

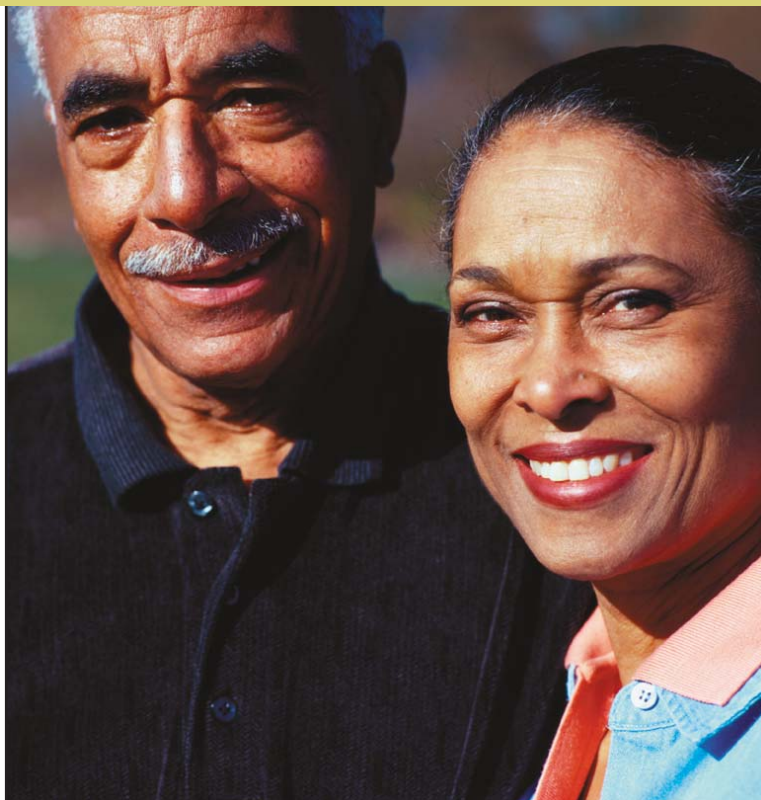
# What's New in the 2003 Hypertension Guidelines?

**Hypertension remains a major public health problem in Canada. Here are the 2003 Canadian Hypertension Education Program Recommendations.**

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on behalf of the Canadian Hypertension  
Education Program

This article outlines the ongoing efforts of the majority of hypertension specialists in Canada to develop and update evidence-based recommendations for the management of hypertension. This effort, initiated on a yearly basis since 1999, represents much more than an academic exercise. It has been clearly recognized that our ability to influence health-care professionals and improve the management of hypertension starts with the dissemination of up-to-date, credible, management recommendations. In this respect, the Canadian Hypertension Education Program (CHEP) has been increasingly coupled with a very active dissemination and implementation program (and more recently an evaluation program to monitor the impact of our efforts).

This initiative is supported by a coalition of professional health-care organizations with a stake in the management of hypertension, including The Canadian Hypertension Society, The Canadian Coalition for High Blood Pressure Prevention and Control, The College of Family



## In this article:

1. What's new in the 2003 CHEP recommendations?
2. What's old, but still important?

Physicians of Canada, Health Canada, and The Heart and Stroke Foundation of Canada.

Hypertension remains a major public health problem in Canada. It is a common reason for physician visits,<sup>1</sup> and a significant cause of morbidity and mortality. In Canada, hypertension is the leading risk associated with death in women and the second leading risk in men.<sup>2</sup> Further, hypertension is only marginally treated (there is no indication that blood pressure [BP] control rates have risen appreciably over the past 10 years since the Canadian Heart Health Survey).<sup>3</sup> However, there have been recent indications that the patterns of management of hypertension in Canada are improving following adoption of our yearly process of updating the hypertension recommendations

(Table 1).<sup>4</sup> This version of the Canadian Hypertension Education Program (CHEP) recommendations for the management of hypertension should be seen as the 2003 blueprint for the ongoing development of tools and programs to improve hypertension management, BP control, and ultimately, reduce BP-related complications.

The current article is designed as a quick glance at the recommendations, highlighting the results of the Antihypertensive and Lipid Lowering Treatment to Prevent Heart Attack (ALLHAT) and the Losartan Intervention for Endpoint Reduction in Hypertension (LIFE) study considerations, and specifically, to identifying those aspects of the recommendations that are new or existing, but still important.

### What's new in the 2003 recommendations?

The major focus of the 2003 update was the incorporation of the findings of the major treatment studies from 2001 and 2002 into the recommendations. The most important studies were LIFE and ALLHAT. These studies influenced the recommendations with regards to therapeutic considerations for:

- Patients with hypertension and diabetes;
- Patients with hypertension and other concurrent cardiovascular diseases; and
- Patients with hypertension without other compelling indications.

The ALLHAT study, published following the completion of the recommendations process, undoubtedly had the biggest impact on this year's

process, although ultimately, the conclusions from ALLHAT resulted in only subtle changes to the actual recommendations. This landmark study examined the effect of amlodipine- or lisinopril-based treatment regimens versus chlorthalidone-based treatment regimens (an alpha blocker arm was prematurely discontinued in 2000 due to excess stroke and heart failure). ALLHAT involved 33,357 participants over 55 with

***In Canada, hypertension is the leading risk associated with death in women and the second leading risk in men.***

hypertension with at least one other coronary heart disease (CHD) risk factor. The primary end point was fatal CHD or non-fatal myocardial infarction. The mean age of the study population was 67, 35% of patients were black, and 36% had diabetes. Baseline BP was 146/84 mmHg (however, pre-existing medications were continued to the point of randomization). Overall, BP control was approximately 20% better in the chlorthalidone group than the lisinopril group, and approximately 10% better in the chlorthalidone group than the amlodipine group. Neither the primary outcome measures nor all-cause mortality differed between the groups. The incidence of heart failure, however, was significantly higher (38%) with amlodipine compared to chlorthalidone. In the comparison of lisinopril and chlorthalidone, there was a 10% higher rate of combined CHD, 15% higher stroke rate, and 19% higher heart failure rate with lisinopril (Figure 1).

There were differences in BP control between treatment arms and concerns over whether the heart failure diagnoses were adequately validated (which may have accounted for some of the differences seen in the secondary end point analyses). Nonetheless, it was concluded by the Evidence-based Recommendations Task Force that ALLHAT demonstrated at least comparable effectiveness of a diuret-

#### **About CHEP...**

**The Canadian Hypertension Education Program (CHEP)** is a network of hypertension experts across Canada committed to the development of evidence-based recommendations for the management of hypertension, the dissemination of these recommendations, and their applications to individual patient groups.

## Hypertension Guidelines

ic-based regimen in both reducing BP and reducing hypertension-related cardiovascular complications. In that respect, ALLHAT was recognized to confirm the tenet, that in the pharmacologic treatment of hypertension in “undifferentiated patients,” thiazide diuretics remain the “first among equals.” Further, subgroup analysis confirmed the relative effectiveness of a diuretic-based regimen in patients with hypertension and diabetes (demonstrated previously in the Systolic Hypertension in the Elderly Program [SHEP] study).<sup>5</sup> Notably, the poorer outcomes with lisinopril in both reducing BP and reducing hypertension-related cardiovascular complications were most evident in the black patient subgroup. ALLHAT was also seen as important in underscoring the message that pharmacologic therapy of hypertension means combination drug therapy for the majority of hypertensives—63% of the patients in ALLHAT required two or more drugs and only 70% achieved BP control (Table 2, Figure 2).

Based on ALLHAT, is it fair to conclude that diuretics should be recommended as sole “first-line” therapy in the management of hypertension in patients “without other compelling indications?” Considering the evidence to date, the answer would have to be no. A formal evaluation of the results of ANBP-2 (Second Australian National Blood Pressure study) was not part of the 2003 recommendations. However, it was appreciated that the results of this study underscored the fallacy of concluding that any one of the five recommended first-line agents demonstrated clear overall superiority (with regards to the effectiveness in either BP lowering or reducing hypertension-related cardiovascular risk). The validity of assuming the superiority of diuretics is further questioned by the lack of comparison with other first-line therapies in ALLHAT (*i.e.*, beta blockers and angiotensin II receptor blockers [ARB]). Finally, the long-term adverse impact of the increase in blood glucose demonstrated in the diuretic arm of ALLHAT is unknown, but remains a concern mitigating against a blanket endorsement of thiazide diuretics as unambiguous preferred therapy in the initial treatment of hypertension (Table 3).

The LIFE trial<sup>6</sup> also had a significant impact on the deliberations. This study compared the benefits of a beta blocker-based regimen (with atenolol) versus an ARB-based regimen (with losartan) in hypertensive subjects over 55 with left ventricular hypertrophy. LIFE demonstrated a significant benefit of ARB-based therapy. It was felt that the LIFE study entry criteria resulted in the inclusion of a high-risk hypertensive population that would be comparable to the highest risk subgroups included in prior large hypertension trials. Thus, it was felt that the extrapolation of LIFE results to patients with “uncomplicated” hypertension was appropriate. However, concerns were raised that the control regimen (atenolol) has uncertain efficacy in older hypertensives. As such, any assertion that ARB-based therapy is superior to “proven first-line therapy” could not be supported (Table 4).

This year’s process also saw further simplification of the recommendations for the management of hypertension in patients with diabetes: ACE inhibitors or ARBs were recommended as first-line therapy in all subgroups of diabetic patients with hypertension. This revision was based on considerations of the diabetic subgroup analysis of LIFE, as well as the ongoing discussions of the 2001 trials that established the renoprotective effect of angiotensin receptor blockers (*i.e.*, RENAAL<sup>7</sup> and IDNT<sup>8</sup>).

## What’s old, but still important?

### **Individualizing management of hypertension based on overall atherosclerotic risk.**

It remains axiomatic (but somewhat paradoxical) that concurrence of other cardiovascular risk factors has a greater impact on both atherosclerotic risk and the absolute benefit of antihypertensive therapy than the extent of BP elevation itself. Further, concurrence of other risk factors of cardiovascular disease continues to have implications both in terms of targets for treatment, as well as specific



Table 1

## Considerations in the Individualization of Antihypertensive Therapy

To maximize the hypotensive effects in dual therapy, see Table 2. Short-acting CCBs are not recommended in the treatment of hypertension.

	Initial Therapy	Second-Line Therapy	Notes and/or Cautions
<b>Hypertension without other compelling indications</b>	Thiazide diuretics, beta blockers, ACE inhibitors, ARBs, or long-acting dihydropyridine CCBs	Combinations of first-line drugs	Alpha blockers are not recommended as initial therapy. Beta blockers are not recommended initially in those over 60. Hypokalemia should be avoided by using potassium-sparing agents in those who are not prescribed diuretics. ACE inhibitors are not recommended for black patients
<b>Isolated systolic hypertension without other compelling indications</b>	Thiazide diuretics, ARBs, or long-acting dihydropyridine CCBs	Combinations of first-line drugs	Hypokalemia should be avoided by using potassium-sparing agents in people prescribed diuretics
<b>Diabetes mellitus with nephropathy</b>	ACE inhibitors or ARBs	Addition of one or more of thiazide diuretics, cardioselective beta blockers, long-acting CCBs or an ARB/ACE inhibitor combination	
<b>Diabetes mellitus without nephropathy</b>	ACE inhibitors, ARBs or thiazide diuretics	Combination of first-line drugs or addition of cardioselective beta blockers and/or long-acting CCBs	If the serum creatinine level is >150 $\mu\text{mol}$ , a loop diuretic should be used to replace low-dose thiazide diuretics if volume control is required
<b>Angina</b>	Beta blockers (consider adding ACE inhibitors)	Long-acting CCBs	Avoid short-acting nifedipine
<b>Prior myocardial infarction</b>	Beta blockers and/or ACE inhibitors	Combinations of additional agents	
<b>Heart failure</b>	ACE inhibitors (thiazide or loop diuretics, beta blockers, spironolactone as additive therapy)	ARBs or hydralazine/isosorbide dinitrate	Avoid nondihydropyridine CCBs (diltiazem, verapamil)
<b>Past cerebrovascular accident or TIA</b>	ACE inhibitor/diuretic combinations		BP reduction reduces recurrent cerebrovascular events
<b>Renal disease</b>	ACE inhibitors (diuretics as additive therapy)	Combinations of additional agents	Avoid ACE inhibitors if bilateral renal artery stenosis
<b>Left ventricular hypertrophy</b>	ACE inhibitors, ARBs, dihydropyridine CCBs, diuretics, (beta blockers for patients under 55)		Avoid hydralazine and minoxidil
<b>Peripheral arterial disease</b>	Does not affect initial treatment recommendations	Does not affect initial treatment recommendations	Avoid beta blockers with severe disease
<b>Dyslipidemia</b>	Does not affect initial treatment recommendations	Does not affect initial treatment recommendations	

ACE: Angiotensin-converting enzyme; TIA: Transient ischemic attack; ARB: Angiotensin II receptor blocker; CCBs: Calcium channel blockers.

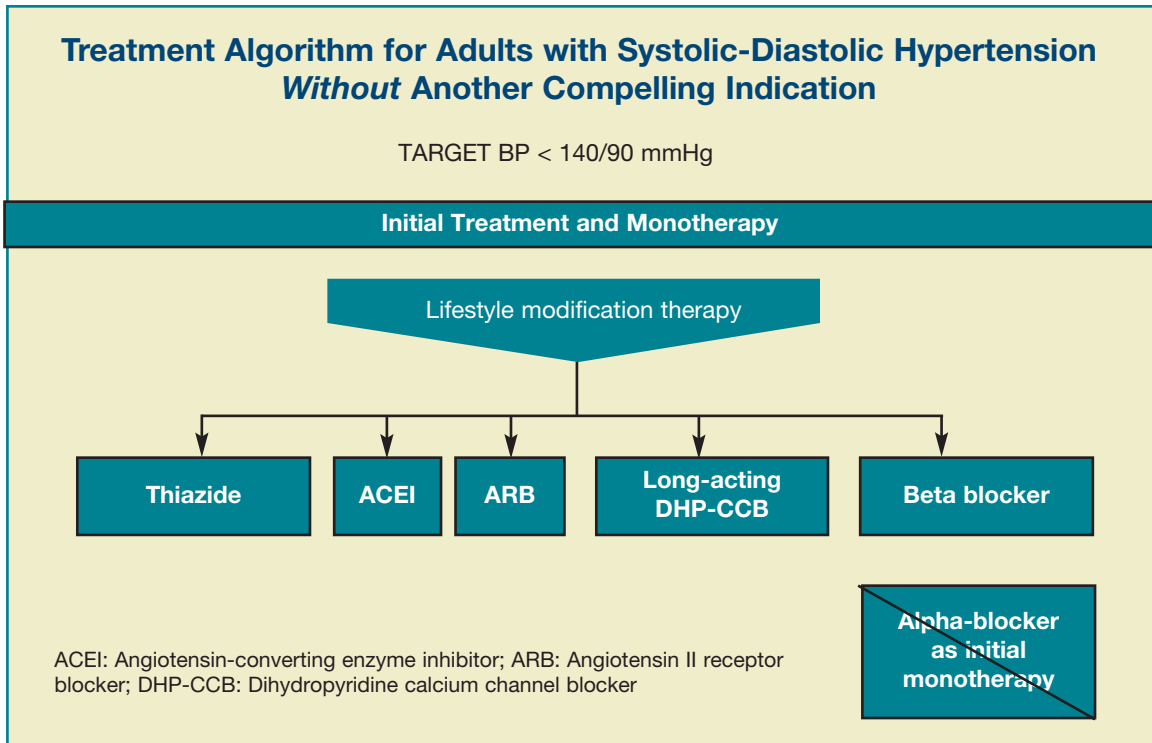


Figure 1.

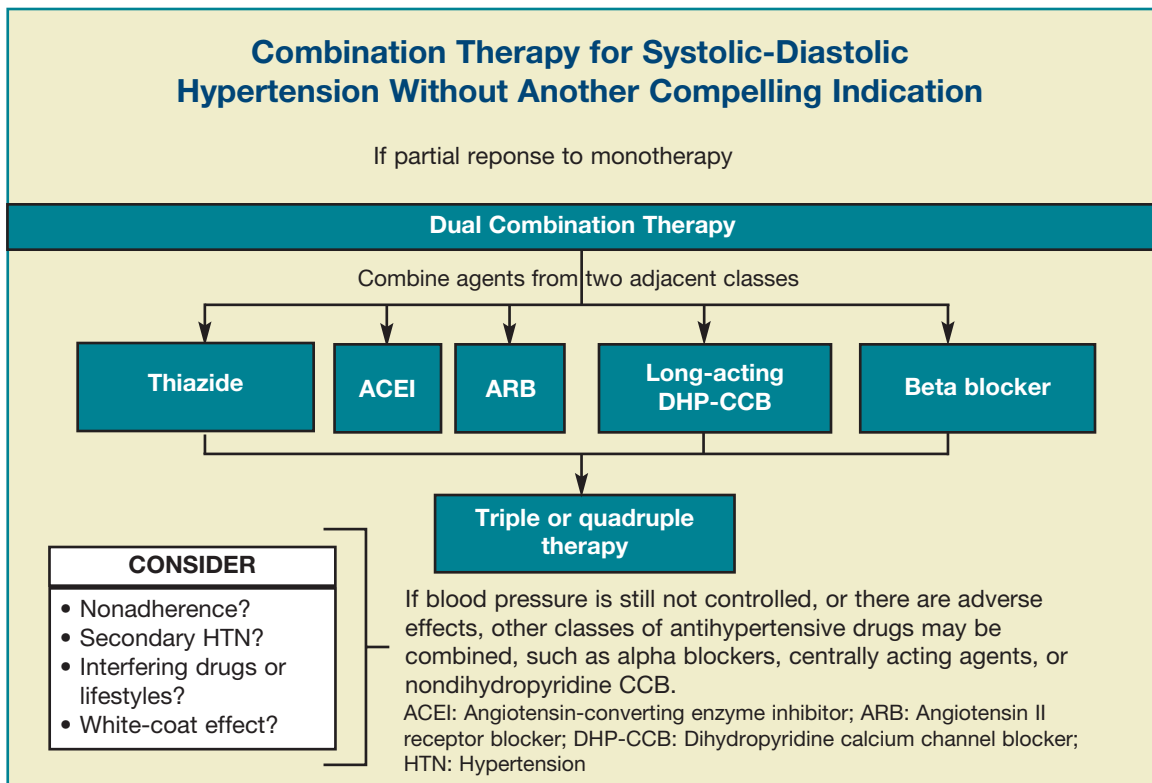


Figure 2.

## Hypertension Guidelines

therapeutic choices. As demonstrated by the Framingham Heart Study Group,<sup>9</sup> in the general population even BP within a “normal” range are positively correlated with cardiovascular risk. Thus, patients with “high normal” BP (130/89 mmHg to 139/85 mmHg) have a three times greater risk of cardiovascular events than those with “optimal” BP (systolic BP < 120 mmHg). Although these data cannot predicate drug management decisions in the general population, they are being seen as increasingly important in identifying BP targets for treatment in patients at highest risk for atherosclerotic events. For example, treatment of hypertension is much more effective, in terms of absolute cardiovascular risk reduction, in patients with diabetes and “high-normal BP” than in premenopausal females with no other risk factors and Level 2 hypertension (> 160/100 mmHg).<sup>10,11</sup> The question of whether lowering BP targets for treatment can be justified for other subgroups at highest risk for atherosclerotic complications (e.g., patients post-stroke, or those patients who fulfill the entry criteria for the Heart Outcomes Prevention Evaluation [HOPE] study)<sup>12</sup> is an ongoing focus of discussion in 2003.

**Lifestyle modifications remain a cornerstone of antihypertensive therapy.** Lifestyle modification is critical both as initial management and in conjunction with pharmacologic therapy. Recent data indicates a life-

Table 2

### Useful Antihypertensive Drug Combinations

For additive hypotensive effect in dual therapy, combine an agent from Column 1 with Column 2.

#### Column 1

- Thiazide diuretic
- Long-acting dihydropyridine CCB

#### Column 2

- Beta blocker
- ACE inhibitor
- ARB

ACE: Angiotensin-converting enzyme; ARB: Angiotensin II receptor blocker; CCB: Calcium channel blocker.

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Table 3

### ALLHAT and the 2003 recommendations

**Overall, the implications of ALLHAT with regards to the 2003 recommendations were reflected in:**

- a. Changes in wording related to choice of first-line therapy, increasing the prominence of thiazide diuretics.
- b. A recommendation **not** to consider ACE inhibitors as first-line therapy in black patients with hypertension without other compelling indications (reflecting the decreased blood pressure-lowering effectiveness of ACE inhibitors in this population).
- c. A recommendation to consider diuretics as a safe alternative to ACE inhibitors and ARBs in patients with hypertension, and diabetes, but normal urinary albumin excretion.

Table 4

### LIFE and the 2003 recommendations

**Overall, the implications of the LIFE study were reflected in:**

- a. The recommendation that ARBs be considered as an additional option for first-line therapy in younger patients, along with thiazide diuretics, beta blockers, dihydropyridine CCBs, and ACE inhibitors.
- b. The recommendation of ARBs as a first-line choice for the treatment of isolated systolic hypertension (ISH), along with diuretics and dihydropyridine CCBs (based, in part, on review of the subgroup analysis of patients with ISH in the LIFE study).
- c. The development of more specific recommendations regarding preferred first-line therapies for the treatment of hypertension in patients with left ventricular hypertrophy. These preferred therapies followed the recommendations for treatment of “hypertension in patients with no other compelling indications.”


time risk for developing hypertension of over 90%.<sup>13</sup> These findings emphasize the importance of lifestyle changes in the prevention, as well as the management, of hypertension.

**The role of combination therapy remains critical in hypertension control (Figure 2).**

This message is important, both in the context of combining lifestyle and pharmacologic treatment, as well as combining antihypertensive drugs effectively. The vast majority of hypertensive patients require combination drug therapy. The most effective combinations should be used preferentially. Whether this predicts an expanded role for the use of fixed dose combinations in the management of hypertension will probably be dependent on their, as yet, unproven role in improving compliance and, ultimately, BP control.

**Establishing and maintaining patient compliance with their antihypertensive management prescription remains a major issue.** However, attention to some simple approaches can improve patient adherence.

In some ways, more important than “what’s new” in the 2003 recommendations is “what has stayed the same.” Many of the issues in the management of hypertension in 2002 remain in 2003. The tools to control hypertension and to reduce cardiovascular disease are in our hands. The CHEP will continue to advocate for hypertension treatment and control, increase awareness of the importance of optimum hypertension management, and

develop tools to aid health-care professionals and evaluate the impact of our activities. We will continue to provide the most current evidence-based recommendations to Canadian health-care practitioners. 

## Take-home message

### The Canadian Hypertension Education Program Recommendations 2003

#### What's New?

- Broadening of recommendations for first-line therapy including ARBs.
- Simplification of recommendations for the management of patients with diabetes and hypertension with the universal recommendation of either ARBs and ACE inhibitors as preferred therapy.

#### What's old, but still important?

- Assessment of global atherosclerotic risk in hypertensive patients, including the appreciation of lower BP targets for patients at highest atherosclerotic risk.
- Importance of lifestyle modifications as a cornerstone of anti-atherosclerotic therapy.
- Emphasis of the benefits of thiazide diuretics in all subgroups of hypertensive patients.
- Importance of drug combinations for BP control.
- Focus on compliance.

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