



## **The 2003 Canadian Recommendations for the Management of Hypertension: Diagnosis**

### **I Accurate Measurement of Blood Pressure**

1. The blood pressure of all adult patients should be assessed at all appropriate visits for determination of cardiovascular risk and monitoring of antihypertensive treatment by health care professionals who have been specifically (re) trained to measure blood pressure accurately (Grade D).
2. Use of standardized measurement techniques is recommended when assessing blood pressure for determination of cardiovascular risk and monitoring of antihypertensive treatment (Grade D).

### **II Criteria for Office or Clinic-based Diagnosis of Hypertension and Recommendations for Follow-up**

1. Patients demonstrating features of a hypertensive emergency/urgency should be diagnosed as hypertensive at their first visit and require immediate management (Grade D).
2. If the initial blood pressure is high, then in the same session at least 2 readings should be taken according to the recommended procedure for accurate blood pressure determination and the patient should be scheduled for further visits (Grade D).
3. Patients with target organ damage can be diagnosed as hypertensive at/after visit 3 (Grade D).
4. The search for target organ damage, associated risk factors and potentially modifiable causes of elevated blood pressure should proceed as follows (Grade D).
  - a) On the first visit, the patient should be questioned and the medical record reviewed for evidence of coronary artery disease (myocardial infarction, angina pectoris, congestive heart failure), cerebrovascular disease (transient ischemic attacks, ischemic or hemorrhagic stroke), peripheral arteriovascular insufficiency (intermittent claudication) or renal insufficiency. Check exogenous factors that can induce/ aggravate hypertension (see Table).

- b) At visit two, if the blood pressure is still elevated, further history and physical examination should be performed. Diagnostic tests should be arranged before visit three.
5. In the absence of target organ damage and/or increased cardiovascular risk, if at visit three, systolic blood pressure remains 160 mmHg or higher (Grade D) and/or diastolic blood pressure 100 mmHg or higher (Grade C), this patient can generally be diagnosed as hypertensive since the greatest fall in blood pressure occurs between visit one and visit two. Two to three more visits may be added prior to assigning a diagnosis of hypertension if the trend in blood pressure values is downward (Grade D).

If at visit three, systolic blood pressure is between 140 and 159 mmHg and/or diastolic blood pressure between 90 and 99 mmHg, up to two to three further visits may be required to diagnose hypertension; these measurements can be taken over a total diagnostic assessment period of up to six months (Grade D).
6. If at the last diagnostic visit, the blood pressure is <140/90 mmHg. and the patient has no evidence of target organ damage or associated risk factors, the patient should be assessed at yearly intervals if the last blood pressure is in the high normal range (130/85 to 139/89 mmHg) or at two yearly intervals if the last blood pressure is in the normal range (120/80 to 129/84 mmHg) as these patients frequently develop hypertension later on (Grade C).
7. Patients receiving lifestyle modification advice (non-pharmacological treatment) should be followed up at three to six month intervals. Shorter intervals (one or two monthly) are needed for patients with higher blood pressures (Grade D).
8. Follow-up of patients on antihypertensive drug treatment: Patients should be seen monthly until 2 blood pressure readings are below their target (Grade D). Shorter intervals between visits will be needed for symptomatic patients, those with severe hypertension, intolerance to antihypertensive drugs or those with target organ damage (Grade D). Once target blood pressure has been reached, patients should be seen at 3-6 month intervals (Grade D).

### **III Assessment of Overall Cardiovascular Risk in Hypertensive Patients**

1. Global cardiovascular risk should be assessed. Multifactorial risk assessment models can be used to predict more accurately an individual's global cardiovascular risk (Grade A) and employ antihypertensive therapy more efficiently (Grade D).

#### **IV Routine and Optional Laboratory Tests for the Investigation of Patients with Hypertension**

1. Routine laboratory tests for the investigation of all patients with hypertension (all Grade D):
  - a) Urinalysis
  - b) Complete blood cell count
  - c) Blood chemistry (potassium, sodium, and creatinine)
  - d) Fasting glucose
  - e) Fasting total cholesterol and high density lipoprotein (HDL) cholesterol, low density lipoprotein (LDL) cholesterol, triglycerides
  - f) Standard 12-lead ECG
2. For specific patient subgroups (all Grade D):
  - a) For those with diabetes or renal disease: assess urinary protein excretion, since lower blood pressure targets are appropriate if proteinuria is present.
  - b) For those with an increased creatinine, history of renal disease or proteinuria: renal ultrasound to assess kidney size and exclude obstruction.
  - c) For those suspected of possibly having an endocrine cause for the high blood pressure, see Section VI below.

#### **V Assessment for Renovascular Hypertension**

1. Patients presenting with two or more of the clinical clues listed below suggesting renovascular hypertension should be investigated (Grade D). These include:
  - a) sudden onset or worsening of hypertension and >age 55 or <age 30
  - b) the presence of an abdominal bruit
  - a) hypertension resistant to  $\geq 3$  drugs
  - b) a rise in creatinine associated with use of an ACE inhibitor or angiotensin II receptor blocker
  - c) other atherosclerotic vascular disease, particularly in patients who smoke or have dyslipidemia
  - d) recurrent pulmonary edema associated with hypertensive surges
2. The captopril-enhanced radioisotope renal scan is the usual screening test of choice (Grade B).

#### **VI Endocrine Hypertension**

##### **a) Recommendations for Hyperaldosteronism Screening and Diagnosis**

1. Screening for hyperaldosteronism should be considered for at least the following patients (Grade D):
  - a) hypertensive patients with spontaneous hypokalemia ( $K^+ < 3.5$  mmol/L)
  - b) hypertensive patients with marked diuretic-induced hypokalemia ( $K^+ < 3.0$  mmol/L)

- c) patients with hypertension refractory to treatment with three or more drugs
  - d) hypertensive patients found to have an incidental adrenal adenoma
2. Screening for hyperaldosteronism should include assessment of a plasma aldosterone and plasma renin activity measured under standardized conditions including the collection of morning samples taken from patients in a sitting position after resting at least 15 minutes (Grade D). Antihypertensive drugs with the exception of aldosterone antagonists may be continued prior to testing.
  3. For patients with suspected hyperaldosteronism (plasma aldosterone/renin activity ratio  $>550$  pmol/L/ng/ml/hr [ $>20$  ng/dL/ng/ml/hr]), a diagnosis of primary hyperaldosteronism should be established by demonstrating inappropriate autonomous hypersecretion of aldosterone using at least one of the following physiological maneuvers:
    - a) Saline loading tests (2L over 4 hours with primary hyperaldosteronism defined as failure to suppress plasma aldosterone to  $<280$  pmol/L; or oral sodium 300 mmol/day for 3 days with primary hyperaldosteronism defined as failure to suppress plasma aldosterone to  $<240$  pmol/L) (Grade C)
    - b) Fludricortisone suppression test (oral sodium loading plus oral fludricortisone over 2 days) positive for primary hyperaldosteronism: plasma aldosterone  $\leq 140$  pmol/l at 12 noon (upright) and/or 8 am (supine) (Grade D)
    - c) A plasma aldosterone/PRA ratio  $>1400$  with a plasma aldosterone  $>440$  pmol/L (Grade C)
    - d) Captopril suppression test (primary hyperaldosteronism defined as failure to suppress plasma aldosterone to  $<240$  pmol/L two hours after 25 mg of oral captopril) (Grade C)
  4. For patients with established primary hyperaldosteronism, attempts to differentiate potential causes should be made and may include the following:
    - a) localization with adrenal CT-scan (standard: 3 mm contiguous cuts) or magnetic resonance imaging (where available) (Grade C)
    - b) assessment of plasma aldosterone before (supine) and after 2-4 hours of upright posture (Grade C)
  5. For patients with established primary hyperaldosteronism and negative imaging studies, selective adrenal venous sampling should be considered because it may be the only way to reliably differentiate unilateral from bilateral overproduction of aldosterone (Grade D).
  6. Adrenal venous sampling should be conducted in centres with experience in performing this diagnostic technique (Grade D).
  7. Treatment of confirmed unilateral aldosterone-producing adenoma is surgical removal by laparoscopic adrenalectomy (Grade C).
  8. Patients should be treated for 8-10 weeks prior to surgery, to correct metabolic abnormalities and to control blood pressure (Grade D).

9. For patients with adrenal hyperplasia, bilateral adenoma, or increased risk of peri-operative complications, treatment is medical (Grade D).
10. Medical treatment should be initiated with spironolactone 25-400 mg per day (usual doses are 100-200 mg). For those intolerant to spironolactone, amiloride 10-20 mg per day is an alternative (Grade D). Addition of thiazide diuretics, beta-blockers and or calcium channel antagonists may be useful to control blood pressure (Grade D).
11. Because many patients will remain hypertensive following the surgical removal of an adrenal adenoma, these patients should be followed and if necessary treated according to the usual guidelines for non-endocrine hypertension (Grade D).

## **VI Endocrine Hypertension**

### **b) Pheochromocytoma Screening and Diagnosis**

1. If pheochromocytoma is strongly suspected, the patient should be referred to a specialized hypertension center, particularly if biochemistry is already found to be positive (Grade D).
2. The following patients should be considered for screening for pheochromocytoma (Grade D):
  - a) patients with paroxysmal and/or severe sustained hypertension refractory to usual antihypertensive therapy
  - b) patients with hypertension and multiple symptoms suggestive of catecholamine excess (e.g., headaches, palpitations, sweating, panic attacks, pallor)
  - c) patients with hypertension triggered by beta-blockers, monoamine oxidase inhibitors, micturition, or changes in abdominal pressure
  - d) patients with incidentally discovered adrenal mass; patients with hypertension and multiple endocrine neoplasia (MEN) 2A or 2B; von Recklinghausen's neurofibromatosis, or von Hippel-Lindau disease
3. To screen for pheochromocytomas, 24-hour urinary total metanephrines (sensitivity 95%) and urinary metanephrine-to-creatinine ratio (sensitivity 100%) should be assessed (Grade C). Plasma catecholamines and, where available, plasma metanephrines may also be considered if clinical suspicion is high, particularly during a hypertensive episode or for those with familial forms (Grade D). Urinary or plasma VMA measurements should not be used as screening tests (Grade C).
4. In the presence of borderline biochemical test results (e.g., plasma NE + E levels ~500 – 2000 ng/L) or potentially false positive results, repeated testing (Grade D) and/or the clonidine suppression test (Grade C) may be employed.
5. For patients with positive biochemical testing, localization of pheochromocytomas should employ magnetic resonance imaging (preferable), computed tomography (if MRI unavailable), and/or iodine I-131 meta-iodobenzylguanidine (MIBG) scintigraphy (Grade C for each modality).

6. For patients with known or suspected malignant pheochromocytoma, MIBG scintigraphy may be used to assess for metastatic disease (Grade D).
7. For patients with familial pheochromocytoma (associated with von Hippel-Lindau disease or MEN 2A/B), long-term follow-up studies measuring urinary or, where available, plasma metanephrines, should be performed, because recurrence after laparoscopic partial or unilateral adrenalectomy is frequent (Grade D).
8. Alpha-blockers (prazosin, doxazosin, phenoxybenzamine) should be used as first line agents in suspected pheochromocytoma (Grade D). Alpha methyldopa or clonidine may also be used (Grade D).
9. Treatment of benign pheochromocytoma should be surgical resection. The following peri-operatively issues should be considered:
  - a) until surgery is performed, the use of beta-blockers should be avoided, unless there are arrhythmias present and adequate alpha-blockade has been achieved (Grade D)
  - b) surgical resection should be carefully planned in advance with involvement of a team of surgical, medical, intensivist and anesthesia consultants who have experience in the management of patients with pheochromocytoma (Grade D)
  - c) laparoscopic surgery should be considered before open surgery for resection of pheochromocytoma except for very large tumors (Grade C)
  - d) administration for 10 to 14 days of the phenoxybenzamine (10 - 20 mg bid-tid) prazosin (1-3 mg bid-tid) or doxazosin (2-4 mg bid) are indicated for patients with severe paroxysmal or sustained hypertension (Grade D)
  - e) the tyrosine hydroxylase inhibitor metyrosine (0.25-1g four times daily) should also be considered (Grade C)
  - f) immediately prior to surgery, administration of intravenous fluids should be considered to ensure adequate volume expansion in order to avoid shock after tumor removal (Grade D)
  - g) for hypertensive crises before or during surgery, phentolamine hydrochloride should be readily available and if necessary, administered intravenously (Grade D)
  - h) intravenous propranolol should be employed for treatment of arrhythmias (Grade D)
10. For patients with pheochromocytoma diagnosed during early pregnancy, if a decision is made to terminate the pregnancy, this should be carried out under alpha and beta blockade (as above), followed immediately by tumor resection. In late pregnancy, alpha and beta blockade, followed by elective cesarean section and immediate tumor resection is recommended (Grade D).
11. For patients with inoperable or metastatic malignant pheochromocytoma, blood pressure control and adrenergic symptoms may be controlled with alpha-adrenergic blockade (phenoxybenzamine, prazosin, doxasozin) plus beta-blockade and/or tyrosine

hydroxylase inhibition with metyrosine (Grade D). A combination of cyclophosphamide, vincristine, and dacarbazine may be used for chemotherapy of metastatic pheochromocytoma (Grade D). Treatment with high dose I<sup>131</sup>-MIBG induces moderate response, but may help control of blood pressure (Grade D).

## **VII Home (Self) Measurement of Blood Pressure**

1. The use of home blood pressure monitoring on a regular basis should be considered for patients suspected to be noncompliant and for diabetic patients (Grade B for noncompliant patients; Grade D for diabetic patients).
2. When using home monitoring to assess patients for white coat hypertension, further assess those with a home-based white coat effect using 24-hour ambulatory blood pressure monitoring. (Grade D).
3. Patients should be advised to purchase and use only home blood pressure monitoring devices that are appropriate for the individual and have met the most recent standards of (i) the Association for the Advancement of Medical Instrumentation, (ii) the British Hypertension Society protocol or (iii) the new International Protocol for validation of automated blood pressure 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 values (Grade D).
4. Home systolic and diastolic blood pressure values above 136/or/83 mmHg respectively should be considered elevated and associated with an increased overall mortality risk analogous to clinic readings greater than 140/or/90 mmHg (Grade C).
5. If patients measure their blood pressure at home, health care professionals should ensure that patients who measure their blood pressure at home have adequate training, and if necessary, repeat training in measuring their blood pressure. Patients should be observed to determine that they measure blood pressure correctly and they should be given adequate information about interpreting these readings (Grade D).
6. The accuracy of all individual patients' validated devices (including electronic devices) must be regularly checked against a device of known calibration (Grade D).
7. Interpretation of home blood pressure values should be based on recorded morning readings taken before medications for a recommended period of four weeks (Grade C). Interpretation of home BP values for assessing white coat effects should be based on duplicate measures, morning and evening on at least three days during each of two weeks (Grade D). Singular and first day home BP values should not be considered (Grade D)

## **VIII Ambulatory Blood Pressure Measurement**

1. Ambulatory blood pressure monitoring should be considered when an office-induced increase in blood pressure is suspected: a) untreated patients with mild to moderate clinic blood pressure elevations and without target organ damage (Grade B). b) treated patients with: apparent resistance to drug therapy (Grade C), symptoms suggestive of hypotension (Grade C) fluctuating office blood pressure readings (Grade D).
2. Physicians should use only ambulatory blood pressure monitoring devices that have been validated independently using established protocols (Grade D).
3. A decision to withhold drug therapy, based upon the ambulatory blood pressure, should take into account normal values for systolic and diastolic 24-hour ambulatory blood pressure (<134/78) and daytime (<136/ 87 for men; <131/ 86 for women) (Grade C).
4. The magnitude of changes in nocturnal blood pressure should be taken into account in any decision to prescribe or withhold drug therapy based upon ambulatory blood pressure (Grade C) because a decrease in nocturnal BP of less than 10% is associated with increased risk of CV events.

## **IX Role of Echocardiography**

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 as well as of systolic and diastolic left ventricular function is recommended for hypertensive patients suspected to have left ventricular dysfunction or coronary artery disease (Grade D).
4. Echocardiography should not be used to track therapeutic regression of left ventricular hypertrophy (Grade D).



## The 2003 Canadian Recommendations for the Management of Hypertension: Therapy

### **I Indications for drug therapy in uncomplicated hypertension**

1. Antihypertensive therapy should be strongly considered if diastolic blood pressure readings average 90 mmHg or more in the presence of hypertensive target organ damage or other independent cardiovascular risk factors such as elevated systolic blood pressure, cigarette smoking, abnormal lipid profile, strong family history of premature cardiovascular disease, truncal obesity, or sedentary lifestyle (Grade A).
2. Antihypertensive therapy should be prescribed for average diastolic blood pressures of 100 mmHg or more (Grade A) or average systolic blood pressures of 160 mmHg or more (Grade A) in patients without hypertensive target organ damage or other cardiovascular risk factors.

### **II Lifestyle Management**

1. For mildly hypertensive individuals, dynamic exercise (including walking, cycling, swimming) should be prescribed to reduce blood pressure (Grade B).
2. Dynamic exercise of moderate intensity for 50-60 minutes, 3 or 4 times per week is preferable to vigorous exercise because it appears to be more effective in lowering blood pressure (Grade B).
3. Exercise should be prescribed as adjunctive therapy for people who have levels of blood pressure that require drug therapy, especially those who are not on beta-adrenergic antagonists (Grade B).
4. Alcohol consumption should be in accordance with Canadian low-risk drinking guidelines: 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).
5. For hypertensive patients in whom stress appears to be an important issue, stress management should be considered as an intervention. Individualized cognitive behavioral interventions are more likely to be effective than single component interventions (Grade B).

6. All overweight hypertensive individuals (BMI > 25) should be advised to lose weight—including those who are receiving antihypertensive drugs (Grade B).
7. In hypertensive individuals, particularly those over the age of 44 years, the dietary intake of sodium should be moderately restricted to a target range of 90-130 mmol/L per day (Grade B).
8. Supplementation above the recommended daily dietary intake of potassium (60 mmol/day), magnesium, or calcium (1 g/day) is not recommended as a treatment for hypertension due to lack of benefit (Grade B).
9. A diet consistent with Canada's Guide to Healthy Eating (i.e. high in fresh fruit and vegetables, high in low fat dairy products and low in salt) is recommended to reduce blood pressure (Grade B).
10. To lower blood pressure, increase the effectiveness of drug therapy and to address other cardiovascular risks, all persons with hypertension (i.e. blood pressure  $\geq$ 140/90 mmHg or on antihypertensive therapy) and all persons at risk for developing hypertension should receive individualized lifestyle advice tailored to their specific lifestyle issues (Grade D).

### **III Choice of Therapy for adults with hypertension without compelling indications**

#### **a) Recommendations for individuals with diastolic $\pm$ systolic hypertension**

1. Initial therapy should be monotherapy with a thiazide diuretic (Grade A), [preferably in low dose]. Other agents appropriate for first-line therapy include: a beta-adrenergic antagonist (Grade B); an angiotensin-converting enzyme inhibitor (Grade B); a long acting dihydropyridine calcium channel blocker (Grade B); or an angiotensin II receptor blocker (Grade B). If there are adverse effects, another drug from this group should be substituted. Hypokalemia should be avoided through the use of potassium sparing agents in patients treated with thiazides (Grade C).
2. Combination therapy should be used if there is only partial response to monotherapy (Grade C). Useful combinations include a thiazide diuretic or calcium channel blocker with either an angiotensin-converting enzyme inhibitor or an angiotensin II receptor blocker or a beta-adrenergic antagonist (Grade D). Caution should be exercised in combining a nondihydropyridine calcium channel blocker and a beta-blocker (Grade D).
3. If blood pressure is still not controlled, or there are adverse effects, other classes of antihypertensive drugs (such as alpha blockers, centrally acting agents, or nondihydropyridine calcium channel blocker) may be tried (Grade D).
4. Possible reasons for poor response to therapy (see Table) should be considered (Grade D).

5. Alpha-blockers are not recommended as first-line agents for uncomplicated hypertension (Grade A); beta-adrenergic antagonists are not recommended as first-line therapy for uncomplicated hypertension in elderly patients (Grade A); ACEI are not recommended as first-line therapy for uncomplicated hypertension in blacks (Grade A). However, these agents may play a role in patients with certain comorbidities or in combination therapy.

### **III Choice of Therapy for adults with hypertension without compelling indications**

#### **b) Recommendations for isolated systolic hypertension**

1. Initial therapy should be monotherapy with a thiazide diuretic (Grade A), [preferably in low dose]. Other agents appropriate for first-line therapy include: a long acting dihydropyridine calcium channel blocker (Grade A) or an angiotensin II receptor blocker (Grade B). If there are adverse effects, other drugs from this group should be substituted. Hypokalemia should be avoided through the use of potassium sparing agents (see text for list) in patients treated with thiazides (Grade C).
2. If blood pressure is still not controlled or there are adverse effects, other classes of drugs (such as alpha blockers, angiotensin converting enzyme inhibitors, centrally acting agents, or nondihydropyridine calcium channel blockers) may be added/substituted (Grade D).
3. Combination therapy should be used if there is only a partial response to monotherapy (Grade C). Useful combinations include a thiazide diuretic or dihydropyridine calcium channel blocker with either an angiotensin converting enzyme inhibitor or angiotensin II receptor blocker or beta-adrenergic antagonist (Grade D).
4. Possible reasons for poor response to therapy (see Table) should be considered (Grade D).
5. Alpha-blockers are not recommended as first-line agents for uncomplicated isolated systolic hypertension (Grade A); beta-adrenergic antagonists are not recommended as first-line therapy for isolated systolic hypertension in elderly patients (Grade A), although both agents may play a role in patients with certain comorbidities or in combination therapy.

### **IV Goal of therapy in uncomplicated hypertension**

1. The systolic blood pressure treatment goal is a pressure level of less than 140 mmHg (Grade C). The diastolic blood pressure treatment goal is a pressure level of less than 90 mmHg (Grade A).

## **V Treatment of hypertension in association with ischemic heart disease**

### **a) Recommendations for patients with stable angina and hypertension**

1. Beta-adrenergic antagonists are preferred as initial therapy (Grade B). Long acting calcium channel blockers may also be used (Grade B).
2. Consideration should be given to the addition of angiotensin-converting enzyme inhibitors (Grade B in patients 55 years or older; Grade D in patients younger than 55).
3. Short acting nifedipine should not be used (Grade D).

## **V Treatment of hypertension in association with ischemic heart disease**

### **b) For patients with hypertension who have had a recent ST-elevation myocardial infarction or non-ST segment elevation myocardial infarction**

1. Initial therapy should include beta-adrenergic antagonists, angiotensin-converting enzyme inhibitors, or both (Grade A).
2. Long acting calcium channel blockers may be used in post myocardial infarction patients when beta blockers are contraindicated or not effective, but non dihydropyridines should only be used when there is no heart failure as evidenced by pulmonary congestion on examination or radiographically (Grade D).

## **VI Treatment of hypertension in association with heart failure**

1. Patients with hypertension and evidence of heart failure should have an objective assessment of left ventricular ejection fraction, either by echocardiogram or nuclear imaging (Grade D).
2. Angiotensin converting enzyme inhibitors are recommended for initial therapy (Grade A for those patients with LVEF < 40%). Beta adrenergic antagonists (Grade A) and diuretics are recommended as additional therapy if needed (Grade B for thiazide diuretics, Grade B for spironolactone, Grade D for loop diuretics).
3. An angiotensin II receptor blocker (Grade B) or a combination of hydralazine and isosorbide dinitrate (Grade B) may be considered if angiotensin-converting enzyme inhibitors are contraindicated or not tolerated. Angiotensin-converting enzyme inhibitors are superior to hydralazine/isosorbide dinitrate (Grade B).
4. For patients with left ventricular systolic dysfunction who remain hypertensive despite optimal doses of angiotensin-converting enzyme inhibitors and/or alternative first-line therapies, additional therapies could include long acting dihydropyridine calcium channel blockers (Grade C).

## **VII Treatment of hypertension in association with cerebrovascular disease**

1. Strong consideration should be given to the initiation of antihypertensive therapy after the acute phase of non-disabling stroke or transient ischemic attack (Grade A).
2. Caution is indicated in deciding whether to lower blood pressure in the acute stroke situation; pharmacological agents and routes of administration should be chosen to avoid precipitous falls in blood pressure (Grade D).
3. Following the acute phase of a stroke, patients should have their blood pressure chronically controlled to a target of less than 140/90 mmHg (Grade C).
4. Consideration should be given to treatment with addition of an angiotensin converting enzyme inhibitor/diuretic combination (Grade B).

## **VIII Treatment of hypertension in association with left ventricular hypertrophy**

1. Hypertensive patients with left ventricular hypertrophy should be treated with antihypertensive therapy to lower 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, angiotensin II receptor blockers, dihydropyridine calcium channel blockers, diuretics, or in those under age 55, beta blockers. Direct arterial vasodilators such as hydralazine or minoxidil should not be used.

## **IX Treatment of hypertension in association with renal disease**

1. For patients with non-diabetic renal disease, target blood pressure is < 130/80 mm Hg (Grade C).
2. For patients with proteinuria >1 g/day, target blood pressure is <125/75 mm Hg (Grade C).
3. For patients with hypertension and renal disease, initial therapy should be an ACE-Inhibitor (Grade A).
4. Thiazide diuretics are recommended as additive antihypertensive therapy (Grade D). For patients with renal insufficiency and volume overload, loop diuretics are an alternative (Grade D).
5. In most cases, combination therapy with other antihypertensive agents may be needed to reach target blood pressures (Grade D).

## **X Treatment of hypertension in association with renovascular disease**

1. Renovascular hypertension should be treated in the same manner as essential hypertension, except for caution in the use of angiotensin converting enzyme inhibitors or angiotensin II receptor blockers due to the risk of acute renal failure in bilateral disease or unilateral disease with a solitary kidney (Grade D).
2. Close follow-up and early intervention (angioplasty and stenting or surgery) should be considered for patients with: uncontrolled hypertension despite therapy with three or more drugs, or deteriorating renal function, or bilateral atherosclerotic renal artery lesions (or tight atherosclerotic stenosis in a single kidney), or recurrent episodes of flash pulmonary edema (Grade D).

## **XI Treatment of hypertension in association with diabetes mellitus**

1. Persons with diabetes mellitus should be treated to attain diastolic blood pressures of 80 mmHg or less (Grade A) and systolic blood pressures of 130 mmHg or less (Grade C). (These target blood pressure levels are the same as the blood pressure thresholds).
2. For persons with diabetes and albuminuria (urinary albumin excretion rates over 30 mg/day) an ACE inhibitor or an angiotensin II receptor blocker is recommended as initial therapy (Grade A). If blood pressure remains greater than 130/80 mmHg despite lifestyle interventions and an ACE inhibitor or angiotensin II receptor blocker, then *addition* of one or more of a thiazide diuretic, long-acting calcium channel blocker, or use of *ACE inhibitor and angiotensin II receptor blocker in combination* can be considered (Grade D). If an ACE inhibitor and angiotensin II receptor blocker cannot be tolerated, a cardioselective beta-adrenergic blocker (Grade B), long acting calcium channel blocker (Grade C), or thiazide diuretic can be substituted (Grade B).
3. For persons with diabetes and normal urinary albumin excretion (less than 30 mg/day) and blood pressure greater than 130/80 mm Hg despite lifestyle interventions, an ACE inhibitor (Grade A for persons aged greater than or equal to 55 years, Grade B for persons aged less than 55 years), or an angiotensin II receptor blocker (Grade A for persons with LVH and age greater than or equal to 55 years, Grade B for persons without LVH irrespective of age) or a thiazide diuretic (Grade A for persons aged greater than or equal to 55 years, Grade B for persons aged less than 55 years) is recommended. If these drugs are contraindicated or cannot be tolerated, a cardioselective beta-adrenergic blocker (Grade B) or long acting calcium channel blocker (Grade C) can be substituted. If blood pressure targets cannot be reached despite an ACE inhibitor, angiotensin II receptor blocker, or thiazide diuretic, then these drugs in combination or addition of one or more of a cardioselective beta-blocker or long acting calcium channel blocker can be considered (Grade D).

4. For persons with diabetes and a serum creatinine over 150  $\mu\text{mol/L}$ , the choice of antihypertensive drugs is the same as above, except that a loop diuretic should be substituted for a thiazide diuretic if control of volume is desired (Grade D).
5. For persons with diabetes and a normal urinary albumin excretion rate (less than 30 mg/day) with isolated systolic hypertension, thiazide diuretic (Grade C) or long acting dihydropyridine calcium channel blocker (Grade C) are alternative initial choices to an ACE inhibitor or an angiotensin II receptor blocker.
6. Alpha-blockers are not recommended as first-line agents for the treatment of hypertension in persons with diabetes (Grade A).

## **XII Adherence**

1. Adherence to an anti-hypertensive prescription can be improved by a multi pronged approach including:
  - a) simplifying medication regimens to once daily dosing (D) and utilizing electronic medication compliance aids (D)
  - b) Tailor pill-taking to fit patients' daily habits (D)
  - c) Encourage greater patient responsibility/autonomy in monitoring their blood pressure and adjusting their prescriptions (C)
  - d) coordinate with a work-site health care givers to improve monitoring of adherence with pharmacological lifestyle modification prescriptions (D)
  - e) educate patients and patients' families about their disease/treatment regimens (C)

Table  
Possible reasons for poor response to therapy\* in adults with uncomplicated hypertension

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Noncompliance	Dietary Medication
Associated Conditions	Obesity Cigarette smoking Excessive alcohol consumption Sleep Apnea Chronic pain and/or mental illness
Drug Interactions	Nonsteroidal anti-inflammatory drugs (including COX-2 inhibitors) Oral contraceptives Corticosteroids and anabolic steroids Sympathomimetics and decongestants Cocaine Amphetamines Erythropoietin Cyclosporine, tacrolimus Licorice
Suboptimal Treatment Regimes	Dosage too low Inappropriate combinations of antihypertensive agents
Volume Overload	Excessive salt intake Renal sodium retention (pseudotolerance)
Secondary hypertension	Renal insufficiency Renovascular disease Primary hyperaldosteronism Thyroid disease Pheochromocytoma and other rare endocrine causes

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\* Note that causes of “pseudo-resistance” (such as white coat hypertension or pseudo-hypertension in the elderly) should be ruled out first. COX-2: Cyclo-oxygenase-2