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Guidelines

Hypertension Canada's 2020 Comprehensive Guidelines for the Prevention, Diagnosis, Risk Assessment, and Treatment of Hypertension in Adults and Children

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ABSTRACT

Hypertension Canada's 2020 guidelines for the prevention, diagnosis, risk assessment, and treatment of hypertension in adults and children provide comprehensive, evidence-based guidance for health care professionals and patients. Hypertension Canada develops the guidelines using rigourous methodology, carefully mitigating the risk of bias in our process. All draft recommendations undergo critical review by expert methodologists without conflict to ensure quality. Our guideline panel is diverse, including multiple health professional groups (nurses, pharmacy, academics, and physicians), and worked in concert with experts in primary care and implementation to ensure optimal usability. The 2020 guidelines include new guidance on the management of resistant hypertension and the management of hypertension in women planning pregnancy.

RÉSUMÉ

Les lignes directrices 2020 d'Hypertension Canada pour la prévention, le diagnostic, l'évaluation des risques et le traitement de l'hypertension chez l'adulte et l'enfant fournissent aux professionnels de la santé et aux patients des conseils complets et fondés sur des données probantes. Hypertension Canada élabore ces lignes directrices en utilisant une méthodologie rigoureuse, en atténuant soigneusement le risque de partialité dans notre processus. Tous les projets de recommandations sont soumis à une évaluation critique par des experts en méthodologie, sans partialité, afin d'en garantir la qualité. Notre panel de lignes directrices est diversifié, comprenant de multiples groupes de professionnels de la santé (soins infirmiers, pharmacie, universitaire et médecins), et a travaillé de concert avec des experts en soins primaires et d'experts en mise en œuvre pour garantir une utilisation optimale. Les lignes directrices 2020 comprennent de nouvelles orientations sur la gestion de l'hypertension résistante et la prise en charge de l'hypertension chez les femmes qui planifient une grossesse.

For the past 2 decades, Canada has been a world leader in hypertension screening, diagnosis, and management. Our national guideline program (which includes our guideline implementation and evaluation teams) has created an international standard for excellence in evidence-based hypertension care. However, cardiovascular disease remains the leading cause of death among Canadians, and we will continue to be diligent in our efforts to prevent, detect, and manage hypertension to optimize population cardiovascular health.

Hypertension Canada is pleased to launch the 2020 guidelines for the prevention, diagnosis, risk assessment and treatment of hypertension in adults and children. Although Hypertension Canada continues to use the rigourous methods that have distinguished our guidelines internationally, our 2020 process was revised to include a comprehensive review of all of our existing recommendations and the elimination of those that were no longer deemed necessary, relevant, or valuable to our end users. We have also reorganized our content into thematic sections and introduced an additional review step to ensure harmony within our guidelines. This year, we have included a series of "key messages" to help directly address areas for which our end users have asked for guidance or information. These key messages reiterate and/or emphasize new or existing recommendations to highlight important clinical information and actions within each section. Finally, primary care advisors were consulted at every stage of guideline development to ensure new/revised recommendations would add value to those providing or receiving hypertension care.

Hypertension Canada is now working on a 2-year review cycle. This longer interval between guidelines production provides more time for educational and implementation activities, while allowing the Hypertension Canada Guidelines Committee (HCGC) more time to innovate the guidelines so that we can be optimally responsive to the needs of our diverse group of users.

In 2020, Hypertension Canada continues to emphasize intensive blood pressure (BP) lowering in patients at high risk for cardiovascular disease, including patients with existing cardiovascular disease, older adults, and persons with nondiabetic chronic kidney disease. This year we have provided more tools to assist in shared decision-making on BP target selection. We continue to encourage accurate and standardized measurement of BP in and out of clinical settings. We have reviewed the evidence on the diagnosis and management of resistant hypertension and, in a separate report, have provided tools to help clinicians evaluate and manage patients whose BP is persistently above target.[1] However, practitioners are advised to consider patient preferences, values, and clinical circumstances when determining how to best apply these guidelines to individual patients.

Methods

Hypertension Canada's guidelines are developed biennially 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 **A**ppraisal of **G**uidelines for **R**esearch and **E**valuation II (AGREE II) instrument for guideline development (guidelines.hypertension.ca/about/overview-process).[2] The HCGC is comprised of a multidisciplinary panel of content and methodological experts divided into 16 subgroups that represent distinct areas of hypertension (see Supplemental Appendix S1 for a list of members and Supplemental Appendix S2 for conflicts of interest). These subgroups are channelled into 7 thematic sections (measurement and diagnosis, cardiovascular health promotion, management: uncomplicated, management: complex comorbidity, resistant hypertension, care delivery, and special populations; Fig. 1). Thematic sections, and corresponding section chairs were introduced in the 2020 guideline development process to provide an additional level of quality assurance, and to minimize internal disharmony and redundancy.

The first step was for the subgroups to review all existing recommendations to identify inconsistencies and

Figure 1. Hypertension Canada Guidelines Committee section structure. CHF, congestive heart failure; CKD, chronic kidney disease; CV, cardiovascular; IHD, ischemic heart disease.

redundancies. Subsequently, comprehensive literature searches up to April 2019 for each subgroup were performed by a highly trained medical librarian, on the basis of key words and terms provided by the subgroups, and according to our established process (details of search strategies and retrieved articles are available upon request). The literature was reviewed independently by subgroup members in a standardized manner. On the basis of the available evidence, the subgroups formed new, or revised existing proposed recommendations, which were then screened and reviewed by the section chair, and subsequently presented to the corresponding unbiased methodological expert of the Central Review Committee. Each Central Review Committee expert performed an independent review on the assigned topic: (1) to ensure accurate, balanced, and complete representation of available evidence; and (2) to assign grading of the proposed guidelines using an evidence-based grading scheme (Table 1). This took the following into consideration: study methodological quality; effects on a hierarchy of validated clinical outcomes (priority given to cardiovascular morbidity and mortality) when appropriate; and that potential benefits must outweigh potential harms. This standardized 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 draft recommendations and supporting evidence were presented by the corresponding Central Review Committee expert to the HCGC consensus meeting in Edmonton, on September 25, 2019. After discussions, the guidelines were further revised and finalized for an electronic vote by all 81 members of the HCGC, with > 70% support required for approval of each new/revised recommendation.

Table 1. Grading scheme for recommendations

Grade A*	Recommendations for interventions are on the basis of randomized trials (or systematic reviews of trials) with high levels of internal validity and statistical precision, and for which the study results can be directly applied to patients because of similar clinical characteristics and the clinical relevance of the study outcomes
Grade B*	Recommendations are on the basis of randomized trials, systematic reviews, or prespecified subgroup analyses of randomized trials that have lower precision, or there is a need to extrapolate from studies because of differing populations or reporting of validated intermediate/surrogate outcomes rather than clinically important outcomes
Grade C*	Recommendations are on the basis of trials that have lower levels of internal validity and/or precision, or trials for which unvalidated surrogate outcomes were reported, or results from nonrandomized observational studies
Grade D*	Recommendations are on the basis of expert opinion alone

*Grade is on the basis of the strength and quality of the clinical evidence. Factors such as patient preferences, cost, and/or resource intensiveness are not included in this grading schema.

Implementation Methods

Implementation and dissemination of the guidelines is a priority for Hypertension Canada. Many strategies are used 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, as well as slide kits and summary documents, which are freely available online in English and French (www.hypertension.ca). Hypertension Canada receives feedback from end users to continually improve guideline processes and content, and address identified needs. The Research and Evaluation Committee conducts hypertension surveillance studies, and reviews existing Canadian health surveys to identify gaps between current and best practices.

1. Diagnosis and Treatment of Hypertension in Adults

Measurement and Diagnosis

Key Messages

- Hypertension remains the most prevalent risk factor for cardiovascular disease in Canada.
- Standardized BP measurement, using validated protocols and devices, continues to be recommended to screen for cases of hypertension.
- Frequency and timing of screening can be tailored to each patient's risk of hypertension. Risk factors for hypertension are: (1) diabetes mellitus; (2) chronic kidney disease; (3) low level of consumption of fresh fruits and vegetables; and (4) sedentary behaviour.
- Use of out-of-office measurement (24-hour ambulatory BP monitoring [ABPM] or home BP monitoring [HBPM]) is recommended for all

adults with: (1) high in-office BP to rule out white coat hypertension; and (2) suspected hypertension (including adults with diabetes) to rule out masked hypertension.
- Adults with confirmed diagnosis of hypertension should have a baseline assessment of: (1) cardiovascular risk factors (including screening for diabetes, hyperlipidemia, and renal disease); (2) target organ damage; and (3) routine lab testing.
- The possibility of pregnancy should be considered in all women of reproductive age with a new diagnosis of hypertension, and during follow-up visits.

I. Accurate measurement of BP

Revised/new recommendations for 2020

- The recommended measurement frequency for ABPM is at 20- to 30-minute intervals throughout the day and night (Supplemental Table S1).

Most studies with data linking ABPM to clinical outcomes used a 24-hour BP measurement frequency of 30 minutes or less.[3-8] In addition, the minimum recommended number of good-quality readings is 20 daytime and 7 night-time readings. Depending on the duration of sleep, 7 good-quality readings might not be achievable if intervals are less frequent than 30 minutes. Moreover, the greater the number of readings, the more precise the average BP.[9] ABPM should be performed according to a standard protocol (Supplemental Table S1).

- HBPM should be considered in adults with inadequately controlled BP.

Home systolic BP (SBP)/diastolic BP (DBP) values 135/85 mm Hg or higher are considered high.[10-13] This is supported by prognostic studies that showed an increased risk of cardiovascular events above or near this threshold.[10-18]

HBPM should be performed according to a standard protocol (Supplemental Table S1). Despite varied measurement protocols, HBPM has been shown to predict health outcomes better than office BP measurements (OBPMs).[14,17,19-22] Although single home readings were shown to be predictive of stroke in a large population,[15] multiple BP readings are required for accurate risk prediction within individuals.[16] BP readings taken on the first day in a series of measurements[23,24] are higher than those on subsequent days, and with respect to duplicate readings, first readings are consistently higher than second readings in the morning as well as in the evening.[24,25]

In the Efficacy of Self-Monitoring of Blood-Pressure, With or Without Telemonitoring, for Titration of Antihypertensive Medication (TASMINH4) study 1182 hypertensive patients were enrolled across 142 primary care clinics in the United Kingdom and randomized to hypertension medication titration on the basis of self-monitoring (HBPM), self-monitoring with telemonitoring, or usual care (clinic-measured BP).[26] BP targets varied according to patient characteristics but were uniformly 5/5 mm Hg lower for HBPM. At 12 months, the average clinic SBP was lower in both HBPM groups by 3.5-7.5 mm Hg, compared with the usual care group. The number of medications used was higher by on average 0.11-0.13 for the HBPM groups. There was no difference in safety outcomes. A shorter (6-month) trial showed similar results,[27] whereas studies that used a common target for HBPM and OBPM did not show benefit of HBPM.[28,29] On the basis of the improvement in BP control using HBPM over 12 months, it is recommended that HBPM be considered in those with inadequately controlled hypertension.

In studies of patients with chronic kidney disease,[30,31] HBPM independently predicted the development of end-stage renal failure. The use of HBPM can increase patient adherence.[32-34] Using population-based home BP measurements from the Ohasama study (N = 128 subjects),[35] it was reported that patients with white coat hypertension followed for 8 years were more likely to develop home hypertension than normotensive patients without white coat hypertension (47% vs 22%, respectively; odds ratio, 2.86; 95% confidence interval [CI], 1.90-4.31). Furthermore, there seems to be a considerable diagnostic agreement between home and ambulatory BP in most of the subjects with and without hypertension.[36]

Patients with a diagnosis of hypertension but with stable normotensive BP averages, "long-term observation" might be achieved with 1 week of HBPM every 3 months.[37] Patients who have difficulty remembering to take medication might benefit from daily home BP measurement[33] and patients with diabetes can benefit from frequent HBPM.[38]

Recommendations

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 independently validated equipment for all methods (automated OBPM [AOBP], OBPM, ABPM, and HBPM) is recommended (Grade D; see Supplemental Table S1 for recommended techniques). Unless specified otherwise, measurement using electronic (oscillometric) upper arm devices is preferred over auscultation (Grade C). Devices that are appropriate for the individual and have met the ISO-81060 protocol (Association for the Advancement of Medical Instrumentation: Non-invasive sphygmomanometers - Part 2: Clinical investigation of automated measurement type. ANSI/AAMI/ISO 81060-2/ANSI-AAMI, 2nd ed. Arlington, VA: AAMI 2013; see https://www.iso.org/standard/57977.html) should be used. For HBPM, patients should be encouraged to use devices with data recording capabilities or automatic data transmission to increase the reliability of reported HBPM (Grade D).
3. In patients with large arm circumferences when standard upper arm cuffs cannot be used, validated wrist devices (used with arm and wrist supported at heart level) may be used for BP estimation (Grade D).

4. Four approaches can be used to assess BP:
   i. AOBP is the preferred method of performing OBPM (Grade D). The BP value calculated and displayed by the device should be used. When using AOBP (see the *Recommended Technique for Automated Office Blood Pressure* section in Supplemental Table S1), displayed mean SBP $\geq$ 135 mm Hg or DBP $\geq$ 85 mm Hg is high (Grade D).
   ii. When using OBPM, the first reading should be discarded and the latter readings averaged (see the *Recommended Technique for Office Blood Pressure Measurement* section in Supplemental Table S1). Mean SBP between 130 and 139 mm Hg or mean DBP between 85 and 89 mm Hg is high-normal, and mean SBP $\geq$ 140 mm Hg or DBP $\geq$ 90 mm Hg is high (Grade C).
   iii. Using ABPM, mean awake SBP $\geq$ 135 mm Hg or DBP $\geq$ 85 mm Hg or mean 24-hour SBP $\geq$ 130 mm Hg or DBP $\geq$ 80 mm Hg are high (Grade C).
   iv. Using HBPM, mean SBP $\geq$ 135 mm Hg or DBP $\geq$ 85 mm Hg are high and associated with an increased overall mortality risk (Grade C). HBPM values should be on the basis of a series comprised of the mean of duplicate measures, for morning and evening, for a 7-day period. First day home BP values should not be considered (Grade D).

Key Messages

- Out-of-office BP measurements are essential to rule out white coat hypertension in subjects with and without diabetes and to diagnose masked hypertension, when suspected. A revised algorithm is presented (Figure 2).

II. Diagnosis of hypertension and follow-up

Hypertension Canada continues to emphasize the use of out-of-office measurements to rule out white coat hypertension in subjects with increased BP in the office (Fig. 2). Its prevalence is estimated to be between 9% and 30%.[39,40] It is more common in women, older subjects, nonsmokers, subjects with mildly elevated office BP, pregnant women, and subjects without target organ damage. Subjects with white coat hypertension have been shown to have an overall cardiovascular risk that approximates that of normotensive subjects.[40-43] Thus, at present, there is no evidence to support pharmacologic treatment of subjects with white coat hypertension. Because treated and untreated subjects have long-term cardiovascular risk similar to that of treated and untreated normotensive individuals, respectively,[40,44,45] it is clinically relevant to identify individuals with white coat hypertension to avoid overtreatment. In individuals with diabetes, diagnosis of hypertension is probable when OBPM is $\geq$ 130/80 for 3 or more measurements on different days; out-of-office measurements could be considered to rule out white coat hypertension, when suspected. Although the diagnostic thresholds for ABPM and HBPM (as well as for AOBP) have not yet been established in subjects with diabetes, they are probably lower than those mentioned for diagnosis of hypertension in the general population.[46]

In cases of normal BP in the office, the possibility of masked hypertension (high out-of-office BP) should be suspected in the following cases: older age, men, current smoking, heavy alcohol drinking, obesity, diabetes mellitus, or other traditional cardiovascular risk factors, as well as in cases of electrocardiographic left ventricular hypertrophy, and high-normal systolic and diastolic office BP.[47,48] Masked hypertension is common in untreated adults, with a possible prevalence of approximately 20%, which is even higher in individuals with controlled office BP (more than 1 of 3 treated individuals).[48] When suspected, masked hypertension should be ruled out by performing out-of-office measurements. In subjects with diabetes, absence of nocturnal dipping in BP (identified using ABPM) is common and correlates with higher cardiovascular mortality.[49-51] Specifically, although mean attended AOBP and daytime ABPM have been shown to be similar in subjects with diabetes, baseline 24-hour SBP (hazard ratio, 1.53; 95% CI, 1.28-2.03) and nighttime SBP (hazard ratio, 1.50; 95% CI, 1.26-1.89) were independent predictors of short-term cardiovascular outcomes.[52] Furthermore, in diabetes the adjusted odds ratio for progression to macroalbuminuria has been shown to be more than eight-fold higher in the masked hypertension group (diagnosed with HBPM) than in the controlled BP group.[53]

Guidelines for diagnosis of hypertension

1. At initial presentation, patients who exhibit features of a hypertensive urgency or emergency (Supplemental Table S2) 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.
2. If the visit 1 OBPM is high-normal (thresholds outlined in section *I. Accurate measurement of BP*, *Recommendation 4. ii*) the patient's BP should be assessed at yearly intervals (Grade C).
3. If the visit 1 mean AOBP or OBPM is high (thresholds outlined in section *I. Accurate measurement of BP*, *Recommendation 4. i and ii*), a history and physical examination should be performed, and, if clinically indicated, diagnostic tests to search for target organ damage (Table 2) and associated cardiovascular risk factors (Table 3) should be arranged within 2 visits. Exogenous factors that can induce or aggravate hypertension should be assessed and removed if possible (Supplemental Table S3). Visit 2 should be scheduled within 1 month (Grade D).
4. If the visit 1 mean AOBP or OBPM SBP is $\geq$ 180 mm Hg or DBP is $\geq$ 110 mm Hg then hypertension is diagnosed (Grade D).
5. If the visit 1 mean AOBP SBP is 135-179 mm Hg or DBP is 85-109 mm Hg or the mean OBPM SBP is 140-179 mm Hg or DBP is 90-109 mm Hg, out-of-office BP measurements should be performed before visit 2 (Grade C).

   i. ABPM is the recommended out-of-office measurement method (Grade D). Patients can be diagnosed with hypertension according to the following thresholds:

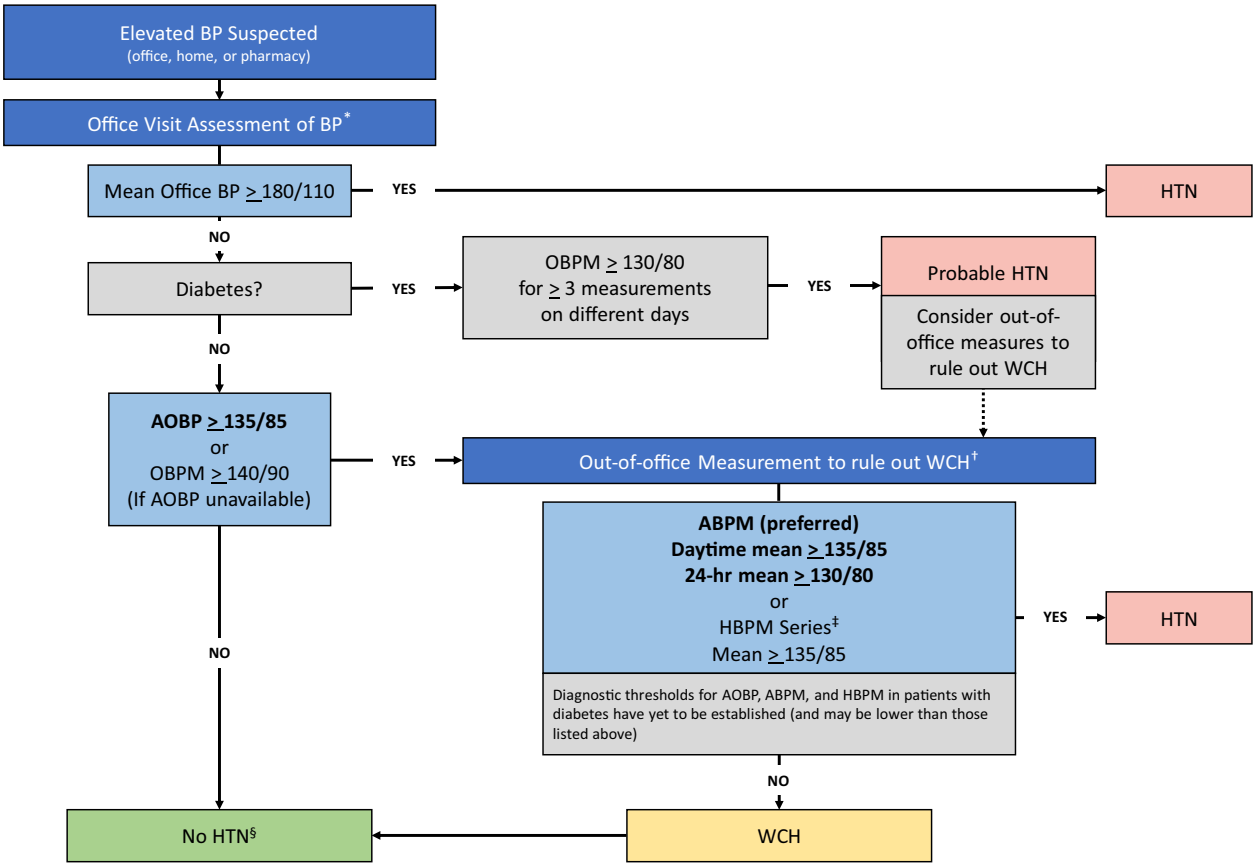

Figure 2. Hypertension diagnostic algorithm for adults. All measurement values in the algorithm are reported as mm Hg. The diagnostic algorithm has been revised for the 2020 Guidelines. In 2017 and 2018, diabetes was included in the diagnostic algorithm to provide a comprehensive overview of the diagnosis of hypertension. However, this introduces several complexities: the OBPM diagnostic threshold is different in patients with diabetes; evidence for defining AOBP and out-of-office (ABPM and HBPM) diagnostic thresholds is lacking; and the potential prognostic value of out-of-office measurements in patients with diabetes, including the identification of white coat hypertension or masked hypertension, exists but definitions are not established. The Hypertension Canada Guidelines Committee considered several options, including no change, revising the algorithm, or creating a separate algorithm for diabetes. The committee elected to revise the 2018 algorithm to include the recommendation that a series of 3-5 office measurements can be used to establish a diagnosis of hypertension in diabetes. Although this was in place for the "no diabetes" side of the algorithm, it was not explicit on the diabetes side, and the algorithm might have given the impression that hypertension could be diagnosed in patients with diabetes on the basis of 1 office visit. This has now been addressed. The algorithm for patients with diabetes might change as future studies are made available. At present, the algorithm specifies 1 threshold above which office BP is considered high in patients with diabetes, primarily on the basis of the **H**ypertension **O**ptimal **T**reatment (HOT) study, in which OBPM was used.[54] Although it is plausible that an AOBP threshold could be lower, there is currently no published evidence to guide a specific AOBP threshold. Similarly, there are no studies to date that have established ABPM or HBPM thresholds in patients with diabetes. Other guideline bodies have elected to estimate corresponding values for HBPM and ABPM on the basis of the established thresholds for the general population,[110,111] however, the evidence is not clear and these are not validated for diabetes.[46] With respect to identifying white coat hypertension in patients with diabetes, there are currently no evidence-based definitions. Elevated ABPM, including 24-hour BP and night-time BP, is associated with cardiovascular disease events and mortality in patients with diabetes.[49-52] However, a comprehensive review of the published evidence is required to establish thresholds upon which diagnostic and treatment decisions can be based. ABPM, ambulatory blood pressure measurement; AOBP, automated office blood pressure (performed with the patient unattended in a private room); BP, blood pressure; HBPM, home blood pressure measurement; HTN, hypertension; OBPM, office blood pressure measurement (measurements are performed in the office using an electronic upper arm device with a provider in the room); WCH, white coat hypertension. * If AOBP is used, use the mean calculated and displayed by the device. If OBPM 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. † Serial office measurements over 3-5 visits can be used if ABPM or HBPM are not available. ‡ 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. § In patient with suspected masked hypertension, ABPM or HBPM could be considered to rule out masked hypertension.

a. if the mean awake SBP is ≥ 135 mm Hg or DBP is ≥ 85 mm Hg, or
b. if the mean 24-hour SBP is ≥ 130 mm Hg or DBP is ≥ 80 mm Hg (Grade C).

ii. HBPM (as outlined in section *I. Accurate measurement of BP, Recommendation 4. iv*) is recommended if ABPM is not tolerated, not readily available, or patient preference (Grade D). Patients can be diagnosed with hypertension if the mean SBP is ≥ 135 mm Hg or DBP is ≥ 85 mm Hg (Grade C).

iii. If the out-of-office ABPM or HBPM average is not elevated, white coat hypertension should be diagnosed and

Table 2. Examples of target organ damage

Cerebrovascular disease
Stroke
Ischemic stroke and transient ischemic attack
Intracerebral hemorrhage
Aneurysmal subarachnoid hemorrhage
Dementia
Vascular dementia
Mixed vascular dementia and dementia of the Alzheimer's type
Hypertensive retinopathy
Left ventricular dysfunction
Left ventricular hypertrophy
Heart failure
Coronary artery disease
Myocardial infarction
Angina pectoris
Acute coronary syndromes
Renal disease
Chronic kidney disease (GFR < 60 mL/min/1.73 m^2)
Albuminuria
Peripheral artery disease
Intermittent claudication

GFR, glomerular filtration rate.
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pharmacologic treatment should not be instituted (Grade C). If the mean HBPM is $<$ 135/85 mm Hg, before diagnosing white coat hypertension, it is advisable to either: (1) perform ABPM to confirm that the mean awake BP is $<$ 135/85 mm Hg and the mean 24-hour BP is $<$ 130/80 mm Hg (preferred); or (2) repeat a HBPM series to confirm the home BP is $<$ 135/85 mm Hg (Grade D).

6. If the out-of-office measurement, although preferred, is not performed after visit 1, then patients can be diagnosed as hypertensive using serial OBPM visits if any of the following conditions are met:
   i. At visit 2, the mean OBPM (averaged across all visits) is $\geq$ 140 mm Hg SBP and/or $\geq$ 90 mm Hg DBP in patients with macrovascular target organ damage, diabetes mellitus, or chronic kidney disease (glomerular filtration rate [GFR] $<$ 60 mL/min/1.73 m^2; Grade D);
   ii. At visit 3, the mean OBPM (averaged across all visits) is $\geq$ 160 mm Hg SBP or $\geq$ 100 mm Hg DBP; and
   iii. At visit 4 or 5, the mean OBPM (averaged across all visits) is $\geq$ 140 mm Hg SBP or $\geq$ 90 mm Hg DBP.
7. Investigations for secondary causes of hypertension should be initiated in patients with clinical and/or laboratory features indicative of hypertension (outlined in sections *III. Routine and optional laboratory tests for the investigation of patients with hypertension*, *XVI. Assessment for renovascular hypertension*, *XVII. Treatment of hypertension in association with renovascular disease*, *XVIII. Assessment for endocrine hypertension*, and *XIX. Treatment of secondary hypertension due to endocrine causes*; Grade D).

Table 3. Examples of key cardiovascular risk factors for atherosclerosis

History of clinically overt atherosclerotic disease indicates a very high risk for a recurrent atherosclerotic event (eg, peripheral arterial disease, previous stroke or transient ischemic attack)
Nonmodifiable
Age $\geq$ 55 years
Male sex
Family history of premature cardiovascular disease (age $<$ 55 in men and $<$ 65 in women)
Modifiable
Sedentary lifestyle
Poor dietary habits
Abdominal obesity
Dysglycemia
Smoking
Dyslipidemia
Stress
Nonadherence

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Guidelines for follow-up of hypertension

1. 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).
2. Hypertensive patients actively modifying their health behaviours should be followed-up at 3- to 6-month intervals. Shorter intervals (every 1 or 2 months) are needed for patients with higher BP (Grade D).
3. Patients receiving 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).
4. Standard OBPM should be used for follow-up. Measurement using electronic (oscillometric) upper arm devices is preferred over auscultation (Grade C).
5. ABPM or HBPM is recommended for follow-up of patients with demonstrated white coat effect (Grade D).

ABPM

A suggested protocol for ABPM is presented in Supplemental Table S1.

Recommendations

1. In addition to a general recommendation for hypertensive patients (in section *II. Diagnosis of hypertension and follow-up*, *5*), ABPM 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); or
   iii. fluctuating office BP readings (Grade D).
2. The magnitude of changes in nocturnal BP should be taken into account in any decision to prescribe or withhold drug therapy on the basis of ABPM (Grade C) because a decrease in nocturnal BP of $<$ 10% is associated with increased risk of cardiovascular events.

HBPM

A suggested protocol for HBPM is presented in Supplemental Table S1.

Recommendations

1. The use of HBPM on a regular basis should be considered for patients with hypertension, particularly those with:
   i. Inadequately controlled hypertension (Grade B; **revised recommendation**);
   ii. Diabetes mellitus (Grade D);
   iii. Chronic kidney disease (Grade C);
   iv. Suspected nonadherence (Grade D);
   v. Demonstrated white coat effect (Grade C); or
   vi. BP controlled in the office but not at home (masked hypertension; Grade C).
2. 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).

Routine Testing

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

New recommendations for 2020

- Consider the potential for pregnancy in women with hypertension.

Women of child-bearing potential should be asked at regular intervals about possible pregnancy. If unsure, a repeat pregnancy test may be done depending upon current or potential antihypertensive treatments. The determination of pregnancy is important in the treatment of women of reproductive age because some medications have relative contraindications in pregnancy (see part *3. Hypertension and Pregnancy* for further details). Similarly, health behaviour changes for hypertension are generally modified during pregnancy.

Recommendations

1. Routine 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 (Grade D);
   iv. Serum total cholesterol, low-density lipoprotein, high-density lipoprotein (HDL), and non-HDL cholesterol, and triglycerides (Grade D); lipids may be drawn fasting or nonfasting (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, fasting lipids, and pregnancy) should be repeated with a frequency reflecting the clinical situation (Grade D; **revised recommendation**).
5. A pregnancy test should be considered before initiation of health behaviour management changes or drug therapy (Grade D; **new recommendation**).
6. Routine echocardiographic evaluation of all hypertensive patients is not recommended (Grade D).
7. An echocardiogram for assessment of left ventricular hypertrophy is useful in selected cases to help define the future risk of cardiovascular events (Grade C).
8. 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 (CAD; Grade D).
9. Patients with hypertension and evidence of heart failure should have an objective assessment of left ventricular ejection fraction, either using echocardiogram or nuclear imaging (Grade D).

Cardiovascular Risk Assessment

IV. Assessment of overall cardiovascular risk in hypertensive patients

Recommendations

1. Global cardiovascular risk should be assessed. Multifactorial risk assessment models can be used to:
   i. Predict more accurately an individual's global cardiovascular risk (Grade A);
   ii. Help engage individuals in conversations about health behaviour change to lower BP (Grade D); and,
   iii. 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).

Cardiovascular Health Promotion

Key Messages

- Health behaviour change plays an important role in hypertension prevention and BP-lowering in people diagnosed with hypertension
- Health behaviour change is strongly recommended as a first-line intervention to lower BP in people with hypertension
- Optimization of lipid levels with the use of statins in higher-risk patients is recommended
- The use of acetylsalicylic acid (ASA) for primary prevention of cardiovascular disease is no longer recommended in people with hypertension

Vascular Protection

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

Removed recommendations for 2020

- The recommendation for the use of low-dose ASA in the primary prevention of cardiovascular disease has been removed.

Hypertension Canada guidelines previously recommended that low-dose ASA be considered in all adults with hypertension who are 50 years of age or older for the primary prevention of cardiovascular disease. In light of emerging evidence on the balance of risks and benefits of low-dose ASA in this population, the HCGC voted to remove this recommendation for 2020. This recommendation was almost entirely on the basis of the **H**ypertension **O**ptimal **T**reatment (HOT) trial.[54] This landmark trial in hypertensive patients showed that ASA use was associated with a 15% reduction in major adverse cardiovascular events but a 74% increase in major bleeds (although no difference in fatal bleeds) and no difference in all-cause mortality. This recommendation was maintained in the face of increasing concerns regarding the benefit (cardiovascular protection) to cost (major bleeds) in patients in the primary prevention of CAD complications.

However, as shown in the recent Effect of Aspirin on All-Cause Mortality in the Healthy Elderly (ASPREE) trial[55] and several recent meta-analyses,[56-58] ASA for primary prevention in patients with hypertension is associated with little overall effectiveness and significant risk of major bleeding. In light of this new evidence, Hypertension Canada decided to remove this recommendation, and aspirin is no longer recommended for primary prevention in individuals with hypertension.

Recommendations

1. Statin therapy is recommended in hypertensive patients with $\geq$ 3 cardiovascular risk factors as defined in Supplemental Table S4 (Grade A in patients older than 40 years) or with established atherosclerotic disease (Grade A regardless of age).
2. 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).
3. Advice in combination with pharmacotherapy (eg, varenicline, bupropion, nicotine replacement therapy) should be offered to all smokers with a goal of smoking cessation (Grade C).

Health Behaviours

VI. Health behaviour management

Revised recommendations for 2020

- Reduce alcohol consumption (or abstain) to reduce BP and prevent hypertension.
- To prevent hypertension, there is no safe limit for alcohol consumption.[59]

In a systematic review and meta-analysis of original cohort studies an increase in incidence of hypertension with any amount of alcohol consumption in men, and an increase in incidence of hypertension with more than 2 drinks per day in women was reported.[60] Additionally, a separate analysis of the risk thresholds from large-scale data sources showed a positive linear association between alcohol consumption and mortality attributed to hypertension (hazard ratio per 100 g/wk greater consumption, 1.24; 95% CI, 1.15-1.33).[61]

In adults with hypertension who consume more than 2 drinks per day, a reduction in alcohol consumption is associated with a decreased BP. In a systematic review and meta-analysis of clinical trials the effect of a change in alcohol consumption on BP in subjects with hypertension was investigated.[62] This analysis showed that there was a significant reduction in BP associated with a reduction in alcohol consumption in hypertensive subjects who consumed 3 or more drinks per day in a dose-dependent manner. The largest reduction in BP (SBP: −5.50 mm Hg [95% CI, −6.70 to −4.30] and DBP: −3.97 mm Hg [95% CI, −4.70 to −3.25]) was reported in subjects with a baseline consumption of 6 or more drinks per day.

Recommendations

A. Physical exercise

1. For nonhypertensive 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 (eg, 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 nonhypertensive or hypertensive individuals with SBP/DBP of 140-159/90-99 mm Hg , 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 18.5-24.9, and waist circumference $<$ 102 cm for men and $<$ 88 cm for women) is recommended for nonhypertensive 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 use a multidisciplinary approach that includes dietary education, increased physical activity, and behavioural intervention (Grade B).

C. Alcohol consumption

1. In healthy adults, abstaining from alcohol or reducing alcohol intake to 2 drinks per day or less is recommended to prevent hypertension (Grade B; **revised recommendation**).

In adults with hypertension who drink more than 2 drinks per day, a reduction in alcohol intake is associated with decreased BP and is recommended. In adults with hypertension who drink 6 or more drinks per day, a reduction in alcohol intake to 2 or fewer drinks per day is associated with decreased BP and is recommended (Grade A; **revised recommendation**).

D. Diet

1. It is recommended that hypertensive patients and normotensive individuals at increased risk of developing hypertension consume a diet that emphasizes

Table 4. Risk factors for hyperkalemia

Before 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 taking other drugs that can cause hyperkalemia (eg, trimethoprim and sulfamethoxazole, amiloride, triamterene)
- Chronic kidney disease (glomerular filtration rate < 45 mL/min/1.73 m^2)
- Baseline serum potassium > 4.5 mmol/L

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[63-66]; Supplemental Table S5; Grade B).

E. Sodium intake

1. To prevent hypertension and reduce BP in hypertensive adults, consider reducing sodium intake toward 2000 mg (5 g of salt or 87 mmol of sodium) per day (Grade A).

F. Calcium and magnesium intake

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

G. Potassium intake

1. In patients not at risk of hyperkalemia (see Table 4), increase dietary potassium intake to reduce BP (Grade A).

H. Stress management

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

Management: Uncomplicated Pharmacotherapy

Key Messages

- Hypertension Canada continues to promote a risk-based approach to treatment thresholds and targets (Tables 5 and 6).
- Hypertension Canada continues to encourage the use of clinical judgement and shared decision-making when identifying BP targets to ensure feasibility in the patient's broader clinical, social, and economic context.
- Patients with existing cardiovascular disease or with elevated cardiovascular risk should be considered for intensive SBP targets (ie, SBP $\leq$ 120 mm Hg).
- Angiotensin converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs), calcium channel blockers (CCBs), and longer-acting thiazide-like diuretics continue to be recommended as effective first-line treatment in all adults with uncomplicated hypertension.
- β-Blockers can be used safely as first-line therapy in younger patients only with uncomplicated hypertension.

Table 5. Blood pressure thresholds for initiation of antihypertensive therapy 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)

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

*See Table 6; on the bass of automated office blood pressure measurement.

- When possible, the use of a single-pill combination (SPC) should be considered to improve treatment efficacy, efficiency, and tolerability.[54]

Considerations for the individualization of pharmacological therapy in adults are provided in Table 7.

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

Recommendations

1. Antihypertensive therapy should be prescribed for average DBP measurements of $\geq$ 100 mm Hg (Grade A; target established using OBPM) or average SBP measurements of $\geq$ 160 mm Hg (Grade A; target established using OBPM) in patients without macrovascular target organ damage or other cardiovascular risk factors.
2. Antihypertensive therapy should be strongly considered for average DBP readings $\geq$ 90 mm Hg (Grade A) or for average SBP readings $\geq$ 140 mm Hg (Grade B for 140-160 mm Hg; Grade A for $>$ 160 mm Hg; targets established using OBPM) in the presence of macrovascular target organ damage or other independent cardiovascular risk factors.
3. For high-risk patients (Table 5), aged 50 years or older, with SBP levels $\geq$ 130 mm Hg, intensive management to target a

Table 6. Clinical indications defining high-risk adult patients as candidates for intensive management

Clinical or subclinical cardiovascular disease; or
Chronic kidney disease (nondiabetic nephropathy, proteinuria $<$ 1 g/d, *estimated glomerular filtration rate 20-59 mL/min/1.73 m^2); or
Estimated 10-year global cardiovascular risk $\geq$ 15%†; or
Age $\geq$ 75 years
Patients with 1 or more clinical indications should consent to intensive management.

*Four-variable Modification of Diet in Renal Disease equation.
† Framingham Risk Score.[109]

Table 7. 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 CCBs. Recommended SPC choices include combinations of an ACE inhibitor with CCB, ARB with CCB, or ACE inhibitor/ARB with a diuretic (consider statins in selected patients)	Combination of first-line drugs	Not recommended for monotherapy: α-blockers, β-blockers in those 60 years of age or older, ACE inhibitors in black people. Hypokalemia should be avoided in those prescribed diuretics. Combination of an ACE inhibitor with an ARB is not recommended
Isolated systolic hypertension without other compelling indications	Thiazide/thiazide-like diuretics, ARBs, or long-acting dihydropyridine CCBs	Combinations of first-line drugs	Same as diastolic hypertension with or without systolic hypertension
Diabetes mellitus			
Diabetes mellitus with microalbuminuria,* renal disease, cardiovascular disease, or additional cardiovascular risk factors	ACE inhibitors or ARBs	Additional use 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
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 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	Nondihydropyridine 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-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-inhibitor is recommended (in place of an ACE inhibitor or ARB) in symptomatic patients with hypertension and HFrEF according to standard guideline-based therapies	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
LVH	ACE inhibitor, ARB, long-acting CCB, or thiazide/thiazide-like diuretic	Combination of first-line agents	Hydralazine and minoxidil should not be used
Past stroke or TIA	ACE inhibitor and a thiazide/thiazide-like diuretic combination	Combination of first-line agents	Treatment of hypertension should not be routinely undertaken in patients with acute stroke unless extreme BP elevation. Combination of an ACE inhibitor with an ARB is not recommended
Nondiabetic chronic kidney disease			
Nondiabetic chronic kidney disease with proteinuria†	ACE inhibitors (ARBs if ACE inhibitor-intolerant) if there is proteinuria Diuretics as additive therapy	Combinations of first-line agents	Carefully monitor renal function and potassium for those receiving an ACE inhibitor or ARB. Combinations of an ACE inhibitor and ARB are not recommended

ACE, angiotensin converting enzyme; ARB, angiotensin receptor blocker; BNP, brain natriuretic peptide; BP, blood pressure; CCB, calcium channel blocker; DBP, diastolic blood pressure; HFrEF, heart failure with reduced ejection fraction $< 40\%$; LVH, left ventricular hypertrophy; NT-proBNP, N-terminal pro B-type naturietic peptide; NYHA, New York Heart Association; SBP, systolic blood pressure; SPC, single-pill combination; TIA, transient ischemic attack.

*Microalbuminuria is defined as persistent albumin to creatinine ratio > 2.0 mg/mmol.

†Proteinuria is defined as urinary protein > 150 mg in 24 hours or albumin to creatinine ratio > 30 mg/mmol in 2 of 3 specimens.

Table 8. 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 past 3 months)
Indication for, but not currently receiving, a β-blocker
Institutionalized elderly individuals
Inconclusive evidence
Diabetes mellitus
Previous stroke
eGFR < 20 mL/min/1.73 m^2
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.

SBP < 120 mm Hg should be considered. Intensive management should be guided by AOBP measurements (see section *I. Accurate measurement of BP*, and the *Recommended Technique for Automated Office Blood Pressure* section of Supplemental Table S1). Patient selection for intensive management is recommended and caution should be taken in certain high-risk groups (Table 8; Grade B).

VIII. 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

Recommendations

1. Initial therapy should be with either monotherapy or 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 nonblack patients; Grade B);
      d. an ARB (Grade B); or
      e. a long-acting CCB (Grade B).
   ii. Recommended SPC choices are those in which an ACE inhibitor is used with a CCB (Grade A), an ARB is used with a CCB (Grade B), or an ACE inhibitor or ARB is used 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 nondihydropyridine 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 S6) 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

Recommendations

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 nondihydropyridine CCBs) may be combined or substituted (Grade D).
4. Possible reasons for poor response to therapy (Supplemental Table S6) 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.

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

Recommendations

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). These targets were established using OBPM.

Management: Complex Comorbidity

Key Messages

- Hypertension frequently coexists with other conditions that influence therapeutic decision-making. Polypharmacy and competing risks need to be considered carefully.
- Adults with diabetes and certain forms of chronic kidney disease (Table 9) might benefit from more intensive BP targets (ie, SPB ≤ 130 mm Hg or ≤ 120 mm Hg).

Table 9. Systolic blood pressure targets in patients with nondiabetic CKD

Nondiabetic CKD	Systolic BP target
Patients meeting SPRINT criteria*	< 120 mm Hg[†]
Patients with APCKD	< 110 mm Hg[‡]
All other patients with nondiabetic CKD	< 140 mm Hg[§]

APCKD, adult polycystic kidney disease; BP, blood pressure; CKD, chronic kidney disease; SPRINT, Systolic Blood Pressure Intervention Trial.

* Patients > 50 years of age, at elevated cardiovascular risk with systolic BP 130-180 mm Hg.

† Measurement is on the basis of automated office BP.

‡ Measurement is on the basis of HBPM.

§ Measurement is on the basis of office BP. Further reduction in systolic BP target may be individualized at the discretion of the treating physician considering the patient's specific kidney disease, comorbidities, and age. Moreover, we recommend that potential benefits and adverse events related to lower systolic BP targets be discussed with each patient and therapeutic decisions should be shared.

Diabetes and Hypertension

There has been significant interest in the potential role of newer diabetes therapies in the management of cardiovascular risk in adults with diabetes and hypertension. This topic has been reviewed and discussed by the HCGC at our 2017 and 2019 consensus conferences and a formal recommendation has not been developed for the use of sodium-glucose co-transporter-2 (SGLT2) inhibitors in the management of persons with comorbid diabetes and hypertension. However, the rationale for reviewing this topic is summarized herein. SGLT2s have been shown to improve survival and improve clinical outcomes in persons with type 2 diabetes, diabetes and heart failure, and diabetes-related kidney disease (GFR 30-60 mL/min/m^2).[67-69] Benefits on heart outcomes (namely reduced hospitalizations for heart failure) have been recently reported in the Dapagliflozin in Patients with Heart Failure and Reduced Ejection Fraction (DAPA-HF) trial, which enrolled 4744 patients with HFrEF, 58% of which did NOT have type 2 diabetes.[70]

Although SGLT2s appear to have clinically significant benefits in persons with diabetes, diabetes-related kidney disease, and HFrEF, SGLT2s are not an approved antihypertensive therapy, and have not been included in the Hypertension Canada guidelines as a recommended therapy for patients with these conditions. However, Hypertension Canada does acknowledge that there is a potential role for SGLT2s in patients to reduce weight, improve hemoglobin A1C, modestly reduce SBP, and improve cardiovascular outcomes in patients with complex comorbidities.[67-69]

IX. Treatment of hypertension in association with diabetes mellitus

Recommendations

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).
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 recommendations 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).

Hypertension in Chronic Kidney Disease

New recommendations for 2020

- Individualize BP targets in patients with chronic kidney disease. Consider intensive targets (SBP < 120 mm Hg) in appropriate patients.

In nondiabetic chronic kidney disease patients who meet the inclusion criteria for the **S**ystolic Blood **Pr**essure **In**tervention **T**rial (SPRINT; age older than 50 years, at elevated cardiovascular risk with SBP 130-180 mm Hg; Table 6),[71] we endorse a target SBP < 120 mm Hg. There was no evidence of heterogeneity of effect across prespecified subgroups; therefore, the benefits observed in the intervention group as a whole should also be experienced by those with nondiabetic kidney disease. However, it should also be acknowledged that SPRINT only enrolled 2646 participants with a GFR < 60 mL/min/1.73 m^2 of an intended 4600, so the evaluation of heterogeneity of effects might be underpowered.

In patients with adult polycystic kidney disease, an SBP < 110 mm Hg should be targeted on the basis of the HALT Progression of Polycystic Kidney Disease (HALT-PKD) trial,[72] which showed a slower increase in total kidney volume, a greater decline in left ventricular mass index, and a greater reduction in urinary albumin excretion compared with standard BP control. The inclusion and exclusion criteria for the SPRINT trial likely captured primarily patients with hypertension-related chronic kidney disease. Consequently, there is currently insufficient evidence to support a target SBP as per the SPRINT trial in nondiabetic chronic kidney disease patients who meet the exclusion criteria for the SPRINT trial (eg, patients with advanced chronic kidney disease [eGFR < 20 mL/min/1.73 m^2], proteinuria > 1 g/d, adult polycystic kidney disease, glomerulonephritis, and those who are institutionalized and/or frail).

Further reduction in SBP target may be individualized at the discretion of the treating physician, considering the patient's specific kidney disease, comorbidities, and age. Moreover, Hypertension Canada recommends that potential benefits and adverse events related to lower SBP targets be discussed with each patient and therapeutic decisions should be shared.

X. Treatment of hypertension in association with nondiabetic chronic kidney disease

Recommendations

1. For patients with hypertension and proteinuric chronic kidney disease (urinary protein level > 150 mg in 24 hours

or albumin to creatinine ratio > 30 mg/mmol), initial therapy should be with an ACE inhibitor (Grade A) or an ARB (Grade B; **revised recommendation**).
2. In most cases, combination therapy with other antihypertensive agents might be needed to reach target BP levels (Grade D).
3. The combination of an ACE inhibitor and ARB is not recommended for patients with chronic kidney disease (Grade B; **revised recommendation**).

Hypertension and Stroke

XI. Treatment of hypertension in association with stroke

Recommendations

A. BP management in acute ischemic stroke (onset to 72 hours)
1. For guidelines on BP management in acute ischemic stroke, refer to the current Canadian Stroke Best Practices recommendations (www.strokebestpractices.ca/recommendations).

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

C. BP management in hemorrhagic stroke (onset to 72 hours)
1. For guidelines on BP management in acute hemorrhagic stroke, refer to the current Canadian Stroke Best Practices recommendations (www.strokebestpractices.ca/recommendations).

Hypertensive Patients With Cardiovascular Disease

XII. Treatment of hypertension in association with ischemic heart disease

A. Recommendations for hypertensive patients with CAD

Recommendations
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 previous 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 might be exacerbated, especially in patients with left ventricular hypertrophy (Grade D).

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

Recommendations
1. Initial therapy should include 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).

XIII. Treatment of hypertension in association with heart failure

Recommendations

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 an aldosterone antagonist is used with an 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 used with an ACE inhibitor and other antihypertensive drug treatment (Grade A). Careful monitoring should be used if an ACE inhibitor and an ARB are used together 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 heart failure with reduced ejection fraction (HFrEF) (ejection fraction < 40%) who remain symptomatic despite treatment with an appropriate dose of guideline-directed heart failure therapy (usually a β-blocker, an ACE inhibitor or ARB, and where appropriate, a

mineralocorticoid receptor antagonist; Grade A). Eligible patients must have a serum potassium level < 5.2 mmol/L, an estimated GFR (eGFR) ≥ 30 mL/min/1.73 m^2, and close surveillance of serum potassium and creatinine (Grade A).

XIV. Treatment of hypertension in association with left ventricular hypertrophy

Recommendations

1. Hypertensive patients with left ventricular hypertrophy should be treated with antihypertensive therapy to decrease 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.

Resistant Hypertension

Key Messages

- Resistant hypertension is defined as BP above target despite 3 or more BP-lowering drugs at optimal doses preferably including a diuretic (and usually a renin-angiotensin-aldosterone system blocker and a CCB).
- Accurate office and out-of-office BP measurement is essential.
- Other reasons for apparent resistant hypertension should be eliminated before diagnosing true resistant hypertension, including nonadherence, white coat effect, and secondary hypertension.
- Pharmacotherapy with the additional use of spironolactone, bisoprolol, doxazosin, amiloride, eplerenone, or clonidine with the baseline regimen decreases BP significantly, with the greatest BP-lowering shown with spironolactone.

XV. Resistant hypertension

New recommendations for 2020

- Patients with resistant hypertension should be referred to providers with expertise in diagnosis and management of hypertension.

Patients with persistent hypertension despite use of ≥ 3 BP-lowering drugs at optimal doses (defined as resistant hypertension) are at high risk of adverse cardiovascular outcomes.[73-77]

Evaluation of resistant hypertension includes ruling out apparent resistant hypertension by using accurate OBPM and/or ABPM and conducting a detailed evaluation of adherence (which is a common risk factor for apparent resistant hypertension; Table 10). Referral to a hypertension specialist may be considered if resistant hypertension is confirmed. Because of the higher cardiovascular risk and increased likelihood that patients with resistant hypertension have secondary causes for hypertension, specialized investigations might be warranted.

Table 10. Diagnostic aspects in suspected resistant hypertension

- Accurate office blood pressure measurement
- Out-of-office blood pressure measurement, preferably with a 24-hour ambulatory blood pressure monitoring
- Optimize blood pressure-lowering drug choice and dosage
- Evaluation of target organ damage
- Review adherence
- Indirect measures (eg, pill counts, pharmacy refill data)
- Direct measures as appropriate (therapeutic drug monitoring, direct observed testing)
- Assess for sleep apnea

Typically, a combination of renin-angiotensin-aldosterone system blocker, CCB, and a diuretic are used to ensure that different mechanisms for increases in BP are blocked.[78] Although Grade A evidence is available to support the dual combination of ACE inhibitor/CCB from the **A**voiding **C**ardiovascular Events Through **Com**bination Therapy in **P**atients **Li**ving With **S**ystolic **H**ypertension (ACCOMPLISH) trial,[79] additional diuretic therapy, to address intravascular volume expansion as a cause for resistant hypertension, is on the basis of expert opinion.[80,81] Garg et al.[82] reported improved BP control with a combination of renin-angiotensin-aldosterone system blocker, CCB, and a diuretic. However, no cardiovascular outcomes were considered.

Several systematic reviews of clinical trials support the introduction of spironolactone (compared with other antihypertensive agents) as a fourth agent for reducing BP.[83-86] However, none of the trials report on cardiovascular outcomes or mortality. Clinical trial data also show doxazosin, bisoprolol, and clonidine reduce BP more than placebo.[86] Moreover, in the Prevention and Treatment of Hypertension with Algorithm-based Therapy-2 (PATHWAY-2) trial it was shown that amiloride reduced BP in a manner similar to spironolactone.[87] There is also a small trial that showed that eplerenone reduced BP in this population compared with placebo.[88] Therapeutic strategies in resistant hypertension are presented in Table 11.

Table 11. Therapeutic strategies in resistant hypertension

- Review and reiterate healthy lifestyle measures (sodium, potassium intake, stress, exercise, alcohol)
- Improve adherence (see Table 12)
- When possible, eliminate drugs and substances that cause higher blood pressure, such as calcineurin inhibitors, licorice, erythropoietin, tyrosine kinase inhibitors, nonsteroidal anti-inflammatory drugs, cocaine, amphetamines, oral contraceptive agents, sympathomimetics, and corticosteroids (see Supplemental Tables S3 and S6)
- Add pharmacotherapy
- Evidence of significant blood pressure-lowering exists for:
  - Spironolactone, eplerenone, amiloride
  - α- and β-adrenergic antagonists
  - Clonidine
- Evaluate and refer if secondary hypertension suspected
- Primary aldosteronism (see guidelines on endocrine hypertension)
- Renovascular hypertension (see guidelines on renovascular hypertension)
- Pheochromocytoma and paraganglioma (see guidelines on endocrine hypertension)
- Other causes of secondary hypertension

Recommendations

1. We recommend that patients with resistant hypertension, defined as BP above target despite ≥ 3 BP-lowering drugs at optimal doses, preferably including a diuretic, be referred to a provider with expertise in hypertension management for diagnosis (Table 10) and therapeutic (Table 11) purposes (Grade D; **new recommendation**).

Renal/Renovascular Hypertension

New recommendations for 2020

- When investigating renovascular hypertension, carefully consider renal function.

For patients with severely reduced kidney function (eGFR < 30 mL/min/1.73 m^2), the preferred diagnostic test for renal artery stenosis screening should be considered on a case-by-case basis and in consultation with a nephrologist. Magnetic resonance angiography with gadolinium-based contrast agents is not universally recommended in this patient population, and alternative diagnostic tests (eg, unenhanced magnetic resonance imaging, computed tomography, ultrasound, scintigraphy, etc) should be considered first. Although conventional angiography is associated with an increased risk of contrast-induced nephropathy, this complication may be reversible, and the procedure itself might offer the opportunity of an intervention (ie, renal angioplasty and/or stenting) should renal artery stenosis be confirmed.

XVI. Assessment for renovascular hypertension

Recommendations

1. Patients who present with 2 or more of the following clinical clues, which suggest renovascular hypertension, should be investigated (Grade D):
   i. Sudden onset or worsening of hypertension and age older than 55 or younger than 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 ACE inhibitor or ARB;
   v. Other atherosclerotic vascular disease, particularly in patients who smoke or have dyslipidemia;
   vi. Recurrent pulmonary edema associated with hypertensive surges.
2. The following tests are recommended for screening for atherosclerotic renal vascular disease: captopril-enhanced radioisotope renal scan (for patients with eGFR > 60 mL/min/1.73 m^2), Doppler sonography, computed tomography angiography, and magnetic resonance angiography (for patients with eGFR > 30 mL/min/1.73 m^2; Grade D; **revised recommendation**).
3. Patients with hypertension who present with at least 1 of the following clinical clues should be investigated for fibromuscular dysplasia (FMD)-related renal artery stenosis (Grade D):
   i. Significant (> 1.5 cm), unexplained asymmetry in kidney sizes;
   ii. Abdominal bruit without apparent atherosclerosis;
   iii. FMD in another vascular territory;
   iv. Family history of 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.

XVII. Treatment of hypertension in association with renovascular disease

Recommendations

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 any of the following (Grade D; **revised recommendation**):
   i. Uncontrolled hypertension resistant to maximally tolerated pharmacotherapy,
   ii. Progressive renal function loss,
   iii. Acute pulmonary edema.
3. Patients with confirmed renal FMD should be referred to a hypertension specialist (Grade D).
4. Renal artery angioplasty without stenting is recommended for treatment of FMD-related renal artery stenosis. Stenting is not recommended unless needed because of a periprocedural dissection. Surgical revascularization should be considered in case of complex lesions less amendable to angioplasty, stenosis associated with complex aneurysm, and restenosis despite 2 unsuccessful attempts of angioplasty (Grade D).

Endocrine Hypertension

XVIII. Assessment for endocrine hypertension

A. Primary aldosteronism: screening and diagnosis

Recommendations

1. Screening for primary aldosteronism 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 primary aldosteronism should include assessment of plasma aldosterone and plasma renin activity or plasma renin (Table 13).
3. For patients with suspected primary aldosteronism (on the basis of the screening test; Table 13, section *II*), a diagnosis of primary aldosteronism should be established by demonstrating inappropriate autonomous hypersecretion of aldosterone using at least 1 of the manoeuvres listed in Table 13, section *III*. When the diagnosis is established, the abnormality should be localized using any of the tests described in Table 13, section *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

Recommendations

1. If pheochromocytoma or paraganglioma is strongly suspected, the patient should be referred to a specialized hypertension centre, particularly if biochemical screening tests (Table 14) have already been shown 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 (eg, 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 anaesthesia;
   iv. Patients with an incidentally discovered adrenal mass;
   v. Patients with a predisposition to hereditary causes (eg, 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 magnetic resonance imaging (preferable), computed tomography (if magnetic resonance imaging unavailable), and/or iodine I-131 meta-iodobenzylguanidine scintigraphy should be used (Grade C for each modality).

XIX. Treatment of secondary hypertension due to endocrine causes

Treatment of primary aldosteronism and pheochromocytoma are outlined in Tables 13 and 14, respectively.

Care Delivery

New recommendations for 2020

- Adherence should be routinely evaluated in adults being treated for hypertension.

Adherence with a small cluster of health behaviours, including physical activity/exercise, smoking cessation, healthy diet, reduction in alcohol consumption, and medication adherence, have been identified as key behaviours aimed at controlling hypertension. Published research in the area typically uses 1 of 3 terms to refer to interventions aimed at changing behaviour: "non-pharmacological," "lifestyle," or "behavioural." Agreeing on a common terminology is important to optimize the efficiency of scientific progress[89]; the 2020 adherence recommendations have been updated to use the term "health behaviour change" in place of "nonpharmacological therapy." A key issue is to prevent naming an intervention by what it is not, to avoid the potential for confusion and poorly delimited concepts.

A second modification to the adherence recommendations for 2020 involves incorporating consideration of medication adherence into decision-making around the stepping-up of treatment. This change reflects a review of 24 retrospective, cross-sectional cohort and randomized controlled trials that examined medication adherence (defined as $\geq$ 80%) for patients with uncontrolled BP despite being prescribed $\geq$ 3 antihypertensive medications of different classes.[90] Using a random effects model, this study reported a pooled prevalence of nonadherence at 31.2% (95% CI, 20.2-44.7; $I^2 = 99.50$), with notably higher rates of nonadherence associated with the use of objective methods, such as liquid chromatography-mass spectrometry in single time point bioassays or directly observed therapy.[91] However, no single measure of adherence can be classified as the gold standard in clinical practice at present.[91] Overall, unrecognized nonadherence with antihypertensive treatment regimens might explain poor treatment response in a small but significant number of patients.

Adherence Strategies

XX. Adherence strategies for patients

Recommendations

1. Adherence to an antihypertensive prescription can be improved by using a multipronged approach (Table 12).

Digital and e-health strategies

Key Messages

- Use of e-health interventions may be used as a means to improve the management of hypertension, reduce the risk of cardiovascular disease, and improve health and well-being.

Table 12. Strategies to improve patient adherence

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

Assist your patient in getting more involved in their treatment by:
- Encouraging greater patient responsibility/autonomy in monitoring their blood pressure and adjusting their prescriptions (Grade C)
- Educating patients and their families about their disease and treatment regimens (Grade C)

Improve your management in the office and beyond by:
- In patients with hypertension who are not at target, adherence to all health behaviour recommendations (including use of prescription medications) should be reviewed before adjustment in therapy is considered (Grade D; **revised recommendation**)
- Encouraging adherence with therapy using out-of-office contact (either phone or mail), particularly during the first 3 months of therapy (Grade D)
- Coordinating with pharmacists and work-site health caregivers to improve monitoring of adherence with pharmacological and health behaviour modification prescriptions (Grade D)
- Using electronic medication compliance aids (Grade D)

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Table 13. Primary aldosteronism

Screening

I. Plasma aldosterone and plasma renin activity or renin mass/concentration (see section *II*, below, for suggested conversion factors) should be collected as follows:
   A. In the morning after the patient has been ambulatory (sitting, standing, or walking) for at least 2 hours
   B. Patients should be seated for 5-15 minutes before the blood draw
   C. Hypokalemia should be corrected and sodium intake should be liberalized
   D. At least 4-6 weeks before testing, agents that markedly affect the results (aldosterone antagonists, potassium-sparing and -wasting diuretics) should be withdrawn
   E. If the results are not diagnostic, and if hypertension can be controlled with medications less likely to affect testing (slow-release verapamil, diltiazem, hydralazine, prazosin, doxazosin, and terazosin), repeat testing 2 weeks after withdrawing the following medications that can interfere with test accuracy: β-blockers, centrally acting α2 agonists, angiotensin receptor blockers, angiotensin converting enzyme inhibitors, directly acting renin inhibitors, and dihydropyridine calcium channel blockers
   F False positive results might occur with direct renin mass/concentration if the patient is a woman using an oral contraceptive pill. If possible, oral contraception should be discontinued for 1 month before testing, or alternately, plasma renin activity should be measured instead

II. The aldosterone to renin ratio is the preferred screening test for primary aldosteronism. Traditionally this was on the basis of measuring aldosterone according to radioimmunoassay and renin activity. Currently most laboratories use automated chemiluminescent assays for aldosterone and renin mass. Interpretation of a positive screening test is dependent on the local laboratory method for renin measurement but assumes standard reporting of aldosterone in pmol/L. Optimal screening cut-offs remain undefined. Suggested cut-offs are:

Renin method used	Aldosterone to renin ratio	
	Higher sensitivity, lower specificity	Lower sensitivity, higher specificity
Plasma renin activity (ng/mL/h)1	555	750
Direct renin concentration (mIU/L)	60	91
Direct renin concentration (ng/L)	100	144

Confirmatory testing

III. If 1 of the following criteria is met, autonomous hypersecretion of aldosterone is confirmed (interfering drugs should continue to be held, as outlined above):
   A Saline loading tests (perform either):
      i Administer 2 L of normal saline intravenously over 4 hours with the patient in a recumbent position. This test is contraindicated in the presence of severe, uncontrolled hypertension or congestive heart failure. Primary aldosteronism is defined as a postinfusion plasma aldosterone > 280 pmol/L. If < 140 pmol/L, primary aldosteronism is unlikely. Values in between are considered indeterminate
      ii. Administer > 200 mmol/d of oral sodium (ie, equivalent to > 5 g/d of sodium; > 12 g/d of sodium chloride; or > 2 tsp/d of salt) for 3 days, with primary aldosteronism defined as a 24-hour urinary aldosterone > 33 nmol/d (measured from the morning of day 3 to the morning of day 4). If < 28 nmol/d, primary aldosteronism is unlikely
   B. A plasma aldosterone to plasma renin activity ratio > 1400 pmol/L/ng/mL/h (or > 270 pmol/L/ng/L), with a plasma aldosterone > 440 pmol/L
   C. Captopril suppression test: Administer 25-50 mg captopril orally after the patient has been sitting or standing for 1 hour. While seated, renin and plasma aldosterone levels should be measured at time 0 and 1 to 2 hours after ingestion. Primary aldosteronism is unlikely if plasma aldosterone is suppressed by > 30% after captopril ingestion. In primary aldosteronism, plasma aldosterone level remains elevated, while renin level remains suppressed

Subtype classification

IV. Differentiating potential causes of confirmed primary aldosteronism (unilateral vs bilateral secretion):
   A. Computed tomography scanning (or magnetic resonance imaging) can help localize the presence of adrenal lesion(s). If imaging shows an adrenal lesion/adenoma, it might be nonfunctional. Therefore, if surgery to remove a suspected unilateral source of primary aldosteronism is planned, selective adrenal venous sampling should be considered first (to verify that an abnormally appearing adrenal gland is the source of hypersecretion)
   B. For patients with established primary aldosteronism and in whom surgery is an option, selective adrenal venous sampling should be considered to differentiate unilateral from bilateral overproduction of aldosterone
   C. Adrenal venous sampling should be conducted in centres with experience in performing this diagnostic technique
   D We suggest selective genetic testing for glucocorticoid-remediable aldosteronism in patients with confirmed primary aldosteronism and either:
      i A family history of primary aldosteronism or stroke at a young age (≤ 40 years); or
      ii Onset of hypertension at 20 years of age or younger and negative imaging

Treatment

V. Treatment is informed by subtype classification (unilateral vs bilateral secretion):
   A. Surgery with ipsilateral adrenalectomy should be considered for unilateral forms of hypersecretion (eg, aldosterone-producing adenomas). Patients should be followed closely after surgery because a significant proportion might remain hypertensive
   B. Mineralocorticoid receptor antagonists (particularly spironolactone in low to moderate doses) are quite effective for those with bilateral disease (eg, idiopathic/bilateral adrenal hyperplasia). Monitoring of potassium and creatinine are required, especially if used with angiotensin receptor blockers or angiotensin converting enzyme inhibitors.
   C. Mineralocorticoid receptor antagonists should be considered for individuals who are not surgical candidates or for those who refuse surgery (even with confirmed unilateral hypersecretion). Blood pressure-lowering responses to other antihypertensive medications (eg, angiotensin receptor blockers, angiotensin converting enzyme inhibitors, and calcium channel blockers) are often only modest to moderate
   D. Primary aldosteronism is associated with a relative hyperfiltration injury to the kidney in excess of that seen in essential hypertension. Treatment of primary aldosteronism (with either surgery or medical therapy) might unmask significant underlying renal disease with an increase in creatinine and decrease in eGFR. Patients should have their renal function monitored closely after treatment

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Despite strong clinical trial evidence supporting the notion that control of hypertension prevents heart disease and strokes, there remains room for improvement in managing hypertension in primary care practice. Technological advancements can help toward this direction. Particularly, limited engagement of patients in the decision-making process and the resulting suboptimal adherence with healthy lifestyle behaviours and prescribed medications can be improved with digital tracking and e-health interventions.

Assessing a patient's cardiovascular risk or cardiovascular age has been shown to improve patient selection for treatment of high BP and dyslipidemia. Success at reaching treatment targets is also increased. Tracking lifestyle habits digitally and/or online has also been shown to increase the adoption of healthy lifestyle behaviours including: regular exercise, healthy eating, and weight management. These behaviours not only lower BP but also reduce cardiovascular risk due to favourable changes in blood lipids and glucose, plus support long-term weight management. Furthermore, healthy lifestyle changes positively affect an individual's health and wellness including improvements in physical health problems (eg, arthritis, chronic pain, diabetes, and cardiovascular disease) and mental health as well (eg, anxiety, stress, depression, and sleep quality).

For these reasons, the HCGC has established a new subcommittee to evaluate and recommend evidence-based digital and e-health strategies to improve the management of hypertension among Canadians for 2022.

Special Populations

2. Hypertension and Pediatrics

Key Messages

- BP should be measured regularly in children 3 years of age or older; the auscultatory method is the gold-standard at present.
- Simplified diagnostic thresholds can be used (in addition to or as an alternative to normative tables) to diagnose hypertension in children and adolescents.
- If office BP readings are elevated, ABPM is recommended using devices independently validated in children and interpreted with appropriate pediatric normative data.
- In children with confirmed hypertension, routine echocardiographic evaluation should be performed, and cardiovascular risk factors should be assessed with routine laboratory tests.
- Health behaviour management should aim for a healthy body weight through a comprehensive approach that includes dietary education and increased physical activity.
- Secondary hypertension should be ruled out before pharmacological therapy is introduced in children with symptomatic hypertension, target organ damage, comorbidities, persistent, or stage 2 hypertension.
- Initial therapy should be monotherapy, with an ACE inhibitor or ARB (not first-line in black children), or a long-acting dihydropyridine CCB.
- The treatment goal is systolic and diastolic office BP and/or ABPM $<$ 95th percentile or $<$ 90th percentile in children with risk factors or target organ damage.
- Complex cases should be referred to an expert in pediatric hypertension.

I. Accurate measurement of BP in children

Recommendations

1. BP should be measured regularly in children 3 years of age and older by a health care professional using standardized pediatric techniques (Table 15) (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 with norms for age, sex, and height (Table 16; Grade D).

II. Criteria for diagnosis of hypertension in children

New recommendations for 2020

- Simplified diagnostic thresholds can also (in addition to or as an alternative to normative tables) be used to diagnose hypertension in children and adolescents.

New criteria for diagnosis of hypertension in children have been introduced in an effort to simplify diagnosis, whereby BP thresholds can be considered. These changes were on the basis of evidence from a longitudinal cohort of 1225 participants from the Bogalusa Heart Study with 27 years of follow-up and repeated BP measurements from childhood to adulthood comparing the traditional definitions vs a simplified approach.[92] The latter used the following BP thresholds: 120/80 for children ages 6-11 years and 130/85 for children ages 12-17 years. Both definitions were equally predictive of adulthood hypertension and subclinical cardiovascular outcomes. When BP is greater than the 95th percentile, a simplified approach is also recommended for staging of hypertension using the 95th percentile alone; this is intended to eliminate the need for using BP tables with the 99th percentile.

- Consider assessing non-HDL cholesterol when evaluating cardiovascular risk in children and adolescents with hypertension.

Non-HDL cholesterol could be considered when analyzing the lipid profile of children with hypertension.

Higher non-HDL cholesterol, above the ideal threshold of 3.1 mmol/L, has been associated with higher body mass index and higher DBP.[93] Furthermore, high non-HDL cholesterol has been associated with two- to threefold increased odds of coronary artery atherosclerotic lesions identified in autopsies on 15- to 34-year-old accident victims.[94]

Recommendations

1. Using OBPMs, children can be diagnosed as hypertensive if SBP or DBP is at the 95th percentile or greater for age, sex, and height, measured on at least 3 separate occasions (Grade C), or if SBP or DBP is $>$ 120/80 mm Hg in children 6-11 years of age, or greater than 130/85 mm Hg in children 12-17 years of age (Grade C; **revised recommendation**).
2. If the SBP and/or DBP is at the 95th percentile or greater, BP should be staged. Stage 1 is defined by BP between the 95th percentile and 95th percentile plus 12 mm Hg. Stage 2 is defined by BP $>$ 95th

Table 14. Pheochromocytoma

Screening and diagnosis
- I To screen for pheochromocytoma:
  - A Twenty-four-hour urinary total metanephrines and catecholamines (sensitivity 90%-95%) or 24-hour urine fractionated metanephrines (sensitivity of approximately 95%) should be measured. Concomitant measurement of 24-hour urine creatinine should also be performed to confirm accurate collection
  - B Plasma free metanephrines and free normetanephrines, where available, might also be considered (sensitivity up to 99%)
  - C Urinary vanillylmandelic acid measurements should not be used for screening
- II Keep in mind that potential false positive results should be considered in the setting of:
  - A Interfering drugs
  - B Incorrect patient preparation and positioning (for plasma metanephrine measures)
  - C Mild elevation of screening values (ie, less than twofold the upper limit of normal)
  - D Normal values on repeat testing
  - E Only 1 abnormal biochemical test in the panel of assays
  - F Atypical imaging results for pheochromocytoma
  - G A low pretest probability of pheochromocytoma
  - H Acute illness/hospitalization
- III In the presence of borderline biochemical test results or potentially false positive results, repeat testing may be performed and/or the clonidine suppression test may be used. This should be done before imaging is requested to avoid identifying potential incidentalomas
- IV Imaging (eg, computed tomography, magnetic resonance, with or without iodine I-131 meta-iodobenzylguanidine scintigraphy) should generally be performed only after biochemical confirmation of disease

Treatment
- I Definitive treatment is surgical resection. Preoperative planning is recommended for blood pressure control and volume expansion
  - A α-Blockade should be started 10-14 days preoperatively. Typical options include phenoxybenzamine (a long-acting, nonselective irreversible α-blocker), prazosin, or doxazosin
  - B Other antihypertensive medications may be added as necessary but diuretics should be avoided if possible. Oral β-blockers may be considered after achieving adequate α-blockade to control tachycardia and prevent arrhythmias during surgery
  - C Volume replacement and liberal sodium intake should be encouraged because volume contraction is common in this condition. Intravenous volume expansion in the perioperative period is recommended to prevent postoperative shock
- II Postoperatively, long-term follow-up is recommended with urinary or plasma metanephrine levels to screen for recurrence, especially in those with a genetic predisposition
- III Genetic testing should be considered for individuals younger than 50 years of age and for all patients with multiple lesions, malignant lesions, bilateral pheochromocytomas, or paragangliomas, or a family history of pheochromocytoma or paraganglioma

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percentile plus 12 mm Hg (Grade D; **revised recommendation**).

i. If BP is stage 1, BP measurements should be repeated on 2 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*)[95] 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 17; Grade C).

III. Assessment of overall cardiovascular risk in hypertensive children

Recommendations

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

IV. Routine laboratory tests for the investigation of children with hypertension

Recommendations

1. Routine tests that should be performed for the investigation of all children with hypertension include:
   i. Blood chemistry (sodium, potassium, chloride, total CO_2, and creatinine; Grade D);

Table 15. Standard approach for BP measurement in children (Grade D)

1. Children who will undergo BP measurement should avoid stimulant medications before evaluation. At the time of evaluation, the child should be seated in a quiet room for 5 minutes with back supported before the measurement of blood pressure
2. The right arm is the preferred location for BP measurement for comparison with normative data because of the possibility of coarctation of the aorta, which might 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. 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 mm Hg 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 mm Hg 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 mm Hg. If Korotkoff sounds persist as the level approaches 0 mm Hg, 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)

BP, blood pressure.

Table 16. Determining normative data for BP values in children (Grade D)

1. The BP tables use growth parameters as defined in the CDC growth charts
2. The normative BP data obtained with the auscultatory method includes the US National Health and Nutrition Examination Survey, 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 on the basis of gender, age, and height

BP, blood pressure; CDC, Centers for Disease Control and Prevention.

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. For diabetes screening refer to Diabetes Canada clinical practice guidelines (https://www.diabetes.ca/health-care-providers/clinical-practice-guidelines/chapter-35#panel-tab_FullText) (chapters on children and adolescence) (**revised recommendation**);
   ii. Serum total cholesterol and HDL cholesterol, low-density lipoprotein cholesterol, non-HDL cholesterol, and triglycerides (Grade C; **revised recommendation**).
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

Recommendations

1. For children with elevated office BP readings, ABPM should be guided by a physician with expertise in pediatric hypertension; ABPM is useful to classify BP (Supplemental Table S7; Grade C).
2. Physicians should use only ABPM devices that have been validated independently in children using established protocols. A standard approach to obtaining ABPM readings should be used (Supplemental Table S7; Grade D).

Table 17. 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.

3. ABPM levels should be interpreted with appropriate pediatric normative data for children 5 years of age or older or height of $\geq$ 120 cm (Grade D).

VI. Role of echocardiography

Recommendations

1. Routine echocardiographic evaluation in children with confirmed hypertension is recommended (Grade D).
2. 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).

VII. Health behaviour management

Recommendations

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).

VIII. Indications for drug therapy for children with hypertension

Recommendations

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 non-pharmacologic 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).

IX. Choice of drug therapy for children with hypertension

A. Recommendations for children with systolic and/or diastolic hypertension

Recommendations

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 because of 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 or diabetes (type 1 or type 2), and high-performance athletes (Grade D).

X. Goals of therapy for children with hypertension

Recommendations

1. The treatment goal is office BP (systolic and diastolic) < 95th percentile (Grade D). The goal for ABPM 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).

3. Hypertension and Pregnancy

Key Messages

- Up to 7% of pregnancies are complicated by a hypertensive disorder of pregnancy, and approximately 5% of women will have chronic hypertension when they become pregnant.
- The prevalence of hypertension in pregnancy is expected to increase with women becoming pregnant later in their reproductive years and the increasing prevalence of cardiovascular comorbidities such as increased preconception body mass index and maternal diabetes.[96-98]
- The possibility of pregnancy should be considered when managing women with hypertension who are of reproductive age.
- Preconception counselling should be offered to all women with hypertension who are considering pregnancy.
- ACE inhibitor and ARB therapy should be avoided before conception and during pregnancy unless there is a compelling indication for their use (ie, proteinuric kidney disease).
- Hypertension during pregnancy can increase the risk of adverse maternal and fetal outcomes, including an increased risk of preeclampsia, placental abruption, prematurity, small for gestational age infants, stillbirth, and maternal renal and retinal injury,[99] thus generally requires involvement of an interdisciplinary team including obstetrical care providers.
- Women with hypertension should be managed as per the Hypertension Canada guidelines for adults with hypertension before and immediately after pregnancy, except if they are breastfeeding. In breastfeeding women, only certain antihypertensive medications should be considered because their concentration in the breastmilk has been shown to be low. During pregnancy refer to Figure 3: Management of Hypertension in Pregnancy.
- Antihypertensive medications commonly used in pregnancy and lactation are presented in Table 18.

I. Preconception care

New recommendations for 2020

- Consider preconception counselling for women with hypertension considering pregnancy.

Beckmann et al. conducted a case control study of approximately 400 nonhypertensive women (ie, subfertility, health condition, and low-risk women) seeking advice preconception.[100] Women were matched 3:1, on age, parity, body mass index, smoking status, and health conditions. One of the secondary outcomes evaluated in this study was the development of a hypertensive disorder of pregnancy. Those that attended preconception care were less likely to develop a hypertensive disorder of pregnancy (0% vs 6.6%; $P = 0.05$). Although this study provides only indirect evidence on the effectiveness of preconception counselling in women with hypertension before pregnancy, preconception consultation is an opportunity for education (ie, chronic condition), assessment of potential risks (ie, preeclampsia, preterm labour, small for gestational age), and interventions for preeclampsia risk reduction (eg, ASA, exercise).[101,102] Because of the balance of benefits to potential harms of preconception counselling, even in the absence of direct evidence, the HCGC agreed that a consensus recommendation for preconception counselling was appropriate.

- Consider discontinuing ACE inhibitor and ARB therapy before conception.

Outside of the reproductive period (ie, considering pregnancy, pregnancy, and lactation), women with hypertension should have their BP managed following Hypertension Canada's guidelines for adults. For women considering a pregnancy, the choice of an antihypertensive agent should be individualized on the basis of the indication and the potential health benefits during the preconception period balanced with the fetal risks of inadvertent first trimester exposures.

For women receiving ACE inhibitors and ARBs in particular, the optimal timing of discontinuation (ie, preconception vs first trimester) has not been established. Thus, the benefits of treatment of kidney disease with significant proteinuria must be balanced with the risks of potential fetal

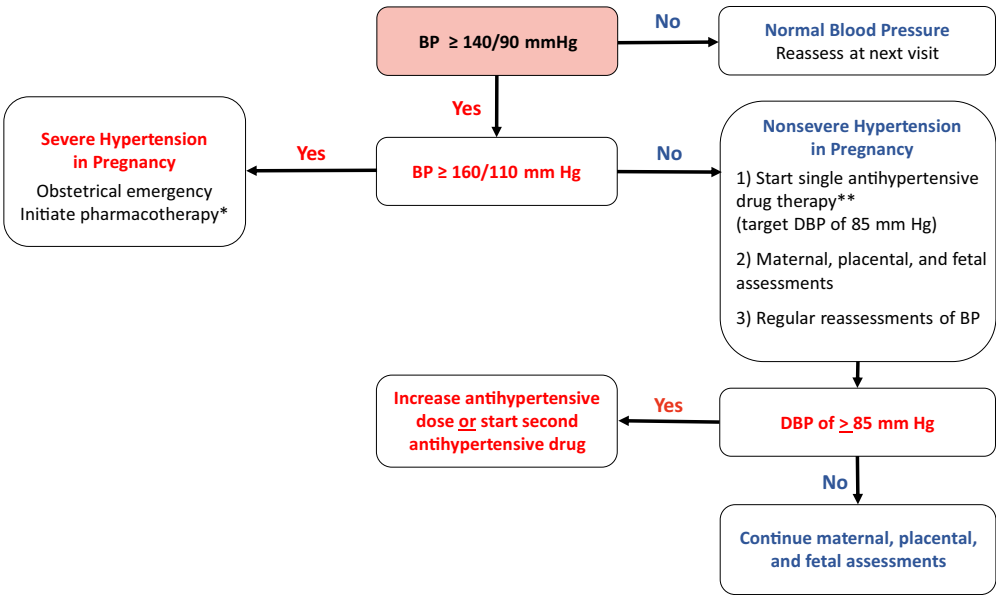

Figure 3. Management of hypertension in pregnancy. BP, blood pressure; DBP, diastolic blood pressure. * See Magee et al.[99] ** See Table 18.

complications from the first trimester exposure.[103] Hoeltzenbein et al. conducted a cohort study of 983 women; 629 women had an ACE inhibitor exposure in pregnancy and 654 had no antihypertensive agent exposure in pregnancy. The risk for major birth defects was significantly increased for women who received ACE inhibitors with hypertension compared with nonhypertensive women (adjusted hazard ratio, 2.41; 95% CI, 1.07-5.43).[104] When women with hypertension who were receiving ACE inhibitors were compared with those receiving methyldopa, the risks were similar (adjusted hazard ratio, 1.47; 95% CI, 0.51-4.23). In a systematic review of population-based studies, Li et al. also reported similar risk associations for ACE inhibitors compared with other antihypertensive medications.[105] However, Bullo et al., in a systematic review of pregnancy outcomes after ACE inhibitor and ARB exposure showed high risks of fetal malformations in those exposed to ACE inhibitors (48%) and even higher among those exposed to ARBs (87%; $P = 0.0001$) at any time during pregnancy.[103] Among fetuses exposed to ARBs in the first trimester, the abnormalities ranged from mild to severe, similar to those described in a case series (N = 7) by Hünseler et al., including neurological, cardiac, renal, and skeletal abnormalities.[106] Although these fetal abnormalities are concerning, the evidence is limited to case series—a level of evidence that can be prone to bias. The HCGC agreed that there was sufficient evidence to caution against the use of ACE inhibitors and ARBs in pregnancy, however, the recommendation is graded D, reflecting the weaknesses of the evidence informing this topic.

- Consider certain antihypertensive medications for safe management of hypertension in breastfeeding women.

Women with chronic hypertension, gestational hypertension, and preeclampsia often require ongoing pharmacologic treatment of hypertension in the postpartum period. There is limited evidence on the safety of possible therapeutic options for women with hypertension who are breastfeeding. The recommendations provided by Hypertension Canada are on the basis of data on the apparent safety on the basis of low breast milk concentrations of specific agents. There is a theoretical concern that ACE inhibitors might cause hypotension, particularly in premature infants. β-Blockers are typically protein-bound with little transfer to breast milk; however, β-blockers can theoretically cause bradycardia in neonates, and neonatal heart rate might require some assessment in mothers using β-blockers while breastfeeding.[107]

Table 18. Antihypertensive medications commonly used in pregnancy and lactation

Pregnancy			Lactation
First-line oral drugs (Grade C)	Second-line oral drugs (Grade D)	Medications to avoid (Grade C)	Oral drugs (Grade D)
Labetalol Methyldopa Long-acting oral nifedipine Other β-blockers (acebutolol, metoprolol, pindolol, and propranolol)	Clonidine Hydralazine Thiazide diuretics	ACE inhibitors* ARBs*	Labetalol Methyldopa Long-acting oral nifedipine Enalapril Captopril

ACE, angiotensin converting enzyme; ARB, angiotensin receptor blocker.
* Fetotoxicity of renal system.

Table 19. Comparison of Hypertension Canada's 2020 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 15) • Oscillometric device or auscultation method for initial measurement • Elevated oscillometric values should be confirmed with auscultation • BP values should be compared with norms on the basis of age, sex, and height (Table 16) • 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 according to BP percentile on the basis of norms for age, sex, and height and level of BP elevation, and number of visits/measurements • See *II. Criteria for diagnosis of hypertension in children*	• Diagnose using absolute BP value according to level of BP elevation, number of visits/measurements, and method of BP measurement • See Figure 2
Assessment	• History and physical examination • Cardiovascular risk factor assessment • Routine investigations for secondary causes of hypertension, cardiovascular risk factors, and target organ damage	• History and physical examination • Cardiovascular risk factor assessment • Routine investigations for secondary causes of hypertension, cardiovascular risk factors, and 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 or single-pill combination with ACE inhibitor and CCB, ARB and CCB, or ACE inhibitor/ARB and 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.

Women with gestational hypertension and preeclampsia also require long-term management of their increased cardiovascular risks.[108]

Recommendations

1. Preconception counselling is recommended for women with prepregnancy hypertension to advise on individualized antihypertensive medication management during pregnancy (Grade D; **new recommendation**).
2. Consider discontinuing ACE inhibitors and ARBs in women planning pregnancy (Grade D, **new recommendation**).

II. Management of nonsevere hypertension (BP 140-159/90-109 mm Hg) in pregnancy

Recommendations

1. Antihypertensive therapy is recommended for average SBP measurements of ≥ 140 mm Hg or DBP measurements of ≥ 90 mm Hg in pregnant women with chronic hypertension, gestational hypertension, or preeclampsia (Grade C).
   i. Initial antihypertensive therapy should be monotherapy from the following first-line drugs: oral labetalol, oral methyldopa, long-acting oral nifedipine, or other oral β-blockers (acebutolol, metoprolol, pindolol, and propranolol; Grade C).
   ii. Other antihypertensive drugs can be considered as second-line drugs including: clonidine, hydralazine, and thiazide diuretics (Grade D).
   iii. ACE inhibitors and ARBs should not be used in pregnant women (Grade C; **revised grade for entire recommendation**).
2. A DBP of 85 mm Hg should be targeted for pregnant women receiving antihypertensive therapy with chronic hypertension or gestational hypertension (Grade B). A similar target could be considered for pregnant women with preeclampsia (Grade D).
3. Additional antihypertensive drugs should be used if target BP levels are not achieved with standard-dose monotherapy (Grade C). Add-on drugs should be from a different drug class chosen from first-line or second-line options (Grade D).

III. Management of severe hypertension (BP ≥ 160/110 mm Hg) in pregnancy and postpartum

Recommendations

1. Women with severe hypertension with SBP ≥ 160 mm Hg or DBP ≥ 110 mm Hg in pregnancy or postpartum require urgent antihypertensive therapy because it is considered an obstetrical emergency (Grade D; **revised recommendation**).

IV. Management of postpartum (up to 6 weeks postpartum) hypertension

Recommendations

1. Antihypertensive drugs used in breastfeeding women include: labetalol, methyldopa, long-acting nifedipine, enalapril, or captopril (Grade D; **new recommendation**).

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 19). The next update for the Hypertension Canada guidelines is planned for 2022 to allow for optimal dissemination of the 2020 guidelines although literature searches will be continued on an annual basis. New evidence identified as being "practice changing" for clinicians (ie, 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 2022 include, among others, updates on BP measurement methods and follow-up, and diagnosis of masked hypertension, as well as updates in the management of complex hypertension with certain comorbidities, and e-health.

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Disclosures

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

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Supplementary Material

To access the supplementary material accompanying this article, visit the online version of the *Canadian Journal of Cardiology* at www.onlinecjc.ca and at https://doi.org/10.1016/j.cjca.2020.02.086.