

## Guidelines

# Hypertension Canada's 2016 Canadian Hypertension Education Program Guidelines for Blood Pressure Measurement, Diagnosis, Assessment of Risk, Prevention, and Treatment of Hypertension

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See page 585 for disclosure information.

A version of the hypertension recommendations designed for patient and public education has been developed to assist health care practitioners managing hypertension. The summary is available electronically (go to <http://www.hypertension.ca>).

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## ABSTRACT

Hypertension Canada's Canadian Hypertension Education Program Guidelines Task Force provides annually updated, evidence-based recommendations to guide the diagnosis, assessment, prevention, and treatment of hypertension. This year, we present 4 new recommendations, as well as revisions to 2 previous recommendations. In the diagnosis and assessment of hypertension, automated office blood pressure, taken without patient-health provider interaction, is now

## RÉSUMÉ

Chaque année, le groupe de travail du Programme éducatif canadien sur l'hypertension d'Hypertension Canada fournit une mise à jour de ses recommandations fondées sur des données probantes en vue de la prévention, du diagnostic, de l'évaluation et du traitement de l'hypertension. Cette année, nous vous présentons quatre nouvelles recommandations et deux recommandations révisées. En clinique, pour évaluer la présence de l'hypertension et poser le diagnostic, on

## Executive Summary

**Objective:** To provide updated 2016 evidence-based recommendations for the prevention, diagnosis, assessment, and treatment of hypertension in adults.

**Methods:** A search was performed in MedLine (up to August 2015) by a medical librarian. Reference lists were reviewed and experts were contacted to identify additional

pertinent studies. Content and methodology experts reviewed and appraised relevant articles using standardized grading algorithms. For pharmacologic interventions, evidence from randomized controlled trials and systematic reviews of trials was preferred. Changes in cardiovascular morbidity and mortality, as well as total mortality were considered the primary outcomes of interest. For health

recommended as the preferred method of measuring in-office blood pressure. Also, although a serum lipid panel remains part of the routine laboratory testing for patients with hypertension, fasting and nonfasting collections are now considered acceptable. For individuals with secondary hypertension arising from primary hyperaldosteronism, adrenal vein sampling is recommended for those who are candidates for potential adrenalectomy. With respect to the treatment of hypertension, a new recommendation that has been added is for increasing dietary potassium to reduce blood pressure in those who are not at high risk for hyperkalemia. Furthermore, in selected high-risk patients, intensive blood pressure reduction to a target systolic blood pressure  $\leq 120$  mm Hg should be considered to decrease the risk of cardiovascular events. Finally, in hypertensive individuals with uncomplicated, stable angina pectoris, either a  $\beta$ -blocker or calcium channel blocker may be considered for initial therapy. The specific evidence and rationale underlying each of these recommendations are discussed. Hypertension Canada's Canadian Hypertension Education Program Guidelines Task Force will continue to provide annual updates.

behaviour management, blood pressure (BP)-lowering was considered as the primary outcome. In those with chronic kidney disease, progressive renal impairment was also accepted as a clinically relevant outcome. All recommendations were graded according to the strength of the supporting evidence, and newly proposed recommendations or changes to existing recommendations were discussed at a consensus conference held on October 22, 2015 in Toronto, Canada. Proposed changes to the recommendations accepted at the consensus conference were subsequently voted upon by the 75 members of the Canadian Hypertension Education Program (CHEP) Recommendations Task Force. Recommendations that received at least 70% task force approval were then accepted as final.

## Recommendations

### Diagnosis and assessment

Two new recommendations and 1 modified recommendation have been introduced this year. First, automated office BP (AOBP), taken without patient-health provider interaction using a fully-automated device, is now recommended as the preferred method of measuring in-office BP. Second, a modified recommendation has been made to the routine workup for individuals with hypertension. A serum lipid panel (consisting of total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein [HDL], non-HDL cholesterol, and triglycerides) is still recommended routinely, but may be drawn in either a fasting or nonfasting state. Finally, a new recommendation was introduced for subtype classification for individuals with secondary hypertension arising from primary hyperaldosteronism. In those who are candidates for potential adrenalectomy, assessment for lateralization should be performed using adrenal vein sampling (AVS).

recommande désormais les mesures électroniques oscillométrique en série qui ne nécessitent pas la présence du professionnel de la santé durant la mesure. Chez les patients hypertendus, le bilan lipidique demeure un examen de laboratoire de routine, mais il est désormais acceptable que la prise de sang soit effectuée que le patient soit à jeun ou non. Chez les patients atteints d'hypertension secondaire liée à un hyperaldostéronisme primaire, on recommande de procéder à un échantillonnage des veines surrénales chez les candidats à une surrénalectomie. En ce qui a trait au traitement de l'hypertension, la nouvelle recommandation porte sur l'augmentation de l'apport en potassium alimentaire pour réduire la pression artérielle des patients qui ne sont pas à risque élevé de présenter une hyperkaliémie. Chez certains patients à risque élevé d'événement cardiovasculaire, on devrait envisager un traitement en vue d'obtenir une importante réduction de la pression artérielle systolique jusqu'à une valeur cible  $\leq 120$  mm Hg afin de réduire le risque de survenue d'un tel événement. Enfin, chez les hypertendus atteints d'angine de poitrine stable, on peut désormais envisager un traitement de première intention par un  $\beta$ -bloquant ou un bloqueur des canaux calciques. Les données probantes appuyant chacune des recommandations et leur justification sont aussi présentées dans cet article. Le groupe de travail du Programme éducatif canadien sur l'hypertension continuera de fournir une mise à jour annuelle de ses recommandations.

## Prevention and treatment

This year, 2 new recommendations were added and another recommendation was modified. First, as a new recommendation, an increase in dietary potassium should be considered in individuals who are not at high risk for hyperkalemia as an effective way to reduce BP. Second, in selected high-risk patients, intensive BP reduction to target a systolic BP (SBP)  $\leq 120$  mm Hg should be considered to lower the risk of cardiovascular events. As a revised recommendation, in individuals with stable angina pectoris (but without previous heart failure, myocardial infarction, or coronary artery bypass), either a  $\beta$ -blocker or calcium channel blocker (CCB) can be considered as equally acceptable choices for initial treatment.

## Updates

CHEP will continue to update recommendations annually.

## Introduction

Hypertension affects approximately 23% of Canadian adults and represents a major risk factor for cardiovascular disease, chronic kidney disease, and death; but it often remains clinically silent until complications arise.<sup>1-3</sup> Worldwide, high BP affects > 40% of adults older than the age of 25 years and is the leading global risk factor for death or disability.<sup>4,5</sup> In Canada, BP control rates have progressively improved from 13.2% in 1992 to 64.6% in 2007,<sup>6</sup> and most recently to 68.1% in 2012-2013.<sup>1</sup> In comparison, global BP control remains at 32.5%.<sup>5</sup>

With the goal of improving hypertension prevention, detection, assessment, and management in Canadians, CHEP has been producing annually updated, evidence-based recommendations for health care providers since 1999. Herein, we provide an updated list of recommendations for the care of adult patients with hypertension, as endorsed by the CHEP

Recommendations Task Force, along with discussion of the supporting evidence for any revised or new additions for 2016. Details pertaining to previously established recommendations are available in previous publications,<sup>6-31</sup> and are also published online (<http://guidelines.hypertension.ca>). This year, we will also introduce new set of pediatric-specific recommendations published in this issue of the *Canadian Journal of Cardiology*.<sup>32</sup>

Our recommendations are intended to guide health care providers but should not replace sound clinical judgement. Practitioners are advised to consider patient preferences, values, and clinical factors when determining how to best apply these recommendations at the bedside. Finally, although individual antihypertensive agents might be mentioned when discussing the current state of evidence, the reader should assume a class effect, unless otherwise stated.

## Methods

Hypertension Canada's CHEP Recommendations Task Force is a multidisciplinary panel of content and methodological experts comprised of a Chair, a Central Review Committee, and 15 subgroups. Each subgroup addresses a distinct content area in hypertension (see [Supplemental Appendix S1](#) for the current CHEP membership list). Members of the Canadian Task Force on Preventive Health Care, Canadian Diabetes Association Guidelines Committee, Canadian Society of Nephrology, Canadian Stroke Network, Canadian Cardiovascular Society, and the Canadian Cardiovascular Harmonized National Guideline Endeavour Initiative regularly collaborate with CHEP members to facilitate harmonization of recommendations across many organizations. In many cases, CHEP Recommendations Task Force members serve as volunteers for multiple organizations.

Systematic literature searches current to August 2015 were performed by a librarian from the Cochrane Collaboration in MedLine/PubMed using text words and Medical Subject Headings. Search terms included "hypertension[MeSH]," "hypertens\*[ti, ab]," and "BP"; these were combined with topic-specific terms. Bibliographies of identified articles were also hand-searched. Details of search strategies and retrieved articles are available upon request. Randomized controlled trials and systematic reviews of randomized controlled trials were reviewed for treatment recommendations, and cross-sectional and cohort studies were reviewed for evidence supporting diagnosis and informing prognosis.

Each subgroup examined the search results pertinent to its content area. Studies that assessed relevant outcomes were selected for further review. Cardiovascular morbidity and mortality as well as total mortality outcomes were prioritized for pharmacotherapy studies. For health behaviour recommendations, BP was considered an acceptable surrogate and, in patients with chronic kidney disease, progressive renal impairment was considered to be a clinically important outcome. Study characteristics and study quality were assessed using prespecified, standardized algorithms developed by CHEP for the critical appraisal of randomized controlled trials and observational studies.<sup>33</sup>

Recommendations were graded according to the strength of their underlying evidence (for details, see [Supplemental Table S1](#)), ranging from Grade A (strongest evidence, on the

basis of high-quality studies) to Grade D (weakest evidence, on the basis of low power, imprecise studies, or expert opinion alone). In addition to classifying recommendations on the basis of study quality, other grading schemes (eg, Grading of Recommendations Assessment, Development and Evaluation [[www.gradeworkinggroup.org](http://www.gradeworkinggroup.org)]), also endorse use of the terms 'strong' and 'weak' to describe the extent to which the guideline creators are confident the benefits outweigh the risks. CHEP does not use these terms because all CHEP recommendations are considered to be 'strong' in nature (ie, CHEP refrains from making 'weak' recommendations). Thus, the CHEP grading scheme refers only to the quality of evidence; all recommendations, regardless of grading, are believed to have benefits that strongly outweigh risks. For pharmacotherapy recommendations, as a general rule, CHEP considers evidence on evaluation of specific agents to be generalizable to a 'class effect.' For diuretic therapy, the term 'thiazides' refers to hydrochlorothiazide (or similar agents) and the term 'thiazide-like' refers to chlorthalidone and indapamide.

Subgroup members, considered content experts in their fields, were responsible for reviewing annual search results and, if indicated, drafting new recommendations or proposing changes to old recommendations. An independent Central Review Committee consisting of methodological experts with no industry affiliations independently reviewed, graded, and refined the proposed recommendations, which were then presented at a consensus conference of the Recommendations Task Force in Toronto, Ontario, Canada on October 22, 2015. This meeting included the Chair, Central Review Committee, and members of all subgroups. Further revisions to proposed recommendations were on the basis of these discussions. Notably, after our consensus conference, the **S**ystolic **B**lood **P**ressure **I**ntervention **T**rial (SPRINT) was released.<sup>34</sup> In light of its significant results, an expedited review of the SPRINT study was performed by the Recommendations Task Force, and therefore was included in this year's discussion.

All recommendations were finalized and submitted electronically to all 75 voting members of the CHEP Recommendations Task Force for approval. Members with potential conflicts of interest recused themselves from voting on specific recommendations (a list of conflicts is available in [Supplemental Appendix S2](#)). Recommendations that received > 70% approval were passed. The CHEP recommendations process is in accordance with the **A**ppraisal of **G**uidelines for **R**esearch and **E**valuation (AGREE) II guidelines,<sup>35</sup> and has been externally reviewed. A summary of how the CHEP process aligns with AGREE II can be found online ([www.hypertension.ca/overview-process](http://www.hypertension.ca/overview-process)). Materials to assist with patient and public education on the basis of these recommendations are freely available on the Hypertension Canada Web site (<http://guidelines.hypertension.ca/about/overview-process/>).

## The 2016 CHEP Diagnosis and Assessment Recommendations

### I. Accurate measurement of BP

#### 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 validated equipment for all methods (office BP measurement taken with a nonautomated device [non-AOBP], AOBP, home BP monitoring, and ambulatory BP monitoring) is recommended (Grade D; see [Supplemental Table S2](#); section VII. *Home BP Measurement*; section VIII. *Ambulatory BP Measurement*; [Table 1](#) in section VII. *Home BP Measurement*; and [Table 2](#) in section VIII. *Ambulatory BP Measurement*). Measurement using electronic (oscillometric) upper arm devices is preferred over auscultation (Grade C). (Unless specified otherwise, electronic [oscillometric] measurement should be used).
3. Four approaches can be used to assess BP:
  - i. For non-AOBP, an SBP  $\geq 140$  mm Hg or a diastolic BP (DBP)  $\geq 90$  mm Hg is high, and an SBP between 130 and 139 mm Hg and/or a DBP between 85 and 89 mm Hg is high-normal (Grade C).
  - ii. AOBP is the preferred method of performing in-office BP measurement (Grade D; **new recommendation**). When using AOBP (see the section on *Recommended Technique for Automated Office Blood Pressure* in [Supplemental Table S2](#)), a displayed mean SBP of  $\geq 135$  mm Hg or DBP  $\geq 85$  mm Hg DBP is high (Grade D).
  - iii. Using ambulatory BP monitoring (see *Recommendations* in section VIII. *Ambulatory BP Measurement*), patients can be diagnosed as hypertensive if the mean awake SBP is  $\geq 135$  mm Hg or the DBP is  $\geq 85$  mm Hg or if the mean 24-hour SBP is  $\geq 130$  mm Hg or the DBP is  $\geq 80$  mm Hg (Grade C).
  - iv. Using home BP monitoring (see *Recommendations* in section VII. *Home BP Measurement*) patients can be diagnosed as hypertensive if the mean SBP is  $\geq 135$  mm Hg or the DBP is  $\geq 85$  mm Hg (Grade C). If the office BP measurement is high and the mean home BP is  $< 135/85$  mm Hg, it is advisable to either repeat home monitoring to confirm the home BP is  $< 135/85$  mm Hg or perform 24-hour ambulatory BP monitoring to confirm that the mean 24-hour ambulatory BP

**Table 1. Standardized protocol for home BP measurement (Grade D)**

- Measurements should be taken using a validated electronic device.
- Choose a cuff with an appropriate bladder size matched to the size of the arm. Bladder width should be close to 40% of arm circumference and bladder length should cover 80%-100% of arm circumference. Select the cuff size as recommended by its manufacturer.
- Cuff should be applied to the nondominant arm unless the SBP difference between arms is  $> 10$  mm Hg, in which case the arm with the highest value obtained should be used.
- The patient should be resting comfortably for 5 minutes in the seated position with back support.
- The arm should be bare and supported with the BP cuff at heart level.
- Measurement should be performed before breakfast and 2 hours after dinner, before taking medication.
- No caffeine or tobacco in the hour and no exercise 30 minutes preceding the measurement.
- Duplicate measurement should be done in the morning and in the evening for seven days (ie, 28 measurements in total).
- Average the results excluding the first day's readings.

BP, blood pressure; SBP, systolic BP.

**Table 2. Standardized protocol for ambulatory BP monitoring (Grade D)**

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

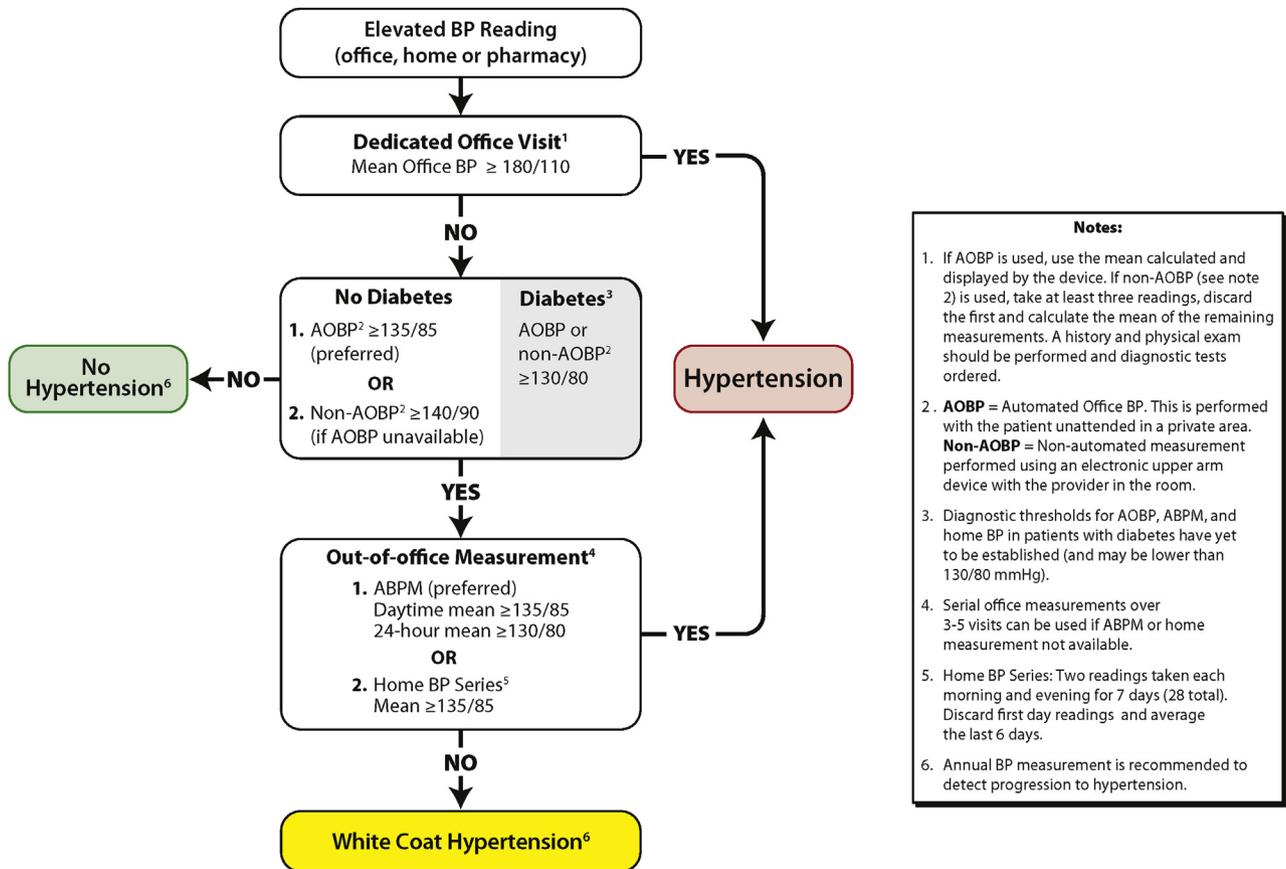
BP, blood pressure; SBP, systolic BP.

measurement is  $< 130/80$  mm Hg and the mean awake ambulatory BP measurement is  $< 135/85$  mm Hg before diagnosing white coat hypertension (Grade D).

**Background.** Building on our previous recommendation in favour of using electronic (oscillometric) upper arm devices,<sup>31</sup> this year we have introduced a new recommendation in support of AOBP as the preferred method of in-office BP measurement. AOBP allows BP to be measured using a fully automated electronic device without any patient-health provider interaction while the patient rests alone in a quiet room or private area (see [Supplemental Table S2](#)).

If AOBP is not used, care providers will typically need to remain in the room and perform sequential electronic measurements (because multiple measurements are recommended). The advantages of AOBP over the non-AOBP approach are that AOBP eliminates the risk of conversation during readings, reduces the risk of the white coat effect, and facilitates multiple measurements with each clinical encounter (and automatically calculates the mean). Measurements collected using AOBP appear to closely approximate mean awake ambulatory BP levels.<sup>36-43</sup> AOBP measurements are also demonstrably consistent from visit to visit.<sup>42,44,45</sup> Furthermore, AOBP measurements do not appear to be significantly altered by the setting in which BP is measured. Measurements taken in an ambulatory BP monitoring unit, office waiting room, and physician's examination room have been shown to be similar<sup>42,46,47</sup>; and, AOBP measurements obtained in a pharmacy and physician's office are likewise comparable.<sup>48</sup>

In addition to providing consistent and reliable readings, AOBP measurements are also useful in predicting the presence of end-organ damage (eg, carotid intima-media thickness, left ventricular mass index, microalbuminuria).<sup>49-51</sup> It has also been recently shown that elevated AOBP measurements are predictive of incident cardiovascular events.<sup>52</sup> In a recent 5-year longitudinal study of 3627 community-dwelling individuals aged 65 years or older with untreated hypertension, the presence of an elevated SBP between 135 and 144 mm Hg (measured using BpTRU [BpTRU Medical Devices, Coquitlam, BC] in various community pharmacies) was associated



**Figure 1.** Hypertension diagnostic algorithm. ABPM, ambulatory BP measurement; AOBP, automated office BP; BP, blood pressure.

with a 66% relative risk increase for developing an adverse cardiovascular event (hazard ratio [HR], 1.66; 95% confidence interval [CI], 1.09-2.54; compared with those with an SBP between 110 and 119 mm Hg); similarly, an elevated DBP between 80 and 89 mm Hg was associated with a 72% increased risk (HR, 1.72; 95% CI, 1.21-2.45; compared with a DBP between 60 and 69 mm Hg).<sup>52</sup> The generalizability of this study might potentially be limited by the older age of the participants (mean 74.2 years), measurement of BP at community pharmacies, and exclusion of individuals already taking antihypertensive medications. Nonetheless, this study provides evidence further supporting AOBP as the preferred method of in-office BP measurement.

## II. Criteria for diagnosis of hypertension and recommendations for follow-up

A hypertension diagnostic algorithm is shown in [Figure 1](#).

### Recommendations

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

averaged. If using AOBP, the BP calculated and displayed by the device should be used.

2. If the visit 1 office BP measurement is high-normal (thresholds outlined in section I, Recommendation 3) annual follow-up is recommended (Grade C).
3. If the visit 1 mean non-AOBP or AOBP measurement is high (thresholds outlined in section I, Recommendation 3), a history and physical examination should be performed and, if clinically indicated, diagnostic tests to search for target organ damage ([Supplemental Table S4](#)) and associated cardiovascular risk factors ([Supplemental Table S5](#)) should be arranged within 2 visits. Exogenous factors that can induce or aggravate hypertension should be assessed and removed if possible ([Supplemental Table S6](#)). Visit 2 should be scheduled within 1 month (Grade D).
4. If the visit 1 mean non-AOBP or AOBP SBP is  $\geq 180$  mm Hg and/or DBP is  $\geq 110$  mm Hg then hypertension is diagnosed (Grade D).
5. If the visit 1 mean non-AOBP SBP is 140-179 mm Hg and/or DBP is 90-109 mm Hg or the mean AOBP SBP is 135-179 mm Hg and/or DBP is 85-109 mm Hg, out-of-office BP measurements should be performed before visit 2 (Grade C).
  - i. Ambulatory BP monitoring is the recommended out-of-office measurement method (Grade D). Patients can be diagnosed with hypertension according to the thresholds outlined in section I, recommendation 3.

- ii. Home BP monitoring is recommended if ambulatory BP monitoring is not tolerated, not readily available, or because of patient preference (Grade D). Patients can be diagnosed with hypertension according to the thresholds outlined in section I, recommendation 3.
  - iii. If the out-of-office BP average is not elevated, white coat hypertension should be diagnosed and pharmacologic treatment should not be instituted (Grade C).
6. If the out-of-office measurement, although preferred, is not performed after visit 1, then patients can be diagnosed as hypertensive using serial office BP measurement visits if any of the following conditions are met:
- i. At visit 2, mean office BP measurement (averaged across all visits) is  $\geq 140$  mm Hg systolic and/or  $\geq 90$  mm Hg diastolic in patients with macrovascular target organ damage, diabetes mellitus, or chronic kidney disease (glomerular filtration rate  $< 60$  mL/min/1.73 m<sup>2</sup>) (Grade D);
  - ii. At visit 3, mean office BP measurement (averaged across all visits) is  $\geq 160$  mm Hg systolic or  $\geq 100$  mm Hg diastolic;
  - iii. At visit 5, mean office BP measurement (averaged across all visits) is  $\geq 140$  mm Hg systolic or  $\geq 90$  mm Hg diastolic.
7. Investigations for secondary causes of hypertension should be initiated in patients with suggestive clinical and/or laboratory features (outlined in sections V and VI) (Grade D).
8. If at the last diagnostic visit the patient is not diagnosed as hypertensive and has no evidence of macrovascular target organ damage, the patient's BP should be assessed at yearly intervals (Grade D).
9. Hypertensive patients actively modifying their health 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 measurements (Grade D).
10. 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).

**Background.** There are no changes to these recommendations for 2016.

### III. Assessment of overall cardiovascular risk in hypertensive patients

#### Recommendations

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

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

**Background.** There are no changes to these recommendations for 2016. Examples of freely available risk calculators include [www.myhealthcheckup.com](http://www.myhealthcheckup.com) and [www.score-canada.ca](http://www.score-canada.ca). The latter is the **S**ystematic **C**erebrovascular and **C**oronary **R**isk **E**valuation [SCORE]) risk calculator. Although not originally developed with Canadian data, Canadian cardiovascular disease prevalence and mortality risk have been integrated into the original SCORE risk engine to produce specific estimates for the Canadian population (SCORE Canada).

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

#### Recommendations

1. Routine laboratory tests that should be performed for the investigation of all patients with hypertension include the following.
  - i. Urinalysis (Grade D);
  - ii. Blood chemistry (potassium, sodium, and creatinine) (Grade D);
  - iii. Fasting blood glucose and/or glycated hemoglobin (Grade D);
  - iv. Serum total cholesterol, LDL, HDL, non-HDL cholesterol, and triglycerides (Grade D); lipids may be drawn fasting or non-fasting (Grade C) (**revised recommendation**);
  - 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 Canadian Diabetes Association guidelines for the new appearance of diabetes (Grade B).
4. During the maintenance phase of hypertension management, tests (including those for electrolytes, creatinine, and fasting lipids) should be repeated with a frequency reflecting the clinical situation (Grade D).

**Background.** This year, we provide a revised recommendation for the measurement of serum lipids. Although a serum lipid panel still remains part of the routine laboratory workup for individuals with hypertension,<sup>31</sup> a nonfasting lipid panel is now considered to be an acceptable method of measurement.

In 2012, a large Canadian community-based cross-sectional study was conducted, on the association between fasting status and serum lipid levels in 209,180 individuals.<sup>53</sup> In that study, the investigators reported that the duration of fasting (from 1 to  $> 16$  hours) had little association with measured lipid levels. Total cholesterol varied by  $< 2\%$  (with an average of 4.3 mmol/L after 1 hour of fasting compared with 4.5 mmol/L after a prolonged fast of 16 hours). Similarly, HDL cholesterol varied by  $< 2\%$  (from 1.2 to 1.3 mmol/L) and LDL cholesterol by  $< 10\%$  (from 2.3 to 2.6 mmol/L). However, there was a wider variation of nearly 20% associated with serum triglycerides

levels with various durations of fasting. Altogether, these findings are consistent with those of other studies, also reporting minimal differences in fasting compared with nonfasting cholesterol levels in the general population.<sup>54,55</sup>

Multiple studies have shown that nonfasting lipid levels are predictive of incident cardiovascular disease.<sup>54-59</sup> A Danish cohort of 9319 individuals was followed prospectively for 14 years,<sup>55</sup> and individuals in the highest tertile of nonfasting total cholesterol were at increased risk for cardiovascular events compared with those in the lowest tertile (HR, 1.7; 95% CI, 1.1-2.6) with similar findings also seen for non-HDL cholesterol (HR, 2.3; 95% CI, 1.5-3.4) and LDL cholesterol (HR, 2.1; 95% CI, 1.4-3.1). In another study, on the basis of the National Health and Nutrition Examination Survey (NHANES) III, 4299 pairs of fasting and nonfasting individuals (matched 1:1) were followed for a mean of 14 years. Regardless of whether LDL cholesterol was collected fasting or nonfasting, the levels were similarly predictive of cardiovascular mortality as well as all-cause mortality in a dose-dependent manner. This remained true for individuals with and without diabetes.<sup>54</sup> Furthermore, using a centralized database of over 125 prospective studies, the Emerging Risk Factors Collaboration conducted a study of 302,430 participants (with a mean age of 58 years representing 2.79 million person-years at risk) and reported similar associations between death attributable to coronary heart disease and lipid levels (for HDL, non-HDL, and LDL), irrespective of fasting status.<sup>58</sup>

Finally, from a practical standpoint, performing nonfasting lipid assessments in routine clinical care might obviate many of the serious challenges associated with prolonged fasting, namely the possibility of decreased patient adherence, increased laboratory burden due to bolus testing in the morning, and preventable hypoglycemia among individuals with diabetes.<sup>60-62</sup>

## V. Assessment for renovascular hypertension

### Recommendations

1. Patients presenting with  $\geq 2$  of the following clinical clues, suggesting renovascular hypertension, should be investigated (Grade D):
  - i. Sudden onset or worsening of hypertension and age  $> 55$  or  $< 30$  years;
  - ii. Presence of an abdominal bruit;
  - iii. Hypertension resistant to  $\geq 3$  drugs;
  - iv. Increase in serum creatinine level  $\geq 30\%$  associated with use of an angiotensin converting enzyme (ACE) inhibitor or angiotensin receptor blocker (ARB);
  - v. Other atherosclerotic vascular disease, particularly in patients who smoke or have dyslipidemia;
  - vi. Recurrent pulmonary edema associated with hypertensive surges.
2. When available, the following tests are recommended to aid in the usual screening for renal vascular disease: captopril-enhanced radioisotope renal scan, Doppler sonography, magnetic resonance angiography, and computed tomography (CT) angiography (for those with normal renal function) (Grade B). Captopril-enhanced radioisotope renal scan is not

recommended for those with chronic kidney disease (glomerular filtration rate  $< 60$  mL/min/1.73 m<sup>2</sup>) (Grade D).

**Background.** There are no changes to these recommendations for 2016.

## VI. Endocrine hypertension

### Recommendations

#### A. Hyperaldosteronism: screening and diagnosis

1. Screening for hyperaldosteronism should be considered for the following patients (Grade D):
  - i. Hypertensive patients with unexplained spontaneous hypokalemia ( $K^+ < 3.5$  mmol/L) or marked diuretic-induced hypokalemia ( $K^+ < 3.0$  mmol/L);
  - ii. Patients with hypertension refractory to treatment with  $\geq 3$  drugs;
  - iii. Hypertensive patients found to have an incidental adrenal adenoma.
2. Screening for hyperaldosteronism should include assessment of plasma aldosterone and plasma renin activity or plasma renin ([Supplemental Table S7](#)).
3. For patients with suspected hyperaldosteronism (on the basis of the screening test, [Supplemental Table S7](#), item iii), a diagnosis of primary hyperaldosteronism should be established by presence of inappropriate autonomous hypersecretion of aldosterone using at least 1 of the manoeuvres listed in [Supplemental Table S7](#), item iv. When the diagnosis is established, the abnormality should be localized using any of the tests described in [Supplemental Table S7](#), item v.
4. In patients with primary hyperaldosteronism and a definite adrenal mass who are eligible for surgery, adrenal venous sampling is recommended to assess for lateralization of aldosterone hypersecretion. AVS should be performed exclusively by experienced teams working in specialized centres (Grade C) (**new recommendation**).

#### B. Pheochromocytoma and paraganglioma: screening and diagnosis

1. If pheochromocytoma or paraganglioma is strongly suspected, the patient should be referred to a specialized hypertension centre, particularly if biochemical screening tests ([Supplemental Table S8](#)) have already been found to be positive (Grade D).
2. The following patients should be considered for screening for pheochromocytoma or paraganglioma (Grade D):
  - i. Patients with paroxysmal, unexplained, labile, and/or severe (BP  $\geq 180/110$  mm Hg) sustained hypertension refractory to usual antihypertensive therapy;
  - ii. Patients with hypertension and multiple symptoms suggestive of catecholamine excess (eg, headaches, palpitations, sweating, panic attacks, and pallor);
  - iii. Patients with hypertension triggered by  $\beta$ -blockers, monoamine oxidase inhibitors, micturition, changes in abdominal pressure, surgery, or 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 should use magnetic resonance imaging (preferable), CT (if magnetic resonance imaging unavailable), and/or iodine I-131 meta-iodobenzylguanidine scintigraphy (Grade C for each modality).

**Background.** This year, we introduced a new recommendation to guide subtype classification for confirmed cases of primary hyperaldosteronism, because differentiation between unilateral and bilateral forms of aldosterone hypersecretion might have important treatment implications. Unilateral forms might be amenable to improvement or even cure with adrenalectomy. In contrast, mineralocorticoid receptor antagonists are the treatment of choice for bilateral hypersecretion. However, in certain cases where surgery is not possible or desired, subtype evaluation might be unnecessary, because treatment is uniformly medical, regardless of whether unilateral or bilateral disease is present (see [Supplemental Table S7](#), item vi).

Numerous studies have reported significant discordance between conventional cross-sectional imaging with CT and AVS.<sup>63-68</sup> In a prospective study of 203 patients with primary hyperaldosteronism, Young et al. reported that the use of CT imaging alone would result in 22% of patients being incorrectly excluded for adrenalectomy while another 25% of individuals potentially receiving unnecessary surgery.<sup>68</sup> In another study by McAlister and Lewanczuk, 18 of 27 individuals with confirmed primary hyperaldosteronism had adrenal masses visualized on CT scan; of these, only 13 had lateralization to the ipsilateral gland proven with AVS or surgery. Further, 5 of 12 patients with bilateral hypersecretion also had a visible adrenal mass on CT scan.<sup>66</sup> Indeed, a systematic review of 38 studies on the performance of CT or magnetic resonance imaging compared with AVS similarly reported a striking high discrepancy rate of 37.8%.<sup>69</sup> Accordingly, reliance on cross-sectional imaging alone to determine lateralization might result in inappropriate treatment decisions.

Direct measurement of aldosterone secretion using AVS is widely considered to be the gold standard technique to determine lateralization. Even so, use of AVS might be limited because of technical challenges and reportedly high procedural failure rates, because of difficulties in localizing the adrenal veins (especially on the right side) because of small vessel size and variations in anatomy.<sup>70</sup> In a retrospective study of 5 centres using the German Conn's Registry, successful bilateral catheterization was only achieved in 30.5% of cases.<sup>71</sup> Performance appeared to be related to technical proficiency. Accordingly, when strictly performed by experienced teams in specialized centres with high throughput, some have reported impressive AVS success rates of > 90%.<sup>68,70,72,73</sup> Therefore, AVS should be exclusively performed at experienced centres to minimize the risk of potential failed catheterizations and unnecessary procedural complications.

## VII. Home BP measurement

### Recommendations

1. Home BP monitoring can be used in the diagnosis of hypertension (Grade C).
2. The use of home BP monitoring on a regular basis should be considered for patients with hypertension, particularly those with:
  - i. Diabetes mellitus (Grade D);
  - ii. Chronic kidney disease (Grade C);
  - iii. Suspected nonadherence (Grade D);
  - iv. Demonstrated white coat effect (Grade C);
  - v. BP controlled in the office but not at home (masked hypertension) (Grade C).
3. When white coat hypertension is suggested by home BP monitoring, its presence should be confirmed by repeat home BP monitoring (Recommendation 7 in this section) or ambulatory BP monitoring before treatment decisions are made (Grade D).
4. Patients should be advised to purchase and use only home BP monitoring devices that are appropriate for the individual and have met standards of the Association for the Advancement of Medical Instrumentation, the most recent requirements of the British Hypertension Society protocol, or the International Protocol for validation of automated BP measuring devices. Patients should be encouraged to use devices with data recording capabilities or automatic data transmission to increase the reliability of reported home BP monitoring (Grade D).
5. Home SBP values  $\geq 135$  mm Hg or DBP values  $\geq 85$  mm Hg should be considered to be elevated and associated with an increased overall mortality risk (Grade C).
6. Health care professionals should ensure that patients who measure their BP at home have adequate training and, if necessary, repeat training in measuring their BP. Patients should be observed to determine that they measure BP correctly and should be given adequate information about interpreting these readings (Grade D).
7. Home BP monitoring for assessing white coat hypertension or sustained hypertension should be on the basis of duplicate measures, morning and evening, for an initial 7-day period. First-day home BP values should not be considered (Grade D).

**Background.** There are no changes to these recommendations for 2016. A suggested, standardized protocol for home BP monitoring is presented in [Table 1](#).

## VIII. Ambulatory BP measurement

### Recommendations

1. Ambulatory BP monitoring can be used in the diagnosis of hypertension (Grade C). Ambulatory BP monitoring should be considered when an office-induced increase in BP is suspected in treated patients with:
  - i. BP that is not below target despite receiving appropriate chronic antihypertensive therapy (Grade C);
  - ii. Symptoms suggestive of hypotension (Grade C);
  - iii. Fluctuating office BP readings (Grade D).

- Ambulatory BP monitoring upper arm devices that have been validated independently using established protocols must be used (see [www.dablededucational.org](http://www.dablededucational.org)) (Grade D).
- Therapy adjustment should be considered in patients with a mean 24-hour ambulatory BP monitoring SBP of  $\geq 130$  mm Hg and/or DBP of  $\geq 80$  mm Hg, or a mean awake SBP of  $\geq 135$  mm Hg and/or DBP of  $\geq 85$  mm Hg (Grade D).
- 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 ambulatory BP monitoring (Grade C) because a decrease in nocturnal BP of  $< 10\%$  is associated with increased risk of cardiovascular events.

**Background.** There are no changes to these recommendations for 2016. A suggested, standardized protocol for ambulatory BP monitoring is presented in [Table 2](#).

## IX. Role of echocardiography

### Recommendations

- Routine echocardiographic evaluation of all hypertensive patients is not recommended (Grade D).
- An echocardiogram for assessment of left ventricular hypertrophy is useful in selected cases to help define the future risk of cardiovascular events (Grade C).
- 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).
- Patients with hypertension and evidence of heart failure should have an objective assessment of left ventricular ejection fraction, either using echocardiography or nuclear imaging (Grade D).

**Background.** There are no changes to these recommendations for 2016.

## The CHEP 2016 Prevention and Treatment Recommendations

Please note, hereafter, all treatment thresholds and targets refer to office BP measurements, because most of the supporting evidence is derived from studies that used this method of BP measurement. Please refer to *The 2016 CHEP Diagnosis and Assessment Recommendations*, section II (*Criteria for Diagnosis of Hypertension and Recommendations for Follow-up*) for corresponding values using other measurement methods. A summary of the potential factors that should be considered when selecting specific drug therapy for individualized treatment is presented in [Table 3](#).

### I. Health behaviour management

#### Recommendations

##### A. Physical exercise

- For nonhypertensive or stage 1 hypertensive individuals, the use of resistance or weight training

exercise (such as free weight lifting, fixed weight lifting, or handgrip exercise) does not adversely influence BP (Grade D). 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).

##### B. Weight reduction

- Height, weight, and waist circumference should be measured and body mass index calculated for all adults (Grade D).
- 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).
- Weight loss strategies should use a multidisciplinary approach that includes dietary education, increased physical activity, and behavioural intervention (Grade B).

##### C. Alcohol consumption

- To reduce BP, healthy adults should limit alcohol consumption to  $\leq 2$  drinks per day, and consumption should not exceed 14 standard drinks per week for men and 9 standard drinks per week for women (Grade B). (Note: One standard drink is considered to be equivalent of 13.6 g or 17.2 mL of ethanol or approximately 44 mL [1.5 oz] of 80-proof [40%] spirits, 355 mL [12 oz] of 5% beer, or 148 mL [5 oz] of 12% wine).

##### D. Dietary recommendations

- It is recommended that hypertensive patients and normotensive individuals at increased risk of developing hypertension consume a diet that emphasizes fruits, vegetables, low-fat dairy products, dietary and soluble fibre, whole grains, and protein from plant sources that is reduced in saturated fat and cholesterol (Dietary Approaches to Stop Hypertension [DASH] diet<sup>74-77</sup>; [Supplemental Table S9](#); Grade B).

##### E. Sodium intake

- To decrease BP, 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

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

##### G. Potassium intake

- In patients not at risk of hyperkalemia (see [Table 4](#)), increase dietary potassium intake to reduce BP (Grade A; **new recommendation**).

##### H. Stress management

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

**Background.** This year, we introduced a new recommendation supporting an increase in dietary potassium to lower BP. Supporting evidence for this recommendation comes from several systematic reviews and meta-analyses that reported a consistent association between increased potassium intake and BP reduction. The most rigorous of these reviews was a meta-analysis of 22 randomized controlled trials by Aburto et al., who reported that increased potassium intake reduced SBP by 3.49 mm Hg (95% CI, 1.82-5.15 mm Hg) and DBP by 1.96 mm Hg (95% CI, 0.86-3.06 mm Hg).<sup>78</sup> Notably, BP reduction was only seen in those with hypertension. There was no significant dose response according to the amount of potassium consumed. However, BP reduction appeared to be greatest in those who consumed the greatest amount of salt (change in SBP of  $-6.9$  vs  $-2.0$  in those with high [ $> 2$  g/d] vs low [ $< 2$  g/d] sodium intake). Although the magnitude of BP reduction is largest when the sodium intake is high, there still appears to be evidence of additive benefit when dietary interventions combine potassium increases with sodium reduction strategies.<sup>74</sup>

The magnitude of expected BP reduction appears to be similar regardless of whether a potassium intervention is delivered through dietary changes or prescribed supplements.<sup>78</sup> If possible, however, we recommend dietary modification as the preferred method of increasing potassium intake because of the additional nutritional benefits of whole foods over prescribed supplements. When appropriate, patients with hypertension should be encouraged to consume foods with higher potassium content (eg, fresh fruits, vegetables, and legumes). Overall, potassium interventions appear to be largely safe with no increase in reported adverse events.<sup>78</sup> However, it should be acknowledged that the generalizability of existing studies is limited by stringent exclusion criteria (eg, excluding those with impaired urinary potassium excretion from renal failure or use of medications that predispose to hyperkalemia).<sup>78</sup> As such, although the literature broadly supports increasing potassium intake to lower BP, caution should be exercised in those at higher risk of developing hyperkalemia (Table 4).

## II. 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) or average SBP measurements of  $\geq 160$  mm Hg (Grade A) in patients without macrovascular target organ damage or other cardiovascular risk factors.
2. Antihypertensive therapy should be strongly considered if DBP readings average  $\geq 90$  mm Hg in the presence of macrovascular target organ damage or other independent cardiovascular risk factors (Grade A).
3. Antihypertensive therapy should be strongly considered if SBP readings average  $\geq 140$  mm Hg in the presence of macrovascular target organ damage (Grade C for 140-160 mm Hg; Grade A for  $> 160$  mm Hg).
4. Antihypertensive therapy should be considered in all patients who meet indications 1-3 in this section, regardless

of age (Grade B). Caution should be exercised in elderly patients who are frail.

5. In the very elderly (aged  $\geq 80$  years) who do not have diabetes or target organ damage, the SBP threshold for initiating drug therapy is  $\geq 160$  mm Hg (Grade C).

**Background.** There are no changes to these recommendations for 2016.

## III. Choice of therapy for adults with hypertension without compelling indications for specific agents

### Recommendations

#### A. Recommendations for individuals with diastolic and/or systolic hypertension

1. Initial therapy should be monotherapy with a thiazide/thiazide-like diuretic (Grade A), a  $\beta$ -blocker (in patients younger than 60 years, Grade B), an ACE inhibitor (in nonblack patients, Grade B), a long-acting CCB (Grade B); 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 choices. Useful choices include a thiazide/thiazide-like diuretic or CCB with either: ACE inhibitor, ARB, or  $\beta$ -blocker (Grade B for the combination of thiazide/thiazide-like diuretic and a dihydropyridine CCB; Grade C for the combination of dihydropyridine CCB and ACE inhibitor; and Grade D for all other combinations). Caution should be exercised in combining a nondihydropyridine CCB and a  $\beta$ -blocker (Grade D). The combination of an ACE inhibitor and an ARB is not recommended (Grade A).
3. Combination therapy using 2 first-line agents may also be considered as initial treatment of hypertension (Grade C) if SBP is 20 mm Hg greater than target or if DBP is 10 mm Hg greater than target. However, caution should be exercised in patients in whom a decrease in BP from initial combination therapy is more likely to occur or in whom it would be poorly tolerated (eg, elderly patients).
4. If BP is still not controlled with a combination of  $\geq 2$  first-line agents, or there are adverse effects, other antihypertensive drugs may be added (Grade D).
5. Possible reasons for poor response to therapy (Supplemental Table S10) should be considered (Grade D).
6.  $\alpha$ -Blockers are not recommended as first-line agents for uncomplicated hypertension (Grade A);  $\beta$ -blockers are not recommended as first-line therapy for uncomplicated hypertension in patients 60 years of age or older (Grade A); and ACE inhibitors are not recommended as first-line therapy for uncomplicated hypertension in black patients (Grade A). However, these agents may be

**Table 3. Considerations in the individualization of pharmacological therapy**

	Initial therapy	Second-line therapy	Notes and/or cautions
<b>Hypertension without other compelling indications</b>			
Diastolic hypertension with or without systolic hypertension	Thiazide/thiazide-like diuretics, $\beta$ -blockers, ACE inhibitors, ARBs, or long-acting CCBs (consider ASA and statins in selected patients). Consider initiating therapy with a combination of first-line drugs if the BP is $\geq 20$ mm Hg systolic or $\geq 10$ mm Hg diastolic above target	Combinations of first-line drugs	Not recommended for monotherapy: $\alpha$ -blockers, $\beta$ -blockers in those $\geq 60$ years of age, ACE inhibitors in black people. Hypokalemia should be avoided in those prescribed diuretics. ACE inhibitors, ARBs, and direct renin inhibitors are potential teratogens, and caution is required if prescribing to women with child-bearing potential. Combination of an ACE inhibitor with an ARB is not recommended
Isolated systolic hypertension without other compelling indications	Thiazide/thiazide-like diuretics, ARBs, or long-acting dihydropyridine CCBs	Combinations of first-line drugs	Same as diastolic hypertension with or without systolic hypertension
<b>Diabetes mellitus</b>			
Diabetes mellitus with microalbuminuria,* renal disease, cardiovascular disease, or additional cardiovascular risk factors	ACE inhibitors or ARBs	Addition of a dihydropyridine CCB is preferred over a thiazide/thiazide-like diuretic	A loop diuretic could be considered in hypertensive chronic kidney disease patients with extracellular fluid volume overload
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
<b>Cardiovascular disease</b>			
Coronary artery disease	ACE inhibitors or ARBs; $\beta$ -blockers or CCBs for patients with stable angina	When combination therapy is being used for high-risk patients, an ACE inhibitor/dihydropyridine CCB is preferred	Avoid short-acting nifedipine. Combination of an ACE inhibitor with an ARB is specifically not recommended. Exercise caution when lowering SBP to target if DBP is $\leq 60$ mm Hg
Recent myocardial infarction	$\beta$ -Blockers and ACE inhibitors (ARBs if ACE inhibitor-intolerant)	Long-acting CCBs if $\beta$ -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 $\beta$ -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	Titrate doses of ACE inhibitors and ARBs to those used in clinical trials. Carefully monitor potassium and renal function if combining any of ACE inhibitor, ARB, and/or aldosterone antagonist
Left ventricular hypertrophy	ACE inhibitor, ARB, long-acting CCB, or thiazide/thiazide-like diuretics	Combination of additional agents	Hydralazine and minoxidil should not be used
Previous stroke or TIA	ACE inhibitor and a thiazide/thiazide-like diuretic combination	Combination of additional agents	Treatment of hypertension should not be routinely undertaken in acute stroke unless extreme BP elevation. Combination of an ACE inhibitor with an ARB is not recommended
<b>Nondiabetic chronic kidney disease</b>			
Nondiabetic chronic kidney disease with proteinuria <sup>1</sup>	ACE inhibitors (ARBs if ACE inhibitor-intolerant) if there is proteinuria. Diuretics as additive therapy	Combinations of additional agents	Carefully monitor renal function and potassium for those receiving an ACE inhibitor or ARB. Combinations of an ACE inhibitor and ARB are not recommended in patients without proteinuria

Continued

**Table 3. Continued.**

	Initial therapy	Second-line therapy	Notes and/or cautions
Renovascular disease	Does not affect initial treatment recommendations. Renal artery stenosis should be primarily managed medically	Combinations of additional agents	Caution with ACE inhibitors or ARB if bilateral renal artery stenosis or unilateral disease with solitary kidney. Renal artery angioplasty and stenting could be considered for patients with renal artery stenosis and complicated, uncontrolled hypertension
<b>Other conditions</b>			
Peripheral arterial disease	Does not affect initial treatment recommendations	Combinations of additional agents	Avoid $\beta$ -blockers with severe disease
Dyslipidemia	Does not affect initial treatment recommendations	Combinations of additional agents	—
Overall vascular protection	Statin therapy for patients with $\geq 3$ cardiovascular risk factors or atherosclerotic disease. Low-dose ASA in patients $\geq 50$ years of age. Advise on smoking cessation and use pharmacotherapy for smoking cessation if indicated	—	Caution should be exercised with the ASA recommendation if BP is not controlled

ACE, angiotensin converting enzyme; ARB, angiotensin receptor blocker; ASA, acetylsalicylic acid; BNP, B-type natriuretic peptide; BP, blood pressure; CCB, calcium channel blocker; DBP, diastolic BP; NT-proBNP, N-terminal pro-B-type natriuretic peptide; NYHA, New York Heart Association; SBP, systolic BP; TIA, transient ischemic attack.

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

† Proteinuria is defined as urinary protein  $> 500$  mg per 24 hours or albumin to creatinine ratio  $> 30$  mg/mmol in 2 of 3 specimens. Reproduced with permission from the Canadian Hypertension Education Program.

used in patients with certain comorbid conditions or in combination therapy.

**Background.** There are no changes to these recommendations for 2016.

**B. Recommendations for individuals with isolated systolic hypertension**

1. Initial therapy should be single-agent therapy with a thiazide/thiazide-like diuretic (Grade A), a long-acting dihydropyridine CCB (Grade A), or an ARB (Grade B). If there are adverse effects, another drug from this group should be substituted. Hypokalemia should be avoided in patients treated with thiazide/thiazide-like diuretic monotherapy (Grade C).
2. Additional antihypertensive drugs should be used if target 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  $\geq 2$  first-line agents, or there are adverse effects, other classes of drugs (such as  $\alpha$ -blockers, ACE inhibitors, centrally

acting agents, or nondihydropyridine CCBs) may be added or substituted (Grade D).

4. Possible reasons for poor response to therapy (Supplemental Table S10) should be considered (Grade D).
5.  $\alpha$ -Blockers are not recommended as first-line agents for uncomplicated isolated systolic hypertension (Grade A); and  $\beta$ -blockers are not recommended as first-line therapy for isolated systolic hypertension in patients aged  $\geq 60$  years (Grade A). However, both agents may be used in patients with certain comorbid conditions or in combination therapy.

**Background.** There are no changes to these recommendations for 2016.

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

**Recommendations**

1. Statin therapy is recommended in hypertensive patients with  $\geq 3$  cardiovascular risk factors as defined in Supplemental Table S11 (Grade A in patients  $> 40$  years) or with established atherosclerotic disease (Grade A regardless of age).
2. Consideration should be given to the addition of low dose acetylsalicylic acid therapy in hypertensive patients  $\geq 50$  years of age (Grade B). Caution should be exercised if BP is not controlled (Grade C).

**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 receiving renin-angiotensin-aldosterone inhibitors
- Patients receiving other drugs that can cause hyperkalemia (eg, trimethoprim and sulfamethoxazole, amiloride, or triamterene)
- Chronic kidney disease (glomerular filtration rate  $< 60$  mL/min/1.73 m<sup>2</sup>)
- Baseline serum potassium  $> 4.5$  mmol/L

**Table 5. Clinical indications defining high-risk 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 <sup>2</sup> )*
or
Estimated 10-year global cardiovascular risk ≥ 15%†
or
Age ≥ 75 years
Patients with ≥ 1 clinical indications should consent to intensive management

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

† Framingham Risk Score.<sup>79</sup>

- 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).
- 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).
- For high-risk patients (Table 5), aged ≥ 50 years, with SBP levels ≥ 130 mm Hg, intensive management to target an SBP ≤ 120 mm Hg should be considered. Intensive management should be guided by AOBP measurements (see *The 2016 CHEP Diagnosis and Assessment Recommendations*, section I [Accurate Measurement of BP], and Supplemental Table S2 [Recommended Technique for Automated Office Blood Pressure]). Patient selection for intensive management is recommended and caution should be taken in certain high-risk groups (Table 6; Grade B; **new recommendation**).

**Background.** This year, we have added a new recommendation to consider intensive BP control, targeting an SBP ≤ 120 mm Hg in selected high-risk patients.

SPRINT was a randomized controlled trial that enrolled 9631 individuals at high risk for cardiovascular disease (but without diabetes or previous stroke) and randomized them to receive either intensive treatment (targeting an SBP < 120 mm Hg) or standard control (targeting an SBP < 140 mm Hg).<sup>34</sup> The trial was terminated after only 3.26 years because of a significant reduction in adverse cardiovascular events with

**Table 6. Generalizability of intensive blood pressure-lowering: cautions and contraindications**

Limited or no evidence
Heart failure (ejection fraction < 35%) or recent myocardial infarction (within past 3 months)
Indication for, but not currently receiving, a β-blocker
Frail or institutionalized elderly individuals
Inconclusive evidence
Diabetes mellitus
Previous stroke
eGFR < 20 mL/min/1.73 m <sup>2</sup>
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.

intensive BP control that was detected before the end of the planned 5 years of follow-up. For the primary outcome of interest (a composite of myocardial infarction, acute coronary syndrome not resulting in myocardial infarction, stroke, acute decompensated heart failure, or death from cardiovascular causes), individuals who received intensive treatment had an event rate of 1.65% per year compared with 2.19% per year in those assigned to standard treatment (HR, 0.75; 95% CI, 0.64-0.89). Among individuals with normal kidney function at baseline, intensive control was associated with an increased risk of renal deterioration compared with standard treatment (HR, 3.49; 95% CI, 2.44-5.10). Serious adverse events commonly occurred but were similar in both groups (38.3% vs 37.1% for intensive vs standard treatment; *P* = 0.25). Although our new treatment recommendation is largely on the basis of the findings of SPRINT, it is also consistent with those of 2 recent meta-analyses of randomized controlled trials, likewise reporting a strong linear association between lower SBP targets and a reduction in major adverse cardiovascular events.<sup>80,81</sup>

In selected high-risk patients who might potentially benefit from lower BP targets, several major considerations should be made before implementing an intensive treatment strategy. First, risk evaluation should be primarily informed by the inclusion criteria used in the SPRINT trial (Table 5).<sup>34</sup> Second, the risks and benefits of intervention should be carefully weighed, because patients with hypertension are at risk for adverse vascular events and also for adverse treatment effects. Caution should be exercised in the setting of clinical conditions in which evidence supporting lower SBP targets < 120 mm Hg remains limited, and therefore intensive BP-lowering is more difficult to justify in light of the increased risk of adverse treatment effects (Table 6). Third, treatment should be guided by AOBP measurements (see *The 2016 CHEP Diagnosis and Assessment Recommendations*, Section I [Accurate Measurement of BP], and Supplemental Table S2 [Recommended Technique for Automated Office Blood Pressure]), as was the case in the SPRINT trial.<sup>34</sup> Finally, patients should be prepared for more clinical encounters, monitoring, and medication usage. Individuals who received intensive treatment in SPRINT were followed monthly until target BP levels were achieved. On average, they were prescribed 2.7 antihypertensive agents, compared with 1.8 agents in the standard control group.<sup>34</sup> Although SBP targets < 120 mm Hg are beneficial in carefully selected cases, intensive treatment also incurs greater health care utilization and potential treatment risks.

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

### Recommendations

- 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).
- In the very elderly (age ≥ 80 years), the SBP target is < 150 mm Hg (Grade C).

**Background.** There are no changes to these recommendations for 2016.

## VI. Treatment of hypertension in association with ischemic heart disease

### Recommendations

#### A. Recommendations for hypertensive patients with CAD

1. For most hypertensive patients with CAD, an ACE inhibitor or ARB is recommended (Grade A).
2. For hypertensive patients with CAD, but without coexisting systolic heart failure, the combination of an ACE inhibitor and ARB is not recommended (Grade B).
3. For high-risk 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  $\beta$ -blocker or CCB can be used as initial therapy (Grade B; **revised recommendation**).
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  $\leq 60$  mm Hg because of concerns that myocardial ischemia might be exacerbated (Grade D).

**Background.** We have revised our previous recommendations in this section with minor wording changes to improve clarity. Additionally, this year, a content revision was made in support of using either a  $\beta$ -blocker or CCB for initial therapy in adults with hypertension and stable angina, but without previous heart failure, myocardial infarction, or coronary artery bypass surgery. This revision is on the basis of a body of evidence that suggests that  $\beta$ -blockers and CCBs are similarly effective in preventing major adverse cardiovascular events in patients with chronic, stable coronary disease, and it harmonizes our recommendations with those of the recent Canadian Cardiovascular Society guidelines.<sup>82</sup>

The largest contributor to this evidence was the **International Verapamil SR Trandolapril Study (INVEST)**, which enrolled 22,576 patients, aged  $\geq 50$  years, with hypertension and stable CAD, and randomized participants to receive either verapamil or atenolol to target a BP of  $< 140/90$  mm Hg (or  $< 130/85$  mm Hg in patients with diabetes or chronic kidney disease).<sup>83</sup> A second agent could be added if patients did not achieve target; trandolapril was added for those initially randomized to verapamil, and hydrochlorothiazide was added for those in the atenolol group. Trandolapril was also added to atenolol if patients had a history of diabetes or chronic kidney disease. The primary outcome was a composite of death, nonfatal myocardial infarction, and nonfatal stroke. After 2.3 years of follow-up, similar BP reductions were seen in both groups ( $-18.7/-10.0$  mm Hg with verapamil vs  $-19.0/-10.2$  mm Hg with atenolol). The average number of medications required to achieve target BP was the same in both groups (mean, 1.7 medications). The overall event rates were also similar in both groups, with a total of 2380 outcome

events confirmed: 1171 in the verapamil group and 1209 in those who received atenolol. The relative risk for the primary outcome was 0.98 (95% CI, 0.90-1.06) with no significant differences detected between those treated with verapamil compared with those treated with atenolol.

The findings of INVEST are congruent with 2 other smaller trials, the **Angina Prognosis Study in Stockholm (APSIS)** and the **Total Ischemic Burden European Trial (TIBET)**.<sup>84,85</sup> These 2 studies enrolled and randomized 809 and 682 patients, respectively, with stable angina to either a  $\beta$ -blocker (ie, metoprolol in APSIS and atenolol in TIBET) or a CCB (verapamil in APSIS and nifedipine in TIBET). Both trials reported a comparable efficacy between  $\beta$ -blockers and CCBs in preventing major adverse cardiovascular events in patients with stable coronary disease. Notably, however, neither trial required hypertension to be present for study inclusion. Only a quarter of participants in APSIS had hypertension compared with approximately half of those in TIBET. Nonetheless, the existing evidence as a whole supports the use of either a  $\beta$ -blocker or CCB as initial therapy in those with stable coronary disease.

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

1. Initial therapy should include a  $\beta$ -blocker and an ACE inhibitor (Grade A).
2. An ARB can be used if the patient is intolerant of an ACE inhibitor (Grade A in patients with left ventricular systolic dysfunction).
3. CCBs may be used in patients after myocardial infarction when  $\beta$ -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).

**Background.** There are no changes to these recommendations for 2016.

## VII. Treatment of hypertension in association with heart failure

### Recommendations

1. In patients with systolic dysfunction (ejection fraction  $< 40\%$ ), ACE inhibitors (Grade A) and  $\beta$ -blockers (Grade A) are recommended for initial therapy. Aldosterone antagonists (mineralocorticoid receptor antagonists) may be added for patients with a recent cardiovascular hospitalization, acute myocardial infarction, elevated B-type natriuretic peptide or N-terminal pro-B-type natriuretic peptide level, or New York Heart Association class II-IV symptoms (Grade A). Careful monitoring for hyperkalemia is recommended when adding an aldosterone antagonist to ACE inhibitor or ARB therapy. 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 reported to be effective in trials unless adverse effects become manifest (Grade B).

2. An ARB is recommended if ACE inhibitors are not tolerated (Grade A).
3. A combination of hydralazine and isosorbide dinitrate is recommended if ACE inhibitors and ARBs are contraindicated or not tolerated (Grade B).
4. For hypertensive patients whose BP is not controlled, an ARB may be added to ACE inhibitor and other antihypertensive drug treatment (Grade A). Careful monitoring should be used if combining an ACE inhibitor and an ARB because of potential adverse effects such as hypotension, hyperkalemia, and worsening renal function (Grade C). Additional therapies may also include dihydropyridine CCBs (Grade C).

**Background.** There are no changes to these recommendations for 2016.

### VIII. Treatment of hypertension in association with stroke

#### Recommendations

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

1. For patients with ischemic stroke not eligible for thrombolytic therapy, treatment of hypertension in the setting of acute ischemic stroke or transient ischemic attack should not be routinely undertaken (Grade D). Extreme BP increases (eg, SBP > 220 mm Hg or DBP > 120 mm Hg) may be treated to reduce the BP by approximately 15% (Grade D), and not more than 25%, over the first 24 hours with gradual reduction thereafter (Grade D). Avoid excessive lowering of BP because this might exacerbate existing ischemia or might induce ischemia, particularly in the setting of intracranial arterial occlusion or extracranial carotid or vertebral artery occlusion (Grade D). Pharmacological agents and routes of administration should be chosen to avoid precipitous decreases in BP (Grade D).
2. For patients with ischemic stroke eligible for thrombolytic therapy, very high BP (> 185/110 mm Hg) should be treated concurrently in patients who receive thrombolytic therapy for acute ischemic stroke to reduce the risk of secondary intracranial hemorrhage (Grade B).

#### B. BP management after acute stroke

1. Strong consideration should be given to the initiation of antihypertensive therapy after the acute phase of a stroke or transient ischemic attack (Grade A).
2. After the acute phase of a stroke, BP-lowering treatment is recommended to a target of consistently < 140/90 mm Hg (Grade C).
3. Treatment with an ACE inhibitor and thiazide/thiazide-like diuretic combination is preferred (Grade B).
4. For patients with stroke, the combination of an ACE inhibitor and ARB is not recommended (Grade B).

**Background.** There are no changes to these recommendations for 2016.

### IX. 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.

**Background.** There are no changes to these recommendations for 2016.

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

#### Recommendations

1. For patients with nondiabetic chronic kidney disease, target BP is < 140/90 mm Hg (Grade B).
2. For patients with hypertension and proteinuric chronic kidney disease (urinary protein > 500 mg per 24 hours or albumin to creatinine ratio > 30 mg/mmol), initial therapy should be an ACE inhibitor (Grade A) or an ARB if there is intolerance to ACE inhibitors (Grade B).
3. Thiazide/thiazide-like diuretics are recommended as additive antihypertensive therapy (Grade D). For patients with chronic kidney disease and volume overload, loop diuretics are an alternative treatment (Grade D).
4. In most cases, combination therapy with other antihypertensive agents might be needed to reach target BP levels (Grade D).
5. The combination of an ACE inhibitor and ARB is not recommended for patients with nonproteinuric chronic kidney disease (Grade B).

**Background.** There are no changes to these recommendations for 2016.

### XI. 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 uncontrolled hypertension resistant to maximally tolerated pharmacotherapy,

progressive renal function loss, and acute pulmonary edema (Grade D).

**Background.** There are no changes to these recommendations for 2016.

## XII. Treatment of hypertension in association with diabetes mellitus

### Recommendations

1. Persons with diabetes mellitus should be treated to attain an 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). Combination therapy using 2 first-line agents may also be considered as initial treatment of hypertension (Grade B) if SBP is 20 mm Hg greater than target or if DBP is 10 mm Hg greater than target. However, caution should be exercised in patients in whom a substantial decrease in BP is more likely or poorly tolerated (eg, elderly patients and patients with autonomic neuropathy).
2. For persons with cardiovascular or kidney disease, including microalbuminuria, or with cardiovascular risk factors in addition to diabetes and hypertension, an ACE inhibitor or an ARB is recommended as initial therapy (Grade A).
3. For persons with diabetes and hypertension not included in other 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).

**Background.** There are no changes to these recommendations for 2016.

## XIII. Adherence strategies for patients

### Recommendations

1. Adherence to an antihypertensive prescription can be improved with a multipronged approach ([Supplemental Table S12](#)).

**Background.** There are no changes to these recommendations for 2016.

## XIV. Treatment of secondary hypertension due to endocrine causes

### Recommendations

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

**Background.** There are no changes to these recommendations for 2016.

### **Implementation**

Considerable ongoing effort is invested into knowledge translation by the CHEP Implementation Task Force to enhance uptake of our recommendations. Recognizing the challenge in reaching a large number of providers who care for patients with hypertension, we use a large number of strategies to increase the dissemination and uptake of our recommendations as broadly as possible; these include knowledge exchange forums, targeted educational materials for primary care providers and patients, “Train the Trainer” teaching sessions, as well as slide kits and summary documents, which are freely available online ([www.hypertension.ca](http://www.hypertension.ca)). Documents are available in French and English, and some documents are additionally translated into other languages. The implementation task force receives feedback from end users to continually improve guideline processes and content.

The CHEP Outcomes Research Task Force conducts hypertension surveillance studies and reviews existing Canadian health surveys to identify gaps between current and best practices.

### **Future Directions**

The present article represents the 16th iteration of the annually updated CHEP recommendations for the management of hypertension. The Recommendations Task Force plans to continue our systematic reviews of the literature and to update our recommendations on an annual basis.

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### **Disclosures**

Please see [Supplemental Appendix S2](#) for a complete list of author 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](http://www.onlinecjc.ca) and at <http://dx.doi.org/10.1016/j.cjca.2016.02.066>.