The 2012-2013 Canadian Hypertension Education Program (CHEP) guidelines for pharmacists: An update

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Since 1999, the Canadian Hypertension Education Program (CHEP) has released annual recommendations on the management of hypertension. Although significant improvements in hypertension treatment and control have been made in Canada, approximately one-third of Canadians continue to have uncontrolled blood pressure.[1]

In 2011, we published a set of guidelines specific to pharmacists based on the CHEP recommendations.[2] Since that publication, new research has been conducted that has prompted changes in the 2012 and 2013 versions of the guidelines. In this article, we will provide an update for pharmacists on these changes and their underlying evidence, as relevant to pharmacy practice.

Enhanced recommendations for the use of out-of-office blood pressure measurements in the diagnosis and management of hypertension

The traditional method of diagnosing and managing hypertension based solely on manual office blood pressure (BP) readings has several potential limitations. Readings may be inaccurate because improper measurement techniques are used. In addition, manual office measurements will not detect masked hypertension (thought to affect about 10% of the general population[3]) in some individuals and, in others, may overestimate the prevalence of hypertension because of the white coat phenomenon (affecting approximately 15% of the general population[4]). As described by Pickering et al.,[5] the addition of out-of-office BP measurement to standard office measurement leads to the identification of 4 groups of patients:

1. True normotensive (normotensive results by both methods)
2. True hypertensive (hypertensive results by both methods)
3. Masked hypertension (normotensive by clinic measurement and hypertensive by ambulatory measurement)
4. White coat hypertension (hypertensive by clinic measurement and normotensive by ambulatory measurement)

Although white coat hypertension has received much attention in the literature and in practice, the impact of masked hypertension has been less studied and reported but may pose greater risk. Patients with masked hypertension have target organ damage and cardiovascular event rates similar to those of true hypertensive patients, whereas those with white coat hypertension have event rates and target organ damage more consistent with those of true normotensive patients.[6,7] With ready access to validated home blood pressure monitors for purchase in community pharmacies, the role of home measurements in the diagnosis of hypertension has received additional attention.

In 2012, the CHEP guidelines were amended to allow for a greater emphasis on home blood

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pressure monitoring. To rule out white coat hypertension in patients with average office BP readings of 140 to 179/90 to 109 mmHg, 1 of 2 methods can be used: either 1 week of home BP monitoring or 24 hours of ambulatory BP monitoring. If home BP monitoring is chosen and the average BP value is <135/85 mmHg, this should be confirmed by either 1 additional week of home monitoring or 24 hours of ambulatory monitoring.[8] The guidelines also recommend regular home BP monitoring and recording of results for patients with hypertension and diabetes, chronic kidney disease or known masked hypertension. Recommendations for pharmacists on the use of home blood pressure monitors by patients have been previously published in *CPJ*.[9] Increased use of out-of-office BP measurements can be expected to increase rates of masked hypertension detection.

Target BP for patients with nondiabetic chronic kidney disease is now <140/90 mmHg

In 2012, CHEP made a significant change to its target BP for patients with nondiabetic chronic kidney disease (CKD), increasing the target from <130/80 mmHg to <140/90 mmHg, whereas those with kidney disease and concomitant diabetes continue to have a target of <130/80 mmHg.[8] This recommendation was based on reevaluation of major studies in the field, including the findings of a systematic review evaluating the effect of different BP targets in patients with CKD. This study, which included 3 randomized controlled trials evaluating different BP targets for this population of patients, specifically evaluated the outcomes of death, kidney failure, cardiovascular events, change in kidney function, adverse events and the number of antihypertensive agents required to achieve target BP.[10]

The studies included were the Modification of Diet in Renal Disease (MDRD) study,[11] the African American Study of Kidney Disease and Hypertension (AASK) study[12] and the Ramipril Efficacy in Neuropathy 2 (REIN-2) trial.[13] The MDRD study randomized patients to both a blood pressure target (either <140/90 or <125/75 mmHg) and 1 of 2 diets of varying protein composition. This study also encouraged the use of angiotensin-converting enzyme (ACE) inhibitors as first-line agents for blood pressure management and calcium channel blockers as second-line agents. The AASK study enrolled black patients with hypertensive kidney disease and randomly assigned participants to either the higher (<140/90 mmHg) or the lower (<125/75 mmHg) blood pressure target, as well as drug therapy (ACE inhibitor, beta-blocker or dihydropyridine calcium channel blocker). The REIN-2 study randomized patients to a BP target of either <130/80 mmHg or a diastolic BP target of <90 mmHg. All patients were treated with ramipril 5 mg/d throughout the trial, whereas those randomized to the lower target also received felodipine 5 to 10 mg/d. Add-on therapy with agents from other antihypertensive drug classes was allowed in each group to achieve the patient's target BP. None of the studies specifically evaluated BP targets in patients with both CKD and diabetes.

All 3 studies failed to find any benefit in their primary clinical outcomes for the lower vs the higher BP target. The only prespecified outcome with a statistically significant benefit was from the 7-year follow-up of patients following the MDRD study, which found a 23% reduction (95% confidence interval [CI], 18%-43%) in the development of kidney failure in the lower target group. In subgroup and extended observational follow-up analysis of the MDRD and AASK studies, outcomes were improved, but these were not considered high-quality evidence. The number of medications required to achieve the lower target blood pressure was greater across all studies compared with the higher target, and adverse effects of hypotension symptoms and cough were more common in the lower target group.

With no clinical benefit seen in the primary end points of these trials, a higher incidence of adverse effects and the need to use more medications, it was felt that evidence did not justify a lower target for nondiabetic patients with CKD. Hence, the target was changed in 2012.

Use of aldosterone antagonists in patients with hypertension and systolic dysfunction

There have been 3 large randomized controlled trials of aldosterone antagonists (spironolactone or eplerenone) in heart failure—RALES,[14] EPHESUS[15] and EMPHASIS-HF.[16] Although the studies were not specifically designed as hypertension studies, approximately two-

thirds of patients enrolled into EPHESUS and EMPHASIS-HF were also hypertensive. All 3 reported significant reductions in mortality, with RALES reporting reductions in all-cause mortality and EPHESUS and EMPHASIS-HF reporting reductions in cardiovascular mortality, as well as significant reductions in heart failure–related hospitalizations.

It is important to note that all 3 studies enrolled patients with ejection fractions of <40% (≤35% in RALES, ≤40% in EPHESUS and EMPHASIS-HF enrolled patients with either ≤30% ejection fraction or an ejection fraction of >30-35% along with a QRS interval of >130 ms). In addition to low ejection fraction, EPHESUS limited its study to patients with a history of acute myocardial infarction and signs of heart failure, and EMPHASIS-HF enrolled patients with a recent hospitalization for heart failure or elevated natriuretic peptides.

With reduced mortality and hospitalizations noted across these studies, the 2012 guidelines were updated to define systolic dysfunction as an ejection fraction of <40% and expand the indications for use of aldosterone antagonists. Whereas previous guidelines recommended these agents as add-on therapy only for patients with New York Heart Association (NYHA) class III or IV symptoms or postmyocardial infarction, the 2012 guidelines also recommend this therapy for patients with a recent cardiovascular hospitalization, elevated natriuretic peptides and class II NYHA symptoms. However, due to their potassium-sparing effect, careful monitoring for hyperkalemia is also recommended when adding aldosterone antagonists to a patient's regimen.

Target systolic BP in the very elderly with isolated systolic hypertension is <150 mmHg

The Hypertension in the Very Elderly Trial (HYVET), published in 2008, was the first randomized controlled trial to specifically evaluate treatment of hypertension in the very elderly.[17] Before HYVET, knowledge of the benefits and risks of treating hypertension in the very elderly was based on pooled subgroup data[18] and epidemiologic data showing improved cardiovascular outcomes with lower blood pressure across all age groups, without special consideration of this population. HYVET randomized 3845 individuals older than 80 years with a sustained systolic BP of >160 mmHg to either placebo or treatment with indapamide 1.5 mg sustained release daily, with the possibility of adding perindopril 2 mg or 4 mg if required to achieve a systolic BP of <150/80 mmHg. The primary end point was fatal or nonfatal stroke, with secondary end points including death from any cause, cardiovascular causes, cardiac causes or stroke.

The study was stopped early, after a mean follow-up of 2.1 years, when significant differences in all-cause mortality were observed. After 2 years, active treatment patients had achieved an average BP of 144/77 mmHg, whereas the placebo group had an average BP of 158/84 mmHg. In the intention-to-treat analysis, there was a 30% rate reduction in fatal or nonfatal stroke (95% CI, –1 to 51; $p = 0.06$) and a 21% reduction (95% CI, 4 to 35; $p = 0.02$) in death from any cause with active treatment compared with the placebo group. Rates of heart failure and major cardiovascular events were also significantly reduced. Although the reduction in rate of stroke was consistent with previous meta-analysis findings,[18] the reduction in all-cause mortality was unexpected.

As the HYVET study findings apply to the very elderly, the 2013 guidelines were amended to recommend a target systolic BP of <150 mmHg for individuals older than 80 years with isolated systolic hypertension. Despite being based on a randomized controlled trial, this recommendation has been assigned a Grade C rating (assigned to recommendations from trials that have lower levels of internal validity and/or precision, report unvalidated surrogate outcomes or are from nonrandomized observational studies) because of concerns regarding study methodology (a priori early stoppage rules were not followed; the trial was stopped early, potentially overestimating benefit; and the trial enrolled relatively healthy participants and may not be representative of many very elderly patients). As in previous iterations of the CHEP guidelines, the task force underscored the importance of tailoring recommendation use to individual patients' preferences and circumstances.

Conclusion

Hypertension is the leading risk factor for global disease burden[19] and the leading cause of premature death worldwide.[20] Pharmacists are a major part of Hypertension Canada's strategy to help Canadians achieve the healthiest blood

TABLE 1 Summary of updates to Canadian Hypertension Education Program (CHEP) guidelines

2012 Updates	
CHEP 2011	**CHEP 2012**
Using home BP measurements, patients can be diagnosed as hypertensive if the average SBP is ≥135 mmHg or the DBP is ≥85 mmHg (Grade C). If the average home BP is <135/85 mmHg, it is advisable to perform 24-hour ABPM to confirm that the mean 24-hour ABPM is <130/80 mmHg and the mean awake ABPM is <135/85 mmHg before diagnosing white coat hypertension (Grade D).	Using home BP measurements, patients can be diagnosed as hypertensive if the average SBP is >135 mmHg or the DBP is >85 mmHg (Grade C). If the average home BP is <135/85 mmHg, **it is advisable to either repeat home monitoring to confirm the home BP is <135/85 mmHg or** perform 24-hour ABPM to confirm that the mean 24-hour ABPM is <130/80 mmHg and the mean awake ABPM is <135/85 mmHg before diagnosing white coat hypertension (Grade D).
For patients with nondiabetic chronic kidney disease, target BP is <130/80 mmHg (Grade C).	For patients with nondiabetic chronic kidney disease, target blood pressure is **<140/90 mmHg (Grade B).**
In patients with systolic dysfunction, ACE inhibitors (Grade A) and beta-blockers (Grade A) are recommended for initial therapy. Aldosterone antagonists (Grade B) are also recommended for patients with NYHA class III or IV symptoms of heart failure or postmyocardial infarction.	In patients with systolic dysfunction **(EF <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 BNP or NT-proBNP level, or NYHA class II to IV symptoms (Grade A). Careful monitoring for hyperkalemia is recommended when adding an aldosterone antagonist.**
2013 Updates	
CHEP 2012	**CHEP 2013**
Isolated systolic hypertension without other compelling indications (target BP is <140/90 mmHg) (Grade C for systolic, Grade A for diastolic)	Isolated systolic hypertension without other compelling indications (target BP **for age <80 years** is <140/90 mmHg; **for age >80 years, the target systolic BP is <150 mmHg)** (Grade C)

ABPM, ambulatory blood pressure monitoring; ACE, angiotensin-converting enzyme; BNP, B-type natriuretic peptide; BP, blood pressure; DBP, diastolic blood pressure; EF, ejection fraction; NT-proBNP, N-terminal prohormone of brain natriuretic peptide; NYHA, New York Heart Association; SBP, systolic blood pressure. **Bold text represents changes in the guidelines from previous versions.**

pressure distribution in the world.[21] As such, pharmacists must keep abreast of this rapidly progressing field. A summary of the changes to the CHEP guidelines in 2012 and 2013 has been provided in Table 1. The 2013 CHEP guidelines are available in full on the Hypertension Canada website (www.hypertension.ca). Pharmacists are also encouraged to use the many other resources available through Hypertension Canada, including short summaries of the recommendations for health professionals and patient education resources. ■

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