An international perspective on cardiovascular risk management: recommendations for high-risk patients

**INTRODUCTION**

For people identified as being at risk of cardiovascular disease (CVD), the degree or intensity of intervention is dictated by the predicted likelihood of a future coronary event. Assessment of cardiovascular risk factors is therefore essential so that individuals can be stratified as accurately as possible into ‘very high’, ‘high’ or ‘moderate-to-low’ risk categories.

The high-risk category (Box 1) includes all those with established cardiovascular, cerebrovascular or peripheral vascular disease, or with diabetes; a subset of these regarded as ‘very high’ risk are targeted for more aggressive intervention (Box 2). Appropriate screening can also identify asymptomatic individuals who are considered to be at high risk because they have multiple risk factors. Although there is some variation between guidelines in the definition of ‘high cardiovascular risk’, this term usually refers to patients whose 10-year risk of an atherosclerotic coronary event (eg myocardial infarction) is ≥20% (see previous article in this series ‘Screening and identifying at-risk patients’). This article aims to provide practitioners with a concise guide to the management of high-risk patients based on recommendations from six of the most up-to-date clinical practice guidelines for prevention of CVD (Box 3).1-7 We refer non-English speakers to the French Health Products Safety Agency and the Spanish local guidelines.8,9

**Box 1: High-risk patients**

Patients in the “high-risk” category have:

- Coronary heart disease and stroke
- Peripheral arterial disease
- Abdominal aortic aneurysm
- Symptomatic carotid artery disease (transient ischaemic attack)
- Diabetes or
- Presence of multiple risk factors to give predicted 10-year CHD risk >20%. These factors include:
  - Cigarette smoking, or cessation less than 3 years
  - High LDL-C (≥4.1 mmol/L) or total cholesterol (≥6.2 mmol/L)
  - Low HDL-C (<1 mmol/L)
  - Hypertension (blood pressure ≥140/90 mmHg or on antihypertensive medication)
  - History of premature coronary heart disease in a first-degree relative (ie event in a male <55 years or female <65 years)

Adapted from Reference 1. Other guidelines (see Box 4) specify LDL-C and total cholesterol cutoffs of 6.0 mmol/L and 8.0 mmol/L, respectively.

Risk calculation tools are available at: European risk calculator for the prediction and management of the risk of heart attack and stroke in Europe: http://www.escardio.org/knowledge/decision_tools/heartscore/

General predictive tool for calculating primary risk analysis over 10 years (not based on country of origin): http://www.bhsoc.org/riskcalc/riskcalculator.exe

Many of these are improved by lifestyle changes (Box 4) but drug therapy will also be needed for the majority of high-risk individuals and should be introduced without undue delay.

We have summarised below the recommended treatment goals in high-risk patients.

**Stop smoking**

Cigarette smoking, one of the strongest risk factors for atherosclerotic disease, has a dose-dependent effect on cardiovascular risk. As recommended by most guidelines (Table 1), all patients who smoke should be encouraged strongly and assisted actively to stop, as a reduction in risk may be observed within a few months of smoking cessation.

**Key points:**

- Lifestyle change should be first line treatment
- Doctors must give assistance and advice to patients for smoking cessation
- Blood pressure should be reduced below 140/90 mmHg or 130/85 mmHg, HbA1c below 7% and LDL-C under 2.5 mmol/L

**TREATMENT GOALS IN HIGH-RISK PATIENTS**

Once a patient’s high-risk status has been established, it is important to address all risk factors amenable to intervention including:

- Cigarette smoking
- Serum lipid levels
- Hypertension
- Hyperglycaemia/insulin resistance
- Excess body weight
- Thrombotic risk

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Using nicotine replacement therapy (NRT) in combination with simple or intensive behavioural support is an effective strategy. In practice, smoking cessation can be achieved in up to 19% of smoking patients. In one study, smoking cessation was achieved in 24.5% of patients using NRT after 12 weeks (compared with 14.2% on placebo) and 10.8% after 12 months (compared with 7.7% on placebo).1

Improve lipid levels

The strong, positive association between total serum cholesterol levels and atherosclerotic disease was recognised more than 50 years ago. Cholesterol in the circulation is carried in low-density lipoprotein (LDL-C), which is atherogenic, and high-density lipoprotein cholesterol (HDL-C), which protects against atherosclerosis.

**Table 1: Recommended management of risk factors in high-risk individuals**

<table>
<thead>
<tr>
<th>Guideline (see Box 3 for full reference)</th>
<th>Australia</th>
<th>Canada</th>
<th>Europe</th>
<th>New Zealand</th>
<th>USA</th>
<th>International</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoking cessation</td>
<td>✔</td>
<td>–</td>
<td>✔</td>
<td>✔</td>
<td>–</td>
<td>✔</td>
</tr>
<tr>
<td>Lifestyle change</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>Dyslipidaemia</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>–</td>
<td>✔</td>
</tr>
<tr>
<td>Blood pressure</td>
<td>✔</td>
<td>–</td>
<td>✔</td>
<td>✔</td>
<td>–</td>
<td>✔</td>
</tr>
<tr>
<td>Antiplatelet therapy</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>Control of hyperglycaemia (diabetes patients)</td>
<td>–</td>
<td>–</td>
<td>✔</td>
<td>✔</td>
<td>–</td>
<td>✔</td>
</tr>
</tbody>
</table>

- 10-year risk of a cardiovascular event ≥20%
- Prudent diet, achievement of optimal bodyweight, increased physical activity
- Optional if low-density lipoprotein cholesterol <2.6 mmol/L
- Recommended in selected patient subgroups only

The use of beta-blockers, angiotensin converting enzyme inhibitors and anticoagulants is recommended by most guidelines, where appropriate.

**Box 2: Very high-risk patients**

Patients in the “very high” risk category have established cardiovascular disease plus:

- The presence of multiple major risk factors (see Box 1) or diabetes
- Severe and poorly controlled risk factors (especially cigarette smoking) (see Box 1)
- Multiple features of the metabolic syndrome (see Box 5)
- Acute coronary syndrome
- Treatment is aggressive with institution of diet and lifestyle modification and immediate commencement of statin therapy
- Goal of lipid-lowering treatment is LDL-C <1.8 mmol/L (<70 mg/dL)

Adapted from Reference 2.

**LDL-C and total cholesterol**

Although total cholesterol is still widely targeted as a goal in preventive strategies, there is agreement among the guidelines that LDL-C should be the primary lipid target in almost all at-risk individuals. For those at high risk, LDL-C should be lowered to <2.5 mmol/L (Table 2). US guidelines recommend that patients at very high risk would benefit from a lower LDL-C goal (<1.8 to 2.0 mmol/L). In addition to an absolute target level, some guidelines recommend that LDL-C be reduced by at least 30% and it is believed that there is a linear relationship between fall in LDL-C and reduction in risk.

**HDL-C and triglycerides**

Some guidelines recommend total cholesterol:HDL-C ratio as an alternative target benchmark for intervention (Table 2). Low levels of HDL-C and...
Low levels of HDL-C and elevated triglyceride levels are both associated with increased cardiovascular risk.
elevated blood pressure by changes in lifestyle, which, if necessary, should be combined with antihypertensive medication. Target systolic pressures of 130 to 140 mmHg and diastolic pressures of 85 to 90 mmHg are recommended by three of the six practice guidelines (Table 3). A lower target level (130/80 mmHg) is appropriate for people with diabetes and CHD. Many studies have confirmed that multiple therapies will usually be necessary to achieve these blood pressure targets, and several guidelines highlight this strategy.

Reduce hyperglycaemia/insulin resistance
The incidence of macrovascular disease in patients with diabetes may be related to blood glucose control. As a result, three of the six practice guidelines recommend that hyperglycaemia should be controlled to maintain HbA1c ≤6% or ≤7% (Table 4).

Reduce overweight
Weight reduction is an important goal in overweight or obese high-risk individuals. Bodyweight is most readily quantified as body mass index (BMI; Figure 1). Individuals with BMI values ≥25 kg/m² should receive counselling and help in achieving bodyweight reduction. Cardiovascular risk is also influenced by the regional distribution of body fat, and abdominal fat is particularly detrimental. Patients with abdominal obesity (commonly defined as a waist circumference >102 cm in American men, >88 cm in American women) should be encouraged to lose weight, regardless of BMI.

Weight loss is difficult to achieve and maintain, but must involve a combination of dietary modification and increased physical activity. In high-risk patients, the recommended level of physical exertion should be based on the results of a comprehensive clinical evaluation. Inclusion of an exercise test in this evaluation is discretionary. Achieving a 5% reduction in bodyweight is a good first step.

Improve diet
For patients at high risk of CVD, dietary modification has three main aims:

i) to lower LDL-C

ii) to increase HDL-C

ii) to allow the patient to achieve an optimal bodyweight.

Table 5 summarises the core dietary recommendations made by the guidelines. In addition to providing detailed recommendations on lipid intake, the guidelines recommend minimum daily intakes of dietary constituents believed to provide protection against CVD, such as omega-3 fatty acids and fruits and vegetables.

Physical activity
A minimum of 30 minutes three times a week of physical activity (eg rapid walk) should be recommended.

Reduce thrombosis risk
With few exceptions, acute cardiovascular events are caused by formation of an intra-arterial thrombus.
Antiplatelet therapy (e.g., aspirin at a dose of between 75 and 150 mg daily) is therefore widely recommended for routine use in all patients at risk of atherothrombosis (Table 1). Anticoagulants may also be employed.

Management of population subgroups
The recommendations discussed above apply to all high-risk individuals. However, in some cases, special consideration may be required in view of the patient’s age or ethnic origin.

Elderly subjects
Historically, healthcare policy makers and physicians have not pursued aggressive modification of cardiovascular risk factors in the elderly. However, recent clinical trials have shown conclusively that LDL-lowering leads to substantial reductions in cardiovascular risk in high-risk elderly individuals. These findings have led three of the six guidelines to emphasise that elderly patients should not be denied treatment of dyslipidaemia on the basis of age alone. After the age of 80 years the treatment of hypercholesterolaemia depends on the extent of cardiovascular risk factors, the general health of the patient, i.e., whether they suffering from an illness other than cardiovascular disease that may decrease their life expectancy, and general tolerance to medication.

Ethnic groups
A patient’s ethnic background may also require consideration because it is well established that the incidence of cardiovascular disease and certain risk factors differs among populations. Some guidelines use ethnicity or country of origin as a major factor in determining total cardiovascular risk. e.g., in the UK, standardised mortality rates for CHD are notably

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**Table 4: HbA1c goals in individuals with diabetes**

<table>
<thead>
<tr>
<th>Guideline</th>
<th>HbA1c (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Australia</td>
<td>–</td>
</tr>
<tr>
<td>Canada</td>
<td>–</td>
</tr>
<tr>
<td>Europe</td>
<td>≤6.1</td>
</tr>
<tr>
<td>New Zealand</td>
<td>≤7</td>
</tr>
<tr>
<td>USA</td>
<td>–</td>
</tr>
<tr>
<td>International</td>
<td>≤7</td>
</tr>
</tbody>
</table>

**Table 5: Major dietary requirements for individuals at high cardiovascular risk**

<table>
<thead>
<tr>
<th>Nutrient</th>
<th>Recommended intake</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total calories</td>
<td>Adjust to achieve/maintain desirable bodyweight (BMI &lt;25 kg/m²)</td>
</tr>
<tr>
<td>Total fat</td>
<td>25–35% of total calories</td>
</tr>
<tr>
<td>Saturated fat &amp; trans fatty acids</td>
<td>&lt;7% of total calories</td>
</tr>
<tr>
<td>Polyunsaturated fat</td>
<td>≤10% of total calories</td>
</tr>
<tr>
<td>Monounsaturated fat</td>
<td>≤20% of total calories</td>
</tr>
<tr>
<td>Cholesterol</td>
<td>&lt;200 mg/day</td>
</tr>
<tr>
<td>Carbohydrate</td>
<td>50–60% of total calories</td>
</tr>
<tr>
<td>Protein</td>
<td>Approximately 15% of total calories</td>
</tr>
<tr>
<td>Fibre</td>
<td>20–30 g/day</td>
</tr>
<tr>
<td>Omega-3 fatty acids</td>
<td>≥1% of total calories or up to 1 g/day</td>
</tr>
<tr>
<td>Fruit &amp; vegetables</td>
<td>≥5 servings/day</td>
</tr>
<tr>
<td>Alcohol</td>
<td>≤20–30 g ethanol/day (men), ≤10–20 g/day (women)</td>
</tr>
</tbody>
</table>

**Table 5: Major dietary requirements for individuals at high cardiovascular risk**

Practical dietary guidelines for patients that provide recommendations similar to those above are available at the American Heart Association website: http://www.americanheart.org/presenter.jhtml?identifier=851

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**Figure 1: Body mass index (BMI)**

BMI ranges recommended by the US National Heart, Lung and Blood Institute (NHLBI). Recommended BMI ranges may vary from country to country.

If weight reduction is necessary, energy intake should be reduced by 500–1,000 kcal/day with the initial aim of reducing bodyweight by 10% within 6 months.

A BMI calculator that uses both metric and imperial measurements is available on the US NHLBI website: http://nhlbi-support.com/bmi/bmicalc.htm
increased among people of South Asian origin and this ethnic background is counted as an independent risk factor. Others adjust the baseline risk according to ethnicity (New Zealand guidelines with Maori, Pacific and Indian subcontinent). However, none of the guidelines recommend modifying treatment goals on the basis of ethnic origin.

**Putting risk factor reduction into practice**

Optimal medical management of high-risk patients requires a holistic approach to care. This should lead to improvements in multiple risk factors, including dyslipidaemia, hypertension, thrombotic state and hyperglycaemia. For a comprehensive risk reduction strategy, patient education and motivation are vital, and communication with the patient is fundamental to successful implementation. Techniques that encourage patient compliance will be discussed later in this series.

**Treatment strategies**

Many risk factors can be modified by lifestyle changes, which form the basis of risk reduction for all patients. However, in high-risk patients adequate improvement in risk profile is rarely achieved using non-pharmacological management alone and these patients usually require treatment with lipid-modifying and antihypertensive drugs. Diabetic patients may also require antihyperglycaemic medication.

**Patient wellbeing**

The cardiovascular health of high-risk patients may be affected by psychosocial factors including depression and social isolation in addition to physical factors. As emphasised by the European guidelines, physicians play an important role in ensuring such patients receive appropriate help.

**CONCLUSION**

Management of the high-risk cardiovascular patient requires simultaneous, aggressive reduction of multiple risk factors to recommended goals. Therefore commitment to the management regimen is of fundamental importance.

Therapeutic changes in lifestyle, which are integral to patient management, can lead to substantial risk reduction. In addition immediate institution of pharmacological therapy – with lipid-lowering, antihypertensive and antiplatelet drugs, where appropriate – is usually recommended to enable risk reduction targets to be achieved.

Patient perceptions and knowledge regarding level of cardiovascular risk differ from those of care providers and may impede risk modification. This has implications for health education and should be considered when providing tailored care for patients.

**Competition Interests**

D. Duhamel and C. Packard are members of the Future Forum. D. Duhamel has received honoraria in the past three years from Bayer, MSD, Lilly, and the French Society of General Medicine (SFMG) and also has a partnership with Sanofi-Aventis. C. Packard has received research honoraria from AstraZeneca, GlaxoSmithKline, MSD, Pfizer, Organon, Schering-Plough and Unilever. Editorial support was provided by E. McGregor of the Future Forum Secretariat, which is supported by an unrestricted grant from AstraZeneca.

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**References**


