	"In patients with hypertension without moderate to advanced CKD and with high daily sodium intake, an increase of potassium intake by 0.5–1.0 g/day—for example through sodium substitution with potassium-enriched salt (comprising 75% sodium chloride and 25% potassium chloride) or through diets rich in fruits and vegetables—should be considered."	Conditional	High
AHA[2]	*"Weight loss is recommended to reduce BP in adults with elevated BP or hypertension who are overweight or obese."*	Strong	High
	"A heart-healthy diet, such as the DASH (Dietary Approaches to Stop Hypertension) diet, that facilitates achieving a desirable weight is recommended for adults with elevated BP or hypertension."	Strong	High
	"Sodium reduction is recommended for adults with elevated BP or hypertension."	Strong	High
	"Potassium supplementation, preferably in dietary modification, is recommended for adults with elevated BP or hypertension, unless contraindicated by the presence of CKD or use of drugs that reduce potassium excretion."	Strong	High
	"Increased physical activity with a structured exercise program is recommended for adults with elevated BP or hypertension."	Strong	High
	"Adult men and women with elevated BP or hypertension who currently consume alcohol should be advised to drink no more than 2 and 1 standard drinks per day, respectively."*	Strong	High
WHO[3]	Not addressed.	N/A	N/A
Adaptation Process	The committee evaluated the evidence syntheses listed below from ESC and AHA (WHO did not provide recommendations on lifestyle modification). The evidence tables provided data from systematic reviews		

	and meta-analysis demonstrating the benefits on improved BP control from a number of different lifestyle modifications including dietary sodium intake, dietary potassium intake, weight loss, exercise, alcohol intake, and smoking cessation. Given the goal of this primary care-specific guideline to provide streamlined recommendations for primary care, the committee felt it more beneficial to provide a single overarching recommendation on healthy lifestyle changes for all adults with hypertension rather than multiple recommendations on each specific lifestyle topic (as AHA and ESC did). However, each of these topics is addressed in the manuscript under the rationale section. When merging these recommendations into a single lifestyle modification recommendation, the committee collectively agreed the strength of evidence for this recommendation was strong and the certainty of evidence was high based on the existing ESC and AHA evidence syntheses/recommendations.
Values and Preferences	This recommendation prioritizes the foundational role of healthy lifestyle changes in managing hypertension, recognizing their broad benefits beyond BP control. It reflects a high value on non-pharmacological interventions that can improve overall health and reduce cardiovascular risk. Given that various healthy lifestyle changes have been shown to potentially reduce BP, the committee chose not to specify particular interventions in the recommendation, recognizing that individuals may have different values and preferences regarding which changes to prioritize.

Links to evidence syntheses:

1. ESC: Evidence table 22-26 available at: https://oup.silverchair-cdn.com/oup/backfile/Content_public/Journal/eurheartj/45/38/10.1093_eurheartj_ehae178/1/2024_hypertension_guidelines_evidence_tables.pdf?Expires=1740736053&Signature=gG9t6zeidOyXkx2yKAvow1R~A1Dj7y1UKs0XGTEtrS31QYV8GU9prHNEiLRANUehQaWnRG97RW3IVgpVxrgi1WUeZ30BY291UWcYaC~17bPBVNOziDzmpF8NwfEP65UmJ5Nvvm8gNUiRh6vc69QZlmyW2vq5zKv7ayV0AaXB2Z06jFu5qislJw4VyxsD8QxLkW-j3~s23YNvC42rLzKhdxlEAEz4-~SD1Fd6thXy3qAAYQOzE5u7kQD1CKPzUaOzuQM3Fhl~FC~cWQn3iPQe~XVsNlqtwWNZp3Ya4-575mlWAmkzLSyawm7CVl~mYGD0Ma98zTuyce7C3TMJozMRMA__&Key-Pair-Id=APKAIE5G5CRDK6RD3PGA.

2. AHA: Online data supplements 9-21 available at: https://www.ahajournals.org/doi/10.1161/hyp.0000000000000065#supplementary-materials.

3. WHO: Not addressed.

Abbreviations:

AHA, American Heart Association; BP, blood pressure; CKD, chronic kidney disease; CVD, cardiovascular disease; ESC, European Society of Cardiology; WHO, World Health Organization.

Supplementary Table 6: Adaptation process for recommendation "*Pharmacotherapy initiation for hypertension is recommended for adults with BP ≥140/90 mmHg and for adults with systolic BP 130-139 mmHg at high cardiovascular disease risk. (Strong recommendation; High-certainty evidence)*."

Source Guideline	Recommendation	Strength of Recommendation	Certainty of Evidence
ESC[1]	*"It is recommended that in hypertensive patients with confirmed BP ≥140/90 mmHg, irrespective of CVD risk, lifestyle measures and pharmacological BP-lowering treatment are initiated promptly to reduce CVD risk."*	Strong	High
	"In adults with elevated BP and sufficiently high CVD risk , after 3 months of lifestyle intervention, BP lowering with pharmacological treatment is recommended for those with confirmed BP ≥130/ 80 mmHg to reduce CVD risk."	Strong	High
AHA[2]	*"Use of BP-lowering medications is recommended for secondary prevention of recurrent CVD events in patients with clinical CVD and an average SBP of 130 mm Hg or higher or an average DBP of 80 mm Hg or higher, and for primary prevention in adults with an estimated 10-year atherosclerotic cardiovascular disease (ASCVD) risk of 10%or higher and an average SBP 130 mm Hg or higher or an average DBP 80 mm Hg or higher."*	Strong	Moderate for systolic BP; low for diastolic BP
	"Use of BP-lowering medication is recommended for primary prevention of CVD in adults with no history of CVD and with an estimated 10-year ASCVD risk <10% and an SBP of140 mm Hg or higher or a DBP of 90 mm Hg or higher."	Strong	Low
WHO[3]	*"WHO recommends initiation of pharmacological antihypertensive treatment of individuals with a confirmed diagnosis of hypertension*	Strong	Moderate-to-high

	and systolic blood pressure of ≥140 mmHg or diastolic blood pressure of ≥90 mmHg."		
	"WHO recommends pharmacological antihypertensive treatment of individuals with existing cardiovascular disease and systolic blood pressure of 130–139 mmHg."	Strong	Moderate-to-high
	"WHO suggests pharmacological antihypertensive treatment of individuals without cardiovascular disease but with high cardiovascular risk, diabetes mellitus, or chronic kidney disease, and systolic blood pressure of 130–139 mmHg."	Strong	Moderate-to-high
Adaptation Process	The committee evaluated the evidence syntheses listed below from ESC, AHA, and WHO. The evidence tables provided data from systematic reviews and meta-analysis of randomized controlled trials demonstrating strong evidence in regard to cardiovascular and mortality benefits for different BP thresholds for when to initiate pharmacotherapy for adults with hypertension. All three guidelines provide similar recommendations of initiating pharmacotherapy for all adults with hypertension and BP ≥140/90 mmHg and for adults with hypertension who are at high cardiovascular disease risk and systolic BP 130-139 mmHg. On review of the evidence tables (where the ESC notably includes the most up-to-date randomized controlled trials for intensive BP lowering targets), the committee endorsed the ESC assessment of the strength of recommendation as strong and the certainty of evidence as high.		
Values and Preferences	This recommendation prioritizes timely pharmacotherapy initiation to reduce cardiovascular risk, emphasizing treatment for all adults with BP ≥140/90 mmHg and for those with systolic BP 130-139 mmHg at high cardiovascular disease risk. It places a high value on preventing complications associated with elevated BP by targeting individuals at the greatest risk and recognizes that the benefit of pharmacotherapy initiation in individuals at lower risk (i.e., systolic BP 130-139 without any high-risk conditions) is uncertain. This recommendation places lower value on pharmacotherapy avoidance, costs, and tolerability, as most agents are now available as low-cost generics and are well-tolerated.		

Links to evidence syntheses:

1. ESC: Evidence table 30-32 available at: https://oup.silverchair-cdn.com/oup/backfile/Content_public/Journal/eurheartj/45/38/10.1093_eurheartj_ehae178/1/2024_hypertension_guidelines_evidence_tables.pdf?Expires=1740736053&Signature=gG9t6zeidOyXkx2yKAvow1R~A1Dj7y1UKs0XGTEtrS31QYV8GU9prHNEiLRANUehQaWnRG97RW3IVgpVxrgi1WUeZ30BY291UWcYaC~17bPBVNOziDzmpF8NwfEP65UmJ5Nvvm8gNUiRh6vc69QZlmyW2vq5zKv7ayV0AaXB2Z06jFu5qislJw4VyxsD8QxLkW-j3~s23YNvC42rLzKhdxlEAEz4-~SD1Fd6thXy3qAAYQOzE5u7kQD1CKPzUaOzuQM3Fhl~FC~cWQn3iPQe~XVsNlqtwWNZp3Ya4-575mlWAmkzLSyawm7CVl~mYGD0Ma98zTuyce7C3TMJozMRMA__&Key-Pair-Id=APKAIE5G5CRDK6RD3PGA.

2. AHA: Online data supplement 23 available at: https://www.ahajournals.org/doi/10.1161/hyp.0000000000000065#supplementary-materials.

3. WHO: Web annex A (tables 1-15) available at: https://iris.who.int/bitstream/handle/10665/344384/9789240033993-eng.pdf.

Abbreviations:

AHA, American Heart Association; BP, blood pressure; CVD, cardiovascular disease; ESC, European Society of Cardiology; WHO, World Health Organization.

Supplementary Table 7: Adaptation process for recommendation "*Treatment, including healthy lifestyle changes with or without pharmacotherapy, is recommended for adults with hypertension to achieve a target systolic BP <130 mmHg provided the treatment is well-tolerated. (Strong recommendation; High-certainty evidence)*."

Source Guideline	Recommendation	Strength of Recommendation	Certainty of Evidence
ESC[1]	*"To reduce CVD risk, it is recommended that treated systolic BP values in most adults be targeted to 120-129 mmHg, provided the treatment is well tolerated."*	Strong	High
AHA[2]	*"For adults with confirmed hypertension and known CVD or 10-year ASCVD event risk of 10% or higher, a BP target of less than 130/80 mmHg is recommended."*	Strong	Moderate for systolic BP; low for diastolic BP
	"For adults with confirmed hypertension, without additional markers of increased CVD risk, a BP target of less than 130/80 mmHg may be reasonable."	Conditional	Moderate for systolic BP; low for diastolic BP
WHO[3]	*"WHO recommends a target blood pressure treatment goal of <140/90 mmHg in all patients with hypertension without comorbidities."*	Strong	Moderate
	"WHO recommends a target systolic blood pressure treatment goal of <130 mmHg in patients with hypertension and known cardiovascular disease (CVD)."	Strong	Moderate
	"WHO suggests a target systolic blood pressure treatment goal of <130 mmHg in high-risk patients with hypertension (whose with high CVD risk, diabetes mellitus, chronic kidney disease."	Conditional	Moderate

Adaptation Process	The committee evaluated the evidence syntheses listed below from ESC, AHA, and WHO. The evidence tables provided data from systematic reviews and meta-analysis demonstrating cardiovascular and mortality benefits for different BP treatment targets for adults with hypertension. Treatment here is implied to include healthy lifestyle changes with or without pharmacotherapy. ESC and AHA both are consistent in recommending a systolic BP target of <130 mmHg. Notably, ESC provides only a systolic BP target while AHA also provides a diastolic BP target though acknowledging that the certainty of evidence for setting a diastolic BP is low. The WHO recommends a systolic BP target <130 mmHg for those adults with hypertension who are at high cardiovascular disease risk based on their comorbidities but a BP target of <140/90 mmHg for those adults with hypertension who are without comorbidities. Given the overarching goal of this primary care-specific guideline to provide streamlined and pragmatic recommendations for primary care, the committee felt it would be optimal to provide a single BP target if possible, largely consistent with the approaches taken by ESC and AHA. Based on the available evidence from randomized controlled trials of intensive BP lowering which were primarily based on systolic (rather than diastolic) BP targets, the committee agreed that providing an isolated systolic BP target alone was most appropriate and consistent with the literature. Therefore, the committee endorsed the ESC and AHA recommendation of a systolic BP treatment target of <130 mmHg. Further, the committee endorsed the ESC assessment of the strength of recommendation as strong and the certainty of evidence as high.
Values and Preferences	This recommendation places a relatively high value on a simplified approach to hypertension management by adopting a single treatment target for all, irrespective of cardiovascular risk and comorbidities. While the committee recognizes that some individuals may benefit from a lower target, and some may only tolerate a higher target, this recommendation prioritizes ease of implementation, and is a response to requests for more pragmatic and streamlined guidance to hypertension management in primary care.

Links to evidence syntheses:

1. ESC: Evidence table 34 available at: https://oup.silverchair-cdn.com/oup/backfile/Content_public/Journal/eurheartj/45/38/10.1093_eurheartj_ehae178/1/2024_hypertension_guidelines_evidence_tables.pdf?Expires=1740736053&Signature=gG9t6zeidOyXkx2yKAvow1R~A1Dj7y1UKs0XGTEtrS31QYV8GU9prHNEiLRANUehQaWnRG97RW3IVgpVxrgi1WUeZ30BY291UWcYaC~17bPBVNOziDzmpF8NwfEP65UmJ5Nvvm8gNUiRh6vc69QZlmyW2vq5zKv7ayV0AaXB2Z06jFu5qislJw4VyxsD8QxLkW-j3~s23YNvC42rLzKhdxlEAEz4-

~SD1Fd6thXy3qAAYQOzE5u7kQD1CKPzUaOzuQM3Fhl~FC~cWQn3iPQe~XVsNlqtwWNZp3Ya4-575mlWAmkzLSyawm7CVl~mYGD0Ma98zTuyce7C3TMJozMRMA__&Key-Pair-Id=APKAIE5G5CRDK6RD3PGA.

2. AHA: Online data supplement 26 available for download at: https://www.ahajournals.org/doi/10.1161/hyp.0000000000000065#supplementary-materials.

3. WHO: Web annex A (tables 82-90) available at: https://iris.who.int/bitstream/handle/10665/344384/9789240033993-eng.pdf.

Abbreviations:

AHA, American Heart Association; ASCVD, atherosclerotic cardiovascular disease; BP, blood pressure; CVD, cardiovascular disease; ESC, European Society of Cardiology; WHO, World Health Organization.

Supplementary Table 8: Adaptation process for recommendation "*For adults with hypertension requiring pharmacotherapy, low-dose combination therapy (ideally as a single-pill combination) is recommended as initial treatment which includes drugs from two of the following three complementary classes of medications: 1. ACEIs/ARBs, 2. Thiazide/thiazide-like diuretics, and 3. Long-acting dihydropyridine CCBs. (Strong recommendation; Moderate-certainty evidence)*."

Source Guideline	Recommendation	Strength of Recommendation	Certainty of Evidence
ESC[1]	*"Among all BP-lowering drugs, ACE inhibitors, ARBs, dihydropyridine CCBs, and diuretics (thiazides and thiazide-like drugs such as chlorthalidone and indapamide) have demonstrated the most effective reduction of BP and CVD events, and are therefore recommended as first-line treatments to lower BP."*	Strong	High
	"Given trial evidence for more effective BP control vs. monotherapy, combination BP-lowering treatment is recommended for most patients with confirmed hypertension (BP ≥140/90 mmHg) as initial therapy. Preferred combinations are a RAS blocker (either an ACE inhibitor or an ARB) with a dihydropyridine CCB or diuretic. Exceptions to consider include patients aged ≥85 years, those with symptomatic orthostatic hypotension, moderate-to-severe frailty, or elevated BP (systolic BP 120–139 mmHg or diastolic BP 70–89 mmHg) with a concomitant indication for treatment."	Strong	Moderate
AHA[2]	*"For initiation of antihypertensive drug therapy, first-line agents include thiazide diuretics, CCBs, and ACE inhibitors or ARBs."*	Strong	High
	"Initiation of antihypertensive drug therapy with 2 first-line agents of different classes, either as separate agents or in a fixed-dose combination, is recommended in adults with stage 2 hypertension and an average BP more than 20/10 mm Hg above their BP target."	Strong	Low

WHO[3]	*“For adults with hypertension requiring pharmacological treatment, WHO recommends the use of drugs from any of the following three classes of pharmacological antihypertensive medications as an initial treatment: 1. thiazide and thiazide-like agents 2. angiotensin-converting enzyme inhibitors (ACEis)/angiotensin-receptor blockers (ARBs) 3. long-acting dihydropyridine calcium channel blockers (CCBs)."*	Strong	High
	"For adults with hypertension requiring pharmacological treatment, WHO suggests combination therapy, preferably with a single-pill combination (to improve adherence and persistence), as an initial treatment. Antihypertensive medications used in combination therapy should be chosen from the following three drug classes: diuretics (thiazide or thiazide-like), angiotensin-converting enzyme inhibitors (ACEis)/angiotensin-receptor blockers (ARBs), and long-acting dihydropyridine calcium channel blockers (CCBs)."	Conditional	Moderate
Adaptation Process	The committee evaluated the evidence syntheses listed below from ESC, AHA, and WHO. The evidence tables provided data from systematic reviews and meta-analysis demonstrating evidence of the benefit of upfront low-dose single pill combination therapy in the pharmacologic management of hypertension. These benefits include improved BP control, quicker time to BP treatment target, improved adherence/persistence, and reduced costs. The committee did note the lack of prospective trial outcome data on upfront combination therapy versus upfront monotherapy in the isolated treatment of hypertension. However, the committee agreed with ESC’s assessment that “given the totality of evidence for outcomes benefit in observational studies, randomized trial data for better BP control and adherence, and importantly, also given CVD outcomes benefit for polypills (a form of single-pill combination) in randomized trials”, it endorsed the ESC assessment of the strength of recommendation as strong and the certainty of evidence as moderate.		
Values and Preferences	This recommendation places a high value on initiating a combination of effective and well-tolerated drugs to reduce therapeutic inertia and increase time in target range. Single-pill combination agents are often available at lower cost than their individual components. While recognizing the potential uncertainty		

	regarding which agent may cause intolerance in a combination pill, the recommendation places lower value on this concern compared to the benefits of timely and efficient treatment.

Links to evidence syntheses:

1. ESC: Evidence table 27-29 available at: https://oup.silverchair-cdn.com/oup/backfile/Content_public/Journal/eurheartj/45/38/10.1093_eurheartj_ehae178/1/2024_hypertension_guidelines_evidence_tables.pdf?Expires=1740736053&Signature=gG9t6zeidOyXkx2yKAvow1R~A1Dj7y1UKs0XGTEtrS31QYV8GU9prHNEiLRANUehQaWnRG97RW3IVgpVxrgi1WUeZ30BY291UWcYaC~17bPBVNOziDzmpF8NwfEP65UmJ5Nvvm8gNUiRh6vc69QZlmyW2vq5zKv7ayV0AaXB2Z06jFu5qislJw4VyxsD8QxLkW-j3~s23YNvC42rLzKhdxlEAEz4-~SD1Fd6thXy3qAAYQOzE5u7kQD1CKPzUaOzuQM3Fhl~FC~cWQn3iPQe~XVsNlqtwWNZp3Ya4-575mlWAmkzLSyawm7CVl~mYGD0Ma98zTuyce7C3TMJozMRMA__&Key-Pair-Id=APKAIE5G5CRDK6RD3PGA.

2. AHA: Online data supplement 27 and online data supplement D available at: https://www.ahajournals.org/doi/10.1161/hyp.0000000000000065#supplementary-materials.

3. WHO: Web annex A (tables 21-66) available at: https://iris.who.int/bitstream/handle/10665/344384/9789240033993-eng.pdf.

Abbreviations:

ACEI, angiotensin-converting enzyme inhibitor; AHA, American Heart Association; ARB, angiotensin II receptor blocker; BP, blood pressure; CCB, calcium channel blocker; CVD, cardiovascular disease; ESC, European Society of Cardiology; WHO, World Health Organization.

Supplementary Table 9: Adaptation process for recommendation "*If BP remains above target despite two-drug combination therapy, three-drug combination therapy consisting of an ACEI/ARB, a thiazide/thiazide-like diuretic, and a long-acting dihydropyridine CCB is recommended (Strong recommendation; Moderate-certainty evidence)*."

Source Guideline	Recommendation	Strength of Recommendation	Certainty of Evidence
ESC[1]	*"If BP is not controlled with a two-drug combination, increasing to a three-drug combination is recommended, usually a RAS blocker with a dihydropyridine CCB and a thiazide/thiazide-like diuretic, and preferably in a single-pill combination."*	Strong	Moderate
AHA[2]	Not addressed.	N/A	N/A
WHO[3]	Not addressed.	N/A	N/A
Adaptation Process	Of the three source guidelines, only ESC had a recommendation specific to if an adult with hypertension required three medications for BP control, which classes of recommendations should be used. That being said, all three source guidelines named the first-line BP medication classes as ACEIs/ARBs, thiazide/thiazide-like diuretics, and long-acting dihydropyridine CCBs. The committee evaluated the evidence syntheses listed below from ESC provided for this recommendation. The evidence tables provided data from systematic reviews and meta-analysis demonstrating the benefit in terms of BP control and cardiovascular risk reduction for these classes of BP medications beyond other classes. Notably, beta blockers provided similar levels of BP reduction but without the same magnitude of cardiovascular risk reduction (especially stroke prevention) which is why they are not considered first-line unless there is a specific recommendation for a beta blocker (e.g., angina, heart failure, post-myocardial infarction, atrial fibrillation, etc.). Upon review of the available evidence, the committee endorsed the ESC assessment of the strength of recommendation as strong and the certainty of evidence as moderate.		
Values and Preferences	This recommendation prioritizes the use of medications with well-established cardiovascular benefits over those for which such benefits have not been as clearly demonstrated.		

Links to evidence syntheses:

1. ESC: Evidence tables 27-29 available at: https://oup.silverchair-cdn.com/oup/backfile/Content_public/Journal/eurheartj/45/38/10.1093_eurheartj_ehae178/1/2024_hypertension_guidelines_evidence_tables.pdf?Expires=1740736053&Signature=gG9t6zeidOyXkx2yKAvow1R~A1Dj7y1UKs0XGTEtrS31QYV8GU9prHNEiLRANUehQaWnRG97RW3IVgpVxrgi1WUeZ30BY291UWcYaC~17bPBVNOziDzmpF8NwfEP65UmJ5Nvvm8gNUiRh6vc69QZlmyW2vg5zKv7ayV0AaXB2Z06jFu5qislJw4VyxsD8QxLkW-j3~s23YNvC42rLzKhdxlEAEz4-~SD1Fd6thXy3qAAYQOzE5u7kQD1CKPzUaOzuQM3Fhl~FC~cWQn3iPQe~XVsNlqtwWNZp3Ya4-575mlWAmkzLSyawm7CVl~mYGD0Ma98zTuyce7C3TMJozMRMA__&Key-Pair-Id=APKAIE5G5CRDK6RD3PGA.

2. AHA: Not addressed.

3. WHO: Not addressed.

Abbreviations:

ACEI, angiotensin-converting enzyme inhibitor; AHA, American Heart Association; ARB, angiotensin II receptor blocker; BP, blood pressure; CCB, calcium channel blocker; ESC, European Society of Cardiology; RAS, renin-angiotensin system; WHO, World Health Organization.

Supplementary Table 10: Adaptation process for recommendation "*If BP remains above target despite three-drug combination therapy consisting of an ACEI/ARB, a thiazide/thiazide-like diuretic, and a long-acting dihydropyridine CCB at their maximally tolerated doses, the addition of spironolactone is suggested (Conditional recommendation; Moderate-certainty evidence)*."

Source Guideline	Recommendation	Strength of Recommendation	Certainty of Evidence
ESC[1]	*"If BP is not controlled with a three-drug combination, adding spironolactone should be considered."*	Conditional	Moderate
AHA[2]	Not addressed.	N/A	N/A
WHO[3]	Not addressed.	N/A	N/A
Adaptation Process	As primary care providers commonly encounter and manage patients with resistant hypertension, the committee felt strongly that this primary care-focused guideline provide a recommendation as to the preferred fourth-line BP medication to be added in such cases. Among the source guidelines, only ESC had a recommendation specific to this issue. The evidence tables provide data demonstrating the benefit in terms of BP control for spironolactone compared to alternative non-first-line BP medication options. However, the committee noted that while the evidence shows the enhanced benefits of spironolactone for BP control, there is a lack of evidence showing that this translates into improved cardiovascular and mortality outcomes. Therefore, the committee agrees with the ESC's assessment that the strength of recommendation should be listed as conditional while the certainty of evidence should be listed as moderate.		
Values and Preferences	This recommendation places high value on the proven BP-lowering benefits of spironolactone compared to other agents, while assigning lower value to the potential side effects, including the risk of hyperkalemia, that may arise with its use. Its lower strength of evidence reflects the limited data available on the long-term cardiovascular benefits of the treatment.		

Links to evidence syntheses:

1. ESC: Evidence tables 27-29 available at: https://oup.silverchair-cdn.com/oup/backfile/Content_public/Journal/eurheartj/45/38/10.1093_eurheartj_ehae178/1/2024_hypertension_guidelines_evidence_tables.pdf?Expires=1740736053&Signature=gG9t6zeidOyXkx2yKAvow1R~A1Dj7y1UKs0XGTEtrS31QYV8GU9prHNEiLRANUehQaWnRG97RW3IVgpVxrgi1WUeZ30BY291UWcYaC~17bPBVNOziDzmpF8NwfEP65UmJ5Nvvm8gNUiRh6vc69QZlmyW2vq5zKv7ayV0AaXB2Z06jFu5qislJw4VyxsD8QxLkW-j3~s23YNvC42rLzKhdxlEAEz4-~SD1Fd6thXy3qAAYQOzE5u7kQD1CKPzUaOzuQM3Fhl~FC~cWQn3iPQe~XVsNlqtwWNZp3Ya4-575mlWAmkzLSyawm7CVl~mYGD0Ma98zTuyce7C3TMJozMRMA__&Key-Pair-Id=APKAIE5G5CRDK6RD3PGA.

2. AHA: Not addressed.

3. WHO: Not addressed.

Abbreviations:

ACEI, angiotensin-converting enzyme inhibitor; AHA, American Heart Association; ARB, angiotensin II receptor blocker; BP, blood pressure; CCB, calcium channel blocker; ESC, European Society of Cardiology; RAS, renin-angiotensin system; WHO, World Health Organization.

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1. McEvoy JW, McCarthy CP, Bruno RM, et al. 2024 ESC Guidelines for the management of elevated blood pressure and hypertension. *Eur Heart J.* 2024;45:3912-4018.
2. Whelton PK, Carey RM, Aronow WS, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: Executive Summary: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Hypertension.* 2018;71:1269-324.
3. World Health Organization. Guideline for the pharmacological treatment of hypertension in adults. Geneva, 2021.