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Hypertension Canada's 2018 Guidelines for Diagnosis, Risk Assessment, Prevention, and Treatment of Hypertension in Adults and Children

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ABSTRACT

Hypertension Canada provides annually-updated, evidence-based guidelines for the diagnosis, assessment, prevention, and treatment of hypertension in adults and children. This year, the adult and pediatric guidelines are combined in one document. The new 2018 pregnancy-specific hypertension guidelines are published separately.

For 2018, 5 new guidelines were introduced, and one existing guideline on the blood pressure thresholds and targets in the setting of thrombolysis for acute ischemic stroke was revised. The use of validated wrist devices for the estimation of blood pressure in individuals with large arm circumference is now included. Guidance is provided for the follow-up measurements of blood pressure, with the use of standardized methods and electronic (oscillometric) upper arm devices in individuals with hypertension, and either ambulatory blood pressure monitoring or home blood pressure monitoring in individuals with white coat effect. We specify that all individuals with hypertension should have an assessment of global cardiovascular risk to promote health behaviours that lower blood pressure. Finally, an angiotensin receptor-neprilysin inhibitor combination should be used in place of either an angiotensin-converting enzyme inhibitor or angiotensin receptor blocker in individuals with heart failure (with ejection fraction < 40%) who are symptomatic despite appropriate doses of guideline-directed heart failure therapies. The specific evidence and rationale underlying each of these guidelines are discussed.

KEY WORDS: hypertension, high blood pressure, guidelines, recommendations, adults, pediatrics, diagnostic algorithm, blood pressure measurement, ambulatory blood pressure

monitoring, home blood pressure monitoring, automated blood pressure, global cardiovascular risk, lipid profile, tobacco, smoking cessation, renovascular disease, renal artery stenosis, primary aldosteronism, pheochromocytoma, pharmacotherapy, lifestyle.

SUMMARY FOR ONLINE TABLE OF CONTENTS

For 2018, 5 new guidelines were introduced and one existing guideline was revised. The use of wrist devices for the estimation of blood pressure in individuals with large arm circumference is included. Guidance is provided for follow-up measurements of blood pressure (hypertension with/without white coat effect). All individuals with hypertension should have an assessment of global cardiovascular risk. Finally, an angiotensin receptor-neprilysin inhibitor combination should be used in individuals with heart failure meeting specific criteria.

Introduction

Hypertension is one of the most common chronic diseases affecting Canadians across their lifespan – from approximately 2% of children and adolescents,¹ to 7% of pregnant women,² to 25% of the adult population.³ Hypertension has broad impacts on the health of Canadians given its association with obesity (from childhood to adulthood)^{3,4} as well chronic kidney disease, cardiovascular disease, and death.^{3,5,6} Management of hypertension in children and adults centres around behavioural changes as well as pharmacotherapy, and is highly informed by individual cardiovascular risk. Hypertension Canada continues to recommend a risk-based approach for treatment thresholds and targets, placing a strong emphasis on cardiovascular risk assessment not only for the purpose of therapeutic decision-making but also to engage and educate patients in risk reduction strategies. This year, adult and pediatric guidelines have been consolidated into a single clinical practice guidelines document. Hypertension Canada's 2018 pregnancy-specific hypertension guidelines are published separately.

Hypertension Canada (formerly the Canadian Hypertension Education Program, CHEP) has been producing annually-updated, evidence-based guidelines for health care providers since 1999. Updated guidelines (new, revised and existing) are presented herein, along with discussion of the supporting evidence for the new and revised guidelines. Evidence along with corresponding references pertaining to previously established guidelines are available in prior publications,⁷⁻³⁶ and online (guidelines.hypertension.ca).

The guidelines are intended to provide a framework for evidence-based care of hypertension and do not supplant clinical judgment. Practitioners are advised to consider patient preferences, values, and clinical circumstances when determining how to best apply these guidelines to individual patients.³⁷

Methods

Hypertension Canada's Guidelines are developed annually through a highly structured and systematic process designed to minimize bias. Hypertension Canada's guideline process has been externally reviewed and is in concordance with the Appraisal of Guidelines for Research and Evaluation II (AGREE II) Instrument for guideline development (guidelines.hypertension.ca/about/overview-process).³⁸ The Hypertension Canada Guidelines Committee (HCGC) is comprised of a multidisciplinary panel of both content and methodological experts divided into 16 subgroups that represent distinct areas of hypertension (Supplemental Appendix S1 for list of members and S2 for conflicts of interest).

Comprehensive literature searches to August 2017 for each subgroup were performed by a trained medical librarian based on key words and terms provided by the subgroups. (Details of search strategies and retrieved articles are available upon request.) The literature was reviewed in a standardized manner and was graded using an evidence-based grading scheme (Supplemental Table S1) which considered the following: study methodologic quality; impacts on a hierarchy of validated clinical outcomes (priority given to cardiovascular morbidity and mortality); and that potential benefits must outweigh potential harms. This process ensures that all Hypertension Canada Guidelines are graded according to the best available evidence. For pharmacotherapy guidelines, Hypertension Canada considers evidence evaluating specific agents to be generalizable to a "class effect" unless otherwise stated.

The guidelines were then reviewed by the Central Review Committee, unbiased experts in clinical epidemiology, to ensure that guidelines accurately reflected the evidence and to verify grading. The draft guidelines and supporting evidence were presented to the HCGC in Toronto,

on October 12, 2017. Following the discussions, the guidelines were further revised and finalized for an electronic vote by all 81 members of the HCGC, with greater than 70% support required for approval of each new/revised guideline.

Hypertension Canada's 2018 Guidelines

Diagnosis and Assessment of Hypertension in Adults

I. Accurate measurement of blood pressure (BP)

Background. BP is traditionally measured using an upper arm cuff, however, recent studies suggest that accurate measurement of BP can be challenging in patients with increased upper arm size, particularly in obese patients with a body mass index (BMI) greater than 35 kg/m^{2,39,40}. In these patients, there is a concern of hidden undercuffing (i.e., the cuff bladder is too small or narrow for the arm size) leading to falsely elevated BP values.³⁹ A 2016 systematic review and meta-analysis examined the diagnostic accuracy of BP measurements of the forearm wrist and fingertip compared with correctly fitting upper arm cuff in obese individuals. Compared with upper arm cuffs, wrist measurements (with the wrist held at the level of the heart) had the highest diagnostic accuracy for hypertension with a sensitivity of 0.92 (0.64-0.99) and specificity of 0.92 (0.85-0.87),⁴⁰ though individual studies reported discordant results for the classification by BP category.³⁹

Given the limitations of the available studies to date, an appropriately sized upper arm cuff remains the standard for BP measurement.⁴⁰ However, when upper arm measurements are not possible due to extreme size of the arm or pain, a wrist measurement (with the arm and wrist

held at the level of the heart) may be used.^{39,40} When possible, concordance of wrist and upper arm device measurements should be demonstrated prior to the use of wrist BP measurements.^{39,40} Measurement of fingertip BP is not recommended.³⁸

Guidelines.

1. Health care professionals who have been specifically trained to measure 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 Supplemental 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. In patients with large arm circumference when standard upper arm measurement methods cannot be used, validated wrist devices (utilized with the arm and wrist supported at heart level) may be used for BP estimation (Grade D; **new guideline**).
4. 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 mm Hg or DBP ≥ 85 mm Hg DBP is high (Grade D).

- ii. When using non-AOBP, a mean systolic BP (SBP) ≥ 140 mm Hg or diastolic BP (DBP) ≥ 90 mm Hg is high, and an SBP between 130-139 mm Hg and/or a DBP between 85-89 mm Hg 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 mm Hg or the DBP is ≥ 85 mm Hg or if the mean 24-hour SBP is ≥ 130 mm Hg or the DBP is ≥ 80 mm Hg (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 mm Hg or the DBP is ≥ 85 mm Hg (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 $< 135/85$ mm Hg or perform 24-hour ambulatory BP monitoring to confirm that the mean 24-hour ambulatory BP monitoring is $< 130/80$ mm Hg and the mean awake ambulatory BP monitoring is $< 135/85$ mm Hg before diagnosing white coat hypertension (Grade D).

II. Criteria for diagnosis of hypertension and guidelines for follow-up

Background. A hypertension diagnostic algorithm for adults is shown in Figure 1. The new guidelines for 2018 address measurement methods for BP follow-up in adults with confirmed hypertension and in cases complicated by white coat effect.

Evidence-based recommendations for follow-up BP assessment are very important as they frequently inform BP treatment initiation and/or intensification. However, there are patient, procedure, and device sources of measurement variation that can have significant clinical implications.^{41,42} Several studies have demonstrated that routine manual BP reading (SBP/DBP) are on average 9/6 mm Hg higher when compared with the corresponding research quality manual BP measurements.^{43,44} This can lead to significant misclassification of hypertensive status and inappropriate treatment.^{43,45} Thus, ensuring standardization and systematic measurement in the follow-up of adults with hypertension will help obtain accurate measurement and promote safe and appropriate BP treatment.

Creating recommendations for specific follow-up measurement methods requires evidence (ideally from randomized controlled trials, RCTs) that evaluate different types of BP measurement methods and have a sufficient length of follow-up to allow comparisons of clinically important outcomes (morbidity and mortality) among the different measurement methods. Unfortunately, these data are not available. To date, there is only one low-quality RCT of nearly 1,300 participants with primary hypertension which compared clinical outcomes for those whose antihypertensive treatment was guided by 24-hour ambulatory BP monitoring versus by usual office-based practice.⁴⁶ While ambulatory BP monitoring-guided management was associated with a significant reduction in cardiovascular events and mortality after 4.7 years of follow-up, this trial had significant methodologic limitations (including differential exclusions after randomization and highly asymmetric loss to follow-up between trial arms). Other trials of measurement strategies have been completed (8 RCTs with almost 1,900 participants) but are of shorter duration and evaluated surrogate outcomes.⁴⁷⁻⁵⁴ These studies compared out-of-office BP

measurement methods (ambulatory or home BP monitoring) with office-based BP measurements and had significant variation in study methodologies, approaches to out-of-office BP management, and BP treatment thresholds. Overall, the out-of-office measurement groups had lower treatment intensity and higher BP values, in keeping with white coat effect being identified and managed less intensively, while the short-term intermediate outcomes were similar to office-based measurement approaches.

In summary, there is limited evidence on measuring follow-up BPs in adults with hypertension, and thus, at present, there are insufficient data to make a recommendation for a single measurement method. What has been established is that measurement variation is common and concerning, thus standardized methods of BP measurement should be employed, preferably using electronic (oscillometric) devices (Supplemental Table S2).

For hypertensive patients with white coat effect, no trial has specifically examined optimal follow-up strategies to date. In RCTs of BP follow-up strategies, patients in whom antihypertensive medications have either been reduced or stopped are thought to represent those individuals with white coat effect. Two RCTs comparing the use of home with office BP measurements demonstrated a significant reduction in antihypertensive medication use without changes in other clinical cardiovascular surrogate outcomes when home BP monitoring was used.^{47,53} Similarly, reduction in antihypertensive medications use was observed in another RCT when ambulatory BP monitoring was used to titrate medications.⁴⁹ All three RCTs are limited, however, by the use of the same BP target in both arms regardless of measurement method. Overall, this limited evidence suggests that either ambulatory or home BP monitoring can be

used for BP follow-up in patients with white coat effect, though there remains a paucity of data on the specific frequency of monitoring to guide clinical practice.

Guidelines.

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, Guideline 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, Guideline 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 mm Hg and/or DBP is ≥ 110 mm Hg then hypertension is diagnosed (Grade D).

5. If the visit 1 mean AOBP SBP is 135-179 mm Hg and/or DBP is 85-109 mm Hg OR the mean non-AOBP SBP is 140-179 mm Hg and/or DBP is 90-109 mm Hg, 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, Guideline 3.
 - ii. Home BP monitoring is recommended if ambulatory BP monitoring is not tolerated, not readily available, or because of patient preference (Grade D). Patients can be diagnosed with hypertension according to the thresholds outlined in Section I, Guideline 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 mm Hg SBP and/or ≥ 90 mm Hg DBP in patients with macrovascular target organ damage, diabetes mellitus, or chronic kidney disease (glomerular filtration rate < 60 mL/min/1.73m²) (Grade D);
 - ii. At visit 3, mean non-AOBP measurement (averaged across all visits) is ≥ 160 mm Hg SBP or ≥ 100 mm Hg DBP;

- iii. At visit 4 or 5, mean non-AOBP measurement (averaged across all visits) is ≥ 140 mm Hg SBP or ≥ 90 mm Hg DBP.
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).
 11. Standardized office BP measurement should be used for follow-up. Measurement using electronic (oscillometric) upper arm devices is preferred over auscultation (Grade C; **new guideline**).
 12. Ambulatory BP monitoring or home BP is recommended for follow-up of patients with demonstrated white coat effect (Grade D; **new guideline**).

III. Home BP measurement

A suggested protocol for home BP monitoring is presented in Supplemental Table S2.

Guidelines.

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);
 - 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 (Guideline 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 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 mm Hg or DBP values ≥ 85 mm Hg 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 for assessing white coat hypertension or sustained hypertension should be based on duplicate measures, morning and evening, for an initial 7-day period. First-day home BP values should not be considered (Grade D).

IV. Ambulatory BP measurement

A suggested protocol for ambulatory BP monitoring is presented in Supplemental Table S2.

Guidelines.

1. Ambulatory BP monitoring 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 antihypertensive therapy (Grade C);
 - ii. Symptoms suggestive of hypotension (Grade C);
 - 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 mm Hg and/or DBP of ≥ 80 mm Hg, or a mean awake SBP of ≥ 135 mm Hg and/or DBP of ≥ 85 mm Hg (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 cardiovascular events.

V. Routine and optional laboratory tests for the investigation of patients with hypertension

Guidelines.

1. Routine laboratory tests that should be performed for the investigation of all patients with hypertension include the following:
 - 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); and,
 - 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

Background. Global cardiovascular risk assessment is often done through the use of risk calculators, including the Framingham risk score, www.myhealthcheckup.com and www.score-canada.ca. Estimation and reporting of an individual's global cardiovascular risk may help improve risk perception,⁵⁵ facilitate informed discussions between physicians and patients regarding health behaviours,⁵⁵⁻⁵⁷ and potentially improve health outcomes,^{57,58} with little evidence of harm on psychological wellbeing.⁵⁷ Counselling efforts aimed at improving health behaviours (such as promoting a healthful diet, weight management, and physical activity) appear effective in lowering BP. A recent meta-analysis of 88 RCTs reported that counseling interventions targeting both a healthful diet and increasing physical activity led to modest lowering of SBP (data from 22 RCTs of 57,953 participants; -1.26 mm Hg; 95% confidence interval [CI], -1.77 to -0.75) and DBP (data from 23 RCTs of 58,022 participants; -0.49 mm Hg; 95% CI, -0.82 to -0.16) over 6 to 12 months in individuals at low cardiovascular risk.⁵⁶ As such, global cardiovascular risk assessment can be considered as a tool to engage individuals in conversations to improve health behaviours to lower BP.

Guidelines.

1. Global cardiovascular risk should be assessed. Multifactorial risk assessment models can be used to:

- a. Predict more accurately an individual's global cardiovascular risk (Grade A);
- b. Help engage individuals in conversations about health behaviour change to lower BP (Grade D; **new guideline**); and,
- c. 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

Guidelines.

- 1. Patients presenting with ≥ 2 of the following clinical clues listed below, suggesting renovascular hypertension, should be investigated (Grade D):
 - i. Sudden onset or worsening of hypertension and age >55 or <30 years;
 - ii. Presence of an abdominal bruit;
 - iii. Hypertension resistant to ≥ 3 drugs;
 - iv. Increase in serum creatinine level $\geq 30\%$ associated with use of an angiotensin converting enzyme (ACE) inhibitor or angiotensin receptor blocker (ARB);
 - 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 computer tomography angiography (for those with normal renal function) (Grade B). Captopril-enhanced radioisotope renal scan is not recommended for those with chronic kidney disease (glomerular filtration rate <60 mL/min/1.73m²) (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):
 - i. Age <30 years, especially in non-obese women;
 - ii. Hypertension resistant to ≥ 3 drugs;
 - iii. Significant (>1.5 cm), unexplained asymmetry in kidney sizes;
 - 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):
 - 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): magnetic resonance angiography and computed tomography angiography.

VIII. Assessment for endocrine hypertension

A. Hyperaldosteronism: screening and diagnosis:

Guidelines.

1. Screening for hyperaldosteronism should be considered in hypertensive patients with the following (Grade D):
 - i. Unexplained spontaneous hypokalemia ($K^+ < 3.5$ mmol/L) or marked diuretic-induced hypokalemia ($K^+ < 3.0$ mmol/L);
 - ii. Resistance to treatment with ≥ 3 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 ii), a diagnosis of primary aldosteronism should be established by demonstrating inappropriate autonomous hypersecretion of aldosterone using at least one of the manoeuvres listed in Supplemental Table S7, Item iii. When the diagnosis is established, the abnormality should be localized using any of the tests described in Supplemental Table S7, Item iv.
4. In patients with primary aldosteronism 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 and paraganglioma: screening and diagnosis

Guidelines.

1. If pheochromocytoma or paraganglioma 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 $\geq$ 180/110 mm Hg) 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 β -blockers, monoamine oxidase inhibitors, micturition, changes in abdominal pressure, surgery, or anesthesia;
 - iv. Patients with an incidentally discovered adrenal mass;
 - v. Patients with a predisposition to hereditary causes (e.g., multiple endocrine neoplasia 2A or 2B, von Recklinghausen 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 magnetic

resonance imaging unavailable), and/or iodine I-131 meta-iodobenzylguanidine (MIBG) scintigraphy (Grade C for each modality).

IX. Role of echocardiography

Guidelines.

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).

Hypertension Canada's 2018 Guidelines

Prevention and Treatment of Hypertension in Adults

Hereafter, all BP treatment thresholds and targets refer to non-AOBP measurements performed in office (see Supplemental Table S2, section on *Recommended Technique for Automated Office Blood Pressure [AOBP]*), because most of the supporting evidence is derived from studies using this BP measurement method. A summary of the potential factors that should be considered

when selecting specific drug therapy for individualized treatment is presented in Table 1. BP thresholds for initiation of treatment and BP treatment targets are summarized in Table 2 and Hypertension Canada's definition of high-risk patients are presented in Table 3.

I. Health behaviour management

Guidelines.

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 30-60 minutes of moderate intensity dynamic exercise (e.g., walking, jogging, cycling, or swimming) 4-7 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/m², and waist circumference <102 cm for men and <88 cm for women) is recommended for non-hypertensive individuals to prevent hypertension (Grade C) and for hypertensive patients to reduce BP (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 reduce BP in hypertensive adults, individuals should limit alcohol consumption to ≤ 2 drinks 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;⁵⁹⁻⁶² Supplemental Table S9) (Grade B).

E. Sodium intake

To prevent hypertension and reduce BP in hypertensive adults, consider reducing sodium intake towards 2000 mg (5 g of salt or 87 mmol 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 4), increase dietary potassium intake to reduce BP (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 used (Grade B).

II. Indications for drug therapy for adults with hypertension without compelling indications for specific agents

Guidelines.

1. Antihypertensive therapy should be prescribed for average DBP measurements of ≥ 100 mm Hg (Grade A) or average SBP measurements of ≥ 160 mm Hg (Grade A) in patients without macrovascular target organ damage or other cardiovascular risk factors.
2. Antihypertensive therapy should be strongly considered for average DPB readings ≥ 90 mm Hg (Grade A) or for average SBP readings ≥ 140 mm Hg (Grade B for 140-160 mm Hg; Grade A for >160 mm Hg) 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. Indications for drug therapy for adults with diastolic hypertension with or without systolic hypertension

Guidelines.

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),
 - b. a β -blocker (in patients younger than 60 years; Grade B),
 - c. an ACE inhibitor (in non-black patients; Grade B),
 - d. an ARB (Grade B), or
 - 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), ARB with a CCB (Grade B), or ACE inhibitor or ARB with a diuretic (Grade B).
 - iii. Hypokalemia should be avoided in patients treated with thiazide/thiazide-like diuretic monotherapy (Grade C).
2. Additional antihypertensive drugs should be used if target BP 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: ACE inhibitor, ARB or β -blocker (Grade B for the combination of thiazide/thiazide-like diuretic and a dihydropyridine CCB; Grade A for the combination of dihydropyridine CCB and ACE inhibitor; and Grade D for all other combinations). Caution should be

exercised in combining a non-dihydropyridine CCB and a β -blocker (Grade D). The combination of an ACE inhibitor and an ARB is not recommended (Grade A).

3. If BP is still not controlled with a combination of 2 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. α -Blockers are not recommended as first-line agents for uncomplicated hypertension (Grade A); β -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. Indications for drug therapy for adults with isolated systolic hypertension

Guidelines.

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 BP levels are not achieved with standard-dose monotherapy (Grade B). Add-on drugs should be chosen from first-line options (Grade D).

3. If BP is still not controlled with a combination of 2 or more first-line agents, or there are adverse effects, other classes of drugs (such as α -blockers, ACE inhibitors, centrally acting agents, or non-dihydropyridine CCBs) may be combined or substituted (Grade D).
4. Possible reasons for poor response to therapy (Supplemental Table S10) should be considered (Grade D).
5. α -Blockers are not recommended as first-line agents for uncomplicated isolated systolic hypertension (Grade A); and β -blockers are not recommended as first-line therapy for isolated systolic hypertension in patients aged 60 years or older (Grade A). However, both agents may be used in patients with certain comorbid conditions or in combination therapy.

IV. Global vascular protection therapy for adults with hypertension without compelling indications for specific agents

Guidelines.

1. Statin therapy is recommended in hypertensive patients with 3 or more cardiovascular risk factors as defined in Supplemental Table S11 (Grade A in patients >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 of age (Grade B). Caution should be exercised if BP 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 or older, with SBP levels ≥ 130 mm Hg, intensive management to target a SBP ≤ 120 mm Hg should be considered. Intensive management should be guided by AOBP measurements (see *Diagnosis and Assessment Guidelines*, Section I [Accurate measurement of BP], and Supplemental Table S2 [Recommended Technique for Automated Office BP]). Patient selection for intensive management is recommended and caution should be taken in certain high-risk groups (Table 5; Grade B).

V. Goals of therapy for adults with hypertension without compelling indications for specific agents

Guidelines.

1. The SBP treatment goal is a pressure level of <140 mm Hg (Grade C). The DBP treatment goal is a pressure level of <90 mm Hg (Grade A).

VI. Treatment of hypertension in association with ischemic heart disease

A. Guidelines for hypertensive patients with coronary artery disease (CAD)

Guidelines.

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 hypertensive 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 artery bypass surgery, either a β -blocker or CCB 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 DBP is ≤ 60 mm Hg because of concerns that myocardial ischemia may be exacerbated, especially in patients with left ventricular hypertrophy (Grade D).

B. Guidelines for patients with hypertension who have had a recent myocardial infarction

Guidelines.

1. Initial therapy should include both a β -blocker as well as 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 myocardial infarction when β -blockers are contraindicated or not effective. Nondihydropyridine CCBs should not be used when

there is heart failure, evidenced by pulmonary congestion on examination or radiography (Grade D).

VII. Treatment of hypertension in association with heart failure

Background. The new 2018 guideline focuses on the use of a combined ARB-neprilysin-inhibition (ARNI) in hypertensive patients with symptomatic heart failure with a reduced ejection fraction (HFrEF) and aligns closely with the Canadian Cardiovascular Society's recent heart failure update.⁶³ The Prospective Comparison of ARNI with ACEI to Determine Impact on Global Mortality and Morbidity in Heart Failure Trial (PARADIGM-HF) RCT,⁶⁴ included 8,442 participants with symptomatic heart failure and a left ventricular ejection fraction of less than 40% on standard evidence-based therapies. Participants were randomized to receive either sacubitril-valsartan 200 mg bid (ARNI) or enalapril 10 mg bid. Treatment with sacubitril-valsartan resulted in a reduction in the primary outcome (combination of cardiovascular death or hospitalization for heart failure) (hazard ratio [HR], 0.80; 95% CI, 0.73-0.87; $p < 0.001$) as well as all-cause mortality (HR, 0.84; 95% CI 0.76-0.93; $p < 0.001$) after a mean follow-up of 27 months.⁶⁴ Furthermore, ARNI was associated with a lower rate of progression of heart failure among surviving participants.⁶⁵ The benefit of ARNI over enalapril was consistent in participants both with and without a history of hypertension, and in participants with baseline SBP both above and below the median value of 122 mm Hg.⁶⁴

Prior to use of an ARNI, as with all renin–angiotensin–aldosterone system inhibitor treatments, patient safety must be assessed. Specifically, we recommend careful patient selection (Table 4) and monitoring patients for excessive hypotension, changes in renal function and potassium values (i.e., hyperkalemia). At present, the combination of valsartan and

sacubitril is the only licensed ARNI product in Canada for the indication of heart failure and does not have a Health Canada indication for the treatment of hypertension.⁶⁶

Guidelines.

1. In patients with systolic dysfunction (ejection fraction <40%), ACE inhibitors (Grade A) and β -blockers (Grade A) are recommended for initial therapy. Aldosterone antagonists (mineralocorticoid receptor antagonists) may be combined for patients with a recent cardiovascular hospitalization, acute myocardial infarction, elevated B-type natriuretic peptide or N-terminal pro-B-type natriuretic peptide level, or New York Heart Association Class II-IV symptoms (Grade A). Careful monitoring for hyperkalemia is recommended when combining 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 BP 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 BP is not controlled, an ARB may be combined with an ACE inhibitor and other antihypertensive drug treatment (Grade A). Careful monitoring should be used if combining an ACE inhibitor and an ARB because of potential adverse

effects such as hypotension, hyperkalemia, and worsening renal function (Grade C).

Additional therapies may also include dihydropyridine CCBs (Grade C).

5. An Angiotensin Receptor-Neprilysin Inhibitor combination should be used in place of an ACE inhibitor or ARB for patients with HFrEF (EF <40%) who remain symptomatic despite treatment with appropriate dose of guideline-directed HF therapy (usually a β -blocker, an ACE-Inhibitor or ARB, and where appropriate, a mineralocorticoid antagonist) (Grade A; **new guideline**). Eligible patients must have a serum potassium <5.2 mmol/L, an eGFR greater or equal to 30 mL/min/1.73m² and close surveillance of serum potassium and creatinine (Grade A; **new guideline**).

VIII. Treatment of hypertension in association with left ventricular hypertrophy

Guidelines.

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.

IX. Treatment of hypertension in association with stroke

Background. The revised guideline specifies target BP values prior to tissue plasminogen activator (tPA) therapy, i.e., alteplase, and for the subsequent 24 hours. It is well-established that patients with ischemic stroke who receive alteplase demonstrate better functional outcomes, as corroborated by a 2016 meta-analysis.⁶⁷ Optimal BP management algorithms in the context of

alteplase have not been specifically evaluated through definitive clinical trials, however there is an increased risk of intracerebral hemorrhage (ICH) with BP >185/110 and BP lowering at this threshold has been encouraged in adults that are candidates for thrombolysis. This year, a target BP of <185/110 prior to alteplase administration and to target of <180/105 in the subsequent 24 hours is recommended. These treatment thresholds and targets have not been explicitly evaluated in the context of an RCT, however these thresholds and targets were used in the National Institute of Neurological Disorders and Stroke (NINDS) rt-PA Stroke Study which demonstrated the effectiveness of alteplase in acute stroke.⁶⁸ It should be noted that not all alteplase stroke trials have used these BP levels during thrombolysis and have not demonstrated a significantly higher rate of ICH. However, given that ICH is a low frequency but concerning outcome, the Hypertension Canada Stroke Subgroup recommends using the NINDS protocol to ensure safe and optimal use of alteplase in the setting of acute stroke.

Guidelines.

A. BP management in acute ischemic stroke (onset to 72 hours)

1. For patients with ischemic stroke not eligible for thrombolytic therapy, hypertension in the setting of acute ischemic stroke or transient ischemic attack should not be routinely treated (Grade D; **revised wording**). Extreme BP increases (e.g., SBP >220 mm Hg or DBP >120 mm Hg) may be treated to reduce the BP by approximately 15% (Grade D), and not more than 25%, over the first 24 hours with gradual reduction thereafter (Grade D). Avoid excessive lowering of BP because this might exacerbate existing ischemia or might induce ischemia, particularly in the setting of intracranial or extracranial arterial

occlusion (Grade D; **revised wording**). Pharmacological agents and routes of

administration should be chosen to avoid precipitous decreases in BP (Grade D).

2. For patients with ischemic stroke who are eligible for thrombolytic therapy, very high BP ($>185/110$ mm Hg) should be treated concurrently with thrombolysis to reduce the risk of hemorrhagic transformation (Grade B; **revised guideline**). Blood pressure should be lowered to below 185/110 mm Hg prior to tPA therapy and to below 180/105 for the next 24 hours (Grade D; **revised guideline**).

B. BP management after acute ischemic 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. After the acute phase of a stroke, BP-lowering treatment is recommended to a target of consistently $<140/90$ mm Hg (Grade C).
3. Treatment with an ACE inhibitor and thiazide/thiazide-like 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. BP 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 mm Hg should be avoided due to an absence of benefit (relative to a target of <180 mm Hg) (Grade A) and some suggestion of harm.

X. Treatment of hypertension in association with non-diabetic chronic kidney disease

Guidelines.

1. For patients with nondiabetic chronic kidney disease, target BP is <140/90 mm Hg (Grade B).
2. For patients with hypertension and proteinuric chronic kidney disease (urinary protein >500 mg per 24 hours or albumin to creatinine ratio >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 might be needed to reach target BP levels (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**Guidelines.**

1. Patients with hypertension attributable to atherosclerotic renal artery stenosis 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).
4. In patients with hypertension attributable to FMD-related renal artery stenosis, revascularization should be considered (Grade D).
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 amenable to angioplasty, stenosis associated with complex aneurysm, and restenosis despite two unsuccessful attempts of angioplasty (Grade D).

XII. Treatment of hypertension in association with diabetes mellitus

Guidelines.

1. Persons with diabetes mellitus should be treated to attain SBP of <130 mm Hg (Grade C) and DBP of <80 mm Hg (Grade A) (these target BP levels are the same as the BP treatment thresholds) (**revised wording**).
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),

ARBs (Grade B), dihydropyridine CCBs (Grade A), and thiazide/thiazide-like diuretics (Grade A).

4. If target BP levels 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

Guidelines.

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

Guidelines.

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

Hypertension Canada's 2018 Guidelines. Diagnosis and Assessment of Hypertension in Children

Background. There are no changes to these guidelines³⁵ for 2018.

I. Accurate measurement of BP in children

Guidelines.

1. BP should be measured regularly in children 3 years of age and older by a health care professional using standardized pediatric techniques (Table 6) (Grade D).
2. BP may be measured with a mercury sphygmomanometer, aneroid sphygmomanometer, or oscillometric device (Grade D). Abnormal oscillometric values should be confirmed with auscultation (Grade C).
3. BP varies with age, sex and height in children and, therefore, BP values should be compared to norms for age, sex, and height (Table 7) (Grade D).

II. CRITERIA FOR DIAGNOSIS OF HYPERTENSION IN CHILDREN

Guidelines.

1. Using office BP measurements, children can be diagnosed as hypertensive if SBP or DBP is ≥ 95 th percentile for age, sex, and height, measured on at least three separate occasions (Grade C).
2. If the BP is ≥ 95 th percentile, BP should be staged. Stage 1 is defined by BP between 95th percentile and 99th percentile plus 5 mm Hg. Stage 2 is defined by BP > 99 th percentile plus 5 mm Hg (Grade D).
 - i. If BP is Stage 1, BP measurements should be repeated on two more occasions within 1 month; if hypertension is confirmed, evaluation (as described in section IV – *Routine Laboratory Tests for the Investigation of Children with Hypertension*)³⁵ and/or appropriate referral should be initiated within 1 month, or both (Grade D).

- ii. If BP is Stage 2, prompt referral should be made for evaluation and therapy (Grade C).
3. All children with suspected or confirmed hypertension should undergo a hypertension focused history and physical evaluation (Table 8) (Grade C).

III. ASSESSMENT OF OVERALL CARDIOVASCULAR RISK IN HYPERTENSIVE CHILDREN

Guidelines.

1. Cardiovascular risk factors should be assessed in hypertensive children (Grade C).

IV. ROUTINE LABORATORY TESTS FOR THE INVESTIGATION OF CHILDREN WITH HYPERTENSION

Guidelines.

1. Routine tests that should be performed for the investigation of all children with hypertension include:
 - i. Blood chemistry (sodium, potassium, chloride, total CO₂, and creatinine) (Grade D);
 - ii. Urinalysis (Grade D);
 - iii. Renal ultrasound (Grade D);
2. Routine laboratory tests that should be performed for the assessment of cardiovascular risk in all children with hypertension include the following:

- i. Fasting blood glucose (Grade C);
 - ii. Serum total cholesterol and high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, and triglycerides (Grade C).
3. Routine tests that should be performed for the assessment of target organ damage in all children with hypertension include:
 - i. Echocardiogram (Grade C);
 - ii. Retinal examination (Grade C);
 - iii. Albumin/creatinine ratio (first morning) (Grade D)

V. AMBULATORY BP MEASUREMENT IN CHILDREN

Guidelines.

1. For children with elevated office BP readings, ambulatory BP monitoring should be guided by a physician with expertise in pediatric hypertension; ambulatory BP monitoring is useful to classify BP (Table 9) (Grade C).
2. Physicians should use only ambulatory BP monitoring devices that have been validated independently in children using established protocols. A standard approach to obtaining ambulatory BP monitoring readings should be used (Supplemental Table S13) (Grade D).
3. Ambulatory BP monitoring levels should be interpreted with appropriate pediatric normative data for children 5 years of age or older or height of ≥ 120 cm (Grade D).

VI. ROLE OF ECHOCARDIOGRAPHY

Guidelines.

2. Routine echocardiographic evaluation in children with confirmed hypertension is recommended (Grade D).
3. The echocardiographic assessment should include measurements of left ventricular mass index, systolic and diastolic left ventricular function, and evaluation of the aortic arch (Grade D).

Hypertension Canada's 2018 Guidelines. Prevention and Treatment of Hypertension in Children

There are no changes to these guidelines³⁶ for 2018.

I. HEALTH BEHAVIOUR MANAGEMENT**Guidelines.**

1. Height and weight should be measured and body mass index calculated for all children at routine health visits (Grade D).
2. Achieving a healthy body weight (body mass index percentile <85%) is recommended for nonhypertensive individuals to prevent hypertension and for hypertensive children to reduce BP (Grade C).
3. A comprehensive approach should include dietary education and increased physical activity (Grade C).

II. INDICATIONS FOR DRUG THERAPY FOR CHILDREN WITH HYPERTENSION

Guidelines.

1. Pharmacological therapy should be initiated when patients have:
 - i. Symptomatic hypertension (Grade D);
 - ii. Hypertensive target organ damage (Grade C);
 - iii. Stage 2 hypertension (Grade D);
 - iv. BP $\geq$ 90th percentile associated with diabetes mellitus type 1 or 2, chronic kidney disease or heart failure (Grade D);
 - v. Stage 1 hypertension without target organ damage that persists ($\geq$ 6 months) despite a trial of nonpharmacologic therapy (Grade D).
2. In children with proven secondary hypertension, specific treatment of the underlying disease must be initiated by an expert in pediatric hypertension (Grade D).

II. CHOICE OF DRUG THERAPY FOR CHILDREN WITH HYPERTENSION**A. Recommendations for individuals with systolic and/or diastolic hypertension****Guidelines.**

1. Initial therapy should be monotherapy.
 - i. Recommended monotherapy choices are:
 - a. An ACE inhibitor (Grade C);
 - b. An ARB (Grade C); or
 - c. A long-acting dihydropyridine CCB (Grade D).

- ii. An alternate option is a β -blocker (Grade D) although they are less preferable due to the side effect profile in children.
 - iii. If there are adverse effects, another drug from this group should be substituted.
2. If BP goals are not achieved with standard-dose monotherapy for ≥ 6 months, children should be referred to an expert in pediatric hypertension (Grade D).
 3. ACE inhibitors (Grade C) and ARBs (Grade D) are not recommended as first-line agents in black patients and β -blockers are not recommended as first-line agents in children with asthma, diabetes (type 1 or type 2) and high-performance athletes (Grade D).

IV. GOALS OF THERAPY FOR CHILDREN WITH HYPERTENSION

Guidelines.

1. The treatment goal is office BP (systolic and diastolic) <95th percentile (Grade D). The goal for ambulatory BP monitoring is BP (systolic and diastolic) <95th percentile (Grade D).
2. For patients with risk factors or target organ damage the goal is BP (systolic and diastolic) <90th percentile (Grade D).

Summary/Future Directions

These guidelines are a summary of the best available evidence to guide clinicians in the measurement, diagnosis, and treatment of hypertension in adults and children (key similarities and differences are summarized in Table 10). The next update for Hypertension Canada's Guideline is planned for 2020 to allow for optimal dissemination of the 2018 Guidelines though

literature searches will be continued on an annual basis. New evidence identified as being “practice changing” for clinicians (i.e., associated with a strong reduction in cardiovascular events or mortality; or a substantial reduction in resource utilization) will be brought forward for an interim update to ensure timely implementation of important evidence. Priorities identified for the development of new guidelines in 2020 include, among others, the management of resistant hypertension (i.e., uncontrolled BP despite the use of ≥ 3 antihypertensive agents of different classes including a diuretic, or controlled BP with ≥ 4 agents),⁶⁹⁻⁷² as well as updates on BP measurement methods and follow-up, and diagnosis of masked hypertension.

Implementation

Implementation and dissemination of the guidelines is a priority for Hypertension Canada. Many strategies are employed to reach a variety of providers who care for patients with hypertension. Efforts include knowledge exchange forums, targeted educational materials for primary care providers and patients, “Train the Trainer” teaching sessions, as well as slide kits and summary documents which are freely available online in French and English (www.hypertension.ca). Hypertension Canada receives feedback from end-users to continually improve guideline processes and content. The Research and Evaluation Committee conducts hypertension surveillance studies and reviews existing Canadian health surveys to identify gaps between current and best practices.

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Disclosures

Please see Supplemental Appendix S2 for a complete list of disclosures.

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Table 1. Considerations in the individualization of pharmacological therapy in adults

	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), β 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: α blockers, β 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	ACE inhibitors or ARBs	Addition of a dihydropyridine CCB is preferred over a thiazide/thiazide-like diuretic.	A loop diuretic could be considered in hypertensive chronic kidney disease patients with extracellular fluid volume overload.

disease or additional cardiovascular risk factors			
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
Cardiovascular disease			
Coronary artery disease	ACE inhibitors or ARBs; β 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 mm Hg, especially in patients with LVH.
Recent myocardial infarction	β blockers and ACE inhibitors (ARBs if ACE inhibitor intolerant)	Long-acting CCBs if β 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 β 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. A combined ARB/neprilysin-	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.

		inhibitor is recommended (in place of an ACE inhibitor or ARB) in symptomatic patients with hypertension and HFrEF on standard guideline-based therapies.	
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.
Non-diabetic chronic kidney disease			
Non-diabetic 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 β 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; HFrEF Heart failure with reduced ejection fraction $< 40\%$; NYHA New York Heart Association; TIA Transient ischemic attack; LVH Left ventricular hypertrophy; SPC Single pill combination.

Table 2. Blood pressure thresholds for initiation of antihypertensive and treatment targets in adults

Patient Population	BP threshold (mm Hg) for initiation of antihypertensive therapy	BP target (mm Hg) for treatment
Low-risk (No target organ damage or cardiovascular risk factors)	SBP $\geq$ 160 (Grade A) DBP $\geq$ 100 (Grade A)	SBP < 140 (Grade A) DBP < 90 (Grade A)
High-risk* of cardiovascular disease	SBP $\geq$ 130 (Grade B)	SBP < 120 (Grade B)
Diabetes mellitus	SBP $\geq$ 130 (Grade C) DBP $\geq$ 80 (Grade A)	SBP < 130 (Grade C) DBP < 80 (Grade A)
All others	SBP $\geq$ 140 (Grade C) DBP $\geq$ 90 (Grade A)	SBP < 140 (Grade A) DBP < 90 (Grade A)

*see table 3; based upon automated office blood pressure measurement

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

Table 3. Clinical indications defining high risk adult 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/1.73m²)

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 **M**odification of **D**iet in **R**enal **D**isease (MDRD) equation

†Framingham Risk Score⁷³

g/d, grams per day

Table 4. 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 $<45 \text{ mL/min/1.73m}^2$)
- Baseline serum potassium $>4.5 \text{ mmol/L}$

Table 5. Generalizability of intensive blood pressure lowering in adults: cautions and contraindications

Limited or No Evidence

Heart failure (left ventricular ejection fraction <35%) or recent myocardial infarction (within last 3 months)

Indication for, but not currently receiving, a β -blocker

Institutionalized elderly

Inconclusive evidence

Diabetes Mellitus

Prior stroke

eGFR < 20 ml/min/1.73 m²

Contraindications

Patient unwilling or unable to adhere to multiple medications

Standing SBP <110 mm Hg

Inability to measure SBP accurately

Known secondary cause(s) of hypertension

eGFR, estimated glomerular filtration rate; SBP, systolic blood pressure

Table 6. Standard approach for BP measurement in children (Grade D)

1. Children who will undergo BP measurement should avoid stimulant medications prior to evaluation. At the time of evaluation, the child should be seated in a quiet room for 5 minutes with back supported prior to the measurement of blood pressure.
2. The right arm is the preferred location for BP measurement for comparison to normative data due to the possibility of coarctation of the aorta, which may result in an erroneously low BP measurement being obtained in the left arm.
3. A cuff size with a bladder width that is at least 40% of the arm circumference and the cuff bladder length should cover 80-100% of the circumference of the arm. The arm should be bare and supported with the BP cuff at heart level. In order to obtain accurate measurements in children a range of pediatric and adult cuff sizes should be available.
4. The pressure should be increased rapidly to 30 mmHg above the level at which the radial pulse is extinguished.
5. The stethoscope should be placed below the bottom edge of the cuff and above the antecubital fossa. The bell or diaphragm of the stethoscope should be held gently and steadily over the brachial artery.
6. The control valve should be opened so that the rate of deflation of the cuff is approximately 2 mmHg per heartbeat.
7. 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)) should be recorded. In some children, Korotkoff sounds can be heard to 0 mmHg. If Korotkoff sounds persist as the level approaches 0 mmHg, then the point of muffling of the sound is used (phase IV Korotkoff) to indicate the diastolic pressure.
8. The BP should be recorded to the closest 2 mm Hg on the manometer (or 1 mm Hg on electronic devices).

Table 7. Determining normative data for BP values in children (Grade D)

1. The BP Tables utilize growth parameters as defined by the Centers for Disease Control and Prevention (CDC) growth charts.
2. The normative BP data obtained with auscultatory method includes the US National Health and Nutrition Examination Survey from 1999-2000. Normative BP data for oscillometric measurements are now available.
3. To determine BP percentile, use the standard CDC height charts to determine the height percentile.
4. Measure the child's blood pressure. Use the appropriate gender table. Locate the child's age on the left side of the table and follow the age row horizontally across the table to the intersection of the line for the height percentile as shown in the vertical column.
5. The 50th, 90th, 95th, and 99th percentiles are defined for systolic and diastolic blood pressure based on gender, age and height.

Table 8. History and physical examination of children (Grade C)

1. Medical History: Symptoms ▫ Of hypertension ▫ Of an underlying disorder* Past Medical History ▫ For underlying cause of hypertension*, including neonatal history Identify other cardiovascular risk factors including inactivity, smoking, and dietary factors Family History
2. Patient physical examination: Height, weight, and body mass index Vital signs including upper and lower limb blood pressures Evaluation for signs of end-organ damage Fundi, cardiovascular and neurologic systems Evaluation for underlying cause of hypertension*

*Systems to review include renal, cardiovascular, endocrine, and neurologic, as well as medications/drugs and sleep disorders

Table 9. Suggested schema to classify blood pressure in children

Classification	Office BP	Mean ambulatory SBP or DBP during wake or sleep period, or both	SBP or DBP load (%)
White coat hypertension	$\geq 95^{\text{th}}$ percentile	$< 95^{\text{th}}$ percentile	< 25
Masked hypertension	$< 95^{\text{th}}$ percentile	$\geq 95^{\text{th}}$ percentile	≥ 25
Ambulatory hypertension	$\geq 95^{\text{th}}$ percentile	$\geq 95^{\text{th}}$ percentile	25-50
Severe ambulatory hypertension	$\geq 95^{\text{th}}$ percentile	$\geq 95^{\text{th}}$ percentile	> 50

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

Table 10. Comparison of Hypertension Canada's 2018 pediatric and adult guidelines for blood pressure measurement, hypertension diagnosis, assessment, and treatment

	Pediatric Guidelines	Adult Guidelines
Measurement	- Use standardized pediatric techniques and validated equipment (Table 6) - Oscillometric device or auscultation method for initial measurement - Elevated oscillometric values should be confirmed with auscultation - BP values should be compared to norms based on age, sex, and height (Table 7) - ABPM should be guided by experts in pediatric hypertension	- Use standardized measurement techniques and validated equipment - Oscillometric devices are preferred over auscultation. Automated office blood pressure is the preferred method of performing in-office BP measurement. - Elevated office BP measurements should be confirmed with out-of-office BP measurements including ABPM (preferable) or home BP monitoring where available
Diagnosis	- Diagnose by BP percentile based on norms for age, sex, and height and: - level of BP elevation - number of visits/ measurements - See Diagnosis and Assessment Section II	- Diagnose by absolute BP value according to: - level of BP elevation - number of visits/ measurements - method of BP measurement - See Figure 1
Assessment	- History and physical examination - Cardiovascular risk factor assessment - Routine investigations for: - secondary causes of hypertension - cardiovascular risk factors - target organ damage	- History and physical examination - Cardiovascular risk factor assessment - Routine investigations for: - secondary causes of hypertension - cardiovascular risk factors - target organ damage
Management	- Dietary education and increased physical activity - Initial pharmacologic therapy for primary hypertension is monotherapy with choice of ACE inhibitor, ARB, or CCB - If BP is not controlled with monotherapy, refer to an expert in pediatric hypertension	- Dietary education, increased physical activity, alcohol limitation and stress management - *Initial pharmacologic therapy with either thiazide/thiazide-like diuretic, β-blocker, ACE inhibitor, ARB, or CCB monotherapy <u>or</u> single pill combination with ACE inhibitor + CCB, ARB + CCB, or ACE inhibitor/ARB + diuretic

ABPM: ambulatory blood pressure monitoring, ACE: angiotensin converting enzyme, ARB: angiotensin receptor blocker, BP: blood pressure, CCB: calcium channel blocker

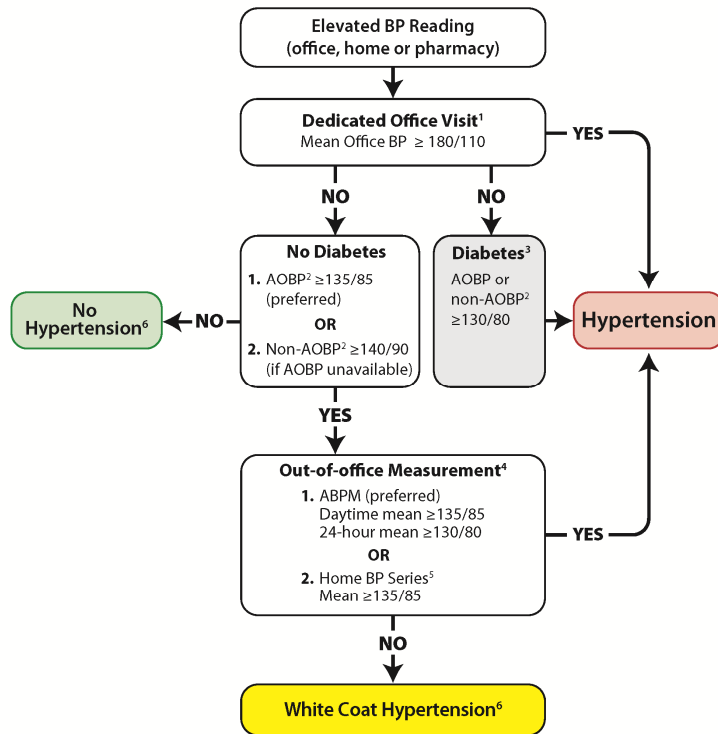
* For adults with diastolic with or without systolic hypertension, without compelling indications for specific agents

FIGURE LEGEND

Figure 1. Hypertension diagnostic algorithm for adults

ACCEPTED MANUSCRIPT

Hypertension Diagnostic Algorithm for Adults

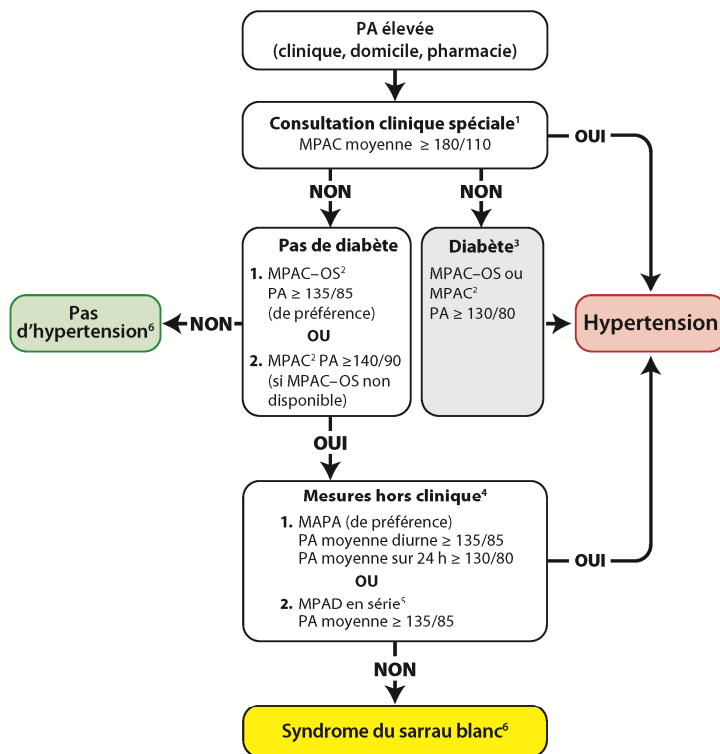


Notes:

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

Algorithme de diagnostic de l'hypertension pour adultes



Notes:

1. Si l'on utilise la MAPC OS, il faut inscrire la moyenne calculée par l'appareil, affichée à l'écran. Si l'on utilise la MPAC (voir note 2), il faut prendre au moins trois mesures, rejeter la première et faire la moyenne des autres. Il faudrait aussi procéder à une anamnèse et à un examen physique, en plus de demander des examens complémentaires.
2. **MPAC-OS** : mesure de la pression artérielle en clinique – oscillométrique en série; elle s'effectue en laissant le patient seul dans un endroit retiré.
MPAC : mesure de la pression artérielle en clinique. Mesurée à l'aide d'un appareil électronique de bras par le professionnel de la santé, dans la salle d'examen.
3. Les seuils de diagnostic de la PA mesurée selon la MPAC OS, le MAPA ou la MPAD chez les diabétiques ne sont pas encore établis (et pourraient être inférieurs à 130/80 mm Hg).
4. On peut procéder à des mesures de la PA en clinique, en série, réparties sur 3 à 5 consultations si l'on ne peut avoir recours au MAPA ou à la MPAD.
5. Pour la MPAD en série, il faut prendre 2 mesures tous les matins et tous les soirs pendant 7 jours (28 au total), rejeter celles de la première journée et faire la moyenne des mesures des 6 autres journées.
6. Il est recommandé de procéder à des mesures annuelles de la PA afin de détecter une évolution vers l'hypertension.

MAPA : monitoring ambulatoire de la pression artérielle

MPAC : mesure de la pression artérielle en clinique

MPAC-OS : mesure de la pression artérielle en clinique – oscillométrique en série

MPAD : mesure de la pression artérielle à domicile