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Hypertension Canada's 2017 Guidelines for Diagnosis, Risk Assessment, Prevention, and Treatment of Hypertension in Adults

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BRIEF SUMMARY

For 2017, new guidelines include: Treatment should be considered for elevated systolic blood pressure, irrespective of age or frailty; single pill combinations are also recommended as an initial treatment option; longer-acting diuretics are preferred; use caution if lowering diastolic blood pressure ≤60 mmHg in patients with ischemic heart disease and left ventricular hypertrophy; immediately after a hemorrhagic stroke, systolic blood pressure lowering <140 mmHg is not recommended; and guidance is provided for managing fibromuscular dysplasia.

ABSTRACT

Hypertension Canada provides annually-updated, evidence-based guidelines for the diagnosis, assessment, prevention, and treatment of hypertension. This year, we introduce 10 new guidelines. Three previous guidelines have been revised and 5 have been removed. Previous age and frailty distinctions have been removed as considerations for when to initiate antihypertensive therapy. In the presence of macrovascular target organ damage, or in those with independent cardiovascular risk factors, antihypertensive therapy should be considered for all individuals with elevated average systolic blood pressure readings ≥140 mmHg. For individuals with diastolic hypertension (with or without systolic hypertension), fixed-dose single pill combinations are now recommended as an initial treatment option. Preference is given to pills containing an angiotensin converting enzyme inhibitor or angiotensin receptor blocker in combination with either a calcium channel blocker or diuretic. Whenever a diuretic is selected as monotherapy, longer-acting agents are preferred. In patients with established ischemic heart disease, caution should be exercised in lowering diastolic pressure ≤60 mmHg, especially in the presence of left ventricular hypertrophy. Following a hemorrhagic stroke, in the first 24 hours, systolic blood pressure lowering to <140 mmHg is not recommended. Finally, guidance is now provided for screening, initial diagnosis, assessment, and treatment of renovascular hypertension arising from fibromuscular dysplasia. The specific evidence and rationale underlying each of these guidelines are discussed.

KEY WORDS: hypertension, high blood pressure, guidelines, recommendations, diagnostic algorithm, electronic oscillometric devices, out-of-office blood pressure measurements,

ambulatory blood pressure monitoring, home blood pressure monitoring, automated blood pressure, lipid profile, tobacco, smoking cessation, renovascular disease, renal artery stenosis, primary aldosteronism, pheochromocytoma.

INTRODUCTION

Hypertension affects nearly a quarter of Canadian adults and represents a major risk factor for cardiovascular morbidity, chronic kidney disease, and death; however, it often remains clinically silent until complications arise.[1-3] Worldwide, high blood pressure (BP) affects over 40% of adults over the age of 25 years, and is the leading global risk factor for death or disability.[4, 5]

With the goal of improving the prevention, detection, assessment, and management of hypertension, Hypertension Canada (formerly the Canadian Hypertension Education Program [or CHEP]) has been producing annually-updated, evidence-based guidelines for health care providers since 1999. (The rebranding of Hypertension Canada was in response to feedback and marketing research from primary care stakeholders). We present herein updated guidelines for 2017, along with discussion of the supporting evidence. Further details along with supporting references pertaining to established guidelines are available in prior publications,[6-32] and online (guidelines.hypertension.ca). Pediatric-specific guidelines are published separately.

Our guidelines are intended to provide a framework but should not replace clinical judgment. Practitioners are advised to consider patient preferences, values, and clinical factors when determining how to best apply these guidelines to the bedside.

Methods

The Hypertension Canada Guidelines Committee (HCGC) is a multidisciplinary panel of both content and methodological experts comprised of a Chair, a Central Review Committee with a designated Chair, and 15 subgroups. Each subgroup addresses a distinct content area in

the field of hypertension (see Supplementary Appendix A for the current membership list). All HCGC members are volunteers.

Systematic literature searches to August 2016 were performed by a librarian from the Cochrane Collaboration in MEDLINE/PubMed using text words and MeSH headings. Details of search strategies and retrieved articles are available upon request. Randomized controlled trials and systematic reviews of randomized controlled trials were reviewed for treatment guidelines, while cross-sectional and cohort studies were reviewed for evidence related to diagnosis and prognosis.

Each subgroup examined the search results pertinent to its content area. Studies assessing relevant outcomes were selected for further review. Cardiovascular morbidity and mortality as well as total mortality outcomes were prioritized for pharmacotherapy studies. For health behaviour guidelines, BP was considered an acceptable surrogate. Similarly, progressive renal impairment was an acceptable surrogate for guidelines relevant to chronic kidney disease. Study characteristics and study quality were assessed using pre-specified, standardized algorithms developed by Hypertension Canada for the critical appraisal of randomized controlled trials and observational studies.[33]

Guidelines were individually graded according to the supporting evidence. All guidelines, regardless of grading, are felt to have benefits that strongly outweigh risks. In this sense, all of Hypertension Canada's guidelines are 'strong' in nature (i.e., the HCGC refrains from making 'weak' guidelines). For pharmacotherapy guidelines, as a general rule, Hypertension Canada considers evidence evaluating specific agents to be generalizable to a 'class effect' unless otherwise stated.

Expert subgroup members were responsible for reviewing annual search results and, if indicated, drafting new guidelines or revising existing guidelines. An independent Central Review Committee consisting of methodological experts with no industry affiliations independently reviewed, graded, and refined proposed guidelines, which were then presented at a consensus conference of the HCGC in Montreal on October 19, 2016.

All guidelines were finalized and submitted electronically to all 81 voting members of the HCGC for approval. Members with potential conflicts of interest recused themselves from voting on specific guidelines (a list of conflicts is available as Supplementary Appendix B). Guidelines receiving over 70% approval were passed. The Hypertension Canada Guidelines process is in accordance with the AGREE2 guidelines (guidelines.hypertension.ca/about/overview-process),[34] and has been externally reviewed.

Hypertension Canada's 2017 Guidelines: Diagnosis and Assessment of Hypertension

I. Accurate measurement of BP

Background. There are no changes to these guidelines for 2017.

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 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 mmHg or 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 guidelines for follow-up

Background. There are no changes to these guidelines for 2017. A hypertension diagnostic algorithm is shown in Figure 1.

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 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, 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 mmHg SBP and/or ≥90 mmHg DBP 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 SBP or ≥90 mmHg 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).

III. Home BP measurement

Background. There are no changes to these guidelines for 2017. 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 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 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

Background. There are no changes to these guidelines for 2017. 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 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 cardiovascular events.

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

Background. There are no changes to these guidelines for 2017.

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).
    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. There are no changes to these guidelines for 2017. Examples of risk calculators include www.myhealthcheckup.com and www.score-canada.ca.

Guidelines.

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

Background. Despite the lack of high-quality evidence, the HCGC deemed it important to provide guidance for the diagnosis of renal FMD. Affecting up to 4% of adults,[35-40] FMD is an idiopathic condition, characterized by segmental, non-atherosclerotic narrowing of small and medium-sized arteries, which commonly affects renal blood flow.[41] There is a marked female-to-

male preponderance of 9:1, more often affecting younger women.[41, 42] It is estimated that more than half of individuals with FMD have renal artery stenosis, one-third have cervicocranial involvement, while few are affected at other sites.[39, 43, 44] Hypertension is the most common manifestation, often requiring multiple drugs.[42] Headache, tinnitus, dizziness, neck pain, and cervical/abdominal bruits may also be present.[42] The diagnosis of FMD is based on diagnostic imaging with catheter-based angiography being the 'gold standard.' Non-invasive imaging modalities include captopril renal scan, duplex ultrasound, computed tomographic angiography and magnetic resonance angiography. Estimates of sensitivity and specificity vary widely and are generally derived from small studies.[38, 40, 44-48] Based on a consensus of expert opinion, we recommend either computed tomographic angiography or magnetic resonance angiography as the initial diagnostic test. If renal FMD is confirmed, patients should be screened for cervicocephalic and intracranial involvement, as these sites are also commonly affected.[42] Screening of other vascular sites should be guided by symptoms.

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 ≥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/1.73m^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 <30 years, especially in non-obese women;
    ii. Hypertension resistant to ≥3 drugs;
    iii. Significant (>1.5cm), 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; **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:

Background. There are no changes to these guidelines for 2017.

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 iii), 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 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 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

Background. There are no changes to these guidelines for 2017.

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 ≥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 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

Background. There are no changes to these guidelines for 2017.

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).

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Please note, hereafter, all treatment thresholds and targets refer to non-AOBP measurements performed in office (see Supplemental Table S2 [Recommended Technique for Office Blood Pressure Measurement (non-AOBP)]), as most of the supporting evidence is derived from studies using this method of BP measurement. Please refer to the *Diagnosis and Assessment Guidelines*, section II (*Criteria for Diagnosis of Hypertension and Guidelines for Follow-up*) for corresponding values using other measurement methods. A summary of the potential factors that should be considered when selecting specific drug therapy for individualized treatment is presented in Table 1.

I. Health behaviour management

Background. There are no changes to these guidelines for 2017.

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/m^2, 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 behavioral 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;[49-52] 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 2), 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

Background. Age and frailty distinctions have been removed from our guidelines for the treatment of uncomplicated hypertension. This revision is based on evidence suggesting that older individuals with hypertension benefit from BP reduction irrespective of baseline frailty.[53, 54] In those with a baseline SBP 140-160 mmHg, treatment reduces the rate of major adverse

cardiovascular events, myocardial infarction, stroke, and mortality, but may also increase the risk of renal dysfunction.[53-56] Caution should be exercised in elderly patients with orthostasis.

In a *post-hoc* analysis of the **Hy**pertension in the **V**ery **E**lderly **T**rial (HYVET), investigators examined the association between frailty and treatment outcomes in 2,656 individuals, aged ≥80 years, and with a baseline SBP ≥160 mmHg.[53] The benefits of BP reduction were similar irrespective of frailty for the outcomes of stroke, cardiovascular events, and mortality (P for interaction=0.52, 0.73, and 0.61, respectively). Similarly, a prespecified subgroup analysis of 2,636 adults ≥75 years of age without history of diabetes, stroke, or baseline orthostasis from the **S**ystolic Blood **Pr**essure **In**tervention **T**rial (SPRINT) showed that intensive treatment (SBP target <120 mmHg) compared to standard treatment (<140 mmHg) resulted in a significant reduction in major adverse cardiovascular events (hazard ratio [HR], 0.66; 95% confidence intervals [CI], 0.51-0.85) and mortality (HR, 0.67; 95% CI, 0.49 to 0.91) over 3.14 years with no detectable difference in outcome benefit with intensive treatment when examined according to baseline frailty.[54, 55] Rates of serious adverse events were not statistically different when examined according to frailty. However, there was a significant increase in renal dysfunction with intensive treatment for those without pre-existent kidney disease (HR, 3.14; 95% CI, 1.66 to 6.37). Individuals with limited life-expectancy (i.e., <1 year or <3 years, respectively), dementia, or those needing institutionalized care were ineligible for HYVET or SPRINT.[53, 54] Altogether, these findings are consistent with those from a large meta-analysis of 19 randomized controlled trials (n=44,989) showing that intensive BP reduction is just as beneficial for the reduction of major cardiovascular events in older adults (≥62 years) as it is in those who are younger.[56]

Guidelines.

1. Antihypertensive therapy should be prescribed for average DBP measurements of ≥100 mmHg (Grade A) or average SBP measurements of ≥160 mmHg (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 mmHg (Grade A) or for average SBP readings ≥140 mmHg (Grade B for 140-160 mmHg; Grade A for >160 mmHg; **revised guideline**) 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 and with or without systolic hypertension

Background. This year, we introduce a number of new and revised guidelines for the initial treatment of hypertension. Although both thiazide and thiazide-like diuretics remain initial treatment options, preference is now given to the longer-acting, thiazide-like diuretics (e.g., chlorthalidone and indapamide). A meta-analysis of 21 randomized controlled trials demonstrated that the use of thiazide-like diuretics resulted in an additional 12% risk reduction for cardiovascular events (p=0.049) and 21% risk reduction in heart failure (p=0.023) compared to thiazide diuretics, after adjusting for differences in BP reduction.[57] Compared to placebo, only thiazide-like diuretics reduced the risk of coronary events and all-cause mortality. In another meta-analysis of 14 randomized controlled trials, the use of indapamide or chlorthalidone resulted in greater SBP reduction compared to hydrochlorothiazide (-5.1 mmHg; 95% CI, -8.7 to -1.6 mmHg; and -3.6 mmHg; 95% CI, -7.3 to 0.0 mmHg, respectively) without any detectable

difference in adverse effects.[58] Consistent with these findings, a 12-week double-blind randomized controlled trial of 54 patients demonstrated a greater reduction in mean 24-hour BP compared to baseline with chlorthalidone and extended-release hydrochlorothiazide, but not with conventional, short-acting hydrochlorothiazide.[59] Collectively, evidence supports the use of longer-acting diuretics for reducing cardiovascular events and BP.

We recommend SPCs as an initial treatment option, based on a global body of evidence, demonstrating their effectiveness in reducing cardiovascular events,[60, 61] improving BP control,[60-64] promoting adherence,[65, 66] and reducing medication side effects.[67] The therapeutic efficacy of combination therapy is well established. A meta-analysis of 42 randomized trials testing the combined use of 2 drugs of different classes compared to doubling the dose of one drug showed a 5-fold greater reduction in BP with combination treatment compared to increasing the dose of one drug alone.[68] Further supporting evidence is derived from the **S**implified **T**reatment **I**ntervention to **C**ontrol **H**ypertension (STITCH) study, a cluster randomized trial of 45 family practices in Ontario.[62] A total of 2,111 patients with uncontrolled hypertension were assigned to initial fixed-dose combination therapy with an ACE inhibitor or ARB and diuretic vs. monotherapy with up-titration as appropriate. After 6 months, there was a larger reduction in BP (-5.2/-2.2 mmHg) and greater proportion of target BP control (64.7% vs. 52.7%; p=0.03) in those receiving initial fixed-dose combination therapy compared to a single agent. Consistent with these findings, observational data also suggest that initial combination treatment compared to monotherapy is associated with a lower likelihood of developing a cardiovascular event, shorter median time to achieve target BP control, and less healthcare utilization.[60, 61] Moreover, fixed-dose antihypertensive combinations (i.e., SPCs) are reasonable as first-line treatment as most

patients require two or even three antihypertensive agents to reach target BP control in practice.[55, 69-73]

When a SPC is selected, the combination of an ACE inhibitor with a CCB, ARB with a CCB, or ACE inhibitor or ARB with a diuretic is recommended. The most compelling evidence comes from the **A**voiding **C**ardiovascular Events through **Com**bination Therapy in **P**atients **Li**ving with **S**ystolic **H**ypertension (ACCOMPLISH) trial, which randomized 11,506 adults at high risk for cardiovascular disease to either a combination of benazepril plus amlodipine or benazepril plus hydrochlorothiazide.[63] A reduction in the composite of cardiovascular death and major adverse cardiovascular events was noted with benazepril plus amlodipine vs. benazepril plus hydrochlorothiazide (HR, 0.80; 95% CI, 0.72 to 0.90). More recently, the **H**eart **O**utcomes **P**revention **E**valuation (HOPE)-3 trial evaluated 12,705 individuals at intermediate-risk of cardiovascular disease and randomized them to receive a fixed-dose combination of candesartan and hydrochlorothiazide or placebo.[64] Although there were no significant differences in outcomes overall, there appeared to be benefit favoring fixed-dose combination therapy in the subgroup of patients with hypertension. For individuals with a baseline SBP >143.5 mmHg, treatment with candesartan and hydrochlorothiazide vs. placebo reduced the risk of the first co-primary outcome (a composite of cardiovascular death, nonfatal myocardial infarction, or nonfatal stroke; HR, 0.73; 95% CI, 0.56 to 0.94) and second co-primary outcome (a composite of the first co-primary outcome, plus resuscitated cardiac arrest, heart failure, or revascularization; HR, 0.76; 95% CI, 0.60 to 0.96). Finally, as discussed above, STITCH provides additional supporting evidence for the use of an ACE inhibitor with diuretic or an ARB with diuretic as initial therapy.[62]

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; **new guideline**),
    b. a β-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), 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; **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 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 C 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. Guidelines for individuals with isolated systolic hypertension

Background. There are no changes to these guidelines for 2017.

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 added 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 (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

Background. There are no changes to these guidelines for 2017.

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, 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 BP]). 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

Background. Consistent with the changes made to section II (Indications for drug therapy for adults with hypertension without compelling indications for specific agents), we have removed the previous guideline for different BP goals for the elderly. Evidence suggests that older patients with hypertension similarly benefit from intensive BP reduction as younger adults.[53-56]

Guidelines.

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

VI. Treatment of hypertension in association with ischemic heart disease

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

Background. *Post hoc* analyses of several large clinical trials in patients with coronary artery disease suggest the possible existence of a J-curve, whereby reducing BP below a specific nadir may be associated with an increased risk of coronary events.[30, 74-76] This may be of greatest concern in individuals with LVH because of increased myocardial demand and decreased coronary perfusion during diastole.

In a retrospective cohort of 92 patients with coronary artery disease, there was reduced coronary blood flow with increasing left ventricular mass, even after adjustment.[77] This association was present for all levels of DBP, but was most pronounced for those with a DBP <70 mmHg. These findings are consistent with and extend those from a systematic review of 8 studies (n=362), which reported an inverse association between coronary blood flow and left ventricular mass, especially in those with hypertension.[78]

Nevertheless, it should be acknowledged that for the majority of high-risk individuals, BP reduction is well-tolerated and beneficial. As such, while we advise exercising caution when lowering BP, antihypertensive therapy is still strongly recommended for individuals with hypertension who tolerate antihypertensive treatment, especially for patients with moderate or severely increased SBP.

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 mmHg because of concerns that myocardial ischemia may be exacerbated, especially in patients with left ventricular hypertrophy (LVH) (Grade D; **revised guideline**).

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

Background. There are no changes to these guidelines for 2017.

Guidelines.

1. Initial therapy should include both a β-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 myocardial infarction when β-blockers are contraindicated or not effective. Non-dihydropyridine 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. There are no changes to these guidelines for 2017.

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 added for patients with a recent cardiovascular hospitalization, acute myocardial infarction, elevated B-type natriuretic peptide or N-terminal (NT) pro-B-type natriuretic peptide level, or New York Heart Association Class II-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 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 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 because of 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

Background. BP is often elevated following intracerebral hemorrhage (ICH). In recent years, several trials have studied the impact of BP lowering in the context of ICH. The **Inte**nsive Blood Pressure **R**eduction in **A**cute **C**erebral Hemorrhage **T**rial (INTERACT)-2 enrolled 2,839 patients within 6 hours of spontaneous ICH, and compared the SBP targets of <140 mmHg vs. <180 mmHg.[79] Targets were applied within the first hour of presentation and maintained for 7 days. No statistical difference was observed between the two strategies for the primary outcome, a composite of death or stroke-related disability at 90 days (52.0% vs. 55.6% for intensive compared to standard treatment, respectively; odds ratio [OR], 0.87; 95% CI, 0.75 to 1.01). In the **A**ntihypertensive **T**reatment of **A**cute **C**erebral **H**emorrhage (ATACH)-2 trial, 1,000 patients presenting within 4.5 hours of spontaneous ICH were randomly assigned to SBP targets of 110 to 139 mmHg vs. 140 to 179 mmHg for the first 24 hours.[80] The primary outcome was the same as in INTERACT-2. There was no difference between the 2 treatment strategies for the main outcome, and the trial was terminated early because of futility. In addition, there was a trend towards more adverse events in the lower SBP target arm. Considered together, these 2 important trials demonstrate no measurable benefit to lowering SBP <140 mmHg in the acute period following spontaneous ICH. There is no trial evidence to delineate an appropriate SBP target, if any, above 140 mmHg. All trials to date have followed the convention in limiting SBP increases beyond 180 mmHg in their control arms.

Guidelines.

A. BP 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 transient ischemic attack should not be routinely undertaken (Grade D). Extreme BP increases (e.g., SBP >220 mmHg or DBP >120 mmHg) 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 arterial occlusion or extracranial carotid or vertebral artery occlusion (Grade D). Pharmacological agents and routes of administration should be chosen to avoid precipitous decreases in BP (Grade D).
2. For patients with ischemic stroke eligible for thrombolytic therapy, very high BP (>185/110 mmHg) should be treated concurrently in patients receiving thrombolytic therapy for acute ischemic stroke to reduce the risk of secondary intracranial hemorrhage (Grade B).

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 mmHg (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 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

Background. There are no changes to these guidelines for 2017.

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.

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

Background. There are no changes to these guidelines for 2017.

Guidelines.

1. For patients with nondiabetic 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 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 non-proteinuric chronic kidney disease (Grade B).

XI. Treatment of hypertension in association with renovascular disease

Background. Accompanying our guidelines for the assessment of renal FMD (see *Diagnosis and Assessment Guidelines*, section VII [Assessment for renovascular hypertension]), we introduce 3 new guidelines for the treatment of this condition. Evidence guiding treatment is primarily based on small case series and case reports. Treatment decisions should be individualized and take into consideration the nature and location of the vascular lesions, severity of symptoms, previous vascular events, and comorbid conditions.[41] Given the complexity in care, consultation with a hypertension expert is advised.

Hypertension arising from renal FMD is primarily mediated by the renin-angiotensin-aldosterone system. Medical therapy should be directed towards BP control and vascular risk reduction. Revascularization should be considered for individuals with elevated BP, particularly for those with recent-onset or resistant hypertension. Highest cure rates are associated with younger age and shorter duration of hypertension.[81, 82] Although there are no data to inform the

most appropriate initial revascularization strategy, percutaneous renal transluminal angioplasty is usually preferred over surgery because it is less costly, less invasive, has a lower morbidity, and can be performed on an outpatient basis.[41, 44] It is associated with a combined rate of cure or BP improvement of 86.4%.[44, 82] Stenting is not routinely recommended for FMD as the risk of restenosis is generally felt to be low,[44] but may be considered for lesions that fail angioplasty or those associated with flow-limiting dissection. It is reasonable to consider surgery for complex lesions less amendable to angioplasty, stenosis associated with complex aneurysm, and restenosis despite 2 unsuccessful attempts of angioplasty.[41, 44]

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; **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 peri-procedural 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

Background. There are no changes to these guidelines for 2017.

Guidelines.

1. Persons with diabetes mellitus should be treated to attain SBP of <130 mmHg (Grade C) and DBP of <80 mmHg (Grade A) (these target BP levels are the same as the BP treatment thresholds). Combination therapy using 2 first-line agents may also be considered as initial treatment of hypertension (Grade B) if SBP is 20 mmHg greater than target or if DBP is 10 mmHg greater than target. However, caution should be exercised in patients in whom a substantial decrease in BP 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), 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

Background. There are no changes to this guideline for 2017.

Guidelines.

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

XIV. Treatment of secondary hypertension due to endocrine causes

Background. There are no changes to this guideline for 2017.

Guidelines.

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

XV. Treatment of resistant hypertension

Background. Resistant hypertension—defined by uncontrolled BP despite the use of ≥3 antihypertensive agents of different classes including a diuretic, or controlled BP with ≥4 agents—is present in 10-20% of individuals treated for hypertension.[83-86] Accordingly, the HCGC has identified resistant hypertension as an area of importance needing to be explicitly addressed in our guidelines. A decision was made to assemble a dedicated subgroup committee

to conduct a comprehensive literature review and to develop specific guidelines in the coming years.

Preliminary discussion was held regarding the **P**revention **A**nd **T**reatment of **H**ypertension **W**ith **A**lgorithm-based therap**y** number **2** (PATHWAY-2) trial, which enrolled 335 individuals with uncontrolled hypertension on 3 drugs, comparing spironolactone, doxazosin, bisoprolol, or placebo as add-on therapy.[87] Spironolactone was most effective in lowering SBP. After 3 months, 58% of patients treated with spironolactone achieved target BP control vs. 42% on doxazosin and 43% on bisoprolol. While noteworthy, the committee decided not to generate any formal guidelines based on PATHWAY-2 alone at this time, given the lack of event-related outcomes. Consistent with our overall guidelines process, studies assessing cardiovascular morbidity and mortality, as well as total mortality are prioritized for establishing guidelines related to pharmacotherapy.

Implementation

Implementation and dissemination of the guidelines is a priority for Hypertension Canada. We employ many strategies to reach out to a variety of providers who care for patients with hypertension. Our 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 A2 for a complete list of disclosures.

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Table 1. Considerations in the individualization of pharmacological 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), 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 mmHg, 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.	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.
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; 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 **M**odification of **D**iet in **R**enal **D**isease (MDRD) equation
†Framingham Risk Score[88]

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
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

FIGURE LEGEND

Figure 1. Hypertension diagnostic algorithm

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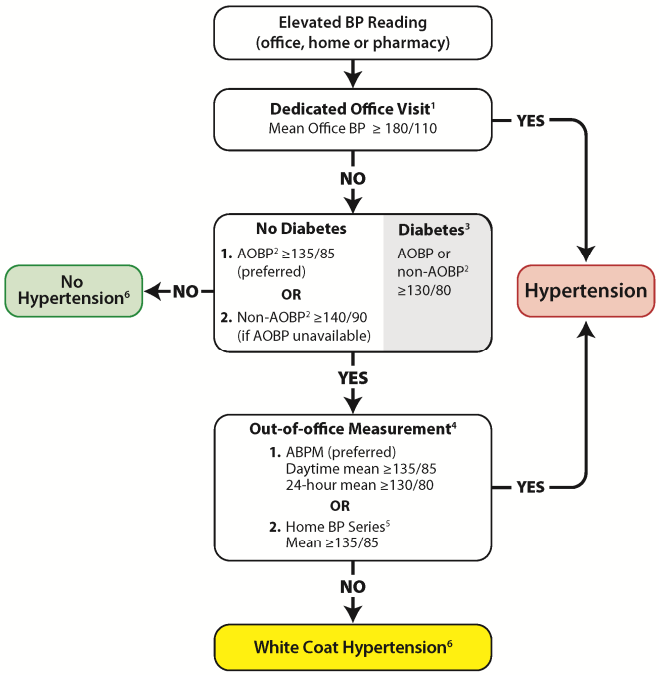
Hypertension Diagnostic Algorithm



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