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# **Guidelines**

# The 2015 Canadian Hypertension Education Program Recommendations for Blood Pressure Measurement, Diagnosis, Assessment of Risk, Prevention, and Treatment of Hypertension

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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 or http://www.heartandstroke.ca).

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See page 564 for disclosure information.

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#### ABSTRACT

The Canadian Hypertension Education Program reviews the hypertension literature annually and provides detailed recommendations regarding hypertension diagnosis, assessment, prevention, and treatment. This report provides the updated evidence-based recommendations for 2015. This year, 4 new recommendations were added and 2 existing recommendations were modified. A revised algorithm for the diagnosis of hypertension is presented. Two major changes are proposed: (1) measurement using validated electronic (oscillometric) upper arm devices is preferred over auscultation for accurate office

#### **Executive Summary**

**Objective:** To provide updated 2015 evidence-based recommendations for the prevention, diagnosis, assessment, and treatment of hypertension in adults.

**Methods:** A medical librarian independently conducted a MEDLINE search current to August 2014. Reference lists were reviewed and experts were contacted to identify additional studies. Content and methodology experts reviewed and appraised relevant articles using standardized grading algorithms. For pharmacologic interventions, evidence from randomized controlled trials and systematic

#### RÉSUMÉ

Le Programme éducatif canadien sur l'hypertension révise annuellement la littérature sur l'hypertension et propose des recommandations détaillées concernant le diagnostic, l'évaluation, la prévention et le traitement de l'hypertension. Le présent rapport fournit les recommandations révisées et fondées sur des données probantes pour 2015. Cette année, il compte l'ajout de 4 nouvelles recommandations et la modification de 2 recommandations. Un algorithme révisé pour le diagnostic de l'hypertension est présenté. Deux changements majeurs sont proposés : 1) la mesure au bras au moyen d'appareils électroniques

reviews of trials was preferred and changes in cardiovascular morbidity and mortality, and total mortality, were the primary outcomes of interest. For health behaviour management, blood pressure (BP)-lowering was accepted as a primary outcome. In patients with chronic kidney disease, progressive renal impairment was accepted as a clinically relevant primary 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 October 16, 2014, in Gatineau, Canada. blood pressure measurement; (2) if the visit 1 mean blood pressure is increased but < 180/110 mm Hg, out-of-office blood pressure measurements using ambulatory blood pressure monitoring (preferably) or home blood pressure monitoring should be performed before visit 2 to rule out white coat hypertension, for which pharmacologic treatment is not recommended. A standardized ambulatory blood pressure monitoring protocol and an update on automated office blood pressure are also presented. Several other recommendations on accurate measurement of blood pressure and criteria for diagnosis of hypertension have been reorganized. Two other new recommendations refer to smoking cessation: (1) tobacco use status should be updated regularly and advice to quit smoking should be provided; and (2) advice in combination with pharmacotherapy for smoking cessation should be offered to all smokers. The following recommendations were modified: (1) renal artery stenosis should be primarily managed medically; and (2) renal artery angioplasty and stenting could be considered for patients with renal artery stenosis and complicated, uncontrolled hypertension. The rationale for these recommendation changes is discussed.

Proposed changes to the recommendations accepted at the consensus conference were subsequently voted on by the 70 members of the Canadian Hypertension Education Program (CHEP) Recommendations Task Force. Recommendations that received at least 70% task force approval were accepted as final.

#### Recommendations

#### Diagnosis and assessment

For 2015, 2 new recommendations were added. A revised algorithm for the diagnosis of hypertension is presented. Two major changes are proposed: (1) measurement using validated electronic (oscillometric) upper arm devices is preferred over auscultation for accurate office BP measurement; (2) if the visit 1 mean BP is increased but < 180/110 mm Hg, out-ofoffice BP measurements using ambulatory BP monitoring (preferably) or home BP monitoring should be performed before visit 2 to rule out white coat hypertension, for which pharmacologic treatment is not recommended. A standardized ambulatory BP monitoring protocol is presented, and an update on automated office BP is provided. Several other recommendations on accurate measurement of BP and criteria for diagnosis of hypertension have been reorganized.

#### Prevention and treatment

For 2015, 2 new recommendations were added and 2 existing recommendations were modified. The 2 new recommendations refer to smoking cessation: (1) tobacco use status should be updated regularly and advice to quit smoking should be provided; and (2) advice in combination with pharmacotherapy for smoking cessation should be offered to all smokers. The 2 modified recommendations refer to

(oscillométriques) validés est préférable à l'auscultation pour obtenir une mesure exacte de la pression artérielle en clinique; 2) si la pression artérielle moyenne à la  $1^{re}$  visite est élevée, mais < 180/ 110 mmHg, des mesures de la pression artérielle en ambulatoire à l'aide de la surveillance ambulatoire du monitoring ambulatoire de la pression artérielle (MAPA) (préférablement) ou de la mesure de la pression artérielle à domicile devraient être réalisées avant la 2<sup>e</sup> visite afin d'exclure l'hypertension de sarrau blanche pour laquelle le traitement pharmacologique n'est pas recommandé. Un protocole standardisé du MAPA ambulatoire de la pression artérielle et une révision de la mesure de la pression artérielle en clinique: oscillométrique en série sont également présentés. De nombreuses autres recommandations sur la mesure exacte de la pression artérielle et les critères de diagnostic de l'hypertension ont été réorganisées. Deux autres nouvelles recommandations font référence à cessation tabagique : 1) le statut tabagique devrait être révisé régulièrement et des conseils pour cesser de fumer devraient être donnés; 2) des conseils pour la cessation tabagique en combinaison avec la pharmacothérapie devraient être offerts à tous les fumeurs. Les recommandations suivantes ont été modifiées : 1) la sténose de l'artère rénale devrait principalement être prise en charge sur le plan médical; 2) l'angioplastie de l'artère rénale et l'implantation d'une endoprothèse pourraient être envisagées chez les patients souffrant de sténose de l'artère rénale et d'hypertension compliquée non maîtrisée. Les raisons justifiant ces changements aux recommandations sont discutées.

renovascular disease: (1) renal artery stenosis (RAS) should be primarily managed medically; and (2) renal artery angioplasty and stenting could be considered for patients with RAS and complicated, uncontrolled hypertension.

#### Updates

The CHEP will continue to update recommendations annually.

#### Introduction

Hypertension affects approximately 20% of the Canadian adult population<sup>1,2</sup> and is a major risk factor for cardiovascular disease, chronic kidney disease, and death, remaining largely silent until the development of complications.<sup>3,4</sup> Worldwide, high BP affects > 40% of adults<sup>5</sup> and is the leading global risk factor for death or disability.<sup>6</sup> BP control rates have significantly improved from 13.2% in 1992 to 64.6% in 2007 in Canada, and the rate of BP control globally is 32.5%.<sup>1,5</sup>

With the goal of improving hypertension prevention, detection, assessment, and management in Canadian adults, the CHEP, with funding from Hypertension Canada, produces annually-updated, evidence-based recommendations for primary care and other health care providers. This document outlines all recommendations endorsed by the CHEP Recommendations Task Force and contains detailed discussion of the evidence base and rationale for recommendations that have been updated or newly added for 2015. Discussion of the rationale for recommendations that remain unchanged is available in previous publications.<sup>1,7-29</sup> A full set of supplementary tables are available as an online supplement to this report.

The recommendations detailed herein are intended to guide health care providers and should not replace sound

clinical judgement. Practitioners are advised to consider patient preferences when applying these recommendations to their patients and should note that the CHEP does not currently take into account economic considerations when formulating recommendations. Although individual antihypertensive agents might be mentioned in discussions of evidence, the reader should assume a class effect, unless otherwise stated.

#### Methods

The CHEP Recommendations Task Force is a multidisciplinary panel of content and methodological experts comprised of 2 Co-Chairs, a Central Review Committee, and 14 subgroups. Each subgroup addresses a distinct content area in the field of 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 hypertension-related recommendations across organizations. In many cases, the CHEP Recommendations Task Force members serve as volunteers for multiple organizations.

Systematic literature searches current to August 2014 were performed by a Cochrane Collaboration librarian in MED-LINE/PubMed using text words and MeSH headings. Search terms included "hypertension[MeSH]", "hypertens\*[ti, ab]", and "BP"; these were combined with topic-specific terms. Bibliographies of identified articles were also manually 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 assessment of diagnosis and 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 and 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 the CHEP<sup>30</sup> for the critical appraisal of randomized controlled trials and cohort studies.

Recommendations were graded according to the strength of their underlying evidence (for details, see Supplemental Table S1), ranging from Grade A (strongest evidence, based on high-quality studies) to Grade D (weakest evidence, based on low-power, imprecise studies or expert opinion alone). In addition to classifying recommendations based on study quality, other grading schemes (eg, Grading of Recommendations Assessment, Development and Evaluation [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. The 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, the CHEP considers evidence that evaluated specific agents to be generalizable to a 'class effect.' For diuretic therapy, the term 'thiazides' refers to hydrochlorthiazide (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 proposed recommendations, which were then presented at a consensus conference of the Recommendations Task Force in Gatineau, Canada on October 16, 2014. This meeting included the Co-chairs, Central Review Committee, and members of all subgroups. Further revisions to proposed recommendations were based on these discussions.

After the consensus meeting, the recommendations were finalized and submitted electronically to all 70 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 receiving > 70% approval were passed. The CHEP recommendations process is in accordance with the Appraisal of Guidelines for Research and Evaluation (AGREE)-2 guidelines<sup>31</sup> and has been externally reviewed. A summary of how the CHEP process aligns with AGREE2 can be found online at: http://www.hypertension.ca/en/chep/overview-a-process AGREE. Materials to assist with patient and public education based on these recommendations are freely available at: http://www.hypertension.ca.

# The 2015 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, automated office BP, home BP monitoring, and ambulatory BP monitoring) is recommended (Grade D; see Supplemental Table S2, section VII. Home BP Monitoring, section VIII. Ambulatory BP Monitoring, and Table 1).
- 3. Four approaches can be used to assess BP:

#### Table 1. Standardized protocol for ambulatory BP monitoring (Grade D)

- The appropriately sized  $cuff^{32}$  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<sup>33</sup>
- The device should be set to record for a duration of at least 24 hours<sup>34.44</sup> with the measurement frequency set at 20- to 30-minute intervals during the day and 30-60 minutes at night<sup>34.36,39.44</sup>
- A patient-reported diary to define daytime (awake), nighttime (sleep), activities, symptoms, and medication administration is useful for study interpretation
- Daytime and nighttime should preferentially be defined using the patient's diary. Alternatively, predefined thresholds can be used (eg, 0800-2200 hours for awake and 2200-0800 hours for nighttime)
- 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, nighttime, 24 hours) and the "dipping" percentage (the percentage the average BP changed from daytime to nighttime)
- 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 nighttime readings are successful

BP, blood pressure; SBP, systolic blood pressure.

- i. Office BP measurement: Measurement using electronic (oscillometric) upper arm devices is preferred over auscultation (Grade C) (new recommendation) (unless specified otherwise, henceforth office BP measurement refers to electronic [oscillometric] measurement). When using mean office BP measurement, a systolic BP (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. Automated office BP: When using automated office BP (see Supplemental Table S2, on automated office BP), a displayed mean SBP  $\geq$  135 mm Hg or DBP  $\geq$  85 mm Hg DBP is high (Grade D).
- iii. **Ambulatory BP monitoring:** Using ambulatory BP monitoring (see Recommendations in section *VIII. Ambulatory BP Monitoring*), 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. Home BP monitoring: (See Recommendations in section VII. Home BP Monitoring.) 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 monitoring is < 130/80 mm Hg and the mean awake ambulatory BP monitoring is < 135/85 mm Hg before diagnosing white coat hypertension (Grade D).

**Background.** Accurate measurement of BP is critical for hypertension diagnosis and management.<sup>45</sup> Different BP measurement methods exist, including office BP measurement (using auscultatory [mercury, aneroid] or oscillometric techniques), automated office BP (oscillometric technique), ambulatory BP monitoring, and home BP monitoring. Traditionally, health

professionals have measured office BP measurement using auscultatory methods. When auscultatory (also known as manual) office BP measurement is properly performed using standardized criteria (Supplemental Table S2) (also called "research-quality office BP measurement") it can predict target organ damage, and correlates well with ambulatory measurements.<sup>46-48</sup> However, many studies have shown that in routine clinical practice standardized office BP measurement is not commonly performed.<sup>32,49-56</sup> Furthermore, it has also been shown that educational programs to improve the quality of manual office BP measurement have not been successful.<sup>50,57-62</sup> To this end, results from several studies have demonstrated that routine manual BP readings (SBP/DBP) are on average 9/6 mm Hg higher compared with the corresponding research-quality manual BP measurements.<sup>63</sup> This can lead to significant misclassification of hypertensive status and inappropriate treatment.<sup>64</sup>

Therefore, auscultatory office BP measurement is discouraged and the use of validated electronic oscillometric upper arm devices (http://www.dableducational.org/sphygmomanometers. html, http://www.bhsoc.org/bp-monitors/bp-monitors) is preferred, because they have been shown to overcome errors associated with auscultation.<sup>46,65-68</sup>

Automated office BP is a specific type of office BP measurement performed using fully automated devices. Multiple BP readings (3-6 readings, depending on the device) are taken automatically and averaged without patient-health care professional interaction (patient rests alone in a quiet room). Thus, a more standardized BP measurement is obtained, which is more reproducible than routine manual BP measurement.<sup>69-71</sup> Commonly used automated office BP devices include the BpTRU (BpTRU Medical Devices, Coquitlam, Canada), Omron HEM 907 (Omron Corporation, Kyoto, Japan), and the MicroLife WatchBP Office (Microlife, Widnau, Switzerland).

Automated office BP has been shown to be lower than routine manual office BP measurement (8-20 mm Hg difference for SBP, and 3-13 mm Hg for DBP),65,71 shows less digit preference, is more consistent from visit to visit, eliminates white coat effect, is associated with less masked hypertension, and is more strongly associated with target organ damage compared with routine manual office BP measurement.<sup>65,67,68,70,72-75</sup> Importantly, automated office BP highly correlates with awake ambulatory BP monitoring, much stronger than routine manual BP,<sup>68,70,72</sup> and produces mean BP values comparable with awake ambulatory BP monitoring values.<sup>70</sup> For automated office BP, an average measurement of  $\geq$  135/85 mm Hg can be considered increased. However, high-quality outcome-driven data are needed to define actual threshold levels independently associated with cardiovascular events. For further information please refer to the accompanying article in this issue of the Canadian Journal of Cardiology by the measurement subgroup entitled, "A New Algorithm for the Diagnosis of Hypertension in Canada."80

# II. Criteria for diagnosis of hypertension and recommendations for follow-up (Fig. 1)

#### Recommendations

1. At initial presentation, patients who demonstrate features of a hypertensive urgency or emergency (Supplemental Table S3) should be diagnosed as hypertensive and

# **Diagnosis of Hypertension**



Measurement using electronic (oscillometric) upper arm devices is preferred over auscultation

ABPM: Ambulatory Blood Pressure Measurement

**AOBP:** Automated Office Blood Pressure

HBPM: Home Blood Pressure Measurement

**OBPM:** Office Blood Pressure Measurement

Figure 1. The expedited assessment and diagnosis of patients with hypertension: focus on validated technologies for BP assessment. BP, blood pressure; DBP, diastolic blood pressure; SBP, systolic blood pressure.

require immediate management (Grade D). In all other patients, at least 2 more readings should be taken during the same visit. If using office BP measurement, the first reading should be discarded and the latter readings averaged. If using automated office BP, 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 office BP measurement or automated office BP 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 office BP measurement or automated office BP 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 office BP measurement SBP is 140-179 mm Hg and/or DBP is 90-109 mm Hg or the mean automated office BP 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 increased, white coat hypertension should be diagnosed and pharmacologic treatment should not be instituted (Grade C) (**new recommendation**).
- 6. If the visit 1 mean office SBP measurement 140-179 mm Hg and/or DBP is 90-109 mm Hg and out-of-office measurement, although preferred, is not performed, 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 (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 3to 6-month intervals (Grade D).

**Background.** In 2015 we continue to recommend that patients who present with hypertensive urgency/emergency should be diagnosed with hypertension at the first visit (note: even when BP is severely increased, multiple readings should be taken on this visit to confirm the increased BP).

This year, the diagnostic algorithm is changed with our recommendation that if the visit 1 mean office BP measurement SBP/DBP is 140-179 mm Hg and/or 90-109 mm Hg or mean automated office BP SBP/DBP is 135-179 mm Hg and/or 85-109 mm Hg, out-of-office BP measurements should be performed before visit 2. The central reasons for these changes are: (1) out-of-office measures (ambulatory BP monitoring and home BP monitoring) can identify white coat hypertension; and (2) out-of-office measures have better predictive ability than office BP measurement in terms of cardiovascular outcomes. It was previously recommended that if the BP is 140-179/90-109 mm Hg at visit 1 and 2, then a diagnosis of hypertension can be made after serial standardized office BP measurement (up to 4-5 visits over the next 6 months), and alternatively out-of-office BP measurements (ie, ambulatory BP monitoring, home BP monitoring) can be performed at visit 3, if available. Although the serial standardized office BP measurement can still be used for diagnosis of hypertension, this path is not preferred.

White coat hypertension is diagnosed when office BP measurement is  $\geq$  140/90 mm Hg, and the out-of-office BP is normal (< 135/85 mm Hg awake ambulatory BP monitoring or home BP monitoring and/or < 130/80 mm Hg with 24-hour ambulatory BP monitoring).<sup>81-83</sup> The prevalence of white coat hypertension ranges from 9% to 30% in different analyses.<sup>82-84</sup> It is critical to diagnose white coat hypertension early in the diagnostic process. The clinical significance of white coat hypertension remains uncertain, partly due to heterogeneity across white coat hypertension studies. However, several meta-analyses have demonstrated that the overall risk of cardiovascular events is similar between adults with white coat hypertension and normotension.<sup>82,83,85-87</sup> A recent review has suggested that cardiovascular event rates among those with white coat hypertension are similar to those of lowrisk, normotensive adults, however, the presence of white coat hypertension might increase the risk of cardiovascular disease if other risk factors are present.<sup>83</sup>

The available evidence at present does not support pharmacologic treatment of subjects with white coat hypertension.<sup>83,88-90</sup> Antihypertensive treatment in white coat hypertension might decrease office BP measurement and might partially reduce the white coat effect but does not modify ambulatory BP monitoring or cardiovascular risk. There is also no evidence that active treatment confers any benefit over placebo with respect to altering electrocardiogram voltages, or reducing incidence of stroke or cardiovascular events.<sup>83,88-90</sup>

Out-of-office measures (ambulatory BP monitoring and home BP monitoring) have been shown to have a stronger association with cardiovascular events than office BP measurement.<sup>34,86,91-99</sup> Ambulatory BP monitoring and home BP monitoring have high diagnostic and prognostic ability, and either method can be used to identify patients with white coat hypertension. Ambulatory BP monitoring provides multiple BP readings during a patient's regular daily activities and has the advantage of providing information on nighttime BP. It has been increasingly recognized that nighttime BP is an important predictor of cardiovascular events.<sup>34,100-105</sup> Currently, a greater amount of evidence exists for ambulatory BP monitoring than home BP monitoring regarding prediction of target organ damage but the evidence for home BP monitoring has been growing in recent years.<sup>106</sup> The diagnostic agreement between ambulatory BP monitoring and home BP monitoring is moderate and it is suggested that the 2 methods are complementary.<sup>107</sup> Although ambulatory BP monitoring is more expensive to set up and to operate, it requires minimal patient training and there is no risk of reporting bias. Home BP monitoring is more widely available, at a lower cost, and the repeatability/long-term follow-up is high compared with ambulatory BP monitoring. The use of home BP monitoring has been shown to improve long-term adherence to drug therapy<sup>108</sup> and hypertension control rates.<sup>109,110</sup> However, home BP monitoring requires patient training and education; there is a significant risk of reporting bias and it does not provide information on nighttime BP. Therefore, based on the current evidence it was believed that ambulatory BP monitoring is the preferred out-of-office measurement technique, with an alternative option being home BP monitoring if ambulatory BP monitoring is not available or not tolerated by the patient. It has been suggested that if high-normal BP is shown on home BP monitoring, white coat hypertension should be confirmed with ambulatory BP monitoring<sup>106</sup> or with a second series of home BP monitoring.<sup>111-114</sup> If white coat hypertension is confirmed (ie, increased office BP measurement and normal out-ofoffice BP measurement), the out-of-office measurement should be used by health care practitioners to guide diagnosis and management of hypertension.

For further information please refer to the accompanying article in this issue of the *Canadian Journal of Cardiology* by the measurement subgroup entitled, "A New Algorithm for the Diagnosis of Hypertension in Canada."<sup>80</sup>

# 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 more accurately predict 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 2015. Risk calculators are freely available at: www. myhealthcheckup.com (www.monbilansante.com) and www. score-canada.ca. The latter Web site is the Systematic Cerebrovascular and Coronary Risk Evaluation (SCORE) risk calculator. Although no risk engine developed from Canadian data exists, 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 (A1c) (Grade D)
  - iv. Fasting serum total cholesterol and high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, and triglycerides (Grade D);
  - 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.** There are no changes to these recommendations for 2015.

#### V. Assessment for renovascular hypertension

#### Recommendations

- Patients presenting with ≥ 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: captoprilenhanced radioisotope renal scan, Doppler sonography, magnetic resonance angiography, and computer tomography angiography (for those with normal renal function)

(Grade B). Captopril-enhanced radioisotope renal scan is not recommended for those with chronic kidney disease (glomerular filtration rate  $< 60 \text{ mL/min}/1.73 \text{ m}^2$ ) (Grade D).

**Background.** There are no changes to these recommendations for 2015.

### 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 spontaneous hypokalemia (K<sup>+</sup> < 3.5 mmol/L);
  - ii. Hypertensive patients with marked diureticinduced hypokalemia (K $^+$  < 3.0 mmol/L);
  - iii. Patients with hypertension refractory to treatment with  $\geq$  3 drugs;
  - iv. 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 aldosteronism should be established by demonstrating 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.
- B. Pheochromocytoma: screening and diagnosis
  - 1. If pheochromocytoma 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 (Grade D):
    - i. Patients with paroxysmal and/or severe (BP  $\geq$  180/ 110 mm Hg) sustained hypertension refractory to usual antihypertensive therapy;
    - 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, or changes in abdominal pressure;
    - iv. Patients with incidentally discovered adrenal mass and patients with hypertension and multiple endocrine neoplasia 2A or 2B, von Recklinghausen neurofibromatosis, or von Hippel-Lindau disease;
    - v. For patients with positive biochemical screening tests, localization of pheochromocytomas should involve the use of magnetic resonance imaging (preferable), computed tomography (if magnetic resonance imaging unavailable), and/or iodine I-131 meta-iodobenzylguanidine scintigraphy (Grade C for each modality).

**Background.** There are no changes to these recommendations for 2015.

### 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 with 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 increased and associated with an increased overall mortality risk (Grade C).
- 6. Health care professionals should ensure that patients who measure their BP at home have adequate training and, if necessary, repeat training in measuring their BP. Patients should be observed to determine that they measure BP correctly and should be given adequate information about interpreting these readings (Grade D).
- 7. Home BP monitoring for assessing white coat hypertension or sustained hypertension should be based on duplicate measures, morning and evening, for an initial 7-day period. First-day home BP values should not be considered (Grade D).

**Background.** There are no changes to these recommendations for 2015.

## 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).

- 2. Ambulatory BP monitoring upper arm devices that have been validated independently using established protocols must be used (see www.dableducational.org) (Grade D).
- 3. Therapy adjustment should be considered in patients with a mean 24-hour ambulatory BP monitoring SBP of  $\geq$  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).
- 4. The magnitude of changes in nocturnal BP should be taken into account in any decision to prescribe or withhold drug therapy based on ambulatory BP monitoring (Grade C) because a decrease in nocturnal BP of < 10% is associated with increased risk of cardiovascular events.</p>

**Background.** Similar to other methods of BP measurement, ambulatory BP monitoring must be performed in a standardized manner. A standardized protocol for ambulatory BP monitoring is presented in Table 1. For further information please refer to the accompanying article in this issue of the *Canadian Journal of Cardiology* by the measurement subgroup entitled, "A New Algorithm for the Diagnosis of Hypertension in Canada."<sup>80</sup>

### IX. Role of echocardiography

### Recommendations

- 1. Routine echocardiographic evaluation of all hypertensive patients is not recommended (Grade D).
- 2. An echocardiogram for assessment of left ventricular hypertrophy is useful in selected cases to help define the future risk of cardiovascular events (Grade C).
- 3. Echocardiographic assessment of left ventricular mass, and 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).
- 4. 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).

**Background.** There are no changes to these recommendations for 2015.

# The CHEP 2015 Prevention and Treatment Recommendations

Please note that treatment thresholds and targets refer to office BP measurement because the studies used to identify targets and evaluate treatment have largely used this mode of BP measurement. Please refer to section II for corresponding values of other measurement methods.

#### I. Health behaviour management

#### Recommendations

## A. Physical exercise

1. 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

- 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. To reduce BP, alcohol consumption should be in accordance with Canadian low-risk drinking guidelines in normotensive and hypertensive individuals. 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>115-118</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. Potassium, calcium, and magnesium intake

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

## G. Stress management

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

**Background.** There are no changes to these recommendations for 2015.

## 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 meeting 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 2015.

# 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 calcium channel blocker (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 2 or more 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 used in patients with certain comorbid conditions or in combination therapy.

**Background.** There are no changes to these recommendations for 2015.

# 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 2 or more first-line agents, or there are adverse effects, other classes of drugs (such as  $\alpha$ -blockers, ACE inhibitors, centrally acting agents, or nondihydropyridine CCBs) may be added or substituted (Grade D).
- 4. Possible reasons for poor response to therapy (Supplemental Table S10) should be considered (Grade D).
- 5.  $\alpha$ -Blockers are not recommended as first-line agents for uncomplicated isolated systolic hypertension (Grade A); and  $\beta$ -blockers are not recommended as first-line therapy for isolated systolic hypertension in patients aged  $\geq 60$  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 2015.

## 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 3 or more cardiovascular risk factors as defined in Supplemental

Table S11 (Grade A in patients > 40 years) or with established atherosclerotic disease (Grade A regardless of age).

- 2. Consideration should be given to the addition of low-dose acetylsalicylic acid therapy in hypertensive patients  $\geq 50$  years of age (Grade B). Caution should be exercised if BP is not controlled (Grade C).
- 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) (new recommendation).
- 4. 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) (**new recommendation**).

**Background.** Cigarette smoking is a well-established, independent, and powerful risk factor for vascular disease.<sup>119</sup> Smoking cessation is thus a critically important component of global vascular risk reduction in hypertensive patients. This year, the Recommendations Task Force reviewed data that demonstrated that advice on smoking cessation and pharmacotherapy for smoking cessation are both effective strategies in assisting patients to quit smoking.

In a 2013 Cochrane collaboration systematic review that examined 42 randomized controlled trials of  $\geq 6$  months duration, brief physician advice to stop smoking led to clinically important increases in smoking cessation.<sup>120</sup> Participants who received brief advice (provided in one 20-minute consultation with only 1 follow-up visit) were 66% (95% confidence interval, 42%-94%) more likely to no longer be smoking at 6 months. Sustained smoking cessation occurred in 455 of the 7913 (5.8%) patients who received minimal advice vs 216 of the 5811 (3.7%) patients who received usual care. More complex interventions (verbal advice combined with printed materials; additional support from another health care worker; or referral to a cessation clinic) were only slightly more effective.

A Cochrane Collaboration network meta-analysis<sup>121</sup> that synthesized results from 12 reviews that included efficacy data from 267 randomized controlled trials reported that combining advice to quit smoking with pharmacotherapy significantly increased smoking cessation rates over follow-up periods of  $\geq 6$  months. Cessation advice combined with nicotine replacement therapy resulted in an 84% higher likelihood of sustained quitting compared with advice combined with placebo (data from 119 randomized controlled trials, odds ratio [OR], 1.84; 95% credible interval, 1.71-1.99). Similarly, advice combined with the antidepressant bupropion resulted in an 82% greater likelihood of sustained quitting (data from 36 randomized controlled trials; OR, 1.82; 95% credible interval, 1.60-2.06). Finally, advice combined with varenicline led to a nearly 3-fold greater likelihood of quitting compared with advice combined with placebo (data from 15 randomized controlled trials; OR, 2.88; 95% credible interval, 2.40-3.47).

# V. 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).

2. In the very elderly (age  $\geq$  80 years), the SBP target is < 150 mm Hg (Grade C).

**Background.** There are no changes to these recommendations for 2015.

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

#### Recommendations

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

- 1. An ACE inhibitor or ARB is recommended for most patients with hypertension and CAD (Grade A).
- 2. For patients with stable angina,  $\beta$ -blockers are preferred as initial therapy (Grade B). CCBs may also be used (Grade B).
- 3. Short-acting nifedipine should not be used (Grade D).
- 4. For patients with CAD, but without coexisting systolic heart failure, the combination of an ACE inhibitor and ARB is not recommended (Grade B).
- 5. In high-risk patients, when combination therapy is being used, choices should be individualized. The combination of an ACE inhibitor and a dihydropyridine CCB is preferable to an ACE inhibitor and a thiazide/thiazidelike diuretic in selected patients (Grade A).
- 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.** There are no changes to these recommendations for 2015.

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

**Background.** There are no changes to these recommendations for 2015.

# 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, increased B-type natriuretic peptide or N-terminal pro-B-type natriuretic peptide level, or New York Heart Association class II-IV symptoms (Grade A). Careful monitoring for hyperkalemia is recommended when combining an aldosterone antagonist with 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 found to be effective in trials unless adverse effects become manifest (Grade B).

- 2. An ARB is recommended if ACE inhibitors are not tolerated (Grade A).
- 3. A combination of hydralazine and isosorbide dinitrate is recommended if ACE inhibitors and ARBs are contraindicated or not tolerated (Grade B).
- 4. For hypertensive patients whose BP is not controlled, an ARB may be combined with ACE inhibitor therapy 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 2015.

# VIII. Treatment of hypertension in association with stroke

## Recommendations

- A. BP management in acute stroke (onset to 72 hours)
  - 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/thiazidelike 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 2015.

# 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 di-uretics. Direct arterial vasodilators such as hydralazine or minoxidil should not be used.

**Background.** There are no changes to these recommendations for 2015.

# 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 (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 2015.

# XI. Treatment of hypertension in association with renovascular disease

## Recommendations

1. Patients with hypertension attributable to atherosclerotic RAS should be primarily medically managed because renal angioplasty and stenting offers no benefit over optimal medical therapy alone (Grade B) (**revised recommendation**). 2. Renal artery angioplasty and stenting for atherosclerotic hemodynamically significant RAS could be considered for patients with uncontrolled hypertension resistant to maximally tolerated pharmacotherapy, progressive renal function loss, and acute pulmonary edema (Grade D) (revised recommendation).

**Background.** This year's revised recommendations for hypertension associated with atherosclerotic RAS reflect recently published data from the Cardiovascular Outcomes with Renal Atherosclerotic Lesions (CORAL) trial and a meta-analysis that incorporated the CORAL results. The changes emphasize optimization of medical management and limitation of the use of renal revascularization procedures to specific clinical indications.

The National Institutes of Health-funded CORAL trial enrolled 947 patients with RAS of at least 80% or at least 60% and evidence of hemodynamic pressure gradients.<sup>122</sup> In addition, subjects had either hypertension not controlled with 2 or more drugs or declining renal function. All subjects had their cardiovascular risk factors (BP, lipids, glycemic control, and antiplatelet therapy) systematically managed according to a protocol and 460 patients were randomly assigned to stenting of stenotic renal arteries. The primary composite outcome included cardiovascular or renal death, myocardial infarction, stroke, heart failure hospitalization, progression of renal dysfunction, or the requirement of renal replacement therapy. After a median follow-up of 43 months, renal artery stenting did not improve either the primary composite outcome or any of its constituent components. SBP was trivially reduced by renal artery stenting.

These results are congruent with the results of 7 other smaller trials. When combined, meta-analyses of the aggregate 2223 patients from these 8 trials did not detect favourable mortality, stroke, heart failure, or renal preservation effects of revascularization for RAS.<sup>123</sup> BP was not reduced and in aggregate, antihypertensive drug use was only reduced by less than half a daily dose per day.

This year's changes focus on those with atherosclerotic causes of their RAS. CORAL adopted a systematic cardiovascular risk factor management protocol for all patients and perhaps as a consequence, recorded an outcome event rate of approximately half of that expected. For these reasons, it is recommended that hypertensive patients with RAS be managed with good BP control to appropriate targets, a high dose of a high-potency statin for lipid management, good glycemic control, and appropriate antiplatelet therapy. Management should also include adoption of health behaviours appropriate to the risk profile.

Caution with appropriate monitoring of serum creatinine and potassium with the use of renin-angiotensin-aldosterone system (RAAS) inhibitors is still recommended, particularly if bilateral RAS disease is present. However, this does not preclude the use of these drugs. Most patients will have been treated with a RAAS inhibitor before the diagnosis of renovascular hypertension is made or suspected. In randomized controlled trials, such as CORAL, a RAAS inhibitor was a proximal part of the treatment protocol.<sup>122</sup>

Despite the negative results of CORAL and the other randomized controlled trials, concern remains that in aggregate, low trial thresholds for subject inclusion might have resulted in underrepresentation of less common but more severely affected patients. This latter group could include those with more severe and bilateral stenosis associated with progressive decline in renal function, recurrent pulmonary edema, and refractory hypertension despite use of 4 or more drugs. In addition, the point estimates for most clinical outcomes in CORAL and the meta-analysis lie slightly on the side of favouring renal artery revascularization and with wide confidence intervals. For these reasons, in the expert opinion of the CHEP Recommendations Task Force, renal angioplasty and stenting could be considered in these uncommon refractory cases.

These 2015 recommendations apply to atherosclerotic hemodynamically significant RAS. Anticipated next year is the inclusion of guidance specific to nonatherosclerotic causes, such as fibromuscular dysplasia, in which estimates of the benefit on hypertension outcomes might be larger.<sup>124</sup> However, there is a paucity of randomized data from such patients and nontrivial risks of procedure-related vascular complications.<sup>124</sup>

# XII. 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). 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 2015.

#### XIII. Adherence strategies for patients

#### Recommendations

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

**Background.** There are no changes to these recommendations for 2015.

# Table 2. Considerations in the individualization of pharmacological therapy

	Initial therapy	Second-line therapy	Notes and/or cautions
Hypertension without other compell	ling indications		
Diastolic hypertension with or without systolic hypertension (target BP < 140/90 mm Hg)	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 (target BP for age $<$ 80 years is $<$ 140/90 mm Hg; for age $\geq$ 80 years: target SBP is < 150 mm Hg	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 (target BP < 130/8	80 mm Hg)		
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
Cardiovascular disease (target BP <	140/90 mm Hg)		
Coronary artery disease	ACE inhibitors or ARBs; β-blockers for patients with stable angina	Long-acting CCBs. When combination therapy is being used for high-risk patients, an ACE inhibitor/dihydropyridine CCB is preferred	Avoid short-acting nifedipine. Combination of an ACE inhibitor with an ARB is specifically not recommended. Exercise caution when lowering SBP to target if DBP is < 60 mm Hg
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, increased BNP or NT-proBNP level, or NYHA class II to IV	<ul> <li>ACE inhibitor and ARB combined. Hydralazine/isosorbide dinitrate combination if ACE inhibitor and ARB contraindicated or not tolerated.</li> <li>Thiazide/thiazide-like or loop diuretics are recommended as additive therapy. Dihydropyridine CCB can also be used</li> </ul>	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	Combination of additional agents	Hydralazine and minoxidil should not be used
Past stroke or TIA	ACE inhibitor and a thiazide/ thiazide-like diuretic combination	Combination of additional agents	Treatment of hypertension should not be routinely undertaken in acute stroke unless extreme BP increase. Combination of an ACE inhibitor with an ARB is not recommended
Nondiabetic chronic kidney disease Nondiabetic chronic kidney disease with proteinuria <sup>†</sup>	(target BP < 140/90 mm Hg) 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 2. 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
Other conditions (target BP < 14	0/90 mm Fig)		
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 3 or more cardiovascular risk factors or atherosclerotic disease. Low-dose ASA in patients ≥ 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; ACR, albumin to creatinine ratio; ARB, angiotensin receptor blocker; ASA, acetylsalicylic acid; BNP, B-type natriuretic peptide; BP, blood pressure; CCB, calcium channel blocker; DBP, diastolic blood pressure; NT-proBNP, N-terminal pro-B-type natriuretic peptide; NYHA, New York Heart Association; SBP, systolic blood pressure; TIA, transient ischemic attack.

\* Microalbuminuria is defined as persistent ACR > 2.0 mg/mmol.

<sup>†</sup>Proteinuria is defined as urinary protein > 500 mg per 24 hours or ACR > 30 mg/mmol in 2 of 3 specimens. Reproduced wither permission from the Canadian Hypertension Education Program.

# 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 2015.

#### Implementation

The implementation task force conducts an extensive knowledge translation effort to enhance uptake and applicability of these recommendations. These efforts include knowledge exchange forums, targeted educational materials for primary care providers and patients, and freely available slide kits and summary documents of all recommendations on the Canadian Hypertension Society Web site, Hypertension Canada (www.hypertension.ca). Documents are available in French and English, and some documents are translated into other languages. The implementation task force also regularly receives feedback from end users to improve guideline processes and content. Although the number of primary care providers who directly receive CHEP materials on a regular basis has dramatically increased, CHEP is continuing to address the challenge of identifying and reaching all active primary care providers across Canada, through use of the Hypertension Canada Web site, "Train the Trainer" teaching sessions, and wide dissemination of educational materials.

The CHEP outcomes task force conducts hypertension surveillance studies and reviews existing Canadian health surveys to identify gaps between current and best practices.

#### **Summary/Future Directions**

Table 2 contains a summary of pharmacological management recommendations for hypertension. The present report represents the 15th iteration of the annually updated CHEP recommendations for the management of hypertension. The Recommendations Task Force will continue to conduct systematic reviews of the clinical trial evidence and update these recommendations annually. Pediatric hypertension and pregnancy/postpartum hypertension have been identified as priority areas for future updates.

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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 and at http://dx.doi.org/10. 1016/j.cjca.2015.02.016.