



Executive summary

European guidelines on cardiovascular disease prevention in clinical practice

Third Joint Task Force of European and other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of eight societies and by invited experts)

Guy De Backer (Chairperson)^{e,*}, Ettore Ambrosioni^e, Knut Borch-Johnsen^{a,b}, Carlos Brotons^h, Renata Cifkova^e, Jean Dallongeville^e, Shah Ebrahim^e, Ole Faergeman^c, Ian Graham^e, Giuseppe Mancia^e, Volkert Manger Cats^d, Kristina Orth-Gomér^g, Joep Perk^e, Kalevi Pyörälä^e, José L. Rodicio^f, Susana Sans^e, Vedat Sansoy^e, Udo Sechtem^e, Sigmund Silber^e, Troels Thomsen^e, David Wood^e

Other experts who contributed to parts of the guidelines, Christian Albus, Nuri Bages, Gunilla Burell, Ronan Conroy, Hans Christian Deter, Christoph Hermann-Lingen, Steven Humphries, Anthony Fitzgerald, Brian Oldenburg, Neil Schneiderman, Antti Uutela, Redford Williams, John Yarnell

ESC Committee for Practice Guidelines (CPG), Silvia G. Priori (Chairperson), Maria Angeles Alonso Garcia, Jean-Jacques Blanc, Andrzej Budaj, Martin Cowie, Veronica Dean, Jaap Deckers, Enrique Fernández Burgos, John Lekakis, Bertil Lindahl, Gianfranco Mazzotta, Keith McGregor, João Morais, Ali Oto, Otto Smiseth, Hans-Joachim Trappe

Document Reviewers, this document has been reviewed by experts, nominated by their societies, who were independent of the Task Force, Andrzej Budaj (CPG Review Coordinator)^e, Carl-David Agardh^a, Jean-Pierre Bassand^e, Jaap Deckers^e, Maciek Godycki-Cwirko^h, Anthony Heagerty^e, Robert Heine^a, Philip Home^b, Silvia Priori^e, Pekka Puska^g, Mike Rayner^d, Annika Rosengren^e, Mario Sammut^h, James Shepherd^c, Johannes Siegrist^g, Maarten Simoons^e, Michal Tendera^e, Alberto Zanchetti^f

Preamble

Guidelines aim to present all the relevant evidence on a particular issue in order to help physicians to weigh the benefits and risks of a particular diagnostic or thera-

* Corresponding author: Prof. Guy De Backer, University Hospital, De Pintelaan 185, B-9000 Ghent, Belgium

E-mail address: guy.debacker@ugent.be

- ^a European Association for the Study of Diabetes (EASD)
- ^b International Diabetes Federation Europe (IDF-Europe)
- ^c European Atherosclerosis Society (EAS)
- ^d European Heart Network (EHN)
- e European Society of Cardiology (ESC)
- f European Society of Hypertension (ESH)
- g International Society of Behavioural Medicine (ISBM)
- h European Society of General Practice/Family Medicine (ESGP/FM)

peutic procedure. They should be helpful in everyday clinical decision-making.

A great number of guidelines have been issued in recent years by different organizations-European Society of Cardiology (ESC), American Heart Association (AHA), American College of Cardiology (ACC), and other related societies. By means of links to web sites of National Societies several hundred guidelines are available. This profusion can put at stake the authority and validity of guidelines, which can only be guaranteed if they have been developed by an unquestionable decision-making process. This is one of the reasons why the ESC and others have issued recommendations for formulating and issuing guidelines.

In spite of the fact that standards for issuing good quality guidelines are well defined, recent surveys of guidelines published in peer-reviewed journals between 1985 and 1998 have shown that methodological standards were not complied with in the vast majority of cases. It is therefore of great importance that guidelines and recommendations are presented in formats that are easily interpreted. Subsequently, their implementation programmes must also be well conducted. Attempts have been made to determine whether guidelines improve the quality of clinical practice and the utilization of health resources. In addition, the legal implications of medical guidelines have been discussed and examined, resulting in position documents, which have been published by a specific Task Force.

The ESC Committee for Practice Guidelines (CPG) supervises and coordinates the preparation of new Guidelines and Expert Consensus Documents produced by Task Forces, expert groups or consensus panels. The Committee is also responsible for the endorsement of these guidelines or statements.

Introduction

The rationale for an active approach to the prevention of cardiovascular diseases (CVD) is firmly based on five observations:

- CVD is the major cause of premature death in most European populations; it is an important source of disability and contributes in large part to the escalating costs of health care
- the underlying pathology is usually atherosclerosis, which develops insidiously over many years and is usually advanced by the time symptoms occur
- death, myocardial infarction and stroke nevertheless frequently occur suddenly and before medical care is available, and many therapeutic interventions are therefore inapplicable or palliative
- the mass occurrence of CVD relates strongly to lifestyles and modifiable physiological factors
- risk factor modifications have been unequivocally shown to reduce mortality and morbidity, especially in people with either unrecognised or recognised CVD.

Cardiovascular disease is generally due to a combination of several risk factors, and, in recognition of the multifactorial nature of this group of diseases, the European Atherosclerosis Society, the European Society of Cardiology, and the European Society of Hypertension agreed in the early 1990s to collaborate to suggest guidelines for prevention of coronary heart disease in clinical practice. The result was a set of recommendations published in 1994. A revision of these early guidelines was published in 1998 by the Second Joint Task Force, which set lifestyle, risk factor and therapeutic goals for coronary prevention. In this 2nd report the original three societies were joined by the European Society of

General Practice/Family Medicine, the European Heart Network and by the International Society of Behavioural Medicine.

Since completion of this report, important new data have been published. Therefore the Third Joint Task Force provides a second revision of the joint European guidelines. The Task Force has been joined by the European Association for the Study of Diabetes and by the International Diabetes Federation Europe. These new guidelines differ from the previous ones in several important aspects:

- (1) From coronary heart disease (CHD) to CVD prevention. The aetiology of myocardial infarction, ischaemic stroke and peripheral arterial disease is similar, and, indeed, recent intervention trials have shown that several forms of therapy prevent not only coronary events and revascularisations but also ischaemic stroke and peripheral artery disease. Hence, decisions about whether to initiate specific preventive action can be guided by estimation of risk of suffering any such vascular event, not just a coronary event, and preventive actions can be expected to reduce risk, not only of coronary heart disease, but also of stroke and peripheral arterial disease.
- (2) In order to assess the risk for development of CVD different multifactorial risk models have been developed. The Task Force recommends using the SCORE Model and Risk Charts as recently developed. The risk assessment using the SCORE database can be easily adapted to national conditions, resources and priorities and takes into account the heterogeneity in CVD mortality across European populations. A core element of the model is that risk is now defined in terms of the absolute 10 year probability of developing a fatal cardiovascular event
- (3) Explicit clinical priorities. As in the 1994 and 1998 recommendations, the first priority of practitioners is patients with established cardiovascular disease and subjects who are at high risk of developing CVD. Subjects at high risk may also be recognised by new imaging techniques which allow visualisation of subclinical atherosclerosis.
- (4) All new and published knowledge from the field of preventive cardiology was considered, particularly results from recent clinical trials showing clinical benefit of dietary changes, of good management of risk factors and of the prophylactic use of certain drugs. This includes data on usage of certain drugs in elderly subjects and in subjects at high risk with a relatively low total cholesterol level.

These guidelines are specifically intended to encourage the development of national guidance on cardiovascular disease prevention. Implementation of these guidelines is possible only through collaboration between very different professional groups at the national level. The guidelines should be considered as the framework in which all necessary adaptations can be made in order to reflect different political, economic, social and medical circumstances.

The Third Joint Task Force recognises that these guidelines which are targeted at those at highest CVD risk

should be complemented by strategies aimed at whole populations at the national and European level as a contribution to a public health policy to reduce the enormous burden of cardiovascular disease in European populations.

Medical priorities

Preventive efforts are most efficient when they are directed at those at highest risk. The present recommendations therefore define the following priorities for CVD prevention in clinical practice:

- 1 patients with established coronary heart disease, peripheral artery disease and cerebrovascular atherosclerotic disease
- 2 asymptomatic individuals who are at high risk of developing atherosclerotic cardiovascular diseases because of
 - a) multiple risk factors resulting in a 10 year risk of ≥5% now (or if extrapolated to age 60) for developing a fatal CVD event
 - b) markedly raised levels of single risk factors: cholesterol ≥8 mmol/l (320 mg/dl), LDL cholesterol ≥6 mmol/l (240 mg/dl), blood pressure ≥180/110 mmHg
 - c) diabetes type 2 and diabetes type 1 with microalbuminuria
- 3 close relatives of
 - a) patients with early onset atherosclerotic cardiovascular disease
- b) asymptomatic individuals at particularly high risk
 4 other individuals encountered in routine clinical practice

Objectives of cardiovascular prevention

The objectives of these guidelines are to reduce the incidence of first or recurrent clinical events due to coronary heart disease, ischaemic stroke and peripheral artery disease. The focus is prevention of disability and early deaths. To this end, the current guidelines address the role of lifestyle changes, the management of major cardiovascular risk factors and the use of different prophylactic drug therapies in the prevention of clinical CVD.

Intermediate end-points such as left ventricular hypertrophy, carotid artery plaques and to a lesser extent endothelial dysfunction as well as alteration in the electrical stability of the myocardium have been shown to increase the risk of cardiovascular morbidity, indicating that subclinical organ damage has clinical relevance. Accordingly such measurements may be incorporated in more sophisticated models to assess the risk for future CVD events.

Total cardiovascular risk as a guide to preventive strategies: the SCORE system

Patients with established cardiovascular disease have declared themselves to be at high total risk of a further vascular event. Therefore, they require the most intensive lifestyle intervention, and where appropriate drug therapies.

In asymptomatic, apparently healthy subjects, preventive actions should be guided in accordance with the total CVD risk level. Those at highest total risk should be identified and targeted for intensive lifestyle interventions and when appropriate drug therapies. Several models have been developed to assess the risk for CVD in asymptomatic subjects. Using different combinations of risk factors these models are all based on a multifactorial risk analysis in populations which have been followed for several years.

These guidelines recommend a new model for total risk estimation based on the SCORE (Systematic Coronary Risk Evaluation) system. The new risk chart based on the SCORE study represents several advantages compared to the previous chart. The SCORE risk assessment system is derived from a large dataset of prospective European studies and predicts any kind of fatal atherosclerotic end-point i.e. fatal CVD events over a ten-year period. In SCORE the following risk factors are integrated: gender, age, smoking, systolic blood pressure and either total cholesterol or the cholesterol/HDL ratio. Since this chart predicts fatal events the threshold for being at high risk is defined as $\geq 5\%$, instead of the previous $\geq 20\%$ in charts using a composite coronary endpoint. Using SCORE it is now possible to produce risk charts tailored for individual countries provided reliable national mortality information is available.

Practitioners should use total CVD risk estimates when decisions are taken to intensify preventive actions i.e. when dietary advice should be more specified, when the physical activity prescription should be more individualized, when drugs should be prescribed, dosages adapted or combinations started to control risk factors; these decisions should usually not be based on the level of any one risk factor alone; neither should they be linked to only one arbitrary cut point from the continuous total CVD risk distribution.

Total CVD risk can easily be derived from printed charts (see illustrations in Figs. 1 and 2) or from the web where in addition the SCORECARD system will provide physicians and patients with information on how total risk can be reduced by interventions (both lifestyles and drugs) that have been proven to be efficacious and safe in descriptive cohort studies and/or in randomized controlled trials.

Both the SCORE and the SCORECARD system also allows the estimation of total CVD risk to be projected to age 60 which may be of particular importance for guiding young adults at low absolute risk at the age of 20 or 30 but already with an unhealthy risk profile which will put them at much higher risk when they grow older. Furthermore, both systems allow the use of relative risk estimates which, in addition to total absolute risk, may be of interest in particular cases.

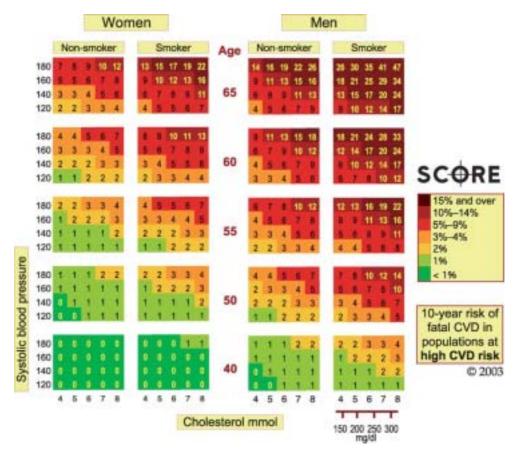


Fig. 1 Ten year risk of fatal CVD in high risk regions of Europe by gender, age, systolic blood pressure, total cholesterol and smoking status.

Definition of high total risk for developing a fatal cardiovascular event

- 1 Patients with established cardiovascular disease 2 Asymptomatic subjects who have:
 - 2.1 Multiple risk factors resulting in a 10 year risk ≥ 5% now or if extrapolated to age 60 (see also box with qualifiers)
 - 2.2 Markedly raised levels of single risk factors: total cholesterol ≥8 mmol/l (320 mg/dl), LDL cholesterol ≥6 mmol/l (240 mg/dl), blood pressure ≥180/110 mmHg
 - 2.3 Diabetes type 2 and diabetes type 1 with microalbuminuria

Instructions on how to use the chart

 The low risk chart should be used in Belgium, France, Greece, Italy, Luxembourg, Spain, Switzerland and Portugal; the high risk chart should be used in all other countries of Europe.

- To estimate a person's total ten year risk of CVD death, find the table for their gender, smoking status and age. Within the table find the cell nearest to the person's systolic blood pressure (mmHg) and total cholesterol (mmol/l or mg/dl).
- The effect of lifetime exposure to risk factors can be seen by following the table upwards. This can be used when advising younger people.
- Low risk individuals should be offered advice to maintain their low risk status. Those who are at 5% risk or higher or will reach this level in middle age should be given maximal attention.
- To define a person's relative risk, compare their risk category with that of a non-smoking person of the same age and gender, blood pressure <140/90 mmHg and total cholesterol < 5mmol/l (190mg/dl).
- The chart can be used to give some indications of the effect of changes from one risk catagory to another, for example when the subject stops smoking or reduces other risk factors.

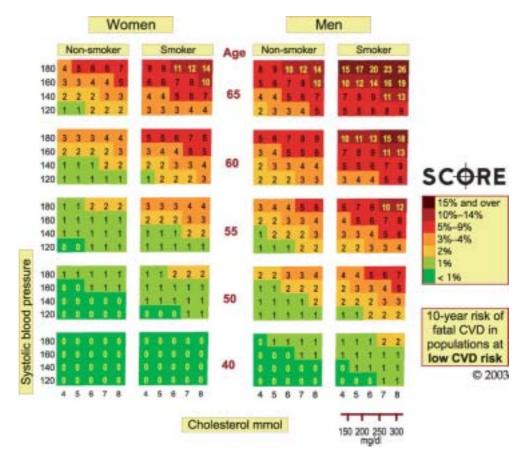


Fig. 2 Ten year risk of fatal CVD in low risk regions of Europe by gender, age, systolic blood pressure, total cholesterol and smoking status.

Qualifiers:

Note that total CVD risk may be higher than indicated in the chart:

- as the person approaches the next age category.
- in asymptomatic subjects with pre-clinical evidence of atherosclerosis (e.g. CT scan, ultrasonography)
- in subjects with a strong family history of premature CVD
- in subjects with low HDL cholesterol levels, with raised triglyceride levels, with impaired glucose tolerance, and with raised levels of C-reactive protein, fibrinogen, homocysteine, apolipoprotein B or Lp(a)
- in obese and sedentary subjects

New imaging methods to detect asymptomatic individuals at high risk for cardiovascular events

Magnetic Resonance Imaging (MRI) allows in vivo imaging of the arterial wall and differentiation of plaque components. Coronary calcifications can be detected and quantified by computed tomography (EC-CT or MS-CT). The resulting calcium score is an important parameter to detect asymptomatic individuals at high risk for future CVD events, independent of the traditional risk factors.

Furthermore, carotid intima-media thickness, measured by ultrasound, is a risk factor for cardiac events and stroke. Left ventricular hypertrophy, either detected by ECG or by echocardiography has also been shown to be an independent risk factor for CVD mortality and morbidity in hypertensive subjects. Each of these measurements has its limitations, yet they may be included in sophisticated models for risk assessment, which may be more precise than current models based on classical risk factors.

Management of CVD risk in clinical practice

Behavioural risk factors

Changes in many patterns of individual behaviour are necessary in a large majority of patients with established CVD or at high risk of CVD, but recent surveys suggest a serious gap between recommendations for behavioural change and the advice actually provided by physicians in routine clinical practice. The management of behavioural risk factors is similar for patients with CVD and high-risk people, but changing risk behaviours (unhealthy diet, smoking, sedentary lifestyle), which have lasted for many years, needs a professional approach.

For many people it can be difficult to change lifestyle according to a physician's advice. This difficulty pertains

especially to people and patients who are socially and economically disadvantaged, who exercise little control over a monotonous and unrewarding job, who are in a stressful family situation, or who live alone and lack social support.

Moreover, negative emotions, including depression, anger and hostility, may constitute barriers to preventive efforts, both in patients and in high-risk people. The physician can recognize these barriers by using a simple set of questions. Although physician's awareness is helpful and in some cases sufficient, persistent and severe negative emotions can require expert consultation and behavioural or pharmacological treatment. As psychosocial risk factors are independent of standard risk factors, efforts to relieve stress and counteract social isolation should be emphasised whenever possible.

Strategic steps that may be used to enhance the effectiveness of behavioural counselling include¹:

- develop a therapeutic alliance with the patient
- ensure that patients understand the relationship between behaviour, health and disease
- help patients to understand the barriers to behavioural change
- gain commitments from patients to behavioural change
- involve patients in identifying and selecting the risk factors to change
- use a combination of strategies including reinforcement of patients' own capacity for change
- design a lifestyle modification plan
- monitor progress through follow-up contact
- involve other health care staff wherever possible

Stop smoking tobacco

All smokers should be professionally encouraged to permanently stop smoking all forms of tobacco. Strategies that may help can be summarized into the following 5 A's:

A – ask: systematically identify all smokers at every opportunity

A – assess: determine the patient's degree of addiction and his/her readiness to cease smoking.

A – advise: urge strongly all smokers to quit

A – assist: agree on a smoking cessation strategy including behavioural counselling, nicotine replacement therapy and/or pharmacological intervention

A – arrange a schedule of follow-up visits

Make healthy food choices

Making healthy food choices is an integral part of total risk management. All individuals should receive professional advice on food and food choices to compose a diet associated with the lowest risk of cardiovascular disease.

A sound diet reduces risk by several mechanisms including weight reduction, lowering of blood pressure, effects on lipids, control of glucose and reduction of the propensity to thrombosis.

General recommendations (to be specified according to local culture):

- foods should be varied, and energy intake must be adjusted to maintain ideal body weight
- the consumption of the following foods should be encouraged: fruits and vegetables, whole grain cereals and bread, low fat dairy products, fish and lean meat
- oily fish and omega-3-fatty acids have particular protective properties
- total fat intake should account for no more than 30% of energy intake, and intake of saturated fats should not exceed a third of total fat intake. The intake of cholesterol should be less than 300 mg/ day
- in an isocaloric diet, saturated fat can be replaced partly by complex carbohydrates, partly by monounsaturated and polyunsaturated fats from vegetables and marine animals

Patients with arterial hypertension, diabetes, and hypercholesterolaemia or other dyslipidaemias should receive specialist dietary advice.

Increase physical activity

Physical activity should be promoted in all age groupsfrom children to the elderly-and all patients and high risk people should be professionally encouraged and supported to increase their physical activity safely to the level associated with the lowest risk of CVD. Although the goal is at least half an hour of physical activity on most days of the week, more moderate activity is also associated with health benefits.

Healthy people should be advised to choose enjoyable activities which fit into their daily routine, preferably 30 to 45 min, 4 to 5 times weekly at 60–75% of the average maximum heart rate. For patients with established CVD, advice must be based on a comprehensive clinical judgement including the results of an exercise test. Detailed recommendations for CVD patients have been given by other expert committees.

Management of other risk factors

Overweight and obesity

Avoiding overweight or reducing existing overweight is important in patients with established CVD as well as in high risk people. Weight reduction is strongly recommended for obese people (BMI \geq 30 kg/m²) or overweight

¹ Adapted from the Report of the US Preventive Services Task Force.

Guide to Blood Pressure Management

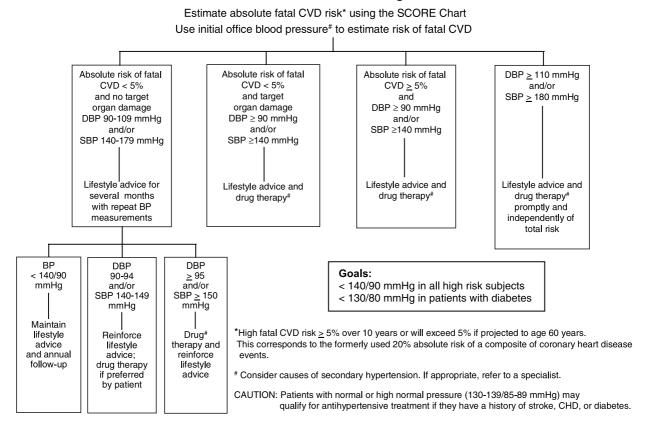


Fig. 3 Guide to blood pressure management.

individuals (BMI \ge 25 and <30 kg/m²) and for those with increased abdominal fat as indicated by waist circumference >102 cm in men and >88 cm in women.

Success in weight reduction is more likely if it supported professionally, but it also requires strong motivation by the individual.

Blood pressure

The risk of cardiovascular diseases increases continuously as blood pressure rises from levels that are considered to be within the normal range. The decision to start treatment, however, depends not only on the level of blood pressure, but also on an assessment of total cardiovascular risk and the presence or absence of target organ damage. In patients with established CVD the choice of antihypertensive drugs depends on the underlying cardiovascular disease.

A guide to blood pressure management in asymptomatic people is given in Fig. 3. The decision to lower blood pressure with drugs depends not only on the total cardiovascular risk but also on presence of target organ damage. Drug therapy should be initiated promptly in individuals with a sustained systolic blood pressure (SBP) ≥180 mmHg and/or a diastolic blood pressure (DBP) ≥110 mmHg regardless of their total cardiovascular risk assessment.

Individuals at high risk of developing CVD with sustained SBP of ≥140 mmHg and/or DBP ≥90 mmHg also require drug therapy. For such individuals, drugs should be used to lower blood pressure to <140/90 mmHg. Similar elevation of blood pressure in low risk people without target organ damage should be followed closely, and lifestyle advice should be given. Drug treatment might be considered after asking the patients' preference.

With few exceptions, individuals with SBP <140 mmHg and/or DBP <90 mmHg do not need drug therapy. Patients with a high or very high cardiovascular risk profile and patients with diabetes can benefit from reducing blood pressure below the goal of SBP<140 mmHg and/or DBP<90 mmHg.

Antihypertensive drugs should not only lower blood pressure effectively. They should have a favourable safety profile and be able to reduce cardiovascular morbidity and mortality.

Five classes of drugs currently meet these requirements: diuretics, beta-blockers, ACE inhibitors, calcium-channel blockers and angiotensin II antagonists.

In many clinical trials, blood pressure control has been achieved by the combination of two or even three drugs, and drug combination therapy is often also necessary in routine clinical practice. In patients with several diseases requiring drug therapy, polypharmacy can become a major problem and good clinical management is

Guide to Lipid Management in asymptomatic subjects

Estimate total fatal CVD risk using the SCORE chart. Use initial total cholesterol (or ratio of total to HDL-cholesterol) to estimate risk. (TC: total cholesterol, LDL-C: LDL cholesterol, HDL-C: HDL cholesterol)

Total risk < 5% Total risk ≥ 5% $TC \ge 5 \text{ mmol/l } (190 \text{ mg/dl})$ $TC \ge 5 \text{ mmol/l}(190\text{mg/dl})$ Measure fasting TC Lifestyle advice to reduce TC below 5 HDL-C and triglycerides. mmol/I (190 mg/dl) and LDL-C below Calculate LDL-C 3 mmol/l (115 mg/dl). Follow-up at a Patient to follow lifestyle advice for minimum of 5 years intervals. at least 3 months. Repeat measurements. TC < 5 mmol/l (190 mg/dl) and $TC \ge 5 \text{ mmol/l (190 mg/dl) or}$ LDL-C < 3 mmol/l (115 mg/dl)LDL-C ≥ 3 mmol/l (115 mg/dl): Maintain lifestyle advice with Maintain lifestyle advice and annual follow-up. If total risk remains start drug therapy ≥ 5%, consider drugs to lower TC to < 4.5 mmol/l (175 mg/dl) and LDL-C to < 2.5 mmol/l (100 mg/dl)

Fig. 4 Guide to lipid management in asymptomatic subjects.

required to resolve it. In all patients, blood pressure reduction should be obtained gradually. For most patients, the goal of therapy is blood pressure less than 140/90 mmHg, but for patients with diabetes and individuals at high total CVD risk, the blood pressure goal should be lower.

Plasma lipids

In general, total plasma cholesterol should be below 5 mmol/l (190 mg/dl), and LDL cholesterol should be below 3 mmol/l (115 mg/dl). For patients with clinically established CVD and patients with diabetes the treatment goals should be lower: total cholesterol <4.5 mmol/l (175 mg/dl) and LDL cholesterol <2.5 mmol/l (100 mg/dl).

No specific treatment goals are defined for HDL cholesterol and triglycerides, but concentrations of HDL cholesterol and triglycerides are used as markers of increased risk. HDL cholesterol <1.0 mmol/l (40 mg/dl) in men and <1.2 mmol/l (46 mg/dl) in women, and similarly, fasting triglycerides >1.7 mmol/l (150 mg/dl), serve as markers of increased cardiovascular risk. Values of HDL cholesterol and triglycerides should also be used to guide the choice of drug therapy.

Asymptomatic people at high multifactorial risk of developing cardiovascular disease, whose untreated values of total and LDL cholesterol are already close to 5 and 3 mmol/l, respectively, seem to benefit from further reduction of total cholesterol to <4.5 mmol/l (175 mg/dl), and from further reduction of LDL cholesterol to <2.5 mmol/l (100 mg/dl), with moderate doses of lipid lowering drugs. However, these lower values are not

goals of therapy for patients with higher untreated values because high-dose therapy, the merits of which have not yet been documented, would be needed to reach such lower goals.

In asymptomatic individuals (see Fig. 4), the first step is to assess total cardiovascular risk and to identify these components of risk that are to be modified. If the 10 year risk of cardiovascular death is <5% and will not exceed 5% if the individuals' risk factor combination is projected to age 60, professional advice concerning a balanced diet, physical activity and stopping smoking should be given to keep the cardiovascular risk low. Risk assessment should be repeated at 5-year intervals. Note that assessment of total risk does not pertain to patients with familial hypercholesterolemia, since total cholesterol >8 mmol/l (320 mg/dl) and LDL cholesterol >6 mmol/l (240 mg/dl) by definition places a patient at high total risk of CVD.

If the 10 year risk of cardiovascular death is $\geq 5\%$, or will become $\geq 5\%$ if the individuals' risk factor combination is projected to age 60, a full analysis of plasma lipoproteins should be performed, and intensive lifestyle advice, particularly dietary advice, should be given. If values of total and LDL cholesterol fall below 5 mmol/l (190 mg/dl) and 3 mmol/l (115 mg/dl), respectively, and the total CVD risk estimate has become <5%, then these persons should be followed at yearly intervals to ensure that cardiovascular risk remains low without drugs. In contrast, if total CVD risk remains $\geq 5\%$, lipid lowering drug therapy should be considered to lower total and LDL cholesterol even further. The goals in such persistently high-risk individuals are to lower total cholesterol to <4.5 mmol/l

(175 mg/dl) and to lower LDL cholesterol to <2.5 mmol/l (100 mg/dl). As stated earlier, these lower values are not goals of therapy for patients with higher untreated values.

The first clinical trials which documented the clinical benefits (improved survival) of lipid lowering therapy with statins were restricted to individuals <70 years and total cholesterol >5 mmol/l. Recently published trials indicate that such treatment can also be effective in the elderly and in subjects with lower cholesterol levels.

Some individuals require combination therapy. In patients with several diseases requiring drug therapy, polypharmacy can become a major problem and good clinical management is required to resolve it. In some patients, goals cannot be reached even on maximal therapy, but they will still benefit from treatment to the extent to which cholesterol has been lowered.

Diabetes

It has been demonstrated that progression to diabetes can be prevented or delayed by lifestyle intervention in individuals with impaired glucose tolerance.

In patients with type 1 and type 2 diabetes, there is convincing evidence from randomised controlled trials that good metabolic control prevents microvascular complications. Regarding the prevention of cardiovascular events, there are also good reasons to aim for good glucose control in both types of diabetes. In type 1 diabetes, glucose control requires appropriate insulin therapy and concomitant professional dietary therapy. In type 2 diabetes, professional dietary advice, reduction of overweight and increased physical activity should be the first treatment aiming at good glucose control.

Drug therapy must be added if these measures do not lead to a sufficient reduction of hyperglycaemia. Recommended treatment targets for type 2 diabetes are given in the table.

Treatment goals for blood pressure and lipids are generally more ambitious in patients with diabetes (see above).

Treatment goals in patients with type 2 diabetes:

		Goal
HbA _{1c} (DCCT- standardized)	HbA _{1c} (%)	≤6.1
Venous plasma	Fasting/pre-prandial	
glucose	mmol/l	≤6.0
	mg/dl	<110
Self-monitored	Fasting/pre-prandial	
blood glucose	mmol/l	4.0-5.0
	mg/dl	70–90
	Post-prandial	
	mmol/l	4.0-7.5
	mg/dl	70-135
Blood pressure	mmHg	<130/80
Total cholesterol	mmol/l (mg/dl)	<4.5(175)
LDL cholesterol	mmol/l (mg/dl)	<2.5(100)

The metabolic syndrome

In clinical practice, the definition given by the US National Cholesterol Education Program can be provisionally used for the identification of individuals with the metabolic syndrome. The diagnosis of the metabolic syndrome is made, when three or more of the following features are present:

- 1 waist circumference >102 cm in males, >88 cm in females
- 2 serum triglycerides ≥1.7 mmol/l (≥150 mg/dl)
- 3 HDL-cholesterol <1 mmol/l (<40 mg/dl) in males or <1.3 mmol/l (<50 mg/dl) in females
- 4 blood pressure ≥130/85 mmHg
- 5 plasma glucose ≥6.1 mmol/l (≥110 mg/dl)

People with the metabolic syndrome are usually at high risk of cardiovascular disease. Lifestyle has a strong influence on all the components of the metabolic syndrome and therefore the main emphasis in the management of the metabolic syndrome should be in professionally supervised lifestyle changes, particularly efforts to reduce body weight and increase physical activity. Elevated blood pressure, dyslipidaemia and hyperglycaemia (in the diabetic range) may, however, need additional drug treatment as recommended in the present guidelines.

Other prophylactic drug therapies

In addition to drugs needed to treat blood pressure, lipids and diabetes, the following drug classes should also be considered in the prevention of CVD in clinical practice:

- aspirin or other platelet-modifying drugs in virtually all patients with clinically established CVD
- betablockers in patients following myocardial infarction or with left ventricular dysfunction due to CHD.
- ACE inhibitors in patients with symptoms or signs of left ventricular dysfunction due to CHD and/or arterial hypertension
- anti-coagulants in those patients with CHD who are at increased risk of thromboembolic events.

In asymptomatic high risk people there is evidence that low dose aspirin can reduce the risk of cardiovascular events in people with diabetes, in people with well controlled hypertension and in men at high multifactorial CVD risk.

Screening close relatives

Close relatives of patients with premature coronary heart disease (men <55 years and women <65 years) and persons who belong to families with familial hypercholesterolaemia or other inherited dyslipidaemias should be examined for cardiovascular risk factors, because all of these persons are at increased risk of developing cardiovascular disease.

Highlights from this executive summary:

In patients with established CVD:

- promote relevant lifestyle changes: stop smoking, make healthy food choices and increase physical activity
- prescribe aspirin and a statin
- consider need for anti-hypertensives, betablockers and ACE-inhibitors

In people at potentially high CVD risk:

- use the SCORE system to define level of total CVD risk
- promote relevant lifestyle changes: stop smoking, make healthy food choices and increase physical activity
- consider need for blood pressure lowering, cholesterol lowering and glycaemic control

Acknowledgement

The authors gratefully acknowledge the secretarial assistance of Christine Ghysbrecht (Ghent).