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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 $\geq 20\%$ (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}

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 risk¹⁰

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) or
- 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 $\geq 140/90$ 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, HbA_{1c} below 7% and LDL-C under 2.5 mmol/L

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

	Guideline (see Box 3 for full reference)					
	Australia 	Canada 	Europe 	New Zealand 	USA 	International 
Goal or treatment recommended?						
Smoking cessation	✓	–	✓	✓	–	✓
Lifestyle change ^b	✓	✓	✓	✓	✓ ^c	✓
Dyslipidaemia	✓	✓	✓	✓	✓	✓
Blood pressure	✓ ^d	–	✓	✓	–	✓
Antiplatelet therapy	✓	–	✓	✓	–	✓
Control of hyperglycaemia (diabetes patients)	–	–	✓	✓	–	✓

^a 10-year risk of a cardiovascular event $\geq 20\%$

^b Prudent diet, achievement of optimal bodyweight, increased physical activity

^c Optional if low-density lipoprotein cholesterol < 2.6 mmol/L

^d 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.

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).¹¹

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.

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

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The strong, positive association between total serum cholesterol levels and atherosclerotic disease was recognised more than 50 years ago



Box 3: Regional and national guidelines for prevention of cardiovascular disease

 Australia	Practical Implementation Taskforce for the Prevention of Cardiovascular Disease (2004) Prevention of cardiovascular disease: an evidence-based clinical aid. <i>Med J Aust</i> 2004; 181 : F1–14 http://www.mja.com.au/public/issues/181_06_200904/ful10382_fm.html
 Canada	Working Group on Hypercholesterolemia and Other Dyslipidemias (2003) Recommendations for the management of dyslipidemia and the prevention of cardiovascular disease: 2003 update. Genest J, Frohlich J, Fodor G, McPherson R. <i>CMAJ</i> 2003; 169 : 921-4. http://www.cmaj.ca/cgi/content/full/169/9/921/DC1
 Europe	Fourth Joint European Task Force (2007) European guidelines on cardiovascular disease prevention in clinical practice. Executive Summary: Graham I, Atar A E, Borch-Johnsen K, <i>et al.</i> <i>Eur Heart J</i> 2007; 28 : 2375-2414. Full text: Graham I, Atar A E, Borch-Johnsen K, <i>et al.</i> <i>Eur J Cardiovasc Prev Rehabil</i> 2007; 14 (Suppl 2): S1-S113 http://www.escardio.org/knowledge/guidelines/CVD_Prevention_in_Clinical_Practice.htm
 New Zealand	The New Zealand Guidelines Group (2003) The assessment and management of cardiovascular risk. http://www.nzgg.org.nz/index.cfm?fuseaction=fuseaction_10&fuse_subaction=docs&documentid=22
 USA	National Cholesterol Education Program (2001;2004) Third report of the National Cholesterol Education Program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adult Treatment Panel III) (2001) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. <i>JAMA</i> 2001; 285 : 2486-97 2004 update – Implications of Recent Clinical Trials for the National Cholesterol Education Program Adult Treatment Panel III Guidelines. Grundy SM, Cleeman JI, Bairley CN, <i>et al.</i> <i>Circulation</i> 2004; 110 : 227-39 http://www.nhlbi.nih.gov/guidelines/cholesterol/index.htm
 International	International Atherosclerosis Society (IAS) (2003) Harmonised guidelines on prevention of atherosclerotic cardiovascular diseases http://www.athero.org/

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Low levels of HDL-C and elevated triglyceride levels are both associated with increased cardiovascular risk
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Box 4: Lifestyle changes that reduce cardiovascular risk

- Smoking cessation
- Dietary modification (see Table 5)
- Achievement of ideal bodyweight (BMI <25 kg/m²; see Figure 1)
- Increased physical activity

elevated triglyceride levels are both associated with increased cardiovascular risk, and are frequently present in individuals with type 2 diabetes or the metabolic syndrome (Box 5).¹² Most of the guidelines regard a triglyceride level <1.7 mmol/L as desirable. Target HDL-C levels are rarely stated, but there is widespread agreement that cardiovascular risk is increased when HDL-C <1.0 mmol/L in men and <1.3 mmol/L in women.

Reduce high blood pressure

Cardiovascular risk rises continuously as the degree of hypertension increases. Effort should be made to reduce

Box 5: Features of the metabolic syndrome

Metabolic syndrome is diagnosed when there is central obesity as assessed by waist circumference

- >94 cm in European men, >80 cm in European women
- >90 cm in South Asian men, >80 cm in South Asian women

plus two of the following

- Triglycerides ≥1.7 mmol/L (1.5 g/L)
- HDL-C <1.03 mmol/L in men (<0.4 g/L in men)
- Blood pressure ≥130/85 mmHg or an antihypertensive prescription
- Glucose ≥5.6 mmol/L (1 g/L) or known diabetic



The IDF definition of the metabolic syndrome.



For the Third Report of the National Cholesterol Education Program (2001), the International Atherosclerosis Society harmonized guidelines (2003) see Box 3

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 HbA_{1c} ≤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).¹³ 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.^{1-7,14} In addition to providing detailed recommendations on lipid intake, the guidelines recommend minimum daily intakes of dietary

Table 2: Lipid goals in high-risk individuals

Guideline	Threshold for initiating treatment ^a	Goal ^b		
		LDL-C (mmol/L)	TC (mmol/L)	TC:HDL-C ratio
 Australia	TC: 3.5/5.0 mmol/L ^c	–	<3.5/5.0 ^c	–
 Canada	Treatment recommended in all patients	<2.5	–	<4.0
 Europe	TC: 5.0 mmol/L LDL-C: 3.0 mmol/L	<2.5	<4.5	–
 New Zealand	TC: 8.0 mmol/L TC:HDL-C: 8.0	<2.0/2.5 ^c	<3.5/4.0 ^c	<4.5
 USA	LDL-C: 2.6 mmol/L (optional if LDL-C <2.6 mmol/L)	↓ by 30-40% and to <1.8/2.6 ^c	–	–
 International	Treatment recommended in all patients	↓ by 30% and to <2.6	–	–

^a Threshold for initiation of lipid-modifying drugs; ^b Attempts should also be made to increase HDL-C and lower triglyceride levels in appropriate patients; ^c Goal/cutpoint depends on disease status/level of risk

Table 3: Blood pressure goals in high-risk individuals

Guideline	Blood pressure goal (mmHg)
 Australia	<140/90 or <130/85 ^{a,b}
 Canada	–
 Europe	<140/90 or <130/80 ^a
 New Zealand	<140/85 or <130/80 ^{a,c,d}
 USA	–
 International	<130/85

The lower goal is recommended for patients with:
^a diabetes; ^b renal disease; ^c clinical cardiovascular disease;
^d Aggressive management of blood pressure is recommended for patients with diabetes and concomitant renal disease

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 thrombotic risk

With few exceptions, acute cardiovascular events are caused by formation of an intra-arterial thrombus.

Table 4: HbA_{1c} goals in individuals with diabetes

Guideline	HbA _{1c} (%)
 Australia	–
 Canada	–
 Europe	≤6.1
 New Zealand	≤7
 USA	–
 International	≤7

Antiplatelet therapy (eg 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, *ie* whether they suffering from an illness other than cardiovascular disease that may decrease their life expectancy, and general tolerance to medication.

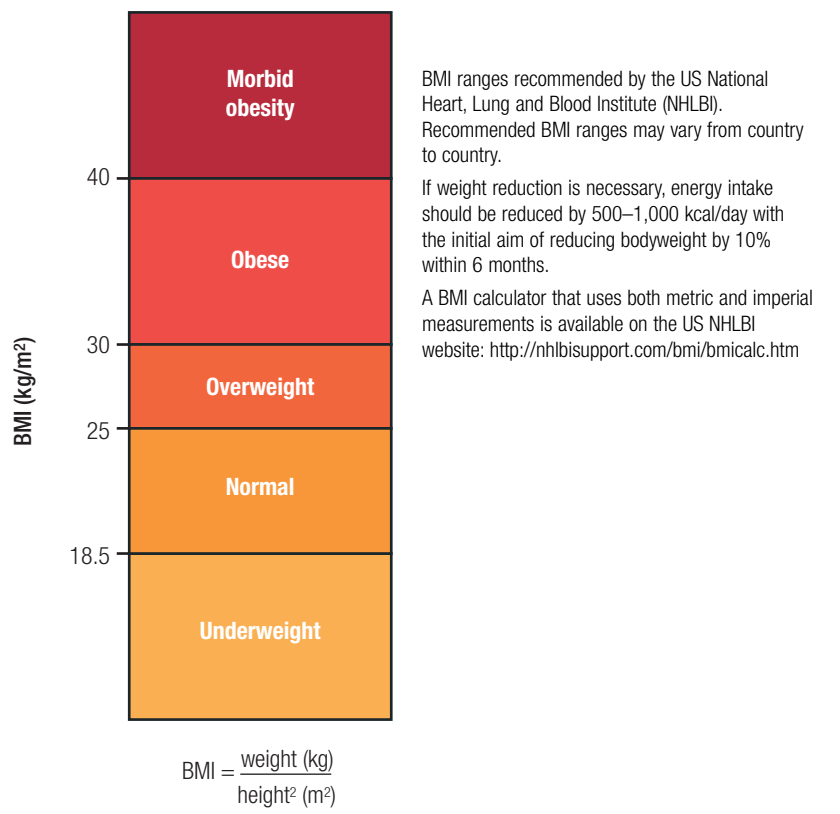
Ethnic groups

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, *eg* in the UK, standardised mortality rates for CHD are notably

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

Nutrient	Recommended intake
Total calories	Adjust to achieve/maintain desirable bodyweight (BMI <25 kg/m ²)
Total fat	25–35% of total calories
Saturated fat & trans fatty acids	<7% of total calories
Polyunsaturated fat	≤10% of total calories
Monounsaturated fat	≤20% of total calories
Cholesterol	<200 mg/day
Carbohydrate	50-60% of total calories
Protein	Approximately 15% of total calories
Fibre	20–30 g/day
Omega-3 fatty acids	≥1% of total calories or up to 1 g/day
Fruit & vegetables	≥5 servings/day
Alcohol	≤20–30 g ethanol/day (men), ≤10–20 g/day (women)

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>

Figure 1: Body mass index (BMI)

increased among people of south Asian origin and this ethnic background is counted as an independent risk factor.¹⁵ Others adjust the baseline risk according to ethnicity (New Zealand guidelines with Maori, Pacific and Indian subcontinent).⁶ 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, and 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.¹⁶

Competing interests

D. Duhot and C. Packard are members of the Future Forum. D. Duhot 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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