Annual Update

2017
Hypertension Canada Guidelines for the Management of Hypertension

(FULL VERSION)

Hypertension CANADA

TABLE OF CONTENTS

2017 Hypertension Canada Guidelines for the Management of Hypertension

2017 Guidelines

PART 1

DIAGNOSIS & ASSESSMENT

I ACCURATE MEASUREMENT OF BLOOD PRESSURE

1) Health care professionals who have been specifically trained to measure blood pressure (BP) accurately should assess BP in all adult patients at all appropriate visits to determine cardiovascular risk and monitor antihypertensive treatment (Grade D).

2) Use of standardized measurement techniques and validated equipment for all methods (automated office BP[AOBP], non-AOBP, home BP monitoring, and ambulatory BP monitoring) is recommended (Grade D; see Supplementary Table S2; section III. Home BP Measurement; section IV. Ambulatory BP Measurement). Measurement using electronic (oscillometric) upper arm devices is preferred over auscultation (Grade C). (Unless specified otherwise, electronic [oscillometric] measurement should be used.)

3) Four approaches can be used to assess BP:

   i) AOBP is the preferred method of performing in-office BP measurement (Grade D). When using *AOBP* (see *Supplemental Table S2, AOBP*), a displayed mean SBP ≥135 mmHg or DBP ≥85 mmHg DBP is high (Grade D).

   ii) When using non-AOBP, a mean systolic BP (SBP) ≥140 mHg or a diastolic BP (DBP) ≥90 mmHg is high, and an SBP between 130-139 mmHg and/or a DBP between 85-89 mmHg is high-normal (Grade C).

   iii) Using ambulatory BP monitoring (see Guidelines in *Section IV, Ambulatory BP Monitoring*), patients can be diagnosed as hypertensive if the mean awake SBP is ≥135 mmHg or the DBP is ≥85 mmHg or if the mean 24-hour SBP is ≥130 mmHg or the DBP is ≥80 mmHg (Grade C).

   iv) Using home BP monitoring (see Guidelines in *Section III, Home BP Monitoring*), patients can be diagnosed as hypertensive if the mean SBP is ≥135 mmHg or the DBP is ≥85 mmHg (Grade C). If the office BP measurement is high and the mean home BP is <135/85 mm Hg, it is advisable to either repeat home monitoring to confirm the home BP is <135/85 mmHg or perform 24-hour ambulatory BP monitoring to confirm that the mean 24-hour ambulatory BP monitoring is <130/80 mmHg and the mean awake ambulatory BP monitoring is <135/85 mmHg before diagnosing white coat hypertension (Grade D).

II CRITERIA FOR DIAGNOSIS OF HYPERTENSION AND RECOMMENDATIONS FOR FOLLOW-UP

1) At initial presentation, patients demonstrating features of a hypertensive urgency or emergency (Supplemental Table S3) should be diagnosed as hypertensive and require immediate management (Grade D). In all other patients, at least 2 more readings should be taken during the same visit. If using AOBP, the BP calculated and displayed by the device should be used. If using non-AOBP measurement, the first reading should be discarded and the latter readings averaged.

2) If the visit 1 office BP measurement is high-normal (thresholds outlined in Section I-3) annual follow-up is recommended (Grade C).

3) If the visit 1 mean AOBP or non-AOBP measurement is high (thresholds outlined in Section I-3), a history and physical examination should be performed and, if clinically indicated, diagnostic tests to search for target organ damage (Supplemental Table S4) and associated cardiovascular risk factors (Supplemental Table S5) should be arranged within 2 visits. Exogenous factors that can induce or aggravate hypertension should be assessed and removed if possible (Supplemental Table S6). Visit 2 should be scheduled within 1 month (Grade D).

4) If the visit 1 mean AOBP or non-AOBP SBP is ≥180 mmHg and/or DBP is ≥110 mmHg then hypertension is diagnosed (Grade D).

5) If the visit 1 mean AOBP SBP is 135-179 mmHg and/or DBP is 85-109 mmHg OR the mean non-AOBP SBP is 140-179 mmHg and/or DBP is 90-109 mmHg, out-of-office BP measurements should be performed before visit 2 (Grade C).

   i) Ambulatory BP monitoring is the recommended out-of-office measurement method (Grade D). Patients can be diagnosed with hypertension according to the thresholds outlined in Section I-3.

   ii) Home BP monitoring is recommended if ambulatory BP monitoring is not tolerated, not readily available, or due to patient preference (Grade D). Patients can be diagnosed with hypertension according to the thresholds outlined in Section I-3.

   iii) If the out-of-office BP average is not elevated, white coat hypertension should be diagnosed and pharmacologic treatment should not be instituted (Grade C).

6) If the out-of-office measurement, although preferred, is NOT performed after visit 1, then patients can be diagnosed as hypertensive using serial office BP measurement visits if any of the following conditions are met:

   i) At visit 2, mean non-AOBP measurement (averaged across all visits) is ≥140 mmHg systolic and/or ≥90 mmHg diastolic in patients with macrovascular target organ damage, diabetes mellitus, or chronic kidney disease (glomerular filtration rate <60 mL/min/1.73m^2) (Grade D);

   ii) At visit 3, mean non-AOBP measurement (averaged across all visits) is ≥160 mmHg systolic or ≥100 mmHg diastolic;

   iii) At visit 4 or 5, mean non-AOBP measurement (averaged across all visits) is ≥140 mmHg systolic or ≥90 mmHg diastolic.

7) Investigations for secondary causes of hypertension should be initiated in patients with suggestive clinical and/or laboratory features (outlined in Sections V, VII and VIII) (Grade D).

8) If at the last diagnostic visit the patient is not diagnosed as hypertensive and has no evidence of macrovascular target organ damage, the patient's BP should be assessed at yearly intervals (Grade D).

9) Hypertensive patients actively modifying their health behaviors should be followed up at 3- to 6-month intervals. Shorter intervals (every 1 or 2 months) are needed for patients with higher BPs (Grade D).

10) Patients on antihypertensive drug treatment should be seen monthly or every 2 months, depending on the level of BP, until readings on 2 consecutive visits are below their target (Grade D). Shorter intervals between visits will be needed for symptomatic patients and those with severe hypertension, intolerance to antihypertensive drugs, or target organ damage (Grade D). When the target BP has been reached, patients should be seen at 3- to 6-month intervals (Grade D).

III HOME BP MEASUREMENT

1) Home BP monitoring can be used in the diagnosis of hypertension (Grade C).

2) The use of Home BP monitoring on a regular basis should be considered for patients with hypertension, particularly those with:

i) diabetes mellitus (Grade D);

ii) chronic kidney disease (Grade C);

iii) suspected non-adherence (Grade D);

iv) demonstrated white coat effect (Grade C); and

v) BP controlled in the office but not at home (masked hypertension) (Grade C).

3) When white coat hypertension is suggested by home BP monitoring, its presence should be confirmed by repeat home BP monitoring (see recommendation 7 in this section) or ambulatory BP monitoring before treatment decisions are made (Grade D).

4) Patients should be advised to purchase and use only home BP monitoring devices that are appropriate for the individual and that have met standards of the Association for the Advancement of Medical Instrumentation, the most recent requirements of the British Hypertension Society protocol or the International Protocol for validation of automated BP measuring devices. Patients should be encouraged to use devices with data recording capabilities or automatic data transmission to increase the reliability of reported home BP monitoring. (Grade D).

5) Home SBP values ≥135 mmHg or DBP values ≥85 mmHg should be considered to be elevated and associated with an increased overall mortality risk (Grade C).

6) Health care professionals should ensure that patients who measure their BP at home have adequate training, and if necessary, repeat training in measuring their BP. Patients should be observed to determine that they measure BP correctly and should be given adequate information about interpreting these readings (Grade D).

7) Home BP monitoring values for assessing white coat hypertension or sustained hypertension should be based on duplicate measures, morning and evening, for an initial seven-day period. First day home BP values should not be considered (Grade D).

IV AMBULATORY BLOOD PRESSURE MEASUREMENT

1) Ambulatory BP monitoring readings can be used in the diagnosis of hypertension (Grade C). Ambulatory BP monitoring should be considered when an office-induced increase in BP is suspected in treated patients with:

i) BP that is not below target despite receiving appropriate chronic anti-hypertensive therapy (Grade C);

ii) symptoms suggestive of hypotension (Grade C); or

iii) fluctuating office BP readings (Grade D).

2) Ambulatory BP monitoring upper arm devices that have been validated independently using established protocols must be used (see www.dableducational.org) (Grade D).

3) Therapy adjustment should be considered in patients with a mean 24-hour ambulatory BP monitoring SBP of ≥130 mmHg and/or DBP of ≥80 mmHg, or a mean awake SBP of ≥135 mmHg and/or DBP of ≥85 mmHg (Grade D).

4) The magnitude of changes in nocturnal BP should be taken into account in any decision to prescribe or withhold drug therapy based upon ambulatory BP monitoring (Grade C) because a decrease in nocturnal BP of <10% is associated with increased risk of CV events.

V ROUTINE AND OPTIONAL LABORATORY TESTS FOR THE INVESTIGATION OF PATIENTS WITH HYPERTENSION

1) Routine laboratory tests that should be performed for the investigation of all patients with hypertension include:

i) urinalysis (Grade D);

ii) blood chemistry (potassium, sodium, and creatinine) (Grade D);

iii) fasting blood glucose and/or glycated hemoglobin (A1C) (Grade D);

iv) Serum total cholesterol, low-density lipoprotein, high-density lipoprotein (HDL), non-HDL cholesterol, and triglycerides (Grade D); lipids may be drawn fasting or non-fasting (Grade C).

v) standard 12-lead electrocardiography (Grade C).

2) Assess urinary albumin excretion in patients with diabetes (Grade D).

3) All treated hypertensive patients should be monitored according to the current Diabetes Canada guidelines for the new appearance of diabetes (Grade B)

4) During the maintenance phase of hypertension management, tests (including those for electrolytes, creatinine and fasting lipids), should be repeated with a frequency reflecting the clinical situation (Grade D).

VI ASSESSMENT OF OVERALL CARDIOVASCULAR RISK IN HYPERTENSIVE PATIENTS

1) Global cardiovascular risk should be assessed. Multifactorial risk assessment models can be used to predict more accurately an individual's global cardiovascular risk (Grade A) and to use antihypertensive therapy more efficiently (Grade D). In the absence of Canadian data to determine the accuracy of risk calculations, avoid using absolute levels of risk to support treatment decisions (Grade C).

2) Consider informing patients of their global risk to improve the effectiveness of risk factor modification (Grade B). Consider also using analogies that describe comparative risk such as "Cardiovascular Age", "Vascular Age" or "Heart Age" to inform patients of their risk status (Grade B).

VII ASSESSMENT FOR RENOVASCULAR HYPERTENSION

1) Patients presenting two or more of the clinical clues listed below, suggesting renovascular hypertension, should be investigated (Grade D).

   i) sudden onset or worsening of hypertension and age greater than 55 or less than 30 years;

   ii) the presence of an abdominal bruit;

   iii) hypertension resistant to three or more drugs;

   iv) increase in serum creatinine level of ≥30% associated with use of an angiotensin-converting enzyme inhibitor or angiotensin II receptor antagonist;

   v) other atherosclerotic vascular disease, particularly in patients who smoke or have dyslipidemia;

   vi) recurrent pulmonary edema associated with hypertensive surges.

2) When available, the following tests are recommended to aid in the usual screening for renal vascular disease: captopril-enhanced radioisotope renal scan, Doppler sonography, magnetic resonance angiography and CT- angiography (for those with normal renal function) (Grade B). Captopril-enhanced radioisotope renal scan is not recommended for those with CKD (GFR <60 mL/min/1.73 m^2) (Grade D).

3) Patients with hypertension and presenting with at least one of the following clinical clues should be investigated for fibromuscular dysplasia (FMD)-related renal artery stenosis (Grade D: ***new guideline***):

i) Age less than 30 years, especially in non-obese women;

ii) Hypertension resistant to three or more drugs;

iii) Significant (>1.5 cm), unexplained asymmetry in kidney size;

iv) Abdominal bruit without apparent atherosclerosis;

v) FMD in another vascular territory;

vi) Positive family history for FMD.

4) In patients with confirmed renal FMD (Grade D; ***new guideline***):

i) Screening for cervicocephalic lesions and intracranial aneurysm is recommended;

ii) Screening for FMD in other vascular beds in the presence of suggestive symptoms is recommended.

5) The following tests are recommended to screen for renal FMD (both with similar sensitivity and specificity) (Grade D; ***new guideline***): magnetic resonance angiography and computed tomography angiography.

VIII ASSESSMENT FOR ENDOCRINE HYPERTENSION

A. Hyperaldosteronism: Screening and Diagnosis:

1) Screening for hyperaldosteronism should be considered for the following patients (Grade D):

i) Unexplained spontaneous hypokalemia (K+ less than 3.5 mmol/L) or marked diuretic-induced hypokalemia (K+ less than 3.0 mmol/L);

ii) Resistant to treatment with three or more drugs;

iii) An incidental adrenal adenoma.

2) Screening for hyperaldosteronism should include assessment of plasma aldosterone and plasma renin activity or plasma renin (Supplemental Table S7).

3) For patients with suspected hyperaldosteronism (on the basis of the screening test, Supplemental Table S7, item iii), a diagnosis of primary aldosteronism should be established by demonstrating inappropriate autonomous hypersecretion of aldosterone using at least one of the maneuvers listed in Supplemental Table S7, item iv. When the diagnosis is established, the abnormality should be localized using any of the tests described in Supplemental Table S7, item v.

4) In patients with primary hyperaldosteronism and a definite adrenal mass who are eligible for surgery, adrenal venous sampling is recommended to assess for

lateralization of aldosterone hypersecretion. Adrenal vein sampling should be performed exclusively by experienced teams working in specialized centres (Grade C).

B) Pheochromocytoma : Screening and Diagnosis :

1) If pheochromocytoma is strongly suspected, the patient should be referred to a specialized hypertension center, particularly if biochemical screening tests (Supplemental Table S8) have already been found to be positive (Grade D).

2) The following patients should be considered for screening for pheochromocytoma or paraganglioma (Grade D):

   i) patients with paroxysmal, unexplained, labile, and/or severe (BP ≥180/110 mmHg) sustained hypertension refractory to usual antihypertensive therapy;

   ii) patients with hypertension and multiple symptoms suggestive of catecholamine excess (e.g., headaches, palpitations, sweating, panic attacks and pallor);

   iii) patients with hypertension triggered by beta-blockers, monoamine oxidase inhibitors, micturition, changes in abdominal pressure, surgery, or anesthesia;

   iv) patients with incidentally discovered adrenal mass,

   v) patients with a predisposition to hereditary causes (e.g. multiple endocrine neoplasia 2A or 2B, von Recklinghausen's neurofibromatosis type 1, or von Hippel-Lindau disease).

   vi) For patients with positive biochemical screening tests, localization of pheochromocytomas or paragangliomas should employ magnetic resonance imaging (preferable), computed tomography (if MRI unavailable), and/or iodine I-131 metaiodobenzylguanidine (MIBG) scintigraphy (Grade C for each modality).

IX ROLE OF ECHOCARDIOGRAPHY

1) Routine echocardiographic evaluation of all hypertensive patients is not recommended. (Grade D).

2) An echocardiogram for assessment of left ventricular hypertrophy is useful in selected cases to help define the future risk of cardiovascular events (Grade C).

3) Echocardiographic assessment of left ventricular mass, as well as of systolic and diastolic left ventricular function is recommended for hypertensive patients suspected to have left ventricular dysfunction or coronary artery disease (Grade D).

4) Patients with hypertension and evidence of heart failure should have an objective assessment of left ventricular ejection fraction, either by echocardiogram or nuclear imaging (Grade D).

Algorithm Notes:

1) If AOBP is used, use the mean calculated and displayed by the device. If non-AOBP (see note 2) is used, take at least three readings, discard the first and calculate the mean of the remaining measurements. A history and physical exam should be performed and diagnostic tests ordered.

2) AOBP = Automated Office BP. This is performed with the patient unattended in a private area. Non-AOBP = Non-automated measurement performed using an electronic upper arm device with the provider in the room.

3) Diagnostic thresholds for AOBP, ABPM, and home BP in patients with diabetes have yet to be established (and may be lower than 130/80 mmHg).

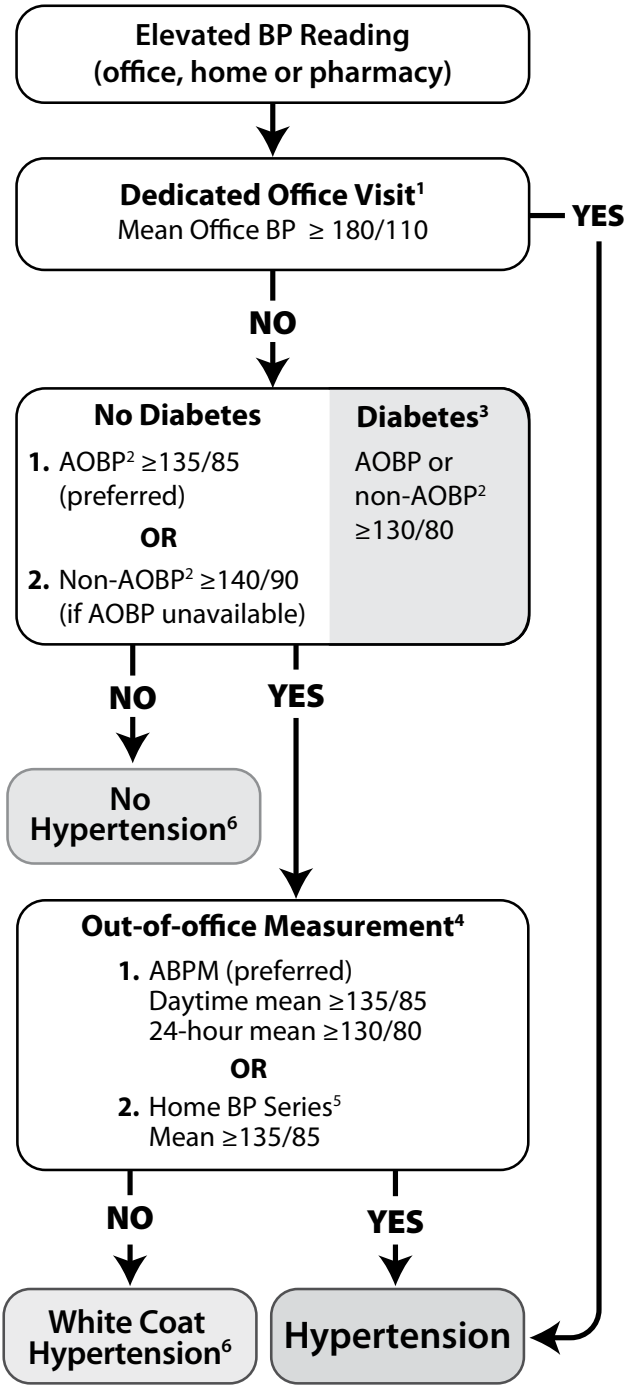
4) Serial office measurements over 3-5 visits can be used if ABPM or home measurement not available.

5) Home BP Series: two readings taken each morning and evening for 7 days (28 total). Discard first day readings and average the last 6 days.

6) Annual BP measurement is recommended to detect progression to hypertension.

ABPM: Ambulatory Blood Pressure Measurement
AOBP: Automated Office Blood Pressure

Hypertension Diagnostic Algorithm



2017 Guidelines

PART 2

PREVENTION & TREATMENT

I HEALTH BEHAVIOUR MANAGEMENT

A) Physical Exercise

For non-hypertensive individuals (to reduce the possibility of becoming hypertensive) or for hypertensive patients (to reduce their BP), prescribe the accumulation of 30 to 60 minutes of moderate intensity dynamic exercise (e.g., walking, jogging, cycling or swimming) four to seven days per week in addition to the routine activities of daily living (Grade D). Higher intensities of exercise are not more effective (Grade D). For non-hypertensive or stage 1 hypertensive individuals, the use of resistance or weight training exercise (such as free weight lifting, fixed-weight lifting or handgrip exercise) does not adversely influence BP (Grade D).

B) Weight Reduction

1) Height, weight, and waist circumference should be measured and body mass index calculated for all adults (Grade D).

2) Maintenance of a healthy body weight (body mass index 18.5 to 24.9 kg/m^2 and waist circumference less than 102 cm for men and less than 88 cm for women) is recommended for non-hypertensive individuals to prevent hypertension (Grade C) and for hypertensive patients to reduce blood pressure (Grade B). All overweight hypertensive individuals should be advised to lose weight (Grade B).

3) Weight loss strategies should employ a multidisciplinary approach that includes dietary education, increased physical activity and behavioural intervention (Grade B).

C) Alcohol Consumption

To prevent hypertension and to reduce BP in hypertensive adults, individuals should limit alcohol consumption to two drinks or less per day, and consumption should not exceed 14 standard drinks per week for men and 9 standard drinks per week for women (Grade B) (**Note:** one standard drink is considered to be equivalent of 13.6 g or 17.2 ml of ethanol, or approximately 44 mL [1.5 oz] of 80 proof [40%] spirits, 355 mL [12 oz] of 5% beer or 148 mL [5 oz] of 12% wine.)

D) Diet

It is recommended that hypertensive patients and normotensive individuals at increased risk of developing hypertension consume a diet that emphasizes fruits, vegetables, low- fat dairy products, whole grain foods rich in dietary fibre, and

protein from plant sources that is reduced in saturated fat and cholesterol (Dietary Approaches to Stop Hypertension [DASH] diet; Supplementary Table S9) (Grade B).

E) Sodium Intake

To prevent hypertension and reduce BP in hypertensive adults, consider reducing sodium intake towards 2,000 mg (5g of salt or 87mmol of sodium) per day (Grade A).

F) Calcium and Magnesium Intake

Supplementation of calcium and magnesium is not recommended for the prevention or treatment of hypertension (Grade B).

G) Potassium Intake

In patients not at risk of hyperkalemia (see Table 2), increase dietary potassium intake to reduce blood pressure (Grade A).

H) Stress Management

In hypertensive patients in whom stress may be contributing to high BP, stress management should be considered as an intervention (Grade D). Individualized cognitive behavioural interventions are more likely to be effective when relaxation techniques are employed (Grade B).

II INDICATIONS FOR DRUG THERAPY FOR ADULTS WITH HYPERTENSION WITHOUT COMPELLING INDICATIONS FOR SPECIFIC AGENTS

1) Antihypertensive therapy should be prescribed for average DBP measurements of 100 mmHg or higher (Grade A), or average SBP measurements of 160 mmHg or higher (Grade A) in patients without macrovascular target organ damage or other cardiovascular risk factors.

2) Antihypertensive therapy should be strongly considered for average DBP readings of 90 mmHg or higher (Grade A) or for average SBP readings of 140 mmHg or higher (Grade B for 140 mmHg to 160 mmHg; Grade A for higher than 160 mmHg) in the presence of macrovascular target organ damage or other independent cardiovascular risk factors.

III CHOICE OF THERAPY FOR ADULTS WITH HYPERTENSION WITHOUT COMPELLING INDICATIONS FOR SPECIFIC AGENTS

A) Recommendations for Individuals with Diastolic and/or Systolic Hypertension

1) Initial therapy should be with either monotherapy or single pill combination (SPC).

   i) Recommended monotherapy choices are:

      a) a thiazide/thiazide-like diuretic (Grade A), with longer-acting diuretics preferred (Grade B; ***new guideline***),

      b) a beta-blocker (in patients younger than 60 years; Grade B),

      c) an angiotensin converting enzyme (ACE) inhibitor (in non-black patients; Grade B),

      d) an angiotensin receptor blocker (ARB) (Grade B),

      e) a long-acting calcium channel blocker (CCB) (Grade B).

   ii) Recommended SPC choices are those in which an ACE inhibitor is combined with a CCB (Grade A; ***new guideline***), ARB with a CCB (Grade B; ***new guideline***) or ACE inhibitor or ARB with a diuretic (Grade B; ***new guideline***).

   iii) Hypokalemia should be avoided in patients treated with a thiazide/thiazide-like diuretic monotherapy (Grade C).

2) Additional antihypertensive drugs should be used if target blood pressure levels are not achieved with standard-dose monotherapy (Grade B). Add-on drugs should be chosen from first-line choices. Useful choices include a thiazide/thiazide-like diuretic or CCB with either an ACE inhibitor, ARB or beta-blocker (Grade B for the combination of thiazide/thiazide-like diuretic and a dihydropyridine CCB; Grade C for the combination of dihydropyridine CCB and ACE inhibitor; and Grade D for all other combinations). Caution should be exercised in combining a nondihydropyridine CCB and a beta-blocker (Grade D). The combination of an ACE inhibitor and an ARB is not recommended (Grade A).

3) If blood pressure is still not controlled with a combination of two or more first-line agents, or there are adverse effects, other antihypertensive drugs may be added (Grade D).

4) Possible reasons for poor response to therapy (Supplemental Table S10) should be considered (Grade D).

5) Alpha-blockers are not recommended as first-line agents for uncomplicated hypertension (Grade A); beta-blockers are not recommended as first-line therapy for uncomplicated hypertension in patients 60 years of age or older (Grade A); and ACE inhibitors are not recommended as first-line therapy for uncomplicated hypertension in black patients (Grade A). However, these agents may be used in patients with certain comorbid conditions or in combination therapy.

B) Guidelines for Individuals with Isolated Systolic Hypertension

1) Initial therapy should be single agent therapy with a thiazide/thiazide-like diuretic (Grade A), a long-acting dihydropyridine CCB (Grade A) or an ARB (Grade B). If there are adverse effects, another drug from this group should be substituted. Hypokalemia should be avoided in patients treated with thiazide/thiazide-like diuretic monotherapy (Grade C).

2) Additional antihypertensive drugs should be used if target blood pressure levels are not achieved with standard-dose monotherapy (Grade B). Add-on drugs should be chosen from first-line options (Grade D).

3) If blood pressure is still not controlled with a combination of two or more first-line agents, or there are adverse effects, other classes of drugs (such as alpha-blockers, ACE inhibitors, centrally acting agents or nondihydropyridine CCBs) may be added or substituted (Grade D).

4) Possible reasons for poor response to therapy (Supplemental Table S10) should be considered (Grade D).

5) Alpha-blockers are not recommended as first-line agents for uncomplicated isolated systolic hypertension (Grade A); and beta-blockers are not recommended as first-line therapy for isolated systolic hypertension in patients aged 60 years of age or older (Grade A). However, both agents may be used in patients with certain co morbid conditions or in combination therapy.

IV GLOBAL VASCULAR PROTECTION THERAPY FOR ADULTS WITH HYPERTENSION WITHOUT COMPELLING INDICATIONS FOR SPECIFIC AGENTS

1) Statin therapy is recommended in hypertensive patients with three or more cardiovascular risk factors as defined in Supplemental Table S11 (Grade A in patients older than 40 years), or with established atherosclerotic disease (Grade A regardless of age).

2) Consideration should be given to the addition of low-dose acetylsalicylic acid (ASA) therapy in hypertensive patients ≥ 50 years (Grade B). Caution should be exercised if blood pressure is not controlled (Grade C).

3) Tobacco use status of all patients should be updated on a regular basis and health care providers should clearly advise patients to quit smoking (Grade C).

4) Advice in combination with pharmacotherapy (e.g., varenicline, bupropion, nicotine replacement therapy) should be offered to all smokers with a goal of smoking cessation (Grade C).

5) For high-risk patients (Table 3), aged ≥50 years, with systolic BP levels ≥130 mmHg, intensive management to target a systolic BP ≤120 mmHg should be considered. Intensive management should be guided by automated office BP measurements (see *Diagnosis and Assessment Guidelines*, Section I [Accurate measurement of BP], and Supplemental Table S2 [Recommended Technique for Automated Office Blood Pressure]). Patient selection for intensive management is recommended and caution should be taken in certain high-risk groups (Table 4) (Grade B).

V GOALS OF THERAPY FOR ADULTS WITH HYPERTENSION WITHOUT COMPELLING INDICATIONS FOR SPECIFIC AGENTS

The systolic blood pressure treatment goal is a pressure level of less than 140 mmHg (Grade C). The diastolic blood pressure treatment goal is a pressure level of less than 90 mmHg (Grade A).

VI TREATMENT OF HYPERTENSION IN ASSOCIATION WITH ISCHEMIC HEART DISEASE

A) Recommendations for Hypertensive Patients with Coronary Artery Disease (CAD)

1) For most hypertensive patients with CAD, an ACE inhibitor or ARB is recommended (Grade A).

2) For hypertensive patients with CAD, but without coexisting systolic heart failure, the combination of an ACE inhibitor and ARB is not recommended (Grade B).

3) For high-risk patients, when combination therapy is being used, choices should be individualized. The combination of an ACE inhibitor and a dihydropyridine CCB is preferable to an ACE inhibitor and a thiazide/thiazide-like diuretic in selected patients (Grade A).

4) For patients with stable angina pectoris but without prior heart failure, myocardial infarction, or coronary bypass surgery, either a beta-blocker or calcium channel blocker can be used as initial therapy (Grade B).

5) Short-acting nifedipine should not be used (Grade D).

6) When decreasing SBP to target levels in patients with established CAD (especially if isolated systolic hypertension is present), be cautious when the diastolic blood pressure is ≤60 mmHg because of concerns that myocardial ischemia may be exacerbated, especially in patients with left ventricular hypertrophy (LVH) (Grade D).

B) Guidelines for Patients with Hypertension Who Have Had a Recent Myocardial Infarction

1) Initial therapy should include both a beta-blocker and an ACE inhibitor (Grade A).

2) An ARB can be used if the patient is intolerant of an ACE inhibitor (Grade A in patients with left ventricular systolic dysfunction).

3) CCBs may be used in patients after postmyocardial infarction when beta-blockers are contraindicated or not effective. Nondihydropyridine CCBs should not be used when there is heart failure, as evidenced by pulmonary congestion on examination or radiography (Grade D).

VII TREATMENT OF HYPERTENSION IN ASSOCIATION WITH HEART FAILURE

1) In patients with systolic dysfunction (EF <40%), ACE inhibitors (Grade A) and β-blockers (Grade A) are recommended for initial therapy. Aldosterone antagonists (mineralcorticoid receptor antagonists) may be added for patients with a recent cardiovascular hospitalization, acute myocardial infarction, elevated BNP or NT-proBNP level, or NYHA Class II to IV symptoms (Grade A). Careful monitoring for hyperkalemia is recommended when adding an aldosterone antagonist to ACE inhibitor or ARB. Other diuretics are recommended as additional therapy if needed (Grade B for thiazide/thiazide-like diuretics for BP control, Grade D for loop diuretics for volume control). Beyond considerations of blood pressure control, doses of ACE inhibitors or ARBs should be titrated to those found to be effective in trials unless adverse effects become manifest (Grade B).

2) An ARB is recommended if ACE inhibitors are not tolerated (Grade A).

3) A combination of hydralazine and isosorbide dinitrate is recommended if ACE inhibitors and ARBs are contraindicated or not tolerated (Grade B).

4) For hypertensive patients whose blood pressure is not controlled, an ARB may be added to an ACE inhibitor and other antihypertensive drug treatment (Grade A). Careful monitoring should be used if combining an ACE inhibitor and an ARB due to potential adverse effects such as hypotension, hyperkalemia and worsening renal function (Grade C). Additional therapies may also include dihydropyridine CCBs (Grade C).

VIII TREATMENT OF HYPERTENSION IN ASSOCIATION WITH STROKE

A Blood Pressure Management in Acute Ischaemic Stroke (Onset to 72 Hours)

1) For patients with ischemic stroke not eligible for thrombolytic therapy, treatment of hypertension in the setting of acute ischemic stroke or TIA should not be routinely undertaken (Grade D). Extreme blood pressure increases (e.g. systolic >220 mmHg or diastolic >120 mmHg) may be treated to reduce the blood pressure by approximately 15 percent (Grade D), and not more than 25%, over the first 24h with gradual reduction thereafter (Grade D). Avoid excessive lowering of blood pressure as this may exacerbate

existing ischemia or may induce ischemia, particularly in the setting of intracranial arterial occlusion or extra cranial carotid or vertebral artery occlusion (Grade D). Pharmacological agents and routes of administration should be chosen to avoid precipitous decreases in blood pressure (Grade D).

2) For patients with ischemic stroke eligible for thrombolytic therapy, very high blood pressure (>185/110mmHg) should be treated concurrently in patients receiving thrombolytic therapy for acute ischemic stroke to reduce the risk of secondary intracranial hemorrhage [Grade B].

B Blood Pressure Management After Acute Ischaemic Stroke

1) Strong consideration should be given to the initiation of antihypertensive therapy after the acute phase of a stroke or transient ischemic attack (Grade A).

2) Following the acute phase of a stroke, blood pressure lowering treatment is recommended to a target of consistently lower than 140/90 mmHg (Grade C).

3) Treatment with an ACE inhibitor/diuretic combination is preferred (Grade B).

4) For patients with stroke, the combination of an ACE inhibitor and ARB is not recommended (Grade B).

C Blood Pressure Management in Hemorrhagic Stroke (Onset to 72 hours)

1) For patients with intracerebral hemorrhage in the hyperacute phase (in the first 24 hours) SBP lowering to <140 mmHg should be avoided due to an absence of benefit (relative to a target of <180 mmHg) (Grade A; ***new guideline***) and some suggestion of harm.

IX TREATMENT OF HYPERTENSION IN ASSOCIATION WITH LEFT VENTRICULAR HYPERTROPHY

1) Hypertensive patients with left ventricular hypertrophy should be treated with antihypertensive therapy to lower the rate of subsequent cardiovascular events (Grade C).

2) The choice of initial therapy can be influenced by the presence of left ventricular hypertrophy (Grade D). Initial therapy can be drug treatment using ACE inhibitors, ARBs, long-acting CCBs or thiazide/thiazide-like diuretics. Direct arterial vasodilators such as hydralazine or minoxidil should not be used.

X TREATMENT OF HYPERTENSION IN ASSOCIATION WITH NON-DIABETIC CHRONIC KIDNEY DISEASE

1) For patients with non-diabetic chronic kidney disease, target BP is < 140/90 mmHg (Grade B).

2) For patients with hypertension and proteinuric chronic kidney disease (urinary protein > 500 mg/24hr or albumin to creatinine ratio [ACR] > 30 mg/mmol), initial therapy should be an ACE inhibitor (Grade A) or an ARB if there is intolerance to ACE inhibitors (Grade B).

3) Thiazide/thiazide-like diuretics are recommended as additive antihypertensive therapy (Grade D). For patients with chronic kidney disease and volume overload, loop diuretics are an alternative (Grade D).

4) In most cases, combination therapy with other antihypertensive agents may be needed to reach target blood pressures (Grade D).

5) The combination of an ACE inhibitor and ARB is not recommended for patients with nonproteinuric chronic kidney disease (Grade B).

XI TREATMENT OF HYPERTENSION IN ASSOCIATION WITH RENOVASCULAR DISEASE

1) Patients with hypertension attributable to atherosclerotic renal artery stenosis (RAS) should be primarily medically managed because renal angioplasty and stenting offers no benefit over optimal medical therapy alone (Grade B).

2) Renal artery angioplasty and stenting for atherosclerotic hemodynamically significant renal artery stenosis could be considered for patients with uncontrolled hypertension resistant to maximally tolerated pharmacotherapy, progressive renal function loss, and acute pulmonary edema (Grade D).

3) Patients with confirmed renal FMD should be referred to a hypertension specialist (Grade D; ***new guideline***).

4) In patients with hypertension attributable to FMD-related renal artery stenosis, revascularization should be considered (Grade D; ***new guideline***).

5) Renal artery angioplasty without stenting is recommended for treatment of FMD-related renal artery stenosis. Stenting is not recommended unless needed because of a periprocedural dissection. Surgical revascularization should be considered in case of complex lesions less amendable to angioplasty, stenosis associated with complex aneurysm, and

restenosis despite 2 unsuccessful attempts of angioplasty (Grade D; ***new guideline***).

XII TREATMENT OF HYPERTENSION IN ASSOCIATION WITH DIABETES MELLITUS

1) Persons with diabetes mellitus should be treated to attain systolic blood pressures of less than 130 mmHg (Grade C) and diastolic blood pressures of less than 80 mmHg (Grade A). (These target blood pressure levels are the same as the blood pressure treatment thresholds.) Combination therapy using two first-line agents may also be considered as initial treatment of hypertension (Grade B) if systolic blood pressure is 20 mmHg above target or if diastolic blood pressure is 10 mmHg above target. However, caution should be exercised in patients in whom a substantial fall in blood pressure is more likely or poorly tolerated (e.g. elderly patients and patients with autonomic neuropathy).

2) For persons with cardiovascular or kidney disease, including microalbuminuria or with cardiovascular risk factors in addition to diabetes and hypertension, an ACE inhibitor or an ARB is recommended as initial therapy (Grade A).

3) For persons with diabetes and hypertension not included in other guidelines in this section, appropriate choices include (in alphabetical order): ACE inhibitors (Grade A), angiotensin receptor blockers (Grade B), dihydropyridine CCBs (Grade A) and thiazide/thiazide-like diuretics (Grade A).

4) If target blood pressures are not achieved with standard-dose monotherapy, additional antihypertensive therapy should be used. For persons in whom combination therapy with an ACE inhibitor is being considered, a dihydropyridine CCB is preferable to a thiazide/thiazide-like diuretic (Grade A).

XIII ADHERENCE STRATEGIES FOR PATIENTS

1) Adherence to an antihypertensive prescription can be improved by a multipronged approach (Supplemental Table S12).

XIV TREATMENT OF SECONDARY HYPERTENSION DUE TO ENDOCRINE CAUSES

1) Treatment of hyperaldosteronism and pheochromocytoma are outlined in Supplemental Tables S7 and S8, respectively.

Table 1: Considerations in the Individualization of Antihypertensive Therapy*†

	Initial therapy	Second-line therapy	Notes and/or Cautions
HYPERTENSION WITHOUT OTHER COMPELLING INDICATIONS			
Diastolic hypertension with or without systolic hypertension	Monotherapy or SPC. Recommended monotherapy choices include thiazide/thiazide-like diuretics (with longer-acting diuretics preferred), ß-blockers, ACE inhibitors, ARBs, or long-acting CCB. Recommended SPC choices include combinations of an ACE inhibitor with CCB, ARB with CCB, or ACE inhibitor/ARB with a diuretic. (Consider ASA and statins in selected patients).	Further addition of first-line drugs	Not recommended for monotherapy: ß-blockers, ß-blockers in those ≥60 years of age, ACE inhibitors in black people. Hypokalemia should be avoided in those prescribed diuretics. ACE inhibitors, ARBs and direct renin inhibitors are potential teratogens, and caution is required if prescribing to women with child-bearing potential. Combination of an ACE-inhibitor with an ARB is not recommended.
Isolated systolic hypertension without other compelling indications	Thiazide/thiazide-like diuretics, ARBs or long-acting dihydropyridine CCBs	Combinations of first-line drugs	Same as diastolic hypertension with or without systolic hypertension
DIABETES MELLITUS			
Diabetes mellitus with microalbuminuria*, renal disease, cardiovascular disease or additional cardiovascular risk factors	ACE inhibitors or ARBs	Addition of dihydropyridine CCB is preferred over thiazide/ thiazide-like diuretic.	A loop diuretic could be considered in hypertensive CKD patients with extracellular fluid overload.
Diabetes mellitus not included in the above category	ACE inhibitors, ARBs, dihydropyridine CCBs or thiazide/ thiazide-like diuretics.	Combination of first-line drugs. If combination with ACE inhibitor is being considered, a dihydropyridine CCB is preferable to a thiazide/thiazide-like diuretic.	Normal urine microalbumin to creatinine ratio <2.0 mg/mmol

	Initial therapy	Second-line therapy	Notes and/or Cautions
CARDIOVASCULAR DISEASE			
Coronary artery disease	ACE inhibitors or ARBs; ß-blockers or CCBs for patients with stable angina.	When combination therapy is being used for high risk patients, an ACE inhibitor/dihydropyridine CCB is preferred.	Avoid short-acting nifedipine. Combination of an ACE-inhibitor with an ARB is specifically not recommended. Exercise caution when lowering SBP to target if DBP is ≤60 mmHg, especially in patients with LVH.
Recent myocardial infarction	ß-blockers and ACE inhibitors (ARBs if ACE inhibitor intolerant).	Long-acting CCBs if ß-blocker contraindicated or not effective.	Non-dihydropyridine CCBs should not be used with concomitant heart failure
Heart failure	ACE inhibitors (ARBs if ACE inhibitor-intolerant) and ß blockers. Aldosterone antagonists (mineralocorticoid receptor antagonists) may be added for patients with a recent cardiovascular hospitalization, acute myocardial infarction, elevated BNP or NT-proBNP level, or NYHA Class II to IV symptoms.	ACE inhibitor and ARB combined. Hydralazine/ isosorbide dinitrate combination if ACE inhibitor and ARB contraindicated or not tolerated. Thiazide/thiazide-like or loop diuretics are recommended as additive therapy. Dihydropyridine CCB can also be used.	Titrate doses of ACE inhibitors and ARBs to those used in clinical trials. Carefully monitor potassium and renal function if combining any of ACE inhibitor, ARB and/or aldosterone antagonist.
Left ventricular hypertrophy	ACE inhibitor, ARB, long acting CCB or thiazide/thiazide-like diuretics.	Combination of additional agents.	Hydralazine and minoxidil should not be used.
Past stroke or TIA	ACE inhibitor and a thiazide/thiazide-like diuretic combination.	Combination of additional agents.	Treatment of hypertension should not be routinely undertaken in acute stroke unless extreme BP elevation. Combination of an ACE inhibitor with an ARB is not recommended.

	Initial therapy	Second-line therapy	Notes and/or Cautions
NON-DIABETIC CHRONIC KIDNEY DISEASE			
Nondiabetic chronic kidney disease with proteinuria†	ACE inhibitors (ARBs if ACE inhibitor intolerant) if there is proteinuria. Diuretics as additive therapy.	Combinations of additional agents.	Carefully monitor renal function and potassium for those on an ACE inhibitor or ARB. Combinations of an ACE-inhibitor and ARB are not recommended in patients without proteinuria.
Renovascular disease	Does not affect initial treatment recommendations. Atherosclerotic renal artery stenosis should be primarily managed medically, while revascularization should be considered for renal fibromuscular dysplasia.	Combinations of additional agents.	Caution with ACE inhibitors or ARB if bilateral renal artery stenosis or unilateral disease with solitary kidney. Renal artery angioplasty and stenting could be considered for patients with renal artery stenosis and complicated, uncontrolled hypertension.
OTHER CONDITIONS			
Peripheral arterial disease	Does not affect initial treatment recommendations.	Combinations of additional agents.	Avoid ß-blockers with severe disease.
Dyslipidemia	Does not affect initial treatment recommendations.	Combinations of additional agents.	
Overall vascular protection	Statin therapy for patients with 3 or more cardiovascular risk factors or atherosclerotic disease. Low dose ASA in patients ≥50 years. Advise on smoking cessation and use pharmacotherapy for smoking cessation if indicated.		Caution should be exercised with the ASA recommendation if BP is not controlled.

*Microalbuminuria is defined as persistent albumin to creatinine ratio >2.0 mg/mmol.
†Proteinuria is defined as urinary protein >500 mg/24hr or albumin to creatinine ratio [ACR] >30 mg/mmol in two of three specimens.
BP: Blood pressure; **ACE:** Angiotensin-converting enzyme; **ARB:** Angiotensin receptor blocker; **ASA:** Acetylsalicylic acid; **CCB:** Calcium channel blocker; **NYHA:** New York Heart Association; **TIA:** Transient ischemic attack ; **LVH:** Left ventricular hypertrophy; **SPC:** Single pill combination

Table 2. Risk factors for hyperkalemia

Prior to advising an increase in potassium intake, the following types of patients, who are at high risk of developing hyperkalemia, should be assessed for suitability, and monitored closely:

- Patients taking renin-angiotensin-aldosterone inhibitors
- Patients on other drugs that can cause hyperkalemia (e.g., trimethoprim and sulfamethoxazole, amiloride, triamterene)
- Chronic kidney disease (glomerular filtration rate <60 mL/min/1.73m^2)
- Baseline serum potassium >4.5 mmol/L

Table 3. Clinical indications defining high risk patients as candidates for intensive management

- Clinical or sub-clinical cardiovascular disease

  OR

- Chronic kidney disease (non-diabetic nephropathy, proteinuria <1 g/d, *estimated glomerular filtration rate 20-59 mL/min/1.73m^2)

  OR

- †Estimated 10-year global cardiovascular risk ≥15%

  OR

- Age ≥ 75 years
- Patients with one or more clinical indications should consent to intensive management.

* Four variable Modification of Diet in Renal Disease (MDRD) equation

† Framingham Risk Score

Table 4. Generalizability of Intensive Blood Pressure Lowering: Cautions and Contraindications

Limited or No Evidence

- Heart failure (ejection fraction <35%) or recent myocardial infarction (within last 3 months)
- Indication for, but not currently receiving, a beta-blocker
- Frail or institutionalized elderly

Inconclusive evidence

- Diabetes Mellitus
- Prior stroke
- eGFR < 20 ml/min/1.73 m^2

Contraindications

- Patient unwilling or unable to adhere to multiple medications
- Standing SBP <110 mmHg
- Inability to measure SBP accurately
- Known secondary cause(s) of hypertension

SUPPLEMENTAL TABLES

Supplemental Table S2: Recommended Technique for Automated Office Blood Pressure (AOBP)

1) Measurements should be taken with a validated sphygmomanometer known to be accurate.
2) Choose a cuff with an appropriate bladder size matched to the size of the arm. Select the cuff size as recommended by its manufacturer.
3) Place the cuff so that the lower edge is 3 cm above the elbow crease and the bladder is centered over the brachial artery. There is no rest period needed before measurement. The arm should be bare and supported with the BP cuff at heart level, as a lower position will result in an erroneously higher SBP and DBP. There should be no talking, and patients' legs should not be crossed.
4) When using automated office oscillometric devices, the patient should be seated in a quiet room (no specified period of rest). With the device set to take measures at 1- or 2-minute intervals. The first measurement is taken by a health professional to verify cuff position and validity of the measurement. The patient is left alone after the first measurement while the device automatically takes subsequent readings.
5) Record the average BP as displayed on the electronic device as well as the arm used and whether the patient was supine, sitting or standing. Record the heart rate.

Recommended Technique for Office Blood Pressure Measurement (non-AOBP)

1) Measurements should be taken with a sphygmomanometer known to be accurate. A validated electronic device should be used. If not available, a recently calibrated aneroid device can be used. Aneroid devices or mercury columns need to be clearly visible at eye level.
2) Choose a cuff with an appropriate bladder size matched to the size of the arm. For measurements taken by auscultation, bladder width should be close to 40% of arm circumference and bladder length should cover 80 – 100% of arm circumference. When using an automated device, select the cuff size as recommended by its manufacturer.
3) Place the cuff so that the lower edge is 3 cm above the elbow crease and the bladder is centered over

the brachial artery. The patient should be resting comfortably for 5 minutes in the seated position with back support. The arm should be bare and supported with the BP cuff at heart level, as a lower position will result in an erroneously higher SBP and DBP. There should be no talking, and patients' legs should not be crossed. The first reading should be discarded and the latter two averaged. BP should also be assessed after 2 minutes standing (with arm supported) and at times when patients report symptoms suggestive of postural hypotension. Supine BP measurements may also be helpful in the assessment of elderly and diabetic patients.

When using automated office oscillometric devices such as the BpTRU (VSM MedTech Ltd, Vancouver, Canada), the patient should be seated in a quiet room (no specified period of rest). With the device set to take measures at 1- or 2-minute intervals, the first measurement is taken by a health professional to verify cuff position and validity of the measurement. The patient is left alone after the first measurement while the device automatically takes subsequent readings. The BpTRU automatically discards the first measure and averages the next 5 measures.

For auscultation, at least three measurements should be taken in the same arm with the patient in the same position. The first reading should be discarded and the latter two averaged.

Steps 4-7 are specific to auscultation.

4) Increase the pressure rapidly to 30 mmHg above the level at which the radial pulse is extinguished (to exclude the possibility of a systolic auscultatory gap).

5) Place the bell or diaphragm of the stethoscope gently and steadily over the brachial artery.

6) Open the control valve so that the rate of deflation of the cuff is approximately 2 mmHg per heart beat. A cuff deflation rate of 2 mmHg per beat is necessary for accurate systolic and diastolic estimation.

7) Read the systolic level -the first appearance of a clear tapping sound (phase I Korotkoff) and the diastolic level- the point at which the sounds disappear (phase V Korotkoff). If Korotkoff sounds persist as the level approaches 0 mmHg, then the point of muffling of the sound is used (phase IV) to indicate the diastolic pressure. Leaving the cuff partially inflated for too long will fill the venous system and make the sounds difficult to hear. To avoid venous congestion, it is

recommended that at least one minute should elapse between readings.

8) Record the BP to the closest 2 mmHg on the manometer (or 1 mmHg on electronic devices) as well as the arm used and whether the patient was supine, sitting or standing. Avoid digit preference by not rounding up or down. Record the heart rate. The seated BP is used to determine and monitor treatment decisions. The standing BP is used to examine for postural hypotension, if present, which may modify the treatment.

9) In the case of arrhythmia, additional readings with auscultation may be required to estimate the average systolic and diastolic pressure. Isolated extra beats should be ignored. Note the rhythm and pulse rate.

10) BP should be taken in both arms on at least one visit and if one arm has a consistently higher pressure, that arm should be subsequently used for BP measurement and interpretation.

Recommended Technique for Home Blood Pressure Measurement

1) Measurements should be taken with a validated electronic device.

2) Choose a cuff with an appropriate bladder size matched to the size of the arm. Bladder width should be close to 40% of arm circumference and bladder length should cover 80 – 100% of arm circumference. Select the cuff size as recommended by its manufacturer.

3) Cuff should be applied to the non-dominant arm unless the SBP difference between arms is >10 mmHg, in which case the arm with the highest value obtained should be used.

4) The patient should be resting comfortably for 5 minutes in the seated position with back support.

5) The arm should be bare and supported with the BP cuff at heart level.

6) Measurement should be performed before breakfast and 2 hours after dinner, before taking medication.

7) No caffeine or tobacco in the hour and no exercise 30 minutes preceding the measurement.

8) Duplicate measurement should be done in the morning and in the evening for seven days (i.e., 28 measurements in total).

9) Average the results excluding the first day's readings.

Recommended Technique for Ambulatory Pressure Monitoring

1) The appropriate sized cuff should be applied to the non-dominant arm unless the SBP difference between arms is >10 mm Hg, in which case the arm with the highest value obtained should be used.
2) The device should be set to record for a duration of at least 24 hours with the measurement frequency set at 20-30 minute intervals during the day and 30-60 minutes at night.
3) A patient-reported diary to define daytime (awake), night-time (sleep), activities, symptoms and medication administration is useful for study interpretation.
4) Daytime and night-time should preferentially be defined using the patient's diary. Alternatively, pre-defined thresholds can be used (e.g. 8 AM to 10 PM for awake and 10 PM and 8 AM for night-time).
5) The ambulatory BP monitoring report should include all of the individual BP readings (both numerically and graphically), the percentage of successful readings, the averages for each time frame (daytime, night-time, 24 hours) and the "dipping" percentage (the percentage the average BP changed from daytime to night-time).
6) Criteria for a successful ambulatory BP monitoring study are:
   i) At least 70% of the readings are successful, AND
   ii) At least 20 daytime readings and 7 night-time readings are successful.

Abbreviations: BP, blood pressure; DBP, diastolic BP; SBP, systolic BP. Unless otherwise mentioned, steps apply to measurement by auscultation and oscillometry using an upper arm cuff.

Supplementary Table S3:
Examples of Hypertensive Urgencies and Emergencies

- Asymptomatic diastolic BP ≥ 130 mmHg
- Severe elevations of BP in the setting of any of:
  - Hypertensive encephalopathy
  - Acute aortic dissection
  - Acute left ventricular failure
  - Acute coronary syndrome
  - Acute kidney injury
  - Intracranial hemorrhage
  - Acute ischemic stroke
  - Pre-eclampsia/eclampsia
  - Catecholamine-associated hypertension

Abbreviations:

BP: Blood Pressure

Supplementary Table S4:
Examples of Target Organ Damage

Cerebrovascular Disease

Stroke
- Ischemic stroke and transient ischemic attack
- Intracerebral hemorrhage
- Aneurysmal sub-arachnoid hemorrhage

Dementia
- Vascular dementia
- Mixed vascular dementia and dementia of the Alzheimer's type

Hypertensive Retinopathy

Left Ventricular Dysfunction

Left Ventricular Hypertrophy

Heart Failure

Coronary Artery Disease
- Myocardial infarction
- Angina pectoris
- Congestive heart failure

Renal Disease
- Chronic Kidney Disease (GFR < 60 ml/min/1.73 m^2)
- Albuminuria

Peripheral Artery disease
- Intermittent claudication

Supplementary Table S5:
Examples of Key Cardiovascular Risk Factors for Atherosclerosis

Prior history of clinically overt atherosclerotic disease *indicates a very high risk for a recurrent atherosclerotic event (e.g., Peripheral arterial disease, previous stroke or TIA).*

Non-Modifiable	Modifiable
• Age ≥ 55 years • Male • Family history of premature cardiovascular disease (age < 55 in men and < 65 in women)	• Sedentary lifestyle • Poor dietary habits • Abdominal obesity • Dysglycemia • Smoking • Dyslipidemia • Stress • Nonadherence

Supplemental Table S6:
Examples of exogenous factors that can induce/aggravate hypertension

Prescription Drugs:	Other substances:
• NSAIDs, including coxibs • Corticosteroids and anabolic steroids • Oral contraceptives and sex hormones • Vasoconstricting/sympathomimetic decongestants • Calcineurin inhibitors (cyclosporin, tacrolimus) • Erythropoietin and analogues • Antidepressants: Monoamine oxidase inhibitors (MAOIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), selective serotonin reuptake inhibitors (SSRIs) • Midodrine	• Licorice root • Stimulants including cocaine • Salt • Excessive alcohol intake

Supplemental Table S7: Hyperaldosteronism

Screening

i) Plasma aldosterone and plasma renin activity or renin mass/concentration (see ii below for conversion factors) should be collected as follows:

   a) In the morning after the patient has been ambulatory (sitting, standing, or walking) for at least 2 hours.

   b) Patients should be seated for 5-15 minutes prior to the blood draw.

   c) Hypokalemia should be corrected and sodium intake should be liberalized.

   d) Agents that markedly affect the results of testing (aldosterone antagonists, potassium sparing and wasting diuretics) should be withdrawn at least 4-6 weeks prior.

   e) If the results are not diagnostic, and if hypertension can be controlled with medications less likely to affect testing (slow-release verapamil, hydralazine, prazosin, doxazosin, and terazosin), repeat testing two weeks after withdrawing the following medications that can interfere with test accuracy: beta-blockers, centrally acting alpha-2 agonists, angiotensin receptor blockers, angiotensin converting enzyme inhibitors, directly acting renin inhibitors, dihydropyridine calcium channel blockers

f) False positive results may occur with direct renin mass/concentration if the patient is a woman using an oral contraceptive pill. If possible, oral contraception should be discontinued for 1 month prior to testing, or alternately, plasma renin activity should be measured instead.

ii) Suggested Conversion Factors:

(A) To estimate:	(B) From:	Multiply (B) by:
Plasma renin concentration (ng/mL)	Plasma renin activity (ng/L/hr)	0.192
Plasma renin activity (ng/L/sec)	Plasma renin activity (ng/mL/hr)	0.278
Plasma aldosterone concentration (pmol/L)	Plasma aldosterone concentration (ng/dL)	28

iii) Interpretation of a positive screening test is dependent upon the local laboratory method for renin measurement but assumes standard reporting of aldosterone in pmol/L:

Renin method used	Aldosterone-to-renin ratio: higher sensitivity, lower specificity	Aldosterone-to-renin ratio: lower sensitivity, higher specificity
Plasma renin activity (ng/ml/h)	555	750
Direct renin concentration (mIU/L)	60	91
Direct renin concentration (ng/L)	100	144

Confirmatory Testing

iv) If one of the following criteria is met, autonomous hypersecretion of aldosterone is confirmed (interfering drugs should continue to be held, as outlined above):

a) Saline loading tests (perform either):

i) Administer two litres of normal saline intravenously over 4h with the patient in a recumbent position. Primary hyperaldosteronism is defined as a post-infusion plasma aldosterone >280 pmol/L. If <140 pmol/L, primary hyperaldosteronism is unlikely. Values in between are considered indeterminate;

ii) Administer oral sodium, 200 mmol/day for three days, with primary hyperaldosteronism defined as a 24-hr urinary aldosterone >33 nmol/d (measured from the

morning of Day 3 to the morning of Day 4). If <28 nmol/day, primary hyperaldosteronism is unlikely.

b) A plasma aldosterone to PRA ratio greater than 1400 pmol/L/ng/ml/hr (or 270 pmol/L/ng/L), with a plasma aldosterone greater than 440 pmol/L.

c) Captopril suppression test: Administer 25-50 mg captopril orally after the patient has been sitting or standing for 1 hour. While seated, renin and plasma aldosterone levels should be measured at time zero and 1-2 hours after ingestion. Primary hyperaldosteronism is unlikely if plasma aldosterone is suppressed by >30% following captopril ingestion. In primary hyperaldosteronism, plasma aldosterone remains elevated, while renin remains suppressed.

Subtype Classification:

v) Differentiating potential causes of confirmed primary hyperaldosteronism (unilateral vs bilateral secretion):

a) CT-scanning or MRI can help localize the presence of adrenal lesion(s). If imaging demonstrates an adrenal lesion/adenoma, it may be non-functional. Therefore, if surgery to remove a suspected unilateral source of primary hyperaldosteronism is planned, selective adrenal venous sampling should be considered first (to verify that abnormally appearing adrenal gland is the source of hypersecretion).

b) For patients with established primary hyperaldosteronism, negative imaging studies, and in whom surgery is an option, selective adrenal venous sampling should be considered to differentiate unilateral from bilateral overproduction of aldosterone.

c) Adrenal venous sampling should be conducted in centers with experience in performing this diagnostic technique.

d) We suggest selective genetic testing for glucocorticoid remediable aldosteronism in patients with confirmed primary hyperaldosteronism and either:

i) a family history of primary hyperaldosteronism or stroke at young age (≤40y);

ii) onset of hypertension ≤20y and negative imaging

Treatment:

vi) Treatment is informed by subtype classification (unilateral vs. bilateral secretion):

a) Surgery with ipsilateral adrenalectomy should be considered for unilateral forms of hypersecretion (e.g., aldosterone-producing adenonas). Patients should be followed closely after surgery as a significant proportion may remain hypertensive.

b) Mineralocorticoid receptor antagonists (particularly spironolactone in low to moderate doses) are quite effective for those with bilateral disease (e.g., idiopathic/bilateral adrenal hyperplasia).

c) Mineralocorticoid receptor antagonists should be considered for individuals who are not surgical candidates or for those who refuse surgery (even with confirmed unilateral hypersecretion). Blood pressure lowering responses to other antihypertensives (e.g., angiotensin receptor blockers, angiotensin converting enzyme inhibitors, and calcium channel blockers) are often only modest-to-moderate.

Supplemental Table S8: Pheochromocytoma
Screening and diagnosis:

1) To screen for pheochromocytoma

a) 24-hr urinary total metanephrines and catecholamines (sensitivity 90-95%) or 24-hr urine fractionated metanephrines (sensitivity of about 100%) should be measured. Concomitant measurement of 24-hr urine creatinine should also be performed to confirm accurate collection.

b) Plasma free metanephrines and free normetanephrines, where available, may also be considered (sensitivity up to 99%).

c) Urinary VMA measurements should not be used for screening.

2) Keep in mind that potential false positives should be considered in the setting of:

a) interfering drugs

b) Incorrect patient preparation and positioning (for plasma metanephrine measures)

c) Mild elevation of screening values (i.e., less than two-fold upper limit of normal)

d) Normal values on repeat testing

e) Only 1 abnormal biochemical test in the panel of assays

f) Atypical imaging results for pheochromocytoma

g) A low pre-test probability of pheochromocytoma

h) Acute illness/hospitalization

3) In the presence of borderline biochemical test results or potentially false positive results, repeat testing may be performed and/or the clonidine suppression test may be used. This should be done before imaging is requested to avoid identifying potential incidentalomas

4) Imaging (e.g., CT, MRI, +/- MIBG) should generally be performed and/or only done after biochemical confirmation of disease.

Treatment:

5) Definitive treatment is with surgical resection. Preoperative planning is recommended for blood pressure control and volume expansion:

a) Alpha blockade should be started 10-14 days preoperatively. Typical options include phenoxybenzamine (a long-acting, non-selective irreversible α-blocker), prazosin, or doxazosin.

b) Other anti-hypertensives may be added as necessary but diuretics should be avoided if possible. Oral beta-blockers may be considered after achieving adequate alpha blockade to control tachycardia and prevent arrhythmias during surgery.

c) Volume replacement and liberal sodium intake should be encouraged as volume contraction is common in this condition. Intravenous volume expansion in the perioperative period is recommended to prevent postoperative shock.

6) Postoperatively, long-term follow-up is recommended with urinary or plasma metanephrines to screen for recurrence, especially in those with a genetic predisposition.

7) Genetic testing should be considered for individuals <50 years of age, multiple lesions, malignant lesions, bilateral pheochromocytomas or paragangliomas, or those with a family history of pheochromocytoma or paraganglioma.

Supplemental Table S9:
Dietary Approaches to Stop Hypertension (DASH) Diet

Food Group	Daily Serving	Examples and Notes
Whole Grains	6-8	Whole wheat breads, cereal, oatmeal, rice, pasta, quinoa, barley, low-fat, low-sodium crackers
Vegetables	4-5	Dark green and orange fresh or frozen vegetables, tomatoes, leafy greens, carrots, peas, squash, spinach, peppers, broccoli, sweet potatoes
Fruits	4-5	Have fruit more often than juice: Apples, apricots, bananas, grapes, oranges, grapefruit, melons, peaches, berries, mango
Low-fat or fat-free milk foods or alternatives	2-3	Skim, 1% milk, fortified soy beverage or yogurt, 6-18% MF, cheese
Meats, poultry, fish	< 6 ounces	Select only lean meats. Choose fish like char, herring, mackerel, salmon, sardines and trout. Trim away fats. Broil, roast or boil. No frying. Remove skin from poultry. Low-sodium, low-fat deli meats
Nuts, seeds, legumes	4-5/week	Almonds, peanuts, walnuts, sunflower seeds, soybeans, lentils, chick peas, dried peas and beans, tofu
Fats and oils	2-3 tsp.	Soft margarines, mayonnaise, vegetable oil (olive, corn, canola, or safflower), salad dressing
Sweets	≤ 5 Tbsp./ Week	Sugar, jelly, jam, hard candy, syrups, sorbet, chocolate

DASH eating plan available at www.nhlbi.nih.gov/files/docs/public/heart/hbp_low.pdf;

Examples of serving sizes are listed in Canada's Food Guide (comparable to DASH) available at www.hc-sc.gc.ca/fn-an/food-guide-aliment/index-eng.php

Supplemental Table S10:
Possible Reasons for Poor Response to Antihypertensive Therapy

Poor Adherence	• Dietary • Physical activity • Medication
Associated Conditions	• Obesity • Tobacco use • Excessive alcohol consumption • Sleep apnea • Chronic pain
Drug Interactions	• Nonsteroidal anti-inflammatory drugs (including cyclo-oxygenase-2 inhibitors) • Oral contraceptives • Corticosteroids and anabolic steroids Sympathomimetics and decongestants • Cocaine • Amphetamines • Erythropoietin • Cyclosporine, tacrolimus • Licorice • Over-the-counter dietary supplements (e.g., ephedra, ma huang, bitter orange) • Monoamine oxidase inhibitors, certain selective serotonin reuptake inhibitors and serotonin-norepinephrine reuptake inhibitors
Suboptimal Treatment Regimens	• Dosage too low • Inappropriate combinations of antihypertensive agents
Volume Overload	• Excessive salt intake • Renal sodium retention (pseudotolerance)
Secondary Hypertension	• Renal insufficiency • Renovascular disease • Primary hyperaldosteronism • Thyroid disease • Pheochromocytoma and other rare endocrine causes • Obstructive sleep apnea

Note that causes of 'pseudo-resistance' (such as white coat hypertension or pseudo-hypertension in the elderly) should be ruled out first.

Supplemental Table S11:
Cardiovascular Risk Factors for Consideration of Statin Therapy in Non-dyslipidemic Patients With Hypertension

Risk Factor

- Male sex
- Age ≥ 55
- Left ventricular hypertrophy
- Other ECG abnormalities:
  - Left bundle branch block, left ventricular strain pattern, abnormal Q-waves or ST-T changes compatible with ischemic heart disease
- Peripheral arterial disease
- Previous stroke or transient ischemic attack
- Microalbuminuria or proteinuria
- Diabetes mellitus
- Smoking
- Family history of premature cardiovascular disease
- Total cholesterol to high-density lipoprotein ratio ≥ 6

If hypertensive patients have ≥3 of these risk factors, statins should be considered.

Supplemental Table S12:
Strategies to Improve Patient Adherence

Assist your patient to adhere by:

- Tailoring pill-taking to fit patients' daily habits (Grade D);
- Simplifying medication regimens to once-daily dosing (Grade D);
- Replacing multiple pill antihypertensive combinations with single pill combinations (Grade C);
- Using unit-of-use packaging (of several medications to be taken together) (Grade D); and
- Using a multidisciplinary team approach to improve adherence to an antihypertensive prescription (Grade B).

Assist your patient in getting more involved in their treatment by:

- Encouraging greater patient responsibility/ autonomy in monitoring their blood pressure and adjusting their prescriptions (Grade C); and
- Educating patients and patients' families about their disease and treatment regimens (Grade C)

Improve your management in the office and beyond by:

- Assessing adherence to pharmacological and non-pharmacological therapy at every visit (Grade D);
- Encouraging adherence with therapy by out-of-office contact (either by phone or mail), particularly during the first three months of therapy (Grade D);
- Coordinating with pharmacists and work-site healthcare givers to improve monitoring of adherence with pharmacological and lifestyle modification prescriptions (Grade D).
- Utilizing electronic medication compliance aids (Grade D).

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The Guidelines in this booklet are presented as a convenient reference tool for health care professionals. They are based on the 2017 Hypertension Canada Guidelines for the Management of Hypertension.

This booklet is designed as an overview based on the complete guidelines. Please visit guidelines.hypertension.ca for more information.

We hope this booklet proves a useful and practical addition to your diagnosis and treatment of hypertension. Please be reminded, however, that all therapeutic decisions are ultimately the responsibility of the health care professional.

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