Advances in the management of cardiovascular disease (CVD) and recognition of its devastating sequelae have led to an overall decline in the age-adjusted mortality from CVD in Europe and North America. CVD remains, however, the most common cause of morbidity and mortality in most industrialized countries, including Canada. In this country, CVD accounts for 37% of total deaths and contributes to more than $7 billion in direct health-care costs annually. Major causes of premature CVD include an unhealthy lifestyle (e.g., lack of physical activity, unhealthy diet, smoking, etc.), along with a high prevalence of cardiac risk factors.

Recent clinical data have convincingly demonstrated the benefit of lifestyle and risk factor modification as secondary prevention mechanisms in patients with established CVD, as well as primary prevention. Effective primary prevention of cardiovascular disease requires both clinical and public health approaches. The family physician’s role consists of risk factor identification, intervention planning and regular follow-up.

By Raja Al-Dashti, MD, FRCPC, and George Honos, MD, FRCPC, FACC

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prevention tools in those at high absolute risk of developing new CVD. It is recognized that the primary-care physician will continue to play a pivotal role in the implementation of primary and secondary prevention measures aimed at reducing the morbidity, mortality and health-care costs of CVD in Canada.

**Estimation of Absolute Coronary Artery Disease Risk**

A simple coronary artery disease (CAD) risk predictor algorithm was established by investigators, using data from the Framingham study.¹ The absolute 10-year risk of developing CAD can be estimated from this chart for most patients. Some patients, however, may have additional risk factors, including abdominal obesity or a strong family history of CAD. This requires the physician to use clinical judgment and individualization when instituting preventive measures.

**Cardiac Risk Factors**

Cardiac risk factors can be categorized as either modifiable or non-modifiable (Table 1). All are important to help predict a patient’s absolute CAD risk and to help define treatment thresholds and targets for intervention on the major modifiable risk factors.

**Hypertension** (HTN) is a major risk factor for CAD, stroke, heart failure (HF), peripheral arterial disease (PAD) and renal failure. According to the Canadian Heart Health Survey, 22% of adult Canadians are hypertensive (26% of men; 18% of women).² Despite the fact that the benefits of treating HTN have been known for several decades (42% reduction in stroke, 25% reduction of CAD, 15% reduction in myocardial infarction [MI], and 50% reduction in chronic heart failure), this survey suggests that 42% of Canadian hypertensives are unaware of their condition, and only 16% are receiving effective treatment (Figure 1).²

To help health-care professionals better manage HTN and prevent its sequelae, the Canadian Hypertension Society and the Canadian Coalition for High Blood Pressure Prevention and Control release yearly updated evidence-based guidelines for HTN management.

Accurate assessment and diagnosis of HTN is an important first step in managing it. The stratification into a high-risk profile can be made immediately if end organ damage (EOD) is present (Table 1). Individuals with borderline HTN are

### Table 1

**Components of Major Cardiovascular Risk Factors**

<table>
<thead>
<tr>
<th>Non-modifiable risk factors</th>
<th>Modifiable Risk Factors</th>
<th>Target Organ Damage</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Sex: men over age 45, postmenopausal women</td>
<td>• Hypertension</td>
<td>• Heart disease: left ventricular hypertrophy, coronary artery disease, heart failure</td>
</tr>
<tr>
<td>• Family history of CVD: men under age 55, women under age 65</td>
<td>• Smoking</td>
<td>• Stroke</td>
</tr>
<tr>
<td></td>
<td>• Dyslipidemia</td>
<td>• Nephropathy</td>
</tr>
<tr>
<td></td>
<td>• Diabetes mellitus</td>
<td>• Peripheral arterial disease</td>
</tr>
<tr>
<td></td>
<td>• Obesity</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Left ventricular hypertrophy</td>
<td></td>
</tr>
</tbody>
</table>
Cardiac Risk Factors

subject to misclassification; therefore, if the blood pressure (BP) at the first visit is between 140/90 mmHg and 180/105 mmHg, at least four additional visits are required to diagnose HTN. If, at the last visit the BP is normal and there is no evidence of EOD or associated risk factors, the patient requires yearly BP follow-up only.3

Home or ambulatory BP monitoring can be used in subsets of patients to rule out white-coat HTN or to characterize potential BP treatment side effects. Measurements greater than 135/85 mmHg should be considered elevated. Absence of the normal nocturnal 10% BP dip is associated with poor cardiovascular prognosis.

Currently, routine echocardiography is not recommended in all hypertensive patients. However, cardiac ultrasound evaluation of left ventricular hypertrophy (LVH), mass index, and systolic and diastolic function may be invaluable in hypertensive patients with symptoms, such as dyspnea or those suspected of having CAD or HF. Serial echocardiograms should not be used to assess the effects of antihypertensive treatment on LVH regression.

Appropriate treatment of HTN should take into account the BP level, along with the presence of other major cardiac risk factors or EOD, such as established CAD. Lifestyle modification should be recommended for all patients, whether or not they require concurrent pharmacologic therapy (Table 2). Aggressive treatment of isolated systolic HTN in the elderly is very important, and has been shown to be safe and helpful in reducing stroke and CVD.4 For most patients,

Table 2

<table>
<thead>
<tr>
<th>Treatment of Hypertension</th>
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</thead>
<tbody>
<tr>
<td><strong>Lifestyle Modification</strong></td>
</tr>
<tr>
<td>• Stop smoking</td>
</tr>
<tr>
<td>• Lose weight (BMI &lt; 25)</td>
</tr>
<tr>
<td>• Eat healthy: less saturated fat, more fiber intake, decrease salt intake to ≤ 6 g/day</td>
</tr>
<tr>
<td>• Limit alcohol intake to ≤ 2 glasses/day and maximum of 9 (female) to 14 (male) drinks/week</td>
</tr>
<tr>
<td>• Exercise regularly (30-45 min, 3-4 times/week) of moderate intensity (aerobic)</td>
</tr>
<tr>
<td>• Learn how to deal with stress</td>
</tr>
<tr>
<td><strong>Pharmacologic Treatment</strong></td>
</tr>
<tr>
<td>• Diuretics</td>
</tr>
<tr>
<td>• Beta-antagonists</td>
</tr>
<tr>
<td>• Calcium-channel blockers</td>
</tr>
<tr>
<td>• ACE inhibitors</td>
</tr>
<tr>
<td>• (\alpha)-adrenergic antagonists and centrally acting agents</td>
</tr>
<tr>
<td>• Pure arterial vasodilators</td>
</tr>
<tr>
<td>• Angiotensin II receptor antagonists</td>
</tr>
</tbody>
</table>

BMI = weight (kg)/height (m²)
the target BP level should be less than 140/90 mmHg. Lower BP targets are recommended for diabetics and renal failure patients (less than 135/80 mmHg) or patients with overt—more than 1g/24 h—proteinuria (less than 125/75 mmHg) (Table 3).5

It is important to advise patients upon initiating pharmacologic treatment about their likelihood of requiring two to three drugs to achieve target BP levels (Figures 2 and 3, Table 2). Consider secondary HTN, white coat HTN, poor compliance or drug interaction in treated patients who fail to reach BP targets, despite treatment with three or more antihypertensive medications. Patient education and the selection of long-acting once-daily regimens is important to improve patient adherence to therapy.

Tobacco use. Cigarette smoking is a strong independent risk factor for CVD and fatal MI. Smokers can sustain their first MI more than one decade earlier than non-smokers. Smokers who have other cardiac risk factors tend to have higher CAD morbidity and mortality.

The mechanism by which tobacco use results in premature CVD is not well established, but is thought to include vascular injury and endothelial dysfunction, vasospasm, thrombosis and platelet aggregation. Smoking cessation increases life
expectancy in both men and women, and after quitting smoking, CAD risk declines rapidly. Three years after quitting, the risk becomes similar to that of non-smokers. All smokers should, therefore, be encouraged to stop the habit.

Physician advice alone is associated with a 10% initial success rate, which is doubled with regular follow-up visits. Behavioral therapy also leads to a 20% cessation rate. The success rate generally improves with concomitant drug therapy. Available options include nicotine substitution (i.e., patch, gum, nasal spray, inhalers), which doubles the cessation rate, and the non-nicotine containing agent, bupropion, with a 10.5% to 24.4% success rate (depending on the dose taken).

While these pharmacologic agents are relatively safe in patients who do not suffer from CVD, their safety profile in patients with CAD and post-MI is a subject of some controversy. The use of nicotine while continuing smoking could lead to worsening myocardial ischemia from increased heart rate, BP and coronary spasm.

Hyperlipidemia. Elevated plasma cholesterol level is directly related to the development of atherosclerosis and, ultimately, to CAD. Over 30 years of clinical and epidemiologic studies have shown that blood cholesterol is a major independent risk factor for CAD. Recent clinical trials have convincingly demonstrated that low-density lipoprotein (LDL) cholesterol lowering through statin therapy lowers CVD morbidity and mortality in both the primary and secondary prevention setting. While relative benefits are similar in all patients’ studies (approximate 30% event reduc-
tion at five years), the magnitude of absolute benefit is greatest in patients with a history of CAD or in those at high absolute risk of developing CAD with a correspondingly lower number needed to treat (NNT).

Current Canadian guidelines recommend that a

<table>
<thead>
<tr>
<th>Condition</th>
<th>Target</th>
</tr>
</thead>
<tbody>
<tr>
<td>18-80 years/systolic + diastolic HTN</td>
<td>&lt; 140/90 mmHg</td>
</tr>
<tr>
<td>60-80 years/isolated systolic HTN</td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>&lt; 135/80 mmHg</td>
</tr>
<tr>
<td>Non-diabetic nephropathy</td>
<td></td>
</tr>
<tr>
<td>Proteinuria &gt; 1 g/24 h</td>
<td>&lt; 120/75 mmHg</td>
</tr>
</tbody>
</table>
screening fasting lipid profile—including total cholesterol, high-density lipoprotein (HDL) and LDL cholesterol and triglycerides—be done in all adults aged 40 or above, or earlier in selected high-risk individuals.\(^8\)

Both the decision to treat hyperlipidemia and the target of therapy depend on the individual patient’s calculated absolute 10-year CAD risk assessment, based on the Framingham table.\(^1\) Patients at the highest risk derive the greatest benefit and, thus, are managed more aggressively with earlier initiation of pharmacologic therapy.\(^8\) Diabetics over age 30 are classified as being at very high risk for CAD, and should be started on pharmacologic therapy immediately to reach the recommended target LDL level of 2.5 mmol/L (Table 4).\(^8\)

Individuals at very high or high risk should be started on drug therapy immediately if cholesterol values are above target levels, whereas those at intermediate or low risk of CAD should be started on a pharmacologic agent only after failure of nonpharmacologic therapy (i.e., diet and lifestyle modification similar to that recommended in HTN). When starting a statin agent, the initial dose can be calculated to the average needed to achieve the target LDL level, with increases at follow-up, as required. An alternative and safe method, especially for patients reluctant to take medications, is to initiate therapy with a high statin dose, which could be titrated down if the LDL is below target value at follow-up.
Statins appear to exert beneficial effects on the atherosclerotic process beyond their ability to lower serum lipids, including improvement in endothelial function and stabilization of vulnerable atherosclerotic plaques. There is insufficient data to suggest the superiority of one statin over another. Physicians should select a statin based on the availability of doses capable of reducing LDL to target values, as well as on the cost of the drug. They should be aware of their principal, albeit rare, side effects of myopathy and hepatotoxicity.

Accordingly, a serum alanine aminotransferase (ALT) and creatinine kinase (CK) should be obtained at baseline, and repeated each time the statin dosage is adjusted. Once the target LDL level is achieved, routine repeat blood tests are not required, unless the patient complains of new symptoms, such as cramps or myalgias.

**Table 4**

**Target Lipid Levels**

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>Risk Category</th>
<th>Target Levels</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men &amp; women</td>
<td></td>
<td>LDL-C (mmol/L)</td>
</tr>
<tr>
<td>History of CVD OR</td>
<td></td>
<td>&lt; 2.5</td>
</tr>
<tr>
<td>Diabetes + &gt; 30 years OR</td>
<td>Very high†</td>
<td></td>
</tr>
<tr>
<td>CHD 10-yr risk &gt; 30%</td>
<td></td>
<td>&lt; 3.0</td>
</tr>
<tr>
<td>CHD 10-yr risk 20-30%</td>
<td>High†</td>
<td></td>
</tr>
<tr>
<td>CHD 10-yr risk 10-20%</td>
<td>Moderate††</td>
<td>&lt; 4.0</td>
</tr>
<tr>
<td>CHD 10-yr risk &lt; 10%</td>
<td>Low††</td>
<td>&lt; 5.0</td>
</tr>
</tbody>
</table>

†Start medication and lifestyle changes concomitantly if values are above target values. ††Start medication if target values are not achieved after lifestyle modification (three months for moderate risk and six months for low-risk groups.)

There are data suggesting that type A personality, particularly with repressed hostility traits or an increased daily stress level, may predispose individuals to CAD.

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**Diabetes mellitus (DM).** There is a clear link between DM and vasculopathy.\(^9\) Of all diabetics, 70% to 80% die due to cardiovascular complications.\(^9\) A diabetic without CAD has the same CVD risk as that of a non-diabetic with CAD.\(^9\) The diagnosis of diabetes is made when the fasting plasma glucose (FPG) is greater than 7.0 mmol/L or greater than 11.0 mmol/L post-75 g of glucose load.

Recent clinical trials (the Diabetes Control and Complications Trial [DCCT] and the U.K. Prospective Diabetes Study [UKPDS]) have shown that intensive treatment using insulin results in a significant reduction in diabetic
microvascular complications, but has less benefit on the macrovascular complications (i.e., cardiovascular events), which respond more to concurrent, aggressive BP reduction.\textsuperscript{10,11} While the optimal level of plasma glucose is uncertain, there is convincing evidence that a diabetic’s optimal target BP should be less than 135/80 mmHg, to minimize long-term CVD complications.

\textit{Increased physical activity} has been associated with reduction in CAD risk, both in primary and secondary prevention. Regular exercise benefits patients by: increasing HDL cholesterol; lowering LDL cholesterol; improving insulin resistance; decreasing body weight; reducing BP; and improving the patient’s sense of well-being. While optimal exercise intensity and duration is not well established, most studies conclude that at least 30 to 40 minutes of moderate aerobic exercise, three to four times per week carries optimal cardio-protective effect. An exercise prescription should be individualized to accommodate the patient’s level of fitness and underlying cardiac status.

\section*{CAD Risk in the Elderly}

While it is an important cause of death and disability among middle-aged adults, CAD is most frequently manifested in older individuals—it is the most common cause of death in men and women aged 60 and older. Recent trials have clearly shown the safety and beneficial effect of treating HTN in the elderly. In contrast, the role of cholesterol-lowering therapy in elderly patients who are in the primary prevention setting is much less well established and should be individualized based on life expectancy, absolute risk of CAD and patient wishes. Care should be taken when prescribing lipid-lowering agents in the elderly because of the higher risk for potential adverse effects and drug interactions.

\section*{Other Cardiac Risk Factors}

There are several other non-traditional and emerging risk factors associated with increased risk of CVD, including:

\begin{itemize}
  \item \textbf{Alcohol.} Moderate consumption of alcohol is known to be cardio-protective, possibly due to increases in HDL cholesterol.
  \item \textbf{Obesity.} Excess weight indirectly increases CAD risk through elevation of BP, cholesterol and blood sugar. Truncal obesity predisposes to CAD (waist measurement > 100 cm in men, and > 90 cm in women). A body mass index (BMI) score of higher than 25 also is a risk factor.
\end{itemize}
Cardiac Risk Factors

- **Genetic background.** People from certain specific genetic backgrounds are at higher risk for CVD (e.g., South Asians).

- **Stress.** There are data suggesting that type A personality, particularly with repressed hostility traits or an increased daily stress level, may predispose individuals to CAD.12

- **Homocysteinemia.** Plasma homocysteine is inversely related to B12 and B6 levels, and, when elevated, is a risk factor for premature atherosclerosis and CAD. Currently, there are no completed clinical trials showing benefit derived from treating hyperhomocysteinemia through increased intake of dietary folic acid, B12 and B6.13

- **Infections.** A number of different infectious agents, including chlamydia pneumonia, cytomegalovirus, herpes simplex and hepatitis B virus have been linked to atherosclerosis and CVD. Large randomized trials are in progress. Until a clear causal relationship is established, however, antibiotics are not recommended for the prevention of CAD.

- **Inflammatory markers.** Elevated C-reactive protein and interleukin-6, tumor necrosis factor-α and others have been reported as predictors of CVD.

- **Hemostatic factors.** Some thrombogenic factors like elevated fibrinogen level, increased factor VII, decrease fibrinolytic activity and plasminogen activator inhibitor (PAI)-1, may predict atherosclerotic events.

Other Issues Related to Primary Prevention Of CVD

**Hormonal Replacement Therapy (HRT).** Estrogen is known to increase HDL cholesterol, decrease LDL cholesterol and improve endothelial function.14 However, oral HRT increases triglycerides, has procoagulant effects, increases inflammation and thrombosis, and predisposes to venous thromboembolic events (VTE).15 These events may neutralize any protective effects or may even cause harm. It is important, therefore, to establish the safety and benefit of HRT in the primary and secondary prevention of CAD through large randomized clinical trials.

The two randomized secondary prevention clinical trials completed thus far, Heart and Estrogen/Progestin Replacement Study (HERS) and Enoxaparin Restenosis after Angioplasty (ERA), have failed to show any clinical benefit from HRT.16,17 A large primary prevention trial, the Women Health Initiative Study (WHI), is under way; results are expected in 2005.18 Based on the available data, the Canadian Cardiovascular Consensus on Women and Heart Disease concludes that HRT is not recommended for the purpose of preventing CAD.19 HRT can, however, be considered in women with multiple CAD risk factors with careful follow-up, for the alleviation of menopausal symptoms and for the prevention of osteoporosis. HRT can be continued in women with stable CAD, but should be stopped on occurrence of an acute ischemic syndrome or MI.19 In women with hypertriglyceridemia, oral HRT should be avoided and replaced by a transdermal preparation.

**Role of acetylsalicylic acid (ASA).** All patients with established CVD (any form of CAD, stroke or PAD) should take daily-coated ASA (80-325 mg), as it has shown overwhelming evidence of risk reduction.20 The benefit of ASA in the primary prevention setting is less clear cut, and treatment has to be individualized based on the patient’s risk of cardiovascular events, while balancing potential benefits with the small hemorrhagic risk from long-term therapy.21

**Role of Vitamin E.** Observational data have shown an inverse relationship between circulatory antioxidants and CAD events.22 The Heart Outcome Prevention Evaluation (HOPE) study,
Cardiac Risk Factors

however, failed to show any benefit of vitamin E (400 IU daily) over 4.5 years in patients over 55 years of age, at high risk for cardiovascular events.  

Role of angiotensin-converting enzyme (ACE) inhibitors. These drugs can lower morbidity and mortality in HTN, as well as in systolic HF. In the recent HOPE study, it was shown that one such ACE inhibitor, ramipril 10 mg daily, can dramatically reduce the risk of MI, stroke, HF, diabetic complications and cardiovascular mortality in patients over age 55 who have normal systolic ventricular function and who are at high risk for CVD (previous CAD, stroke, PAD or DM plus an additional risk factor).  

The benefits were not explained by the modest BP reduction observed, and were likely related to a direct effect of the drug on potentially vulnerable atherosclerotic plaques.

Who To Screen?

Dyslipidemia. Based on the latest Canadian Recommendations for the Management of Dyslipidemia, routine screening for hyperlipidemia (total cholesterol, HDL cholesterol, triglycerides and LDL cholesterol) is recommended in the following individuals: men over age 40; women over age 50; adults with two or more risk factors for CAD; patients with DM; patients with signs and symptoms of PVD; patients with xanthomas; and patients with a family history of CAD or dyslipidemia.  

DM. According to the 1998 Canadian Clinical Practice Guidelines for the Management of Diabetes, mass screening of the general population for type II DM is not recommended. Testing for DM using FPG should be done every three years in those over age 45. More frequent or earlier testing should be considered in those with additional risk factors for DM.  

Exercise stress testing (EST). Routine EST should be avoided in asymptomatic, very low risk individuals. The test has very limited diagnostic and prognostic value in this situation, and frequent false-positive results may lead to additional, expensive and potentially invasive investigations. It is important to remember that most MIs occur on previously low-grade stenotic lesions (<50%), which cannot be detected by routine EST. It is, therefore, not uncommon to present with an MI or even die suddenly from a cardiac cause following a recent normal- or low-risk EST.

The American College of Cardiologists/American Heart Association (ACC/AHA) Task Force Statement for EST in 1990 states that routine EST is indicated only in the following individuals: asymptomatic male patients over the age of 40 with special occupations (i.e., pilots, air traffic controllers, fire fighters, police officers, critical process operators, bus or truck drivers, and railroad engineers); asymptomatic males over age 40 with two or more risk factors for CAD; and sedentary male patients over age 40, who plan to enter a vigorous exercise program.

Summary

Effective primary prevention of CVD requires both clinical and public health approaches. The family physician’s role consists of risk factor identification, intervention planning and regular follow-up. A particular effort should be made to identify high-risk patients, who will benefit most from effective prevention measures. Through an effective doctor-patient relationship, physicians should prioritize the approach to lifestyle and risk factor modification, and encourage patient adherence to treatment through effective communication, encouragement and patient education.

Public health programs help to educate patients about the importance of a healthy, active lifestyle.
They also help educate patients about risk factors for CVD and appropriate risk factor modification to lower future risk of cardiovascular morbidity and mortality. Society may need to decide at what 10-year CAD risk level can it afford to pay for large-scale pharmacologic prevention measures.

References
19. Canadian Cardiovascular Consensus on Women and Heart Disease: Draft Report 2000 is available to members at URL: http://www.ccs.ca.