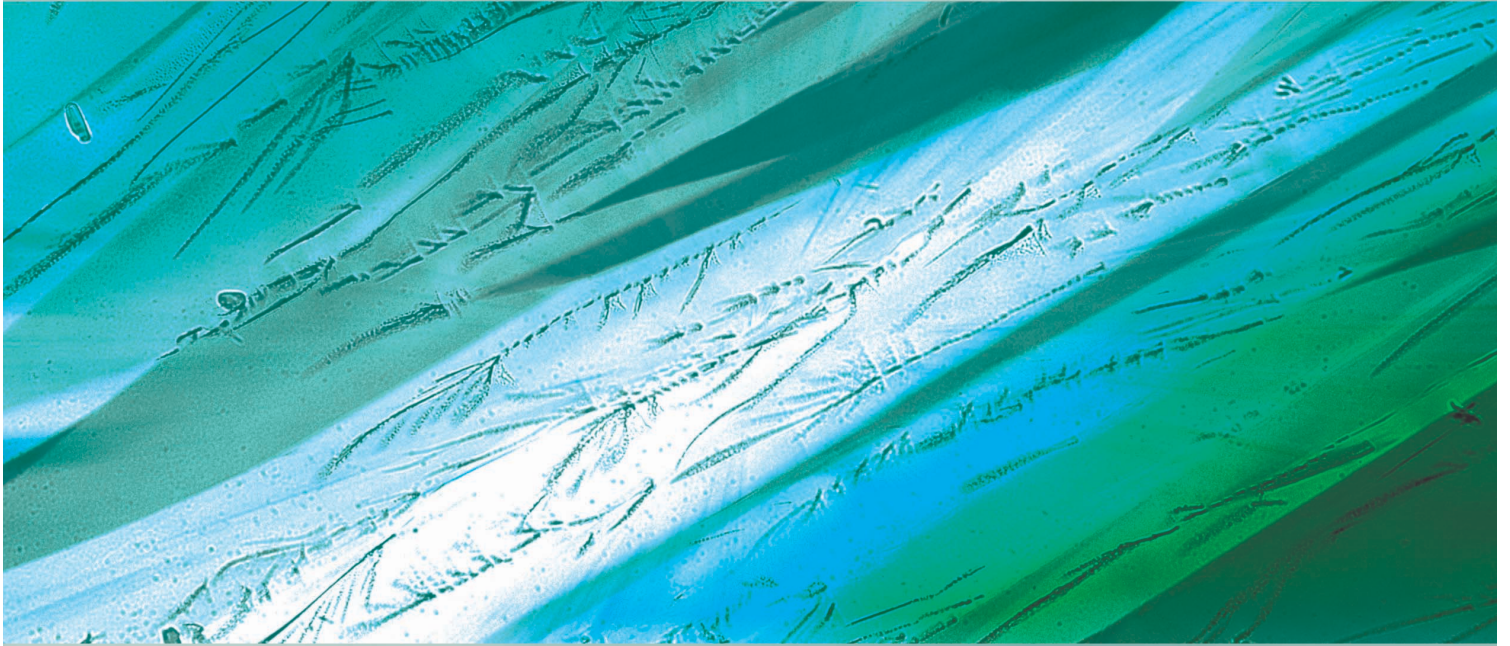




Policy Analysis Centre



European Cholesterol Guidelines Report

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Foreword by Professor Elias Mossialos, Director,
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Foreword

Professor Elias Mossialos, Director, LSE Health, London School of Economics & Political Science

Cholesterol and the Burden of Disease

Throughout the World Health Organization (WHO) European Region cardiovascular disease is estimated to be the leading cause of death, accounting for more than 5 million deaths as well as almost one-quarter of the region’s disease burden. In 2002 cardiovascular disease (CVD) was estimated to have accounted for more than a quarter of all disability-adjusted life years (DALYs) lost in the EU¹, with heart disease or stroke as the leading cause of death in all WHO European member states. CVD is forecast to remain the leading cause of disability in developed countries up until 2020². Risk factors such as smoking, physical inactivity, obesity, high blood pressure, lipids (raised total cholesterol and LDL cholesterol, low HDL cholesterol and raised triglycerides), raised glucose levels and family history of premature coronary disease are responsible for a sizeable proportion of the total burden of cardiovascular disease in the region. The WHO attributes 8.7% of the total burden of disease in the region to high blood cholesterol³, and comments that existing knowledge on disease detection; treatment and rehabilitation should be *“better and more equitably applied, so that all stand to share in the benefits”*⁴

As the chart demonstrates (Figure 1) there is little correlation between death rates from heart disease and average personal income⁵. Death rates from ischaemic heart disease (IHD) vary from 36.9 per 100,000 population in France to 120.1 per 100,000 in Finland, whilst per capita income, at purchasing power parities, varies between \$17,440 in Slovenia and \$60,890 in

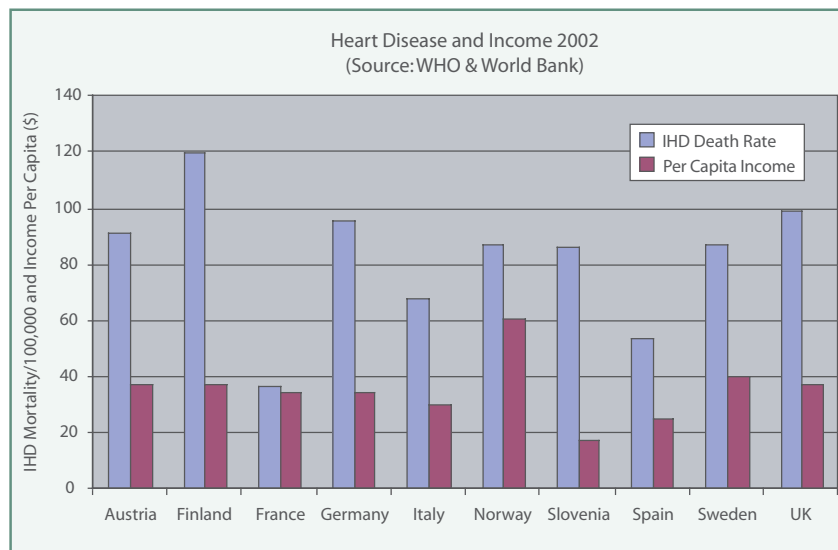
Norway. This would suggest that variations in the prevalence and impact of IHD are not directly associated with issues of the costs of prevention and treatment. As this report demonstrates, there are also significant variations in targets for LDL-cholesterol that are not associated with risk levels or the affordability of medical intervention. The report shows targets for

LDL-cholesterol that vary from 1.8mmol/l in Austria to 3.4mmol/l in Italy, ranging around 30% either side of the agreed European target.

The populations of Finland and the UK have the highest CVD death rates in the European countries covered in the report, with similar levels of per capita income from which to fund investments in prevention and treatment. Yet it is not clear why official cholesterol guidelines for high risk patients in both countries differ from those of their own specialist medical societies and their European counterparts.

Some of the explanation for the absence of a clear relationship between the burden of CVD in a country and its clinical guidelines to tackle this burden might lie in the way in which health systems are funded. When put in a global context, the distinguishing feature of European health systems is the degree to which they are funded by state expenditure. In the sample countries of this report the share of public spending in total health spending varies between around 70% and 85%⁶. Nevertheless, the share of funding from private sources has been rising in recent

Figure 1



years, with increasing co-payments by patients themselves, whether voluntary or compulsory, and rising levels of private health insurance. Despite this gradual shift, the share of spending from the state remains remarkably high by international standards, and absolute levels of spending on health care have continued to rise.

This continued growth in health spending, to more than 10% of GDP, in France and some other countries, is the focus of many health policies. Pharmaceutical spending, although a rather small (but rapidly growing) component of health spending, is very visible and more easily controlled than other aspects (i.e. labour costs). Guidelines can be used therefore, not only to pursue best practice, but also to balance this against the management of growing demands on a country's health resources. However, it is not clear why the French guidelines favour fibrates as the first choice of lipid lowering drug (LLD) rather than statins which are the first-line LLD elsewhere. Moreover, the UK has risen to the challenge of very high levels of CHD mortality and morbidity, with policies that focus on the efficiency and effectiveness of secondary care, with safety net targets for total and LDL-cholesterol, rather than seeking to widen action in this disease area into the asymptomatic or undiagnosed population and adopt best current practice in cholesterol targets.

It is noteworthy, for example, that in 2002 when the British Treasury published a review of the future funding needs of the National Health Service (NHS)⁷, that pointed to much more widespread use of statins, the Department of Health responded very promptly with a proposal to make low-dose simvastatin and several other leading drugs available for private purchase without prescription. The UK faces a particularly difficult policy challenge. Amongst men, ischaemic heart disease mortality, as a proportion of all

cause mortality below the age of 75 years, is amongst the worst in the enlarged European Union (EU), despite falling significantly between 1990 and 2000⁸.

During the Irish Presidency of the European Union in 2004, the Irish government hosted a "consensus" summit on heart health, and the subsequent Council of EU Health Ministers identified CVD as a major threat to public health in the European Union, calling for the European Commission to incorporate this into its programme of work. Since then, as part of the "Lisbon Strategy", the focus of EU policy has shifted from avoidable mortality to the promotion of healthy living, as part of the EU's ambitions for its global competitiveness. As part of this strategy, the EU must tackle rising levels of CVD-related ill health and disability in the population, which are offsetting many of the gains that have been made from falling CVD death rates.

However, many effective measures to tackle CVD are not implemented. The EUROASPIRE II study found that there were still considerable opportunities in Europe to reduce the risk of recurrent CHD through lifestyle changes, rigorous control of other risk factors, and more effective use of proven drug therapies⁹. Moreover, European physicians rarely screen family members of patients with premature CHD for cardiac risk factors. General lifestyle advice or active treatment for these risk factors are also rarely given¹⁰.

Clinical practice guidelines could play an important part in the dissemination and application of existing knowledge, and could potentially be a useful tool for tackling health inequalities in the newly enlarged European Union. Therefore, there are several lessons to learn from the experience of those who develop, implement and evaluate them¹¹. This review of

10 countries within the region not only focuses on guidelines for LDL-cholesterol management, but provides a useful insight into the extent in which European countries have applied knowledge in developing practice guidelines. It raises questions, however, that only member states themselves can answer, to explain the variations in practice that are evident even where there exist similar burdens of disease and levels of income. These answers are rooted in the traditions and practices of individual health systems, including the ways in which total health spending is shared between the state and households, in pharmaceutical reimbursement policies, and in incentive systems for clinicians.

Introduction

Cholesterol Guidelines: Cause for Concern?

Two main forms of cholesterol are generated in the human body. The most relevant to our study is low-density-lipoprotein cholesterol (LDL-C). This is often known as “bad” cholesterol because it can build up in the artery walls, causing them to narrow. The World Health Organization (WHO) believes that 60% of coronary heart disease and 40% of strokes are due to elevated cholesterol levels¹². Reducing LDL-C has long been the primary target of cholesterol policy and this remains the case today. The second form of cholesterol is high-density lipoprotein (HDL-C), known as “good” cholesterol due to its role in taking excess cholesterol away from the arteries.

The cholesterol threat to health has grown out of dietary changes in developed countries, with increasing consumption of saturated fats, to which the human body has been unable to fully adapt¹³. Steps to reduce bad cholesterol, firstly through dietary and lifestyle changes, and subsequently through drug therapy, are proven to be effective in tackling the increasing burden of cardiovascular disease (CVD), particularly coronary heart disease (CHD)¹⁴.

The annual financial cost of CVD in the European Union has been calculated to exceed €169 billion, the majority of which consists of the cost of treatment; primarily the cost of hospitalisation¹⁵, plus the economic costs from CVD as a leading cause of disability¹⁶. It is not surprising, therefore, that when the Council of Ministers of the EU met in Cork in 2004; they called on the European Commission to identify best practice guidelines in CVD prevention as part of a new programme to promote public health in Europe.

When the eight member societiesⁱ represented by the Third European Joint Taskforce on CVD Prevention published their new guidelines¹⁷ in 2003 it made it clear that they should be adapted to local circumstances. The Taskforce described the new guidelines as:

“a framework in which all necessary adaptations can be made in order to reflect different political, economic, social and medical circumstances”¹⁸

This survey of 10 European countriesⁱⁱ raises important questions as to whether the countries of Europe have achieved this ambition during the subsequent four years. There appears to be only limited evidence of the 2003 framework being widely used in practice. Furthermore, studies have shown a widespread failure to treat patients to goal, and this report shows once again that there can be a chasm between professional standards of best practice, reflected in professional guidelines, and guidelines written or influenced by European governments.

The rising European challenge of cholesterol as a risk factor for CVD is clear, yet the variations in practice have no obvious clinical explanation. The variations in local guidance give particular cause for concern in the context of consistent failures to achieve cholesterol targets. The EUROASPIRE II study, for example, found that only 51% of patients on lipid lowering therapy were achieving the treatment goals of the European guidelines¹⁹. The REALITY study found even lower levels of achievement²⁰. This study shows that, at least in part, this failure to achieve widely-accept-

ed treatment goals and the growing toll of CVD-related ill health may in part be due to confusion in the use of risk assessment tools to identify patients for intervention and the targets they need to reach. In contrast to the NCEP (ATP)IIIⁱⁱⁱ standards in the US the lack of clarity on these issues in Europe has created a lottery of patient care. This “treatment gap”²¹ between good evidence-based clinical practice and European clinical reality may widen further if, as expected, the existing European guidelines are revised to expand their scope, in terms of the inclusion of a wider range of asymptomatic patients or elderly patients, and applying more aggressive targets in response to the latest evidence on the management of cholesterol in CVD prevention and treatment.

This study was completed shortly before the publication of revised guidance from the Fourth European Joint Taskforce, which is expected to be released at the 2007 Congress of the European Society of Cardiology (ESC).

ⁱ European Association for the Study of Diabetes (ASD), International Diabetes Federation Europe (IDF-Europe), European Atherosclerosis Society (EAS), European Heart Network (EHN), European Society of Cardiology (ESC), European Society of Hypertension (ESH), International Society of Behavioural Medicine (ISBM), and European Society of General Practice/Family Medicine (ESGP/FM)

ⁱⁱ Austria, Finland, France, Germany, Italy, Norway, Slovenia, Spain, Sweden, United Kingdom

ⁱⁱⁱ National Cholesterol Education Program (Adult Treatment Panel) III; 2001 (updated 2004)

Executive Summary^{iv}

Variations in Risk Assessment

The Framingham Equation has provided a widely-used basis for CHD risk assessment. Its development followed the Framingham study in the USA, between 1948 and 1951, which identified elevated blood pressure, elevated cholesterol, and smoking as the three major risk factors for CHD. Subsequent studies built on this early work in preventative cardiology, and various types of Framingham Equation are still widely used as risk assessment tools.

A new model for risk assessment using a simple chart known as “SCORE”^v in place of a Framingham Equation was at the core of the 2003 European guidelines. SCORE charts show the patient’s risk of any fatal atherosclerotic event within a 10 year period, in contrast to the Framingham Equation’s calculation of a patient’s current 10-year risk of a fatal *or* non-fatal coronary event. If reliable mortality data is available, then the new approach can provide a risk chart specific to each country or region. Additionally, the new system allows the physician to readily predict even a young patient’s risk up until the age of 60, rather than just their current 10-year risk, thus assisting with early preventative intervention on diet and lifestyle.

In practice, a wide variety of risk assessment schemes are still in use across Europe, and the switch to the SCORE system in the European guidelines appears to have created considerable confusion. All of the schemes assess an individual’s percentage risk over a ten year period of suffering a cardiovascular event. In the case of SCORE this is calculated as the risk of a fatal CVD event, whilst other systems usually calculate the risk of any CVD event. Some guideline bodies across the sample European countries have adopted a form of SCORE, but the focus on fatal incidents, and the resulting use of a 5 percent 10-

year risk level for intervention (compared to 15 or 20 percent in schemes that include non-fatal CVD events) can appear to be a low risk to many patients. This has provided important grounds for opposition to the use of SCORE. Instead, various formal and informal equations for calculating the risk of any CVD event, based on a range of risk factors, remain widely used. Sometimes, as in France and the United Kingdom, the choice of risk assessment system is largely left to the individual physician. The Sickness Funds in Austria recommend the use of a New Zealand scale (a Framingham Equation) for adults over 40 years of age. The charts from the Joint British Societies, known as “JBS”, were rejected by the National Health Service (NHS) in England in November 2006, but adopted by the national guidelines programme (PNLG) in Italy.

The European guidelines include all people with Type 2 diabetes and those Type 1 diabetics with microalbuminuria in the “high risk” group. This inclusion is regardless of the presence of other risk factors for CVD. In most of the guidelines included in our survey, diabetes is considered to be one of several risk factors in a patient’s risk assessment, rather than an independent factor that automatically puts a patient at high risk of CVD. With rising obesity and an associated rise in Type 2 diabetes this makes

a significant difference to the number of people targeted for aggressive CVD prevention.

Variations in Cholesterol Testing

All forms of risk assessment require cholesterol testing. For primary prevention the testing of asymptomatic patients is necessary, and the European guidelines recommend specifically that relatives of anyone with premature CHD should be tested. The survey found, however, that testing can be a rarity in many European countries, particularly for the primary prevention of CVD.

Out of the 10 countries in the survey we found routine testing of all adults in just three: Austria, Germany, and Slovenia. In France too, it is recommended that every adult should be tested on a five-yearly basis, but no system exists to deliver this. In the three countries that we were told do undertake preventative screening, the intervals reduce with age or the onset of CVD and other conditions.

For secondary prevention testing is usually covered by the relevant guidelines. One particular anomaly that we found was that the contract for GPs in England can remunerate a physician more than £1400 (€2000) for cholesterol testing patients with established CVD or diabetes, but nothing at all for testing asymptomatic individuals, regardless of their risk profile.

^{iv} Throughout this paper cholesterol levels measured in mg/dl have been converted to mmol/l, by multiplying by 0.02586. The result has been rounded to one decimal place. Descriptions of the two measurement systems are included in the Glossary

^v See Glossary for a list of technical terms and acronyms used in this paper

Variations in Targets

In the treatment of high risk patients the target for LDL cholesterol varies from <1.8mmol/l recommended in 2007 by Update Europe (an independent expert consensus group based in Austria) to <3.3mmol/l recommended by the Italian organisation guidelines.

Norway and the UK both use a target of <3mmol/l, which is the same as the optimal level in the *asymptomatic* population set by the European guidelines, and some 20 percent above the level of 2.5mmol/l recommended by the European guidelines in 2003 for high risk patients.

Targets for total cholesterol in high risk patients range from 4.1mmol/l, advised by the Austrian and German nutrition societies, to 5mmol/l in England, and compared to 4.5mmol/l in the current European guidelines.

Variations in Treatment

All 10 countries have recently focused on diet and lifestyle issues, often in response to reports of “obesity epidemics”, with a range of local and national initiatives on heart health. When it comes to pharmaceutical treatment, all but the French

AFSSAPS guidelines recommend statins as the first choice of lipid lowering drug (LLD), following interventions based on dietary and lifestyle advice. In contrast to every other country, the French guidance appears to be designed to limit the use of statins, in favour of cheaper fibrates. Additionally, the use of fibrates and resins as an alternative to a statin is widely supported in the various guidelines across Europe. Newer therapies, principally the cholesterol absorption inhibitor, ezetimibe, are endorsed as second line drug therapy by:

- Austrian Sickness Funds – in combination with a statin
- Current Care Board, Finland – if other drugs are unsuitable
- AFSSAPS, France – in combination with a statin or alone if a statin is not tolerated
- SLK, Norway – for patients with high total cholesterol
- Läkemedelsverket, Sweden – in combination with a statin

In several countries the recommendations extend to the use of niacin and nicotinic acids, phytosterols, and omega-3 fatty acids.

Conclusions

The Fourth European Joint Taskforce guidelines are due once again for review in 2007. In response to improving knowledge of the challenge presented by cholesterol and the therapeutic options to meet that challenge, this survey of 10 European countries highlights the dramatic variations between local responses. These variations exist at all levels; in risk assessment, screening, and treatment.

In the context of major concerns over demographic issues relating to ageing, obesity and diabetes, the neglect of any system for primary prevention in hypercholesterolaemia in some countries is surprising. Amongst patients who are identified and treated, lipid targets in some countries are more than 30 percent weaker than the standards set in the current European Guidelines, and more than 80 percent weaker than the level suggested in the latest American (NCEP ATP III) national guidance for the highest risk patients.

Methodology

This report is a pan-European review of clinical guidelines for the management of hypercholesterolaemia, using a sample of 10 countries: Austria; Finland; France; Germany; Italy; Norway; Slovenia; Spain; Sweden; and the United Kingdom. The review includes both official/governmental national and local guidelines, and professional guidelines.

Guideline data was gathered from contacts within each country, supplemented where necessary by additional desk-based research of online sources.

The second stage of the research consisted of a series of telephone interviews with a clinical expert from each of the countries. The interviewees were found through the leadership of national member organisations of the European Society of Cardiology and European Atherosclerosis Society, and then by local recommendation for their knowledge of the topic and English language skills. In several countries we were referred to governmental sources or medicines agencies. The interviews, therefore, produced both factual statements on guidelines, and individual subjective opinions on clinical practice. Two of the interviews^{vi} were

conducted by email in order to overcome linguistic difficulties. In some cases these interviews prompted further desk-based research, where the interviews had revealed gaps in the guideline data. We decided to treat the names of the interviewees as being confidential given that their individual comments would be readily identifiable, because we conducted one interview in each country. The limited number of interviews and use of a sample of European countries means that this research must be taken as a survey that is indicative of the current situation with regard to cholesterol guidelines, and not a comprehensive review of guidelines and clinical practice.

The section on “Future Challenges” draws both on the guidelines data, telephone interview results, and a literature search of

Medline and other online search engines, for documents published since 1 January 2000 using a combination of the following search terms:

“cholesterol; cholesterol management; cholesterol treatment; LDL; LDL-C; lipid(s); hypercholesterolemia; future; new; therapies.”

The project began in mid-March 2007, and the telephone interviews took place between Thursday 12th April and Friday 11th May. The text was completed on Thursday 24th May.

^{vi} Spain, Slovenia

Review of European Cholesterol Guidelines Risk Assessment

The Third European Joint Taskforce Guidelines²² recommend a SCORE^{vii} system to assess an asymptomatic and apparently healthy person’s total risk of a fatal CVD event in 10 years, with a range of preventative responses according to the level of risk identified. The new system was agreed to be of widespread applicability because it had been based on a large dataset of studies from across Europe. It produced separate charts for high and low-risk European countries, based on the ready availability of reliable CVD mortality data. Since its launch the European Society of Cardiology has gradually developed specific charts for each country, based on local mortality data, and launched an interactive web-based version.

The European guidelines authors also claimed that the SCORE charts produced an easily understandable tool that could be used by young adults currently at low risk, to enable them to make necessary lifestyle changes in order to avoid putting themselves at higher risk in future. The charts make it very simple to transfer an individual’s current blood pressure and cholesterol results into later age ranges, or between the smoker and non-smoker charts, to predict future risk levels and highlight the benefits of early diet and lifestyle changes.

Despite these apparent advantages of the new system, and the development of nationally-specific versions, our review of guidelines in the 10 countries of the study revealed continued reliance upon earlier and alternative methods of risk assessment. We were told, for example, that **Slovenia** had rejected SCORE for a variety of reasons, not least because it focuses on CVD mortality rather than quality of life with CVD, citing the inclusion of Belgium in the list of “low-risk” countries as evidence of its fallibility.

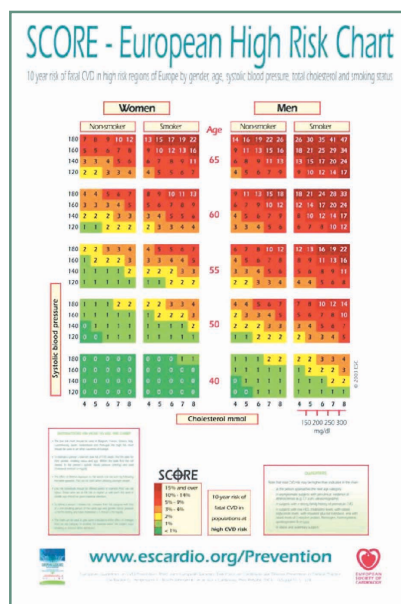
Variety of Risk Assessments

In several countries a variety of risk assessment systems operate according to the choice of the individual physician. In **Austria**, for example, the Sickness Funds recommend the use of the American Heart Association risk calculator for those aged

under 40, and a scale drawn from New Zealand for those aged 40 and over. In February 2007 Update Europe developed an “Expert Statement” which used risk factors including, for example, family history of CVD, or a diagnosis of diabetes and a Framingham Equation.

In **Finland** the Finnish Medical Society and the Current Care board both recommend the use of a SCORE system; in France no such system is specified, but doctors base their decisions on the *number* of risk factors, with a reduction in the total number if a patient’s HDL-C is lower than 1.6mmol/l. Both an adapted SCORE chart and the PROCAM chart are used in **Germany**, although the Lipid Liga recommends a different approach based on cholesterol levels and the presence of other risk factors.

Italy too has a wide variety of risk assessment tools in use. The Istituto Superiore di Sanita (ISS) recommends CUORE, whilst the national guidelines programme (PNLG) proposes the most recent chart from the Joint British Societies, and physicians also make use of SCORE and other risk charts. In **Norway** the Medicines Agency and the widely-used Physician’s Handbook both use the Framingham Equation, and the national Medical Association has produced a risk chart using the Framingham Equation and national epidemiological data. The **Slovenian** health system has retained the system from the older (1998) second



European set of Guidelines, based on a Framingham Equation, although the national authorities are participating in the European Society’s development of a SCORE chart specific to the country. The Spanish interdisciplinary committee for CVD prevention is using the European SCORE charts, adapted for **Spain** as a “low risk” country, although it is unclear whether these are used in practice. The principal source of guidelines in **Sweden** is the medical products agency, which has maintained use of a Framingham Equation, but with acknowledgement that SCORE can be used.

^{vii} Systematic Coronary Risk Evaluation

Variety of Thresholds for Intervention

The European guidelines suggest a threshold in selecting patients for medical intervention who have not yet suffered a CVD event set at a 5 percent risk of a fatal CVD event over a 10 year period. Thresholds vary widely across Europe, but all seem to have retained a threshold based on the risk of a CVD event, including a non-fatal myocardial infarction, rather than the ESC recommendation of using the risk of a fatal event.

In **Austria**, where a variety of guidelines are in use, the social health insurance system suggests a threshold of a “15 percent risk of a CVD event”, and in the similarly diverse situation of **Germany**, the Lipid Liga defines high risk as being a “20 percent risk”, which is also the level at which treatment is reimbursed in **Italy** by the National Health System. A 20 percent risk is most commonly applied in **Norway**, stipulated in **Sweden**, and applied through the PRODIGY decision-support system in **England**. Several of the other guideline issuing organisations do not stipulate such a threshold. Most guidelines make some inclusion for diabetes as an independent factor putting a patient at high risk of CVD, particularly when combined with hypertension.

Strangely, in the **United Kingdom**, public health policy contained within “National Service Frameworks” for England & Wales, and a public health policy paper for Scotland set national targets based on death rates. However guidance to the NHS uses a risk assessment system based on the probability of both fatal and non-fatal events, rather than the SCORE system based only on probability of a fatal event.

More recently joint specialist societies in Britain have produced revised guidelines²³, with new charts for risk assessment. These use the ratio of HDL-C to total cholesterol on one axis and systolic blood pressure on the other, but similarly with the SCORE

charts they provide different charts for different age groups and for smokers and non-smokers. Most significantly, these new guidelines included not only those assessed to have a 10 year risk of a CVD incident ≥ 20 percent and those with established CVD, but also *all* people with diabetes, *all* people with a systolic blood pressure ≥ 160 mmHg or diastolic ≥ 100 mmHg, and *all* people with a ratio of total cholesterol to HDL-cholesterol ≥ 6 . For the National Health System (NHS), this would represent a significant expansion of the population prioritised for medical intervention if it was put into clinical practice.

Variations within Countries

Where there were more than one set of guidelines included in our survey from a single country, this produced some interesting variations that highlight the tension between the clinical aspirations of professionals involved in CVD care and state authorities. In **France**, for example, the state medicines agency AFSSAPS provides a general limit for optimal LDL-C in the population of 5.7mmol/l, whereas the independent Doctissimo suggests a limit of 4.1mmol/l. In the **United Kingdom**, as mentioned above, risk assessment standards and targets are substantially weaker in official government guidance than in the guidance from the Joint British Societies.

Screening

The European guidance makes it clear that while patients with established cardiovascular disease (CVD) are the first medical priority, the second priority is asymptomatic individuals who are at high risk, whether this is due to the presence of multiple risk factors, markedly high levels of a single risk factor (including LDL cholesterol ≥ 6 mmol/l), or diabetes. Additionally, the guidelines call for CVD screening of all close relatives of patients with premature coronary heart disease,

and for ongoing annual cholesterol testing for any patient who manages to reduce their CVD risk below the 5%/10 year level after diet and lifestyle changes.

In addition to “traditional risk factors” such as blood cholesterol measurements and systolic blood pressure, the guidelines advocate new imaging methods to detect asymptomatic individuals who might be at high risk. They suggest that MRI and CT scanning and ultrasound measurement have a role in delivering precision in risk assessment. Despite these new methods explained by the European Taskforce four years ago, our survey revealed that most European countries still have far to go even in making use of traditional blood tests.

Limited routine screening

For three of the ten countries in our sample we were told that routine, regular cholesterol testing of asymptomatic adults takes place: **Austria**, **Germany**, and **Slovenia**.

In **France** every adult *should* be tested every five years, but the country lacks a systematic method of achieving this, so that screening is usually limited to patients who attend a general practitioner. The most extensive screening system within the three countries in which regular screening was reported, appears to be in **Austria**, where the social insurance funds reimburse screening for all enrollees over 18 years of age every three years, and increasing in frequency to every two years from the age of 40 onwards.

In February 2007 the **Italian** government produced a public health policy document on obesity and healthy lifestyles which, amongst other plans, stated the ambition to increase the number of adults having regular checks of their blood pressure and cholesterol, although the details of the plan are yet to be developed.

Testing high risk patients

For patients who are *found* to be at high risk, most of the countries in the sample appear to provide regular cholesterol testing, although the lack of screening of the asymptomatic population means that many individuals at high risk will fall outside this category.

In the **United Kingdom** the 2003 revision of the General Medical Services contract included a new “Quality and Outcomes Framework” (QOF) that set out a list of 76 indicators in the “clinical domain” (with a similar number of non-clinical indicators) listing items of service for which primary care providers would gain points, up to a maximum of 550. For these points they would receive additional reimbursement. The current rate of reimbursement is around £120 per point, and in 2005-6 providers on average achieved around 97 percent of this maximum²⁴. Primary prevention of coronary heart disease is absent from the list, but the sections on secondary prevention in patients with coronary heart disease, stroke and transient ischaemic attacks, and diabetes offer a cumulative total of 12 points for the recording of a total cholesterol measurement in these patients within the preceding 15 month period. Providers, therefore, have a very strong incentive, worth as much as £1440, to provide cholesterol testing for secondary prevention in patients who have been diagnosed with one or more of the listed conditions, but no incentive to do so for primary prevention or in undiagnosed patients.

With the exception of **Austria, Germany and Slovenia** which we were informed have routine and widespread screening of

their adult populations, we found no readily available evidence to suggest that any country specifically screens close relatives of patients with premature coronary heart disease, as recommended in the European guidelines. Specific investigation of this would be required to determine whether this apparent absence of screening prevails in local clinical practice.

Lipid Targets

The European guidelines from 2003 state that:

*“In general total plasma cholesterol should be below 5mmol/l and LDL cholesterol should be below 3mmol/l. For patients with clinically established CVD and patients with diabetes the treatment goals should be lower: total cholesterol <4.5mmol/l and LDL cholesterol <2.5mmol/l”.*²⁵

In the United States the Third Report of the US Expert Panel of the National Cholesterol Education Program, known as NCEP (ATP) III^{viii}, guidance from 2001 applies a general LDL-C goal of around 2.6mmol/l for high risk patients, 3.4mmol/l for those at moderate risk, and 4.1mmol/l more generally. Additionally, in a 2004 update, NCEP set an optional target of around 1.8mmol/l for the highest risk patients. A movement towards more aggressive targets has followed the publication of extensive clinical trials data, such as the TNT^{ix} study, on the benefits of doing so.

Recent guidance in Europe includes the revised advice from the Joint British Societies “JBS2”, issued in December 2005²⁶. This applies a general recommen-

dation of 4mmol/l for total cholesterol and 2mmol/l for LDL-cholesterol, although with “audit standards” set at the same levels as the existing European guidelines. In November 2006 the Department of Health in England took the unprecedented step of issuing a statement²⁷ to clarify that doctors should not follow this, but that they should await the December 2007 review of guidance on statin prescribing from the National Institute for Health & Clinical Excellence (NICE).

The JBS2 Guidance has therefore been excluded from the tables that follow, as it is not in use. Currently the NHS applies a target of either a 30% reduction in cholesterol, or total cholesterol \leq 5mmol/l and LDL \leq 3mmol/l, whichever amounts to the greater reduction from the untreated level.

Lagging targets

By the time of their publication, the European standards already lagged behind those in the May 2001 NCEP-ATP III. This put a renewed focus on LDL cholesterol and established an optional target for very high risk patients of around 2.6mmol/l or less. This was updated in 2004²⁸ following analysis of five major clinical trials. The update provided clinical options for the use of more aggressive targets for patients with a moderate or high risk of CVD (approx. 2.6mmol/l and 1.8mmol/l respectively); the inclusion of diabetics without CVD in the high risk category (because of the serious consequences for them if they do develop CVD); and the extension of intervention to older age groups. The new NCEP (ATP) III target for LDL-C in the highest risk patients was set at 70mg/dl, equivalent to about 1.8mmol/l.

^{viii} National Cholesterol Education Program – Adult Treatment Panel III
^{ix} Treating to New Targets

If 5mmol/l is taken as the current European guideline ambition for optimal total cholesterol, and 3mmol/l for LDL-C, in those at lower levels of CVD risk the comparable standards used within our sample countries for organisations that we were told do not simply recommend the ESC guidance were as set out in the table (Figure 2):

The data from our survey also showed significant variations in treatment targets for those patients who are identified to be at risk. The European guidelines set treatment goals for high risk patients, meaning those with a 10 year risk of cardiovascular death ≥ 5 percent, with very high single risk factors (e.g. LDL-C ≥ 6 mmol/l), or diabetes with microalbuminuria.

For these patients the European guideline targets are <4.5 mmol/l for total cholesterol and <2.5 mmol/l for LDL-C, although they also make it clear that these targets should not be sought as treatment goals in patients with very high untreated levels of cholesterol because, at the time, the high doses of therapy that would be required to make such a large difference had not been documented in data from relevant clinical trials. It is for this reason that guidelines in some countries, such as the United Kingdom and Norway (DNL), give an alternative target of a percentage reduction in cholesterol.

Figure 2

Country		Optimal Cholesterol (<mmol/l) ^x	
		Total	LDL-C
ESC Guidelines 2003		5.0	3.0
Austria	Update Europe	n/a	4.1
	ÖGE & DGE	5.1	3.4
	OEKG	5.0	3.0
Finland	Current Care	5.0	3.0
	Suomen Sydänliitto	5.0	3.0
	Duodecim	5.0	3.0
France	AFSSAPS	6.5	5.7
	Doctissimo	5.2 – 6.5	4.1
Germany	DGK	5.2	4.9
	Lipid Liga	5.2	4.1
Italy	ISS	5.2	n/a
	SIMG	5.2	n/a
	PNLG	5.2	4.1
Norway	SLK	5.0	3.0
Slovenia	National Forum	n/a	n/a
Spain	CEIPC	5.2	3.4
	FEC	5.2	2.6
Sweden	Läkemedelsverket	5.0	3.0
UK	Government	5.0	3.0

Figure 3

Country		Cholesterol Target for High Risk Patients (<mmol/l) ^x	
		Total	LDL-C
European Guidelines 2003		4.5	2.5
Austria	Update Europe	n/a	1.8 /2.6
	ÖGE & DGE	4.1	2.6
	OEKG	4.5	2.5
Finland	Current Care	n/a	n/a
	Suomen Sydänliitto	n/a	n/a
	Duodecim	4.5	2.5
France	AFSSAPS	n/a	2.6
Germany	DGK	n/a	2.6
Italy	ISS	5.2	n/a
	SIMG	5.2	3.4
	PNLG	5.2	3.4
Norway	SLK	5.0	3.0
Slovenia	National Forum	n/a	2.5
Spain	CEIPC	4.5	2.5
Sweden	Läkemedelsverket	4.5	2.5
UK	Government	5.0	3.0

^x The presence of many odd numbers in the table is due to the conversion of mg/dl measures to mmol/l. For example, 130mg/dl has become 3.33 mmol/l and 250mg/dl has become 6.41mmol/l

Therapies: Lifestyle Changes

All of the guidelines in our survey highlight lifestyle changes as the first approach to reducing the risks of cardiovascular disease. The European guidance notes, however, that:

“Recent surveys suggest a serious gap between recommendations for behavioural change and the advice actually provided by physicians in routine clinical practice.”²⁹

Further to this observation the guidance sets out nine “strategic steps” to enhance the effectiveness of behavioural counselling, with specific recommendations on:

- Stopping smoking
- Increasing physical activity
- Management of other risk factors:
 - overweight and obesity
 - blood pressure
 - plasma lipids
 - metabolic syndrome

It is notable that in **Austria** and **Germany** the national nutrition societies appear to be mainstream players in the development of clinical guidelines on cardiovascular disease. Several countries have developed new health promotion policies, particularly following the general rise in obesity and diabetes. In **Austria** the City of Vienna launched an awareness campaign on heart health, “Ein Herz für Wien” (A Heart for Vienna), and in **Finland** the heart association Suomen Sydänliito has developed an action plan to improve the heart health of the Finnish population between 2005 and 2011. The Government of **France** sponsors a national programme running from 2003 to 2008 on nutrition, with the specific aim of reducing the average cholesterol level in the population by five percent. In February 2007 the **Italian** government issued a document under the title of “Gaining Health” (Guadagnare Salute); an interdepartmen-

tal action plan intended to promote healthy lifestyles and prevent obesity. In June 2007 Madrid is hosting **Spain’s** first conference for Health Promotion and Prevention, including CVD as a major topic. In **Slovenia** the Government adopted a nutrition policy for the period 2005 to 2010, which also emphasises the importance of exercise within a healthy lifestyle. Several years earlier CINDI^{xiii} Slovenia adapted the World Health Organization (WHO) Food Based Diet Guidelines to the country. In the **United Kingdom**, in addition to public health white papers in each of the countries of the UK, the Quality and Outcomes Framework (QOF) negotiated with the 2003 general medical services contract to reward GPs for giving smoking cessation advice to people with coronary heart disease or diabetes, or who have experienced a stroke or transient ischaemic attack. The NHS National Service Framework (NSF) on Coronary Heart Disease, published in 2000, is heavily focused on treatment issues, with specific actions on prevention largely limited to smoking cessation policies.

Therapies: Pharmaceutical

The European guidelines recommend that if, after intensive dietary and lifestyle advice, a patient’s 10 year CVD risk remains ≥ 5 per cent, or will become so if projected to age 60, then lipid lowering drug (LLD) therapy should be considered. (See Figure 4).

The **Austrian** Sickness Funds recommend LLDs if a patient with a 10 year risk of CVD ≥ 15 per cent fails to reduce their risk after three to six months of lifestyle interventions. More specifically, the Update Europe Expert Statement of February 2007 identifies statins as the first choice for drug therapy, which can possibly be supplemented with a resin, or replaced by a statin-ezetimibe combination. For patients with raised triglyceride levels, fibrates and nicotinic acid are also suggested.

The Current Care Board in **Finland** recommends statins as first-line drug therapy, although Duodecim makes no specific recommendation, but suggests that LLDs should be used if target cholesterol levels are not reached within one to two months in symptomatic patients and

Figure 4

Common Lipid Lowering Drugs (LLD)	Purpose
Ezetimibe	Prevents the absorption of cholesterol in the intestine
Fibrates	Mainly used in the treatment of high levels of triglyceride
Nicotinic Acid (Vitamin B ₃ /Niacin)	A lipoprotein synthesis inhibitor, that reduces the body’s ability to synthesise cholesterol
Resins	“Bile acid-binders”. That causes bile acids to be excreted from the intestine and not reabsorbed to be used in the production of cholesterol.
Statins	Drugs that interrupt the production of LDL-C in the liver

^{xiii}WHO Countrywide Integrated Non-communicable Diseases Intervention

Sources: American Heart Association; BMJ Best Treatments; Merck Manual; Patient UK

within two to three months for asymptomatic patients. The Current Care Board also suggests that fibrates can be used in male patients, and resins together with a statin, or ezetimibe, if other medications are unsuitable.

France is notable for its ongoing reliance upon locally manufactured and heavily marketed fibrates, and the policies of the relevant agency, AFSSAPS, put considerable pressure on doctors to prescribe fibrates and limit the “overuse” of statins. AFSSAPS does, however, recommend that drug therapy is initiated immediately for any patient with a history of CVD. In asymptomatic but “at risk” patients drug therapy should be started after three months of diet and lifestyle intervention if the risk has not been reduced. AFSSAPS lists statins as one of the potential LLDs available, but recommends fibrates for the treatment of endogenous hypercholesterolaemia, and advises that fibrates should not be combined. Additionally, the guidance from AFSSAPS states that resins can be prescribed with a statin, or on their own if the patient cannot tolerate a statin. It also advises that ezetimibe, if it is prescribed, should be in combination with a statin or alone if a statin is inappropriate.

The French guidance also promotes nicotinic acid in combination with a statin to boost HDL-cholesterol. In the case of patients with diabetes, with or without hypercholesterolaemia, the AFSSAPS guidance recommends the prescription of fibrates.

The DGK guidance for **Germany** recommends the use of LLDs if non-medical behavioural change has not reduced LDL-cholesterol below the suggested levels. Statins are listed as the first-choice therapy, and the Lipid Liga guidance says that if statins prove insufficient for a patient to reach the target LDL-C level then physicians should prescribe ezetimibe.

For patients with high triglycerides, Lipid Liga also suggest that fibrates, nicotinic acid, or fish oil derivatives might be used.

The PNLG and SIMG guidelines for **Italy** list statins as first choice therapy, after lifestyle changes have been tried. The PNLG also indicates that for patients with high triglycerides, normal LDL-C, or normal or low HDL-C, the prescription of niacin and fibrates is an option. SIMG also lists resins and fibrates if statins have proven inadequate.

Both the SLK and DNL in **Norway** propose statins as first choice therapy, with the former listing resins and ezetimibe as options when patients have high total cholesterol, and fibrates and omega-3 fatty acids when patients have high LDL-C. Patients with high triglycerides can also be prescribed fibrates, omega-3 fatty acids and/or nicotinic acid.

The FEC in **Spain** suggests statins as first line therapy, with the reimbursement system promoting generic simvastatin, with options for the use of resins, fibrates, nicotinic acids and phytosterols. In **Sweden** the guidance from Läkemedelsverket, also starts with statins, with an optional combination with a resin, or with ezetimibe. Patients with high triglycerides can be prescribed fibric acid, niacin, or omega-3 fatty acids.

Throughout all countries of the **United Kingdom** guidelines recommend statins as the first choice. There is an apparent conflict between the NICE guidance and the NSF on coronary heart disease inasmuch as the former recommends the use of statins for patients with a 20 percent risk of CVD over 10 years, and the latter uses a 30 percent threshold. PRODIGY indicates that GPs should prescribe statins for patients whose total cholesterol to HDL-cholesterol ratio is six or more. The SIGN (**Scotland**) and JBS2 recommend other LLDs for patients who cannot toler-

ate statins; resins or a statin-ezetimibe combination. The Scottish Medicines Consortium also lists ezetimibe as a treatment option, but the NHS in England awaits NICE guidance on this, scheduled for publication in July 2007. In June 2007 NICE issued revised guidance on secondary prevention of heart attack that included a recommendation that some patients should be offered 1g daily of omega-3-acid ethyl esters for up to 4 years³⁰.

Diabetes and Cholesterol

The European guidelines identify Type 2 (“adult onset” and non-insulin dependent) diabetics and those Type 1 (insulin dependent) diabetics with microalbuminuria as medical priorities even if they are free of symptoms of CVD and regardless of the presence of other risk factors. The guidance places these people in the high risk category. In terms of treatment targets, it argues in favour of aiming to achieve a systolic blood pressure below 140mmHg and total cholesterol below 4.5mmol/l and LDL-C below 2.5mmol/l, as for symptomatic and other high risk groups, whilst emphasising the particular importance of diet and lifestyle change in diabetics. As mentioned earlier, the US NCEP(ATP) III guidance was updated in 2004 following clinical trial evidence to include all diabetics in the priority group, and this approach was repeated by the JBS2 professional guidance published in the United Kingdom a year later.

All of the guidelines in our survey include diabetes as a risk factor, although diabetes alone will not usually put an asymptomatic individual in the high risk group warranting intervention on blood lipids. Nevertheless, most do provide more stringent targets for those diabetics who are assessed to be at risk.

Unsurprisingly, as the most recent of the guidelines in our small survey, Update Europe in **Austria** provides the most

rigorous target for LDL-C in diabetics of less than 1.8mmol/l, the same as NCEP (ATP) III, while most others set a target of around 2.6mmol/l, similar to the current European target. The weakest targets appear to be in the NHS in the **United Kingdom** which applies the same formula to all patients, whether diabetic or in any other risk group, with a target LDL-C below or equal to 3mmol/l.

Guideline Reviews

Several of the major guideline-issuing organisations within the sample European countries recommend that physicians follow the European guidelines, and can be expected to do so again when the European guidelines are revised in 2007. We were informed, for example, that this has been the case with the OEKG in **Austria**, and the Current Care Board in **Finland**.

On the other hand we were also told that in Norway the **NCS** reviewed and rejected the European guidelines, having decided that they were inappropriate for the Norwegian population.

Many guidelines are developed in a collaborative exercise across the range of related medical societies, often led by state agencies. The state has a dominant role in this

in France, Italy, Norway, Slovenia, Sweden, and throughout the United Kingdom. In Sweden and England the agencies that deal with guidelines on medicines play an important role, although this tends not to cover the preventative and risk assessment aspects of cholesterol guidance. In the case of England the latter is largely determined by the remuneration system for primary care providers, particularly the recurrent contractual negotiations between the state and the British Medical Association.

Several have a formal process based on expert committees, often including a proportion of primary care prescribers. We were told that this is particularly the case in France, and that the Directorate for Health and Social Affairs in Norway is following a similar approach. Cardiology societies and other organisations independent of the state tend to concentrate discussion within expert groups of specialists. The 2007 Update Europe guidelines for Austria were the result of a process involving 30 experts.

The editors of the SLK guidelines in Norway use a team of experts in their periodic reviews of the available evidence, requiring each item of research evidence to be reviewed by three or more experts.

In Slovenia guidelines are developed by working groups of the national cardiology society, although they are also working with the European society on the development of a SCORE chart specific to Slovenia.

Several organisations are developing or revising guidelines on cholesterol in the light of recent evidence from clinical trials.

- Lipid Liga in Germany is expected to adopt the NCEP (ATP) III guidance, but with the exclusion of diabetes as an independent risk factor, although the process for this review was unclear and apparently unsystematic.
- The Directorate for Health and Social Affairs in Norway is expected to complete guidelines in August 2007.
- The National Forum on CVD Prevention in Slovenia is expected to publish its new guidance at the end of 2007, for adoption at the cardiology society's plenary in the Spring of 2008.
- In England, NICE is scheduled to publish guidelines for the NHS on ezetimibe in July 2007, followed around six months later by revised guidance on statins.

Future Challenges

It is now more than 10 years since statins came into widespread use in the treatment of cholesterol, and recent years have brought significant new study evidence.

Demographic change

The health threat from cholesterol has been increasing, as part of the ageing and increasing obesity of European society. Gains from the decline in smoking are being offset by these factors. The association with diabetes, which was recognized in the development of the 2003 third set of European guidelines, is having increasing significance in CVD prevention and care. It is predicted that the diabetic population of Europe will increase from 23 million in 2000 to 30 million in 2020³¹.

Slow change in clinical practice

Despite these worrying demographic trends the full potential of lipid lowering therapies has not been realised, due to the slow pace of change in many European countries. The EUROASPIRE II study in 1999-2000³², for example, found that on average just 55.3 percent of CHD patients were taking a statin, with the rate ranging from 38.8 percent in the Czech Republic to 75.1 percent in the Netherlands. The MRC/HPS study found that the use of 40mg simvastatin, with two-thirds compliance, could reduce the rate of first vascular events by about one-third³³.

Declining CVD death rates, but increasing disability

By 2020 ischaemic heart disease will be the leading cause of disability in Europe³⁴. Identifying individuals at risk and treating them to an effective target is, therefore, of considerable economic importance as well as being important to the patients themselves³⁵.

New treatment regimes

The MRC/HPS study demonstrated the potential benefits of statin therapy, and particularly the benefits of reducing cholesterol levels amongst diabetics and

amongst high-risk patients with untreated cholesterol levels that meet the “optimal” levels in most current guidelines. The use of high dose statins and the pursuit of more aggressive targets were investigated in the PROVE-IT³⁶ and TNT studies³⁷. The PROVE-IT study reported in April 2004 and the TNT study reported in March 2005. PROVE-IT showed that amongst patients who had recently suffered an acute coronary syndrome “*an intensive lipid-lowering statin regimen provides greater protection against death or major cardiovascular events than does a standard regimen*”³⁸, and TNT demonstrated “*substantial clinical benefit*”³⁹ in using high dose atorvastatin to reduce LDL-cholesterol below 2.6mmol/l in patients with stable CHD, including patients with diabetes⁴⁰.

Tougher targets for high risk patients

On the basis of the emerging evidence on more aggressive targets, principally PROVE-IT and HPS, the third set of NCEP(ATP) guidelines provided an optional target for very high risk patients of 1.8mmol/l, even if their untreated levels were already below 2.6mmol/l. It is highly probable, therefore, that future European guidelines will follow suit and apply more aggressive targets for high risk patients.

During the study we were told that Lipid Liga, in Germany, will probably follow the NCEP targets in its forthcoming guidance, and we were told that the NCEP(ATP)III guidance is taken into account in current Spanish practice. In England the JBS2 guidance of 2005 set a new goal of LDL-cholesterol ≤ 2 mmol/l, although this is not being followed by the NHS, which retains a target some 30 percent higher than this. There is a widespread expectation that the more aggressive targets will eventually

find their way into NHS contracts and guidance⁴¹, with some now recommending LDL-cholesterol targets as low as 1.3mmol/l for high risk patients⁴¹. However, future guidelines may combine more aggressive targets for high risk patients with recommendations for combination therapies, and a renewed focus on total cardiovascular health and preventative therapy⁴³. This is the direction in which NCEP (ATP)III has gone in the US. Hypertension followed a similar path, with considerable debate over how low to go and whether to treat elderly patients, but with the emergence of aggressive targets for high risk patients and an increase in the number of drugs used in each patient in order to reach treatment goals⁴⁴.

Although therapies, old and new, for cholesterol management have been shown to be effective^{45 46}, findings from the REALITY study⁴⁷ suggest that as few as 41% of patients are reaching their LDL-C goals. The REALITY study suggests that this may be due to physician fear of high dose statins with only 16% of patients across the European countries surveyed having had their statin dosage increased when they failed to reach LDL-C goals with treatment.

Combination therapy using statins and other therapies may be required to help patients reach their LDL-C goals. Several of the national guidelines have included combination therapy with ezetimibe as a recommended therapeutic option. Ezetimibe is the first in a new class of cholesterol-lowering agents called cholesterol absorption inhibitors⁴⁸ that can be used with statins or as monotherapy to inhibit the absorption of biliary and dietary cholesterol in the intestine.

Additionally, there are several other new approaches in development that are also showing considerable promise.

Boosting HDL-Cholesterol: The Scandinavian Simvastatin Survival Study, known as “4S” showed low HDL-cholesterol to be a strong predictor of CHD. The HPS2-THRIVE study, launched in May 2006, is currently testing a new drug in combination with niacin (to overcome the side-effects of niacin) as a means to boost HDL-cholesterol. There is also considerable clinical interest in targeting the cholesterol ester transfer protein (CETP) as a means of raising HDL-cholesterol, and Barter and Kastelein reported on three drug trials in this area: a vaccine that binds and inhibits CETP; a drug that causes an irreversible binding to CETP, and a selective inhibitor of CETP. Although phase III trials on the CETP inhibitor, torcetrapib, have been halted due to increased mortality in patients receiving the combination compared to those receiving atorvastatin alone⁴⁹ further results from clinical trials

on other compounds in this new class are expected during 2007⁵⁰.

Other areas of investigation include the microsomal triglyceride transfer protein (MTP), which is thought to have a potent role, perhaps as part of a combination therapy for certain groups of patients⁵¹ and liver X receptor antagonists (LXR)⁵².

Trials are also demonstrating benefits for use of a dietary portfolio of cholesterol lowering food, rather than reliance upon a single food item. One study reported by Jenkins et al in 2006 showed that 21 out of 66 hyperlipidaemic participants in the trial achieved LDL-cholesterol reductions of >20 percent after one year on a portfolio diet high in plant sterols, soy protein, viscous fibres and almonds⁵³. This reinforced evidence from an earlier study on the effects of a plant-based diet, combining several routinely consumed foods with cholesterol-lowering effects⁵⁴. Additionally, plant sterol esters are available in capsule form, as well as enriched foods, to improve lipid profiles⁵⁵.

Conclusions

The direction of travel is clear. Clinical trial evidence is widening the scope of cholesterol management in the prevention and treatment of CVD, particularly in the inclusion of most or all people with diabetes. It is also leading to increasingly aggressive targets for those at most risk.

Whilst improvements in diet and lifestyle remain the first option for cholesterol reduction, assisted by developments in plant sterol-enhanced foods, the focus of guidelines remain on reducing LDL-C with lipid lowering drugs as the first line of therapy when this proves necessary in the achievement of cholesterol targets. There is a clear and significant time lag between the incorporation of clinical trial evidence into pan-European standards of best practice, widely endorsed by lipid experts and their national associations, and their incorporation into national and local practice across Europe. Thus CVD remains a leading cause of avoidable death and disability in Europe.

GLOSSARY

By Country

Austria

AAS	Austrian Atherosclerosis Society
ÖGE	Österreichische Gesellschaft für Ernährung (Austrian Nutrition Society)
OEKG	Austrian Cardiology Society

Finland

Duodecim	Finnish Medical Society
Suomen Sydänliitto	Finnish Heart Association

France

AFSSAPS	Agence Française de Sécurité Sanitaire des Produits de Santé (French Medical Products Agency)
Doctissimo	Health Website www.doctissimo.fr
NSFA	La Nouvelle Société Française d'Arthérosclérose (French Artherosclerosis Society)

Germany

DGK	Deutsche Gesellschaft für Kardiologie (German Cardiology Society)
DGE	Deutsche Gesellschaft für Ernährung (German Nutrition Society)
Lipid Liga	German Cholesterol Society

Italy

AIFA	Agencia Italiana de Farmaco (National Drug Agency)
ISS	Instituto Superiore di Sanità (National Health authority)
PNLG	Programma Nazionale Linee Guida (National Guidelines Group)
SIMG	Società Italiana di Medicina Generale (General Medicine Society)

Norway

DNL	Den Norske Lægeforening (National Medical Association)
NCS	Norsk Cardiologisk Seiskap (Cardiology Society)
SLK	Statens Legemiddelverk (State Medicines Agency)

Spain

CDS	Catalunya Departament de Salut (Catalan Health Department)
CEIPC	Comité Español Interdisciplinario para la Prevención Cardiovascular (Spanish Interdisciplinary Committee for Cardiovascular Prevention)

FEC

Fundación Española del Corazón (Medical Foundation)

ICS

Institut Català de la Salut (Catalan Health Institute)

Sweden

Läkemedelsverket
Socialstyrelsen

Medical Products Agency
National Board of Health and Welfare

United Kingdom

AWMSG	All-Wales Medicines Strategy Group
JBS	Joint British Societies
NICE	National Institute for Health & Clinical Excellence
NSF	Department for Health National Service Framework
QOF	Department for Health Quality and Outcomes Framework
SIGN Network	Scottish Intercollegiate Guidelines
SMC	Scottish Medicines Consortium

General

EAS	European Atherosclerosis Society
CHD	Coronary Heart Disease; narrowed arteries, leading to angina or heart attack
CVD	Cardiovascular Disease: Disease of heart and blood vessels
ESC	European Society of Cardiology
Framingham	Heart study published in 1991, producing an equation to predict risk
HDL-C	Cholesterol ("Good" Cholesterol; that removes LDL-C)
LDL-C	Low Density Lipoprotein Cholesterol ("Bad" Cholesterol)
Lipids	Fatty substances in blood
mg/dl	Milligrams per deciliter (concentration by weight)
Microalbuminuria	A protein in blood, which is a marker for CVD
mmol/l	Millimoles per litre (concentration by molecule count)
NCEP(ATP)	US National Cholesterol Education Programme (Adult Treatment Panel)
SCORE	Systematic Coronary Risk Evaluation

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