Highlights and summary of the 2006 Canadian Hypertension Education Program recommendations

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The present paper summarizes and highlights key messages of the 2006 Canadian Hypertension Education Program recommendations for the management and diagnosis of hypertension. An important message in the 2006 Canadian Hypertension Education Program recommendations is to improve patient adherence to antihypertensive therapy by incorporating a number of techniques. These new recommendations still need to be incorporated into what remain as the older but still important considerations for the diagnosis, management and treatment of the patient with hypertension, namely, to assess blood pressure in all adults at all appropriate visits, to expedite the diagnosis of hypertension, to assess and manage global cardiovascular risk, to emphasize that lifestyle modifications are the cornerstone of antihypertensive therapy, to treat to target, and to use combinations of antihypertensive medications and lifestyles to achieve recommended targets. Minor changes in pharmacological therapies are discussed, and potentially important aspects related to home and self-monitoring, particularly with respect to patients with masked hypertension (blood pressure controlled in the office but not at home), are introduced.

Key Words: *Clinical trials; Diagnosis; Hypertension; Recommendations; Treatment*

Hypertension is a significant health problem that is predicted to become a greater global burden in the next 20 years, particularly in the developing world (1-3). The estimates of the burden of disease attributable to blood pressure are almost double those of the previous Global Burden of Disease Study (4,5). It is predicted that by 2025, the number of adults worldwide with hypertension will increase by approximately 60% (1). The estimated total number of adults with hypertension in 2000 was 972 million (range 957 to 987 million); 333 million (range 329 to 336 million) in economically developed countries and 639 million (range 625 to 654 million) in economically developing countries. The number of adults with hypertension in 2025 is predicted to increase by approximately 60%, to a total of 1.56 billion (range 1.54 to 1.58 billion) (1). Hence, hypertension is an important public health challenge worldwide. Prevention, detection, treatment and control of this condition should receive high priority, especially because a substantial

Programme d'éducation canadien sur l'hypertension – Résumé des principales recommandations 2006

L'article présente un résumé des principaux messages liés aux recommandations 2006 du Programme d'éducation canadien sur l'hypertension, relatives au diagnostic et à la prise en charge de l'hypertension artérielle (HTA). L'un des messages clés, liés aux recommandations du Programme est l'amélioration de l'observance thérapeutique par les patients, et ce, à l'aide d'un certain nombre de techniques. Il reste toutefois à intégrer ces nouvelles recommandations aux aspects traditionnels mais non moins importants du diagnostic, de la prise en charge et du traitement de l'HTA, qui consistent en la mesure de la pression artérielle chez tous les adultes au cours de toutes les consultations appropriées; en la pose du diagnostic d'hypertension artérielle; en l'évaluation et le traitement du risque global de maladie cardiovasculaire; en la nécessité d'apporter des modifications au mode de vie, pierre angulaire du traitement antihypertenseur; en la poursuite du traitement jusqu'à l'atteinte des valeurs cibles et en l'association du traitement médicamenteux et des modifications du mode de vie, si besoin est. Il sera également question de légères modifications apportées au traitement médicamenteux et d'éléments potentiellement importants, liés à l'autosurveillance et à la surveillance de la pression artérielle à domicile, surtout chez les patients atteints d'hypertension masquée (normale au cabinet du médecin mais pas à domicile).

proportion of cardiovascular disease is attributable to nonoptimal blood pressure levels (3). The Canadian Hypertension Education Program (CHEP) has a mandate to improve hypertension management, to develop tools to aid health care professionals and to evaluate the impact of its activities. The CHEP continues to provide the most current evidence-based recommendations to Canadian health care workers.

The year 2006 marks the seventh consecutive year that the CHEP has updated recommendations for the diagnosis, management and treatment of hypertension. This year, the CHEP's recommendations focused on adherence to antihypertensive therapy. In addition, based on new and additional evidence, a few changes relating to pharmacological treatment were introduced. Furthermore, the CHEP identified that treated hypertensive patients with masked hypertension (blood pressure controlled in the office but not at home) should monitor home and self-measured blood pressure.

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KEY MESSAGES OF CHEP RECOMMENDATIONS

The new key message identified in the 2006 recommendations is to improve patient adherence to antihypertensive therapy by assisting patients with adherence, assisting patients with getting more involved in their treatment, and improving management in the office and beyond.

However, this 'new message' needs to be incorporated into what remain as the older but still important considerations for the diagnosis, management and treatment of the patient with hypertension, namely to:

- assess blood pressure in all adults at all appropriate visits;
- expedite the diagnosis of hypertension;
- assess and manage global cardiovascular risk;
- emphasize that lifestyle modifications are the cornerstone of antihypertensive therapy;
- treat to target; and
- use combinations of antihypertensive medications and lifestyles to achieve recommended targets.

KEY ELEMENTS OF THE 2006 RECOMMENDATIONS PROCESS

The 2006 CHEP recommendations process incorporated all trials and epidemiological studies published in the previous 12 months (2005 to 2006) that were considered to be relevant for the diagnosis, management and treatment of individuals with hypertension. The impact of these studies was considered in the context of the cumulative evidence of the past 50 years of major clinical trials in hypertension, and in the context of the prior iterations of the evidence-based CHEP recommendations developed over the past 25 years. For the 2006 CHEP recommendations, the clinical studies incorporated included the Anglo-Scandinavian Cardiac Outcomes Trial – Blood Pressure Lowering Arm (ASCOT-BLA) study (6,7), Antihypertensive and Lipid-Lowering treatment to prevent Heart Attack Trial (ALLHAT) (8), VALsartan In Acute myocardial iNfarcTion (VALIANT) trial (9) and Self-measurement of blood pressure at Home in the Elderly: Assessment and Follow-up (SHEAF) study (10), as well as a number of smaller studies, systemic reviews and the Cochrane Database.

IMPROVING PATIENT ADHERENCE TO ANTIHYPERTENSIVE THERAPY

Adherence to an antihypertensive prescription can be improved by a multipronged approach. Recommendations made by CHEP include:

Assist patients with adherence

1. Teach patients to take their pills on a regular schedule associated with a routine daily activity (eg, brushing teeth).
2. Simplify medication regimens using long-acting once-daily dosing.
3. Utilize fixed-dose combination pills.
4. Utilize unit-of-use packaging (eg, blister packaging).

Assist patients with getting more involved in their treatment

5. Educate patients and patient's families about their disease and treatment regimens, verbally and in writing.
6. Encourage greater patient responsibility and autonomy in regular monitoring of their blood pressure.

Improve blood pressure management in the office and beyond

7. Assess adherence to nonpharmacological and pharmacological therapy at every visit.
8. Encourage adherence to therapy by health care practitioner-based telephone contact, particularly over the first three months of therapy.
9. Coordinate with work-site health care givers, if available, to improve hypertension management and monitoring.

These recommendations were based on an initial survey of related studies from PsycINFO (including 210 original papers and reviews) and MEDLINE (including 769 original papers and reviews) over the past three years.

Low adherence of patients to prescribed, self-administered antihypertensive drugs is a major problem contributing, in part, to poor control of hypertension. In general, patients who are prescribed self-administered medications typically take less than one-half of the prescribed doses. Efforts to assist patients in following medication protocols may improve the efficiency of care and enhance the benefits. In Canada, suboptimal control of hypertension is attributed, in part, to patients who stop taking their antihypertensive drugs after one year. Accordingly, adherence needs to be stressed, and this is a major focus of the 2006 CHEP recommendations.

With the cut-off point between 'normal' and 'high' blood pressure being pushed increasingly downward, particularly for patients with multiple cardiovascular risk factors, most hypertensive patients need more than one antihypertensive agent to reach target blood pressure. Furthermore, guidelines indicate that low doses of multiple drugs may be even more efficacious than higher doses of fewer drugs. There is an increasing trend to use fixed-dose combination pills, which should facilitate improved adherence. Rational antihypertensive drug combinations are based on their ability to produce additive blood pressure-lowering and to reduce the incidence of dose-dependent side effects. Furthermore, by simplifying medication regimes, adherence is likely to be improved (11).

The 2006 CHEP recommendations suggest simplification of the drug regimen as a strategy to improve adherence. Seventy five per cent of patients require at least two drugs and 25% of patients require at least three drugs to reduce blood pressure to target levels. An even higher proportion of hypertensive patients with diabetes require multidrug therapy. While once-daily dosing and the use of electronic medication aids are currently recommended as ways to simplify the medication regimen and improve adherence, the increase in complexity of self-administration with the use of multiple drugs and the consequent possibility for reduction in adherence remains a problem requiring further attention. Other interventions that aim to simplify dosages involve the use of fixed-dose combination pills (ie, pills that include two or more drugs in fixed proportions in the

same formulation) and unit-of-use packaging (eg, blister packaging of several medications in fixed combination to be taken together). For example, a recent retrospective analysis of medication adherence by Taylor and Shoheiber (12) compared 2754 patients prescribed a single-capsule, fixed-dose combination of amlodipine besylate and benazepril hydrochloride with 2978 patients prescribed an angiotensin-converting enzyme (ACE) inhibitor and a dihydropyridine calcium channel blocker (CCB) as separate drugs. Results indicated improved adherence and fewer medical resource requirements in the fixed-dose combination pill group.

A systematic review of randomized trials evaluating the effects of fixed-dose combination pills and unit-of-use packaging (13) concluded that in 12 of 15 trials identified, there were trends to improved clinical and/or adherence outcomes. While the trials reviewed were heterogeneous in their settings, the medical conditions being treated and the outcome measures used, three of the four trials that involved unit-of-use packaging for the treatment of hypertension reported clinically significant reductions in blood pressure associated with this intervention. Although interpretation of these findings is limited by the methodological quality of the studies (most were small or had inadequate follow-up time), those with greater methodological rigour were typically associated with larger improvements in measures of adherence and clinical outcomes, including blood pressure reduction.

In addition to simplifying drug regimens, there is growing evidence that reinforcements and reminders via telephone calls by health care providers improves adherence. The proposed 2006 recommendations, in regard to encouraging a role of follow-up by telephone, are based primarily on generalization from management of dyslipidemia and specifically are based on the systematic review by Schedlbauer et al (14). In that review, reinforcement and reminders via telephone, as well as postal back-ups, were the interventions of interest in three studies selected among 2380 articles. Weekly phone calls were reported as improving adherence to lovastatin plus colestipol in the intervention group judged by prescription refill rate – the rate was improved by 24% (63% in the intervention group versus 39% in the control group; $P < 0.05$, $n = 30$) (15). It is notable that telephone and postal reminders in the remaining two randomized, controlled trials did not result in any significant improvement (79.7% in the intervention group versus 77.4% in the control group, $P = \text{not significant}$, $n = 4548$ [16] and 88% in the intervention group versus 82% in the control group, $P = 0.32$, $n = 120$ [17]). However, the study by Faulkner et al (15) was viewed as being of higher quality than the other two (notwithstanding the smaller sample size) and is the primary basis of the proposed revision in the 2006 CHEP recommendations. In addition, studies that predominantly enrolled adherent patients are not able to improve the adherence of these patients, regardless of the intervention.

NEW AND ADDITIONAL EVIDENCE IN THE PHARMACOLOGICAL TREATMENT OF PATIENTS WITH HYPERTENSION

Beta-blockers in the treatment of hypertension

The 2006 CHEP recommendations suggest the use of beta-blocker therapy in hypertensive patients of all ages who have specific indications, such as postmyocardial infarction, angina and congestive heart failure. However, with respect to first-line therapy of uncomplicated hypertension, it is recommended that beta-blockers be used only in patients younger than 60 years of age.

New evidence to support the use of beta-blockers as a first-line treatment in the management of hypertension only in patients younger than 60 years was from a large meta-analysis (18,19). The recommendation is not new, but is further supported by the recent studies. Trials demonstrated the inferiority of beta-blockers in reducing cardiovascular events in uncomplicated hypertension in older patients compared with diuretics, angiotensin receptor blockers (ARBs) and CCBs.

Combination of a dihydropyridine CCB and an ACE inhibitor

The 2006 recommendations state that additional antihypertensive drugs should be used if target blood pressure levels are not achieved with standard dose monotherapy. Add-on drugs should be chosen from first-line choices. Useful choices include a thiazide diuretic or CCB with either an ACE inhibitor, ARB or beta-blocker. Caution should be exercised in combining a nondihydropyridine CCB with a beta-blocker.

This year, the grade of evidence supporting the combination of a dihydropyridine CCB and an ACE inhibitor was increased from a D to a C. This change is based in large part on the results of the ASCOT-BLA trial, which showed significantly lower rates of coronary and stroke events in individuals allocated an amlodipine-based combination drug regimen than in those allocated an atenolol-based combination drug regimen (6,7). This trial was complicated by the use of beta-blockers as initial therapy in a predominantly older study population. Therefore, the design of the trial would be expected to favour the amlodipine-based combination therapy.

ARBs and ACE inhibitors in hypertensive patients with myocardial infarction

The 2006 CHEP recommendations state that initial therapy in patients with hypertension who have had a recent ST elevation myocardial infarction or non-ST segment elevation myocardial infarction should include both a beta-adrenergic antagonist and an ACE inhibitor. An ARB can be used if the patient is intolerant of an ACE inhibitor.

These recommendations are based on findings from the VALIANT trial (9), which assessed effects of valsartan or captopril, or the combination of the two, in postmyocardial infarction patients with heart failure or systolic dysfunction, or both. Total mortality, and the combined secondary end point of cardiovascular death, myocardial infarction or heart failure were not significantly different in the three groups after 24.7 months of follow-up. Valsartan was not inferior to captopril in terms of total mortality, and cardiovascular death, myocardial infarction and heart failure. Hence, valsartan can be considered to be an alternative treatment to ACE inhibitors in these patients.

Combined ACE inhibitors and ARBs in hypertensive patients with cardiac failure

2006 CHEP recommendations suggest that patients with uncontrolled hypertension and cardiac failure may benefit from combined ACE inhibitors and ARBs. Although ACE inhibitors combined with ARBs have a positive role in the management of cardiac failure, a higher rate of hospitalization for hypotension, hyperkalemia and worsening renal failure

have been seen in clinical practice (20). Accordingly, careful monitoring is required to ensure patient safety during this combination of therapies.

ISSUES IDENTIFIED BY CHEP AS BEING POTENTIALLY IMPORTANT IN THE DIAGNOSIS AND MANAGEMENT OF HYPERTENSION

An issue that was identified by the 2006 CHEP Recommendations Task Force to be potentially important in the diagnosis and treatment of hypertension relates to home and self-measurement of blood pressure in patients in whom clinic blood pressures either overestimate (white coat hypertension) or underestimate (masked hypertension) their true hypertension-related risks.

Growing evidence indicates the importance of home and self-measurement. In 2004, release of the SHEAF study demonstrated not only the prognostic strength of home blood pressure measuring, but provided, for the first time, data documenting the mortality risk of 'masked hypertension' (21). Masked hypertension is defined as clinic blood pressure less than 140/90 mmHg (three measurements at two office visits) and home blood pressure greater than 135/85 mmHg (three measurements in the morning and the evening over two days). More recent analyses of the SHEAF data focused on the number of measurements necessary to determine masked hypertension (22). The SHEAF data provide perhaps the clearest evidence that the risk profile of those with masked hypertension is similar to the risk profile of those with sustained hypertension.

The prognostic significance of home blood pressure measurement was demonstrated again in an 11-year follow-up study of elderly patients (23). The study results suggest that the prognostic value of home blood pressure is better than clinic blood pressure and similar to daytime ambulatory blood pressure. Results further demonstrated the importance of the setting for blood pressure measurement (home versus clinic), strengthening the need to emphasize 'home' rather than 'self' in the terminology used to describe these measurements.

With respect to prognosis, data from the Ohasama study (24) show that in addition to the blood pressure measured at home, the home heart rate is a powerful independent predictor of cardiovascular risk.

The concept of masked hypertension is not new (25). In general, the term describes the phenomenon when clinic blood pressure is normal, but out-of-office readings are in the hypertensive range. Masked hypertension has been variously called 'reverse white coat hypertension', 'isolated home' or 'isolated ambulatory' hypertension, depending on the method used to find it. Several of the issues and the history surrounding masked hypertension were discussed in the 2005 subcommittee report (26,27).

Important issues still to be resolved centre around how to define masked hypertension in a patient and what method (ambulatory or home blood pressure) is most appropriate for making the diagnosis. These aspects will be further addressed in the 2007 to 2008 CHEP recommendations.

THE OLD BUT STILL IMPORTANT MESSAGES IN THE 2006 RECOMMENDATIONS (26,27)

Measure blood pressure in all adults at all appropriate visits
In the last survey of blood pressure (1985 to 1992), 43% of adults with high blood pressure were not aware that their blood pressure was elevated. This places a large proportion of the Canadian population at preventable risk for cardiovascular

disease due to uncontrolled hypertension. Recent data from the Framingham Study have indicated that over 90% of normotensive participants aged 55 to 65 years developed hypertension over the 20 to 30 years of follow-up. Forty-six per cent of Canadians aged 55 to 65 years already have hypertension. It is therefore expected that the vast majority of Canadians will develop hypertension. Measuring the blood pressure of all adults every time they visit is an important mechanism to detect hypertension and an opportunity to discuss preventive strategies using lifestyle modification.

The diagnosis of hypertension can be (should be) expedited

For patients with hypertensive urgencies or emergencies, a diagnosis of hypertension can be made at an initial hypertension-related visit. A diagnosis of hypertension can be made at a second visit for patients with blood pressure of at least 140/90 mmHg and with one of the following: target organ damage, chronic kidney disease, diabetes mellitus or blood pressure 180/110 mmHg or higher. For patients with blood pressure between 160 mmHg to 179 mmHg/100 mmHg to 109 mmHg (and not already diagnosed based on the criteria above), a diagnosis can be made at a third visit.

Diagnosis can be expedited by home and self-measurement of blood pressure. Office-based diagnosis of hypertension has remained the gold standard for the diagnosis of hypertension. However, it is now firmly established that out-of-office modalities for blood pressure measurement are as or more effective in assessing the prognostic importance of blood pressure elevations. To be effective, these technologies, including automatic ambulatory blood pressure monitoring, and home and self-blood pressure monitoring, must be used by properly educated practitioners (for automatic ambulatory blood pressure monitoring) or patients (for home and self-monitoring); this assumes the use of validated, properly calibrated equipment. However, when available (and properly used), these modalities are effective and can expedite the diagnosis of hypertension – especially for those patients with Level 1 hypertension (and without diabetes, chronic kidney disease or target organ damage) that would otherwise require up to six visits and six months before a diagnosis could be made.

Assess and manage global cardiovascular risk

Over 90% of hypertensive patients have additional cardiovascular risks that require assessment and management. Acetylsalicylic acid should be considered in controlled hypertensive patients. Statins are recommended in hypertensive patients with established cardiovascular disease or the presence of three or more other cardiovascular risks.

Lifestyle modifications are the cornerstone of antihypertensive therapy

Lifestyle modifications are safe and inexpensive, can prevent hypertension, can lower blood pressure in hypertensive patients and when combined with drug therapy, and may result in better blood pressure control and improved quality of life (28). Many of the individual factors, if successfully adopted, may lead to blood pressure changes in the magnitude of that associated with single-drug therapy. Although each factor typically has a modest effect, the combined effects may be substantial. From a public health perspective, even a small reduction in blood pressure should have a significant, beneficial effect on the occurrence of hypertension and its complications.

Lifestyle changes recommended by CHEP to reduce blood pressure include:

- maintaining a diet low in salt and saturated fats, and high in fresh fruit and vegetables and low-fat dairy products (DASH diet [29]);
- continuous or accumulated moderate intensity dynamic exercise (such as walking, jogging, cycling or swimming) for 30 min to 60 min four to seven days per week;
- weight reduction in those who are overweight;
- reduction in alcohol consumption in those who drink more than two drinks per day; and
- a smoke-free environment and smoking cessation to reduce cardiovascular risk.

Treat to target

Population surveys demonstrate that only small proportions of patients have blood pressure treated to target, resulting in sub-optimal cardiovascular risk reduction. In particular, in high-risk patients, greater benefits occur with achieving recommended targets. The systolic blood pressure target is the more difficult to achieve in most patients. Achieving systolic blood pressure targets, however, is important, because systolic blood pressure is at least as important, if not more important, than diastolic blood pressure in determining cardiovascular prognosis. The current recommended targets to reduce blood pressure are, in general, less than 140 mmHg systolic and less than 90 mmHg diastolic, and in patients with diabetes or chronic kidney disease, less than 130/80 mmHg. The drugs recommended to individualize therapy in patients are provided in Table 1.

Use combinations of medications and lifestyle modification to achieve blood pressure targets

Most patients require two or more drugs to achieve recommended blood pressure targets. In general, the average reduction in blood pressure with a single blood pressure-lowering medication is 10/5 mmHg. Combining medications is therefore to be expected in the therapy of hypertension. Using lifestyle modification can reduce the number and doses of medications that are required for blood pressure control, and should be recommended for all hypertensive patients.

CONCLUSIONS

The 2006 CHEP recommendations focus on adherence to antihypertensive therapy. In addition, based on new and additional evidence, a few changes relating to pharmacological treatment are introduced. Furthermore, the CHEP identified that treated hypertensive patients with masked hypertension (blood pressure controlled in the office but not at home) should home and self-monitor blood pressure. As in previous years, it needs to be reiterated that the CHEP hypertension management recommendations are based solely on efficacy data. Considerations relating to individual patient and physician preferences, and cost-effectiveness of different drug classes have not been a component of this process, and need to be considered by the physician and patient when individualizing therapy.

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TABLE 1
Individualized drug therapy in patients based on their condition

Patient's condition	Initial therapy	Second-line therapy	Notes and/or cautions
Hypertension without compelling indications for other medications	Thiazide diuretics, beta-blockers (for patients <60 years of age), ACE inhibitors (in non-black patients), ARB, or long-acting CCBs (consider ASA and/or statins in selected patients)	Combinations of first-line drugs	Alpha-blockers are not recommended as initial monotherapy. Beta-blockers are not recommended as initial monotherapy in those over 60 years of age. Hypokalemia should be avoided in those who are receiving diuretics. ACE inhibitors are not recommended as initial monotherapy for black patients. ACE inhibitors and ARBs are contraindicated in women of child-bearing potential
Isolated systolic hypertension without other compelling indications	Thiazide diuretics, ARBs or long-acting dihydropyridine CCBs	Combinations of first-line drugs	Hypokalemia should be avoided in people receiving diuretics
Diabetes mellitus with nephropathy	ACE inhibitors or ARBs	Addition of one or more of thiazide diuretics, cardioselective beta-blockers, or long-acting CCBs or use of combination of ARB and ACE inhibitor	
Diabetes mellitus without nephropathy	ACE inhibitors, ARBs, thiazide diuretics or long-acting CCBs	Combination of first-line drugs or addition of cardioselective beta-blockers	

Continued on next page

TABLE 1 – continued
Individualized drug therapy in patients based on their condition

Patient's condition	Initial therapy	Second-line therapy	Notes and/or cautions
Angina	Beta-blockers (strongly consider adding ACE inhibitors)	Long-acting CCBs	Avoid short-acting nifedipine
Prior myocardial infarction	Beta-blockers and ACE inhibitors (ARBs if intolerant of ACE inhibitors)	Combinations of additional agents	
Heart failure	ACE inhibitors (ARBs if intolerant of ACE inhibitors), beta-blockers, and spironolactone in selected patients	ARBs or hydralazine/isosorbide dinitrate (thiazide or loop diuretics as additive therapy)	Avoid nondihydropyridine CCBs
Past cerebrovascular accident or transient ischemic attack	Combinations of ACE inhibitor and diuretic		Blood pressure reduction reduces recurrence of cerebrovascular events
Chronic kidney disease	ACE inhibitors (diuretics as additive therapy)	Combinations of additional agents (ARBs if intolerant of ACE inhibitors)	Avoid ACE inhibitors and ARBs if bilateral renal artery stenosis is present
Left ventricular hypertrophy	ACE inhibitors, ARBs, CCBs, thiazide diuretics (beta-blockers for patients <60 years of age)		Avoid hydralazine and minoxidil
Peripheral arterial disease	Does not affect treatment recommendations		Avoid beta-blockers for patients with severe disease
Dyslipidemia	Does not affect treatment recommendations		

Reproduced with permission from the Canadian Hypertension Education Program. ACE Angiotensin-converting enzyme; ARB Angiotensin receptor blocker; ASA Acetylsalicylic acid; CCB Calcium channel blocker

REFERENCES

- Kearney PM, Whelton M, Reynolds K, Muntner P, Whelton PK, He J. Global burden of hypertension: Analysis of worldwide data. *Lancet* 2005;365:217-23.
- Lawes CM, Hoorn SV, Law MR, Elliott P, Macmahon S, Rodgers A. Blood pressure and the global burden of disease 2000. Part I: Estimates of blood pressure levels. *J Hypertens* 2006;24:413-22.
- Lawes CM, Hoorn SV, Law MR, Elliott P, Macmahon S, Rodgers A. Blood pressure and the global burden of disease 2000. Part II: Estimates of attributable burden. *J Hypertens* 2006;24:423-30.
- Ezzati M, Lopez AD, Rodgers A, Vander Hoorn S, Murray CJ; Comparative Risk Assessment Collaborating Group. Selected major risk factors and global and regional burden of disease. *Lancet* 2002;360:1347-60.
- Murray CJ, Lopez AD. Global mortality, disability, and the contribution of risk factors: Global Burden of Disease Study. *Lancet* 1997;349:1436-42.
- Dahlof B, Sever PS, Poulter NR, et al; ASCOT Investigators. Prevention of cardiovascular events with an antihypertensive regimen of amlodipine adding perindopril as required versus atenolol adding bendroflumethiazide as required, in the Anglo-Scandinavian Cardiac Outcomes Trial – Blood Pressure Lowering Arm (ASCOT-BPLA): A multicentre randomised controlled trial. *Lancet* 2005;366:895-906.
- Poulter NR, Wedel H, Dahlof B, et al; ASCOT Investigators. Role of blood pressure and other variables in the differential cardiovascular event rates noted in the Anglo-Scandinavian Cardiac Outcomes Trial – Blood Pressure Lowering Arm (ASCOT-BPLA). *Lancet* 2005;366:907-13.
- Whelton PK, Barzilay J, Cushman WC, et al; ALLHAT Collaborative Research Group. Clinical outcomes in antihypertensive treatment of type 2 diabetes, impaired fasting glucose concentration, and normoglycemia: Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT). *Arch Intern Med* 2005;165:1401-9.
- Solomon SD, Zelenkofske S, McMurray JJ, et al; Valsartan in Acute Myocardial Infarction Trial (VALIANT) Investigators. Sudden death in patients with myocardial infarction and left ventricular dysfunction, heart failure, or both. *N Engl J Med* 2005;352:2581-8.
- Bobrie G, Genes N, Vaur L, et al. Is “isolated home” hypertension as opposed to “isolated office” hypertension a sign of greater cardiovascular risk? *Arch Intern Med* 2001;161:2205-11.
- Haynes R, Yao X, Degani A, et al. Interventions to enhance medication adherence. *Cochrane Database Syst Rev* 2005;(4):CD000011.
- Taylor AA, Shoheiber O. Adherence to antihypertensive therapy with fixed-dose amlodipine besylate/benazepril HCl versus comparable component-based therapy. *Congest Heart Fail* 2003;9:324-32.
- Connor J, Rafter N, Rodgers A. Do fixed-dose combination pills or unit-of-use packaging improve adherence? A systematic review. *Bull World Health Organ* 2004;82:935-9.
- Schedlbauer A, Schroeder K, Peters TJ, Fahey T. Interventions to improve adherence to lipid lowering medication. *Cochrane Database Syst Rev* 2004;(4):CD004371.
- Faulkner MA, Wadibia EC, Lucas BD, Hilleman DE. Impact of pharmacy counseling on compliance and effectiveness of combination lipid-lowering therapy in patients undergoing coronary artery revascularization: A randomized, controlled trial. *Pharmacotherapy* 2000;20:410-6.
- Guthrie RM. The effects of postal and telephone reminders on compliance with pravastatin therapy in a national registry: Results of the first myocardial infarction risk reduction program. *Clin Ther* 2001;23:970-80.
- Schectman JM, Stoy DB, Elinsky EG. Association between physician counseling for hypercholesterolemia and patient dietary knowledge. *Am J Prev Med* 1994;10:136-9.
- Lindholm LH, Carlberg B, Samuelsson O. Should beta-blockers remain first choice in the treatment of primary hypertension? A meta-analysis. *Lancet* 2005;366:1545-53.
- Beever DG. The end of beta blockers for uncomplicated hypertension? *Lancet* 2005;366:1510-2.
- Pfeffer MA, Swedberg K, Granger CB, et al; CHARM Investigators and Committees. Effects of candesartan on mortality and morbidity

- in patients with chronic heart failure: The CHARM-Overall programme. *Lancet* 2003;362:759-66.
21. Bobrie G, Chatellier G, Genes N, et al. Cardiovascular prognosis of "masked hypertension" detected by blood pressure self-measurement in elderly treated hypertensive patients. *JAMA* 2004;291:1342-9.
 22. Mallion JM, Genès N, Vaur L, et al. Detection of masked hypertension by home blood pressure measurement: Is the number of measurements an important issue? *Blood Press Monit* 2004;9:301-5.
 23. Fagard RH, Van Den Broeke C, De Cort P. Prognostic significance of blood pressure measured in the office, at home and during ambulatory monitoring in older patients in general practice. *J Hum Hypertens* 2005;19:801-7.
 24. Hozawa A, Ohkubo T, Kikuya M, et al. Prognostic value of home heart rate for cardiovascular mortality in the general population: The Ohasama study. *Am J Hypertens* 2004;17:1005-10.
 25. Pickering TG, Davidson K, Gerin W, Schwartz JE. Masked hypertension. *Hypertension* 2002;40:795-6.
 26. Khan NA, McAlister FA, Lewanczuk RZ, et al; Canadian Hypertension Education Program. The 2005 Canadian Hypertension Education Program recommendations for the management of hypertension: Part II – Therapy. *Can J Cardiol* 2005;21:657-72.
 27. Hemmelgarn BR, McAllister FA, Myers MG, et al; Canadian Hypertension Education Program. The 2005 Canadian Hypertension Education Program recommendations for the management of hypertension: Part I – Blood pressure measurement, diagnosis and assessment of risk. *Can J Cardiol* 2005;21:645-56.
 28. Dickinson HO, Mason JM, Nicolson DJ, et al. Lifestyle interventions to reduce raised blood pressure: A systematic review of randomized controlled trials. *J Hypertens* 2006;24:215-33.
 29. National Heart, Lung, and Blood Institute. The DASH Eating Plan. <www.nhlbi.nih.gov/health/public/heart/hbp/dash/> (Version current at April 28, 2006).
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