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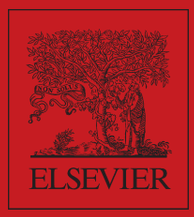

Volume 10, issue 1, June 2009

ISSN 1507-5086

atherosclerosis

supplements

Health Policy Issues in Multiple Risk Factor Management in Cardiovascular Diseases

Official Journal of the European Atherosclerosis Society
Affiliated with the International Atherosclerosis Society and
the Society of Atherosclerosis Imaging and Prevention

Atherosclerosis Supplements Vol. 10/1 (2009) 1–30

Health Policy Issues in Multiple Risk Factor Management

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ATHEROSCLEROSIS

Official Journal of the European Atherosclerosis Society
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Aims and Scope. Atherosclerosis brings together from all sources papers concerned with research and investigation on atherosclerosis, its complications and related diseases, including: lipoprotein metabolism, arterial and vascular biology and disease, thrombosis, inflammation, disorders of lipid transport, diabetes and hypertension as related to atherosclerosis, and cardiovascular risk factors. The editors are also interested in clinical papers dealing with case studies of specific or general interest, new or unusual lipid syndromes, and the genetic basis and familial incidence of atherosclerosis and related diseases. High quality reports of controlled clinical trials of drugs or diets will be considered provided the paper deals with the mechanism of action of the drug or diet.

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Publication information: *Atherosclerosis Supplements* (1567-5688) publishes supplements to *Atherosclerosis* (0021-9150). For 2009, volumes 202–207 are scheduled for publication. Subscription prices are available upon request from the Publisher or from the Regional Sales Office nearest you or from this journal's website (http://www.elsevier.com/locate/atherosclerosis). Further information is available on this journal and other Elsevier products through Elsevier's website: (http://www. elsevier.com). Subscriptions are accepted on a prepaid basis only and are entered on a calendar year basis. Issues are sent by standard mail (surface within Europe, air delivery outside Europe). Priority rates are available upon request. Claims for missing issues should be made within six months of the date of dispatch.

ATHEROSCLEROSIS

SUPPLEMENTS

Official Journal of the European Atherosclerosis Society
Affiliated with the International Atherosclerosis Society and
the Society of Atherosclerosis Imaging and Prevention

Volume 10/1 (2009)

ELSEVIER

Amsterdam • Boston • London • New York • Oxford • Paris • Philadelphia • San Diego • St. Louis

Printed by Polestar Wheatons Ltd, Exeter, UK

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Atherosclerosis is the disease of arteries that is the usual cause of heart attacks and stroke. The European Atherosclerosis Society, founded in 1964, is devoted to advancing knowledge of the causes, natural history, treatment and prevention of the disease, as stipulated by the Society's constitution. Currently composed of over 450 researchers in basic as well as clinical science, membership is open to scientists working in Europe and corresponding membership can be obtained by non-Europeans.

The European Atherosclerosis society organizes a large annual congress and several additional yearly educational activities including our Summer School for young scientists and several collaborative workshops with the IAS and other European Scientific Societies. The society develops guidelines for the treatment and prevention of Atherosclerosis and is a member of the European Joint Prevention Committee. EAS supports outstanding young scientists and EAS members through a series of Grants, Awards and Fellowships. This financial support helps with travel to meetings, research stipends and other educational possibilities.

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European Atherosclerosis Society

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(a) Persons residing in Europe or neighbouring countries engaged in, or who direct research for, the purpose set out in Article 2 shall be eligible for membership of the Society.
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4th International Symposium on Integrated Biomarkers in Cardiovascular Diseases, October 7–9, 2010, Berlin (Germany).
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I extend to you a warm welcome and hope that you will wish to join our Society.

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We stand ready to represent many of the interests that are important to you and your colleagues. Your support is needed and is greatly appreciated.

Sincerely,

Allen J. Taylor, MD, President

SOCIETY OF ATHEROSCLEROSIS IMAGING AND PREVENTION

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Health Policy Issues in Multiple Risk Factor Management in Cardiovascular Diseases

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List of abbreviations

AFCAPS/TexCAPS	Air Force/Texas Coronary Atherosclerosis Prevention Study
ASCOT-LLA	Anglo-Scandinavian Cardiac Outcomes Trial-Lipid-Lowering Arm
BHS	British Hypertension Society
BMI	Body Mass Index
BP	Blood Pressure
CARDS	Collaborative Atorvastatin Diabetes Study
CARE	Cholesterol and Recurrent Events Study
CHD	Coronary Heart Disease
CME	Continuing Medical Education
CV	Cardiovascular
CVD	Cardiovascular Disease
EHHC	European Heart Health Charter
EU	European Union
EUROASPIRE	European Action on Secondary Prevention through Intervention to Reduce Events
4S	Scandinavian Simvastatin Survival Study
GISE	Italian Society of Interventional Cardiology
GP	General Practitioner
HCS	Health Care System
HPS	Heart Protection Study
ICT	Information and Communication Technology
IDEAL	Incremental Decrease in End-points through Aggressive Lipid-Lowering Trial
IHD	Ischemic Heart Disease
LDL-C	Low-Density Lipoprotein Cholesterol
LIPID	Long-Term Intervention with Pravastatin in Ischaemic Disease
LIPS	Lescol Intervention Prevention Study
MI	Myocardial Infarction
MIRACL	Myocardial Ischemia Reduction with Aggressive Cholesterol Lowering
MLD	Minimum Luminal Diameter
MONICA	MONItoring Trends and Determinants in CArdiovascular Diseases Project
NCEP ATP III	National Cholesterol Education Program Adult Treatment Panel III
NHANES	National Health and Nutrition Examination Survey
NHS	National Health Service
NICE	National Institute for Health and Clinical Excellence
NT-proBNP	N-Terminal Prohormone Brain Natriuretic Peptide
PROCOM	Prospective Cardiovascular Münster Study
PROVE IT-TIMI 22	Pravastatin or Atorvastatin Evaluation and Infection Therapy-Thrombolysis In Myocardial Infarction 22
PTCA	Percutaneous Transluminal Coronary Angioplasty
QALY	Quality Adjusted Life Year
QCA	Quantitative Coronary Angiography
QOF	Quality Outcomes Framework
SCORE	Systematic Coronary Risk Evaluation
SCA	Sudden Cardiac Arrest
TNT	Treating to New Targets Trial
UK	United Kingdom
UKPDS	United Kingdom Prospective Diabetes Study
WHO	World Health Organisation
WOSCOPS	West of Scotland Coronary Prevention Study

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Barriers to multiple risk factor management in cardiovascular disease

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Giovanni Lorenzini Medical Science Foundation, Milan, Italy, and Houston, Texas, USA

Keywords: Non-communicable diseases; Cardiovascular disease; Risk factors; Health policy; Prevention; Lipids

Major non-communicable diseases (NCDs) – primarily cardiovascular disease (CVD), cancer, chronic obstructive pulmonary disease (COPD), and diabetes – are responsible for 85% of the deaths and 70% of the burden of disease in Europe. In addition to the human suffering, the costs of managing the clinical sequalae of these diseases create an enormous economic burden for many countries throughout the European Union – even in the more affluent Member States where NCD mortality is trending downwards. The economic situation is likely to deteriorate further in light of the growing prevalence of CVD, the ever-expanding population at risk for future CVD events, the increased life span of individuals in many countries, and the paucity of funding for global disease primary prevention programs to citizens (1–3% of health care expenditures in the US [1] and <0.4% of the total National Health System in Italy) [2]. Skepticism about effectiveness, bureaucratic inertia, and competing interests all contribute to the resistance in preventing NCD diseases and promoting healthy lifestyles. As a result, the health systems of most European countries, and indeed, throughout the world, are not adequately structured or funded to respond to these emerging health care needs. Further, the ongoing worldwide economic crisis is also expected to jeopardize the availability of resources within individual countries for investment in health care systems in both the private and public sectors.

Substantial clinical evidence shows that the clinical and socioeconomic burden of CVD can be markedly attenuated through appropriate integrated approaches to health policies, including individual risk reduction (aimed at high-risk individuals), population risk reduction (aimed at social determinants), the rational use of health services (by empowering primary health care providers), and referral system support [3]. The targeting of total cardiovascular risk and the appropriate management of multiple risk factors, in particular, represents a critical component in the prevention and treatment of NCD as well as CVD.

The Framingham Study initiated in 1948 first characterised individual risk factors such as age, hypertension, smoking, diabetes, and hyperlipidaemia as major determinants of coronary artery disease [4,5]. More recent data from the cross-sectional INTERHEART study in 52 countries indicate that nine major risk factors (smoking, ApoB/ApoA1 ratio, diabetes, hypertension, abdominal obesity, psychosocial factors, sedentarity, low fruit and vegetable consumption, and alcohol consumption) account for more than 90% of the population-attributable risk [6]. In light of these and numerous other epidemiological findings, individual risk factors have been amalgamated into a global (or total) risk score, thereby allowing an overall assessment of CVD risk [7–9]. This multiple risk factor approach is evolving as the foundation of all clinical strategies to reduce CVD risk and is bolstered by evidence of its effectiveness in reducing mortality and disability [8,9]. For example, in the UK, Finland, and US, 44% to 72% of the decline in deaths from coronary heart disease (CHD) from the early 1980s through 2000 may be attributed to reductions in major risk factors, with the remainder attributable to the judicious use of evidence-based medical therapies [10–12].

Despite the growing evidence of mortality and morbidity benefits from lifestyle changes, risk factor management, and use of cardioprotective drugs [9], numerous barriers to

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CVD prevention and management remain to be conquered, both in the individual patient and in the at-risk population as a whole. Specifically, an urgent need exists:

- To develop a consensus among specialists in understanding the global (or total) risk of CVD and to transfer the multiple risk factor approach to actual clinical practice.
- To identify barriers to proper CVD management with a focus on lowering global (or total) risk and to develop an effective plan to overcome these barriers.
- To assist health care decision makers in their policy development directed at improving the prevention and management of CVD at the EU, national, and regional levels.

These needs are particularly germane in the context of the European Union, where 27 countries with different health policies and health organisations are now unified under the same regulatory and economic rules.

Results from recent studies in treating CVD events and the development of innovative medical tools for CVD risk assessment and prevention are already beginning to have a dramatic impact on everyday clinical practice. As a result, the Giovanni Lorenzini Medical Science Foundation decided to organise the 7th International Symposium on Multiple Risk Factors in Cardiovascular Diseases: Prevention and Intervention – Health Policy in Venice, on 22–25 October, 2008, with the goal of providing an integrated overview of new approaches to reduce CVD risk (including, for example, combined control of lipid disorders, hypertension, thrombosis, and diabetes as well as use of polytherapy) and of providing practical solutions for prioritizing and sequencing the treatment of multiple risk factors. Particular emphasis was placed on offering suggestions and providing a forum for lively debates on how to effectively bridge the gap between medical science and health policy. It is important to note, however, that a main mission of the Lorenzini Foundation is to facilitate and reinforce the European Guidelines on Cardiovascular Disease Prevention in Clinical Practice, as put forth by the 4th Fourth Joint Task Force of the European Society of Cardiology and other societies [9,13].

This supplement summarises the material presented and discussed during the Symposium and is dedicated to two main areas where existing barriers impede the transfer of medical scientific innovation to the betterment of the individual and/or the population. These include:

- Bridging Science and Health Policy in CVD – Focus on Lipid Management (see pages 3–21).
- From Hospital to Home: Continuity of Care in Internal Medicine, and Health Policy Strategies (see pages 22–28).

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[1] Woolf SH. The big answer: rediscovering prevention at a time of crisis in health care. Harv Health Policy Rev 2006; 7:5–20.

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Bridging science and health policy in cardiovascular disease: focus on lipid management

A Report from a Session held during the 7th International Symposium on Multiple Risk Factors in Cardiovascular Diseases: Prevention and Intervention – Health Policy, in Venice, Italy, on 25 October, 2008

Session Speakers:

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Abstract

In Europe, cardiovascular disease (CVD) represents the main cause of morbidity and mortality, costing countries € 190 billion yearly (2006). CVD prevention remains unsatisfactory across Europe largely due to poor control of CVD risk factors (RFs), growing incidence of obesity and diabetes, and sedentary lifestyle/poor dietary habits. Hypercholesterolaemia is a proven CVD RF, and LDL-C lowering slows atherosclerotic progression and reduces major coronary events. Lipid-lowering therapy is cost-effective, and intensive treatment of high-risk patients further improves cost effectiveness. In Italy, models indicate that improved cholesterol management translates into potential yearly savings of € 2.9–4 billion. Identifying and eliminating legislative and administrative barriers is essential to providing optimal lipid care to high-risk patients. Public health and government policy can influence clinical practice rapidly, and guideline endorsement via national health policy may reduce the CVD burden and change physician and patient behaviour. Action to reduce CVD burden should ideally include the integration of strategies to lower the incidence of major CV events, improvement in total CV risk estimation, database monitoring of CVD trends, and development of population educational initiatives on CVD prevention. Failure to bridge the gap between science and health policy, particularly in relation to lipid management, could result in missed opportunities to reverse the burgeoning epidemic of CVD in Europe.

Keywords: Cardiovascular disease; Cholesterol; LDL-C; Economics; Health policy; Risk factors; Public health; Government

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1. Introduction

[Volpe M.]

Despite remarkable progress in our understanding of the causes, diagnosis, and management of cardiovascular disease (CVD), strategies to prevent this potentially devastating condition remain largely unsatisfactory throughout the European Union (EU). Although variations in secular trends exist across Europe, the large and increasing incidence of CVD is largely due to poor control of traditional CVD risk factors (such as hypertension and hypercholesterolaemia), the growing incidence of obesity and diabetes in adults and young people, and the sedentary lifestyle and poor dietary habits of modern society.

The progressive and marked increase in the incidence of CVD is a matter of intense and growing concern among many regulators and professionals involved in maintaining and promoting public health. Current health care systems dedicated to acute CVD care (such as coronary care, stroke, and rehabilitation units, intensive care units (ICUs), and specialised outpatient clinics) could quickly become overwhelmed by the growing number of patients requiring prolonged intensive care and assistance. Indeed, disease projections and demographic trends in the European region combined with the routine difficulties admitting patients to ICUs suggest that the health care system may already be imperilled in some countries. In Italy, for example, about half of patients experiencing sudden cardiac arrest (SCA) or acute myocardial infarction (MI) are treated outside of ICUs. In light of these trends, sustaining the advance of medical assistance in terms of the economic costs of drugs, therapeutic devices, diagnostic and interventional technologies, and follow-up programmes will be challenging.

[Wood D.]

It is clear that, in the absence of effective CVD health policy, robust medical evidence and physician expertise do not necessarily translate into high standards of preventive care. In recent years, therefore, European physicians have become more actively engaged in CVD health policy development, as evidenced by the development of the Joint European Societies Prevention Guidelines [1–4] and the creation of the European Heart Health Charter (EHHC) [5] launched in Brussels on 12 June, 2007. While acknowledging and respecting individual country autonomy, EHHC advocates a unified approach to CV health, promoting the translation, adaptation, and dissemination of CVD prevention guidelines. In particular, the EHHC called for establishment of national strategies for the detection and management of patients at high risk of CVD and the prevention and care of those with established CVD. The overall objective is to bridge the treatment gap between what is recommended and what is achieved in daily practice regarding CVD prevention.

To help support the increasing activities of the EU and national parliaments with respect to CVD health policy (particularly as it relates to lipids), a panel of European experts in CVD management, economics, and health policy, convened at an international symposium on Bridging Science and Health Policy in Cardiovascular Disease: Focus on Lipid Management, in Venice, Italy, on October 25, 2008, to review and discuss the following issues:

- The clinical and socioeconomic impact of CVD in the EU
- The impact of lipid-lowering strategies (particularly LDL-C reduction) on CVD outcomes
- Targeted "high-risk" versus population approaches to reduce CVD risk
- The cost-effectiveness of lipid-lowering strategies and their potential role in improving long-term financial health care sustainability
- The barriers and incentives to CVD prevention
- Overcoming barriers to proper lipid management and implementing strategies to improve CVD prevention: the Italian experience.

This article serves as a compilation of the broad range of material presented and discussed during the meeting and summarises the conclusions made.

2. Global and European burden of CVD

[Volpe M.]

The clinical and socioeconomic impact of CVD is substantial. According to World Health Organisation (WHO) 2004 statistics, CVD represents the number one cause of death worldwide, accounting for 29% of total mortality (Fig. 1) [6]. In Europe, CVD represents the main cause of morbidity, mortality, and hospitalisation [7–9]. CVD is the largest contributor to the European burden of disease in terms of mortality – considerably larger than infectious and parasitic diseases, malignant neoplasms, and respiratory infections and diseases (Fig. 1) [9].

In Italy alone, CVD claims more than 300,000 potential years of life lost (that is, years that the person would have lived if he/she had died at an age equal to his/her life expectation) to subjects below the age of 65 years [9]. Survivors of an acute CVD event gradually become chronic patients, with subsequent consequences on quality of life and economic and social costs [9].

2.1. CVD mortality projected to increase

The burden of CVD is progressively expanding, with projected deaths from CVD in 2030 increasing to 23.6 million (34.8%) of the world population and 4.7 million (49.7%) of the European population (Table 1) [10]. This explosion in CVD is due largely to the ongoing epidemic of

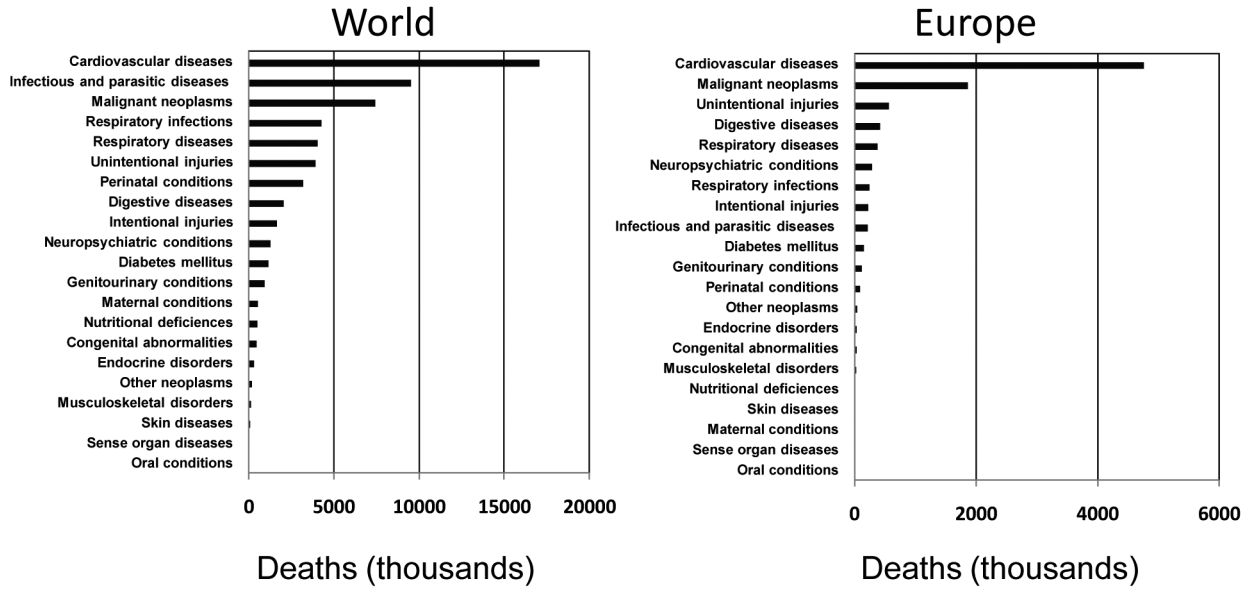


Fig. 1. Global and European burden of disease for the year 2004, according to WHO statistics [6].

Table 1
Projected global and European deaths due to CVD in 2030. Data extracted from WHO [10]

Cause	World (total deaths 67.8 million)		Europe (total deaths 9.5 million)	
	Million	% of total deaths	Million	% of total deaths
Ischemic heart disease	9.6	14.1	2.1	22.6
Hypertensive heart disease	1.5	2.2	0.2	2.0
Stroke	8.2	12.1	1.4	14.9
Total CVD	23.6	34.8	4.7	49.7

metabolic disease, and particularly of type 2 diabetes and metabolic syndrome.

On the basis of data from WHO MONICA (MONItoring trends and determinants in CArdiovascular diseases project), the incidence of coronary events increased from 354,000 to 368,000 (5%) over the period 1990 to 2000 [11]. Although mortality rate due to acute MI is reduced, WHO data indicate that a conservative increase of acute MI events will be 25% by 2030 and will likely involve older and more complex patients such as those with major comorbidities.

Recent statistics from the Italian Society of Interventional Cardiology [12] also reveal marked increases in diagnostic and interventional procedures over the period 2003 to 2007: coronary angiography increased by approximately 25%, percutaneous transluminal coronary angioplasty (PTCA) by approximately 50%, and primary PTCA by approximately 90%.

3. Economic burden of CVD

[Volpe M.]

In the US in 2006, the cost of CVD was estimated to be $ 368 billion (two-thirds of the overall in-hospital medical assistance cost); a 25% increase over the next 25 years would result in CVD costs increasing to $ 550 billion [13]. In Italy, the effective gross cost of the intra-hospital phase of acute MI could be around € 6000 per patient (€ 720 million per year); a 25% increase in MI over the next 25 years (without considering the costs related to rehabilitation, leave of absence from work, drug therapies, after-discharge diagnostic tests, jobs, and working days lost) would lead to an estimated cost of more than € 1 billion per year [9].

3.1. Cost of CVD in the EU

[Leal J.]

In the 27 countries of the EU, the societal economic burden of CVD was estimated to be € 186 billion in 2006 compared to the EU budget expenditure of € 107 billion for the same period. The estimated economic burden not only included health care consumption but also the opportunity costs and productivity losses associated with unpaid care, premature death and absence from work due to illness. These estimates were informed by the most recent CVD epidemiological, resource use and unit cost data obtained from international databases, national ministries and statistical institutes, and published studies. Previous work using similar methodology estimated the cost of CVD at € 169 billion for the 25 countries of the EU in 2003 [14].

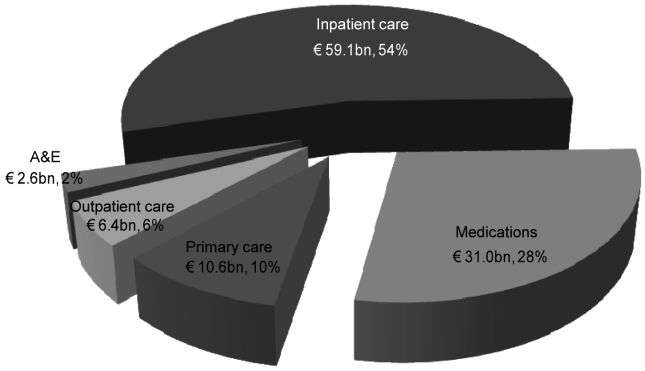


Fig. 2. Total health care costs in the EU.

3.2. Major components of CVD-related health care costs

In 2006, CVD was found to cost the EU around € 110 billion (58%) on health care, € 40 billion (21%) in unpaid care costs, € 27 billion (14%) and € 13 billion (7%) in productivity losses due to premature mortality and absence from work, respectively. Hospital inpatient care was the largest component of CVD-related health care costs, followed by medications, primary care, outpatient care, and accident and emergencies (Fig. 2). However, there was a wide variation in the pattern of health care expenditure across the EU member states. For example, medication costs were estimated to be higher than inpatient costs in some countries.

In terms of total EU expenditure on health care, CVD was estimated to account for 10% of its total, which is equivalent to an annual cost of € 223 per EU citizen. CVD expenditure as a proportion of total health care expenditure was also found to vary considerably between the member states. These differences seemed to be positively correlated with the country's national income. Coronary heart disease (CHD) and cerebrovascular diseases represented 26% and 20% of the total CVD societal costs, respectively.

This work highlights the significant economic burden of CVD across the EU. In the process, it reveals the need for comparable and accurate information on the epidemiology, resource use and unit costs associated with CVD across the member states. It also shows that other cardiovascular diseases which are not given as much priority as CHD and cerebrovascular disease account for a significant proportion of total costs.

3.3. Aims of assessing economic burden of disease

It is important to understand that the aim of an economic burden of disease study is to inform decisions concerning the distribution of the available research funding and not to determine the appropriate level of health care spending. For example, the 7th framework programme (FP7) of the European Community for research and technological development for the period of 2007 to 2013 allocated € 6.1 billion for health research [15]. Understanding the burden of different diseases is a useful tool to help prioritise the scarce research funds to areas with the highest burden.

Previous studies have shown that the allocation of US research funding by the National Institutes of Health appears to be significantly related to measures of disease burden [16]. Furthermore, in the UK, where CVD-related health care expenditure was estimated at 18% of all health care expenditure in 2004, the largest publicly-funded medical research organisation (i.e., Medical Research Council) spent 8.2% of their total budget on CVD research [17].

3.4. Conclusions

Any judgment concerning the appropriate level of health care expenditure across the EU member states needs to measure the population health benefit arising directly from such expenditure. This, unfortunately, is far from straightforward. Nevertheless, a way of maximising the health of the population with the available health care resources is to increase investment on cost-effective interventions while removing non cost-effective interventions from clinical practice. At the EU level, the feasibility of such approach depends on joint research efforts between its member states to identify those curative and preventive interventions that are cost-effective not only in one jurisdiction but across the several member states.

4. Clinical outcome benefits of lowering LDL-C

[Atella V.]

Several key factors contribute to CVD, including age, high blood pressure (BP), smoking, high cholesterol levels, high body mass index (BMI), obesity, and diabetes. The median age in most member states of the EU is now over 30 years (Italy is the highest with 41.6 years). By 2020, 20% of people in Europe will be over 60 years and more than 5% will be over the age of 80 years. Obesity and diabetes are estimated to be 30 million in 2020, with obesity and overweight, in particular, affecting 30 to 80% of adults in countries comprising WHO Europe.

4.1. Hypercholesterolaemia in CVD

[Catapano A.L.]

Hypercholesterolaemia is a proven risk factor for CHD and plays a key role in the development and progression of atherosclerosis (a chronic inflammatory disease) [18–21]. Data on the incidence of ischemic heart disease (IHD) and serum cholesterol concentration (Fig. 3) were analyzed from 10 prospective (cohort) studies, 3 international studies, and 28 randomised controlled trials (500,000 men and 18,000 events) and clearly show that a long term reduction in serum cholesterol concentration of 0.6 mmol/L (∼23 mg/

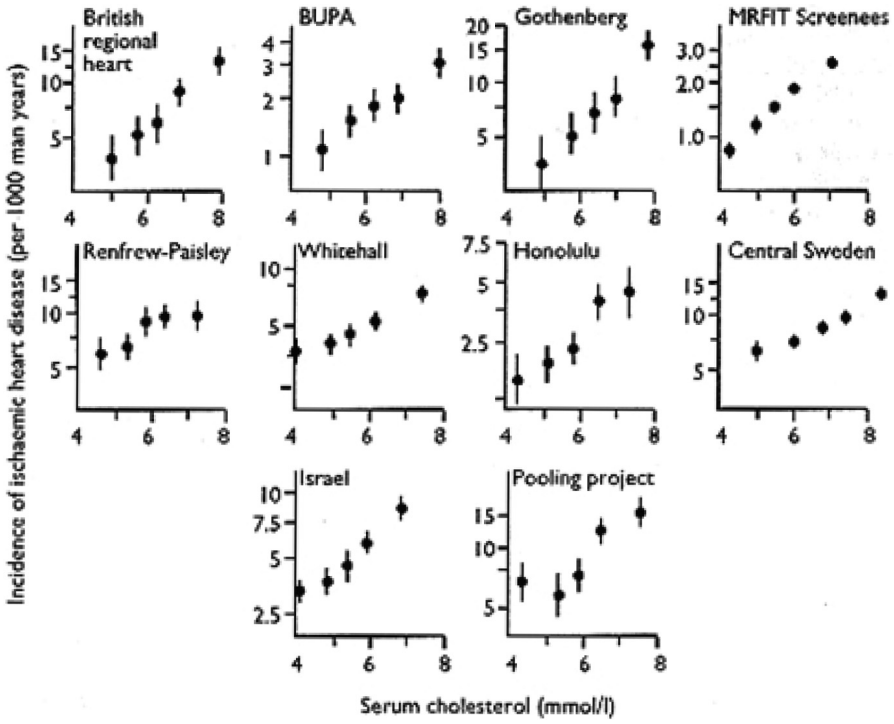


Fig. 3. Incidence of IHD, age adjusted with 95% confidence intervals, according to quintiles of serum cholesterol level. Reproduced with permission from BMJ Publishing Group Limited [22].

dL or 10%) lowers the risk of IHD by 50% and that the full effect of the reduction in risk is achieved by five years [22].

4.2. Impact of lipid-lowering therapy on CVD

Therapeutic interventions to lower LDL-C levels show a clear reduction in the progression of atherosclerosis, and this translates into a decline in the incidence of major coronary and vascular events. The association of effects on LDL-C with measures of stenosis by quantitative coronary angiography (QCA) was recently analyzed in large trials of statin therapy [23]. Regression analysis showed a linear relationship between LDL-C level achieved (or the percent reduction in LDL-C) and the change in percent diameter stenosis or change in minimum luminal diameter (MLD).

Interventions that lower LDL-C significantly reduce the incidence of CHD and other major vascular events in a wide range of individuals, as shown by findings of a prospective meta-analysis of data from 90,056 individuals in 14 randomised trials of statins [24]. This meta-analysis showed that each mmol/L (∼38 mg/dL) reduction in LDL-C was associated with an approximately 20% reduction in the 5-year incidence of major coronary events, coronary revascularisation, and stroke, an effect largely independent of the initial lipid profile or other presenting characteristics.

More recently published major outcomes studies such as Pravastatin or Atorvastatin Evaluation and Infection Therapy-Thrombolysis In Myocardial Infarction 22 (PROVE IT-TIMI 22) and Treating to New Targets (TNT) [25,26], provide evidence that an LDL-C value of 100 mg/dL (∼2.6 mmol/L) may not be the threshold for cardiovascular (CV) benefits and that additional CV benefits may be attainable by lowering LDL-C below this value.

PROVE IT-TIMI 22 [25] showed that an intensive lipid-lowering statin regimen in patients with acute coronary syndrome (ACS) provided greater protection against death or major CV events compared with a standard lipid-lowering regimen. TNT showed that patients with stable coronary artery disease whose mean LDL-C levels were lowered to 77 mg/dL (∼2 mmol/L) had a 22% relative reduction in risk of a major CV event including death from CHD, nonfatal nonprocedure-related MI, resuscitation after cardiac arrest, and fatal and nonfatal stroke ($p < 0.001$), compared with patients whose mean LDL-C levels were reduced to 101 mg/dL (∼2.63 mmol/L). [26]. Taken together, these data show a continuous log-linear relationship between LDL-C levels and relative risk for CHD (Fig. 4), such that for every 30 mg/dL (∼0.77 mmol/L) change in LDL-C, the relative risk for CHD is changed in proportion by about 30% [27].

4.3. New clinical trial evidence supports ever lower LDL-C goals

The new clinical trial evidence, including PROVE IT-TIMI 22 and TNT, is driving lipid management guidelines toward ever lower LDL-C goals. The 2002 National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) guidelines were revised in 2004 to help reduce patients' risk of CVD [27]. The updated guidelines propose an LDL-C level of less than 100 mg/dL (∼2.6 mmol/L)

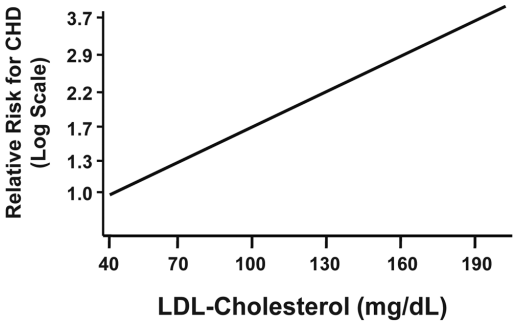


Fig. 4. Log-linear relationship between LDL-C levels and relative risk for CHD. Epidemiological and trials evidence suggests that for every 30 mg/dL (0.77 mmol/L) change in LDL-C the CHD RR is changed by 30%. The relative risk is set at 1.0 for an LDL-C of 40 mg/dL (1.03 mmol/L). Reproduced with permission © 2004, American Heart Association, Inc. [27].

for persons at high risk of CVD and an LDL-C level of less than 70 mg/dL (∼1.8 mmol/L) as an optional therapeutic goal for persons at very high risk of developing CVD. These lower LDL-C levels may be closer to what is physiologically normal, as evidenced by the LDL-C levels of 29 mg/dL (∼0.75 mmol/L) in newborns [28]. Indeed, 30 mg/dL (∼0.77 mmol/L) of LDL-C saturates the LDL-C receptor, and higher levels simply fail to get metabolised.

4.4. Reduction in CHD risk by statins: absence of molecule-specific effects unrelated to LDL-C lowering

It is important to note that the reduction in CHD risk in the statin trials is primarily driven by lower LDL-C levels rather than the anti-inflammatory, immunomodulatory, antithrombotic, vascular, and other non-LDL-C-lowering effects of statins. This assertion comes from a regression analysis of data from diet, bile acid sequestrant, surgery, and statin trials, involving a total of 81,859 patients [29]. The regression lines for LDL-C lowering and CHD and stroke reduction over five years of treatment were similar in non-statin and statin trials, indicating the absence of pleiotropic effects of statins (that is, molecule-specific effects unrelated to LDL-C lowering). In other words, regardless of the population studied or the type of lipid-lowering agent employed, this linear relationship between events and LDL-C levels entirely accounts for any outcomes benefits.

4.5. Conclusions

Plasma LDL-C levels are un-physiologically high in the Western world. LDL-C less than 100 mg/dL (∼2.6 mmol/L) is safe and is associated with a low rate of CV events in the population. Reduction of un-physiologically high LDL-C levels is also safe and reduces events, although adherence and persistence with statin therapy is poor and remains to be addressed in order to spend health care funds effectively.

5. Targeted “high-risk” versus population approaches to reduce CVD risk

[Critchley J.]

Public policies outside of the health service play a major role in influencing public health, generally by facilitating (or hindering) healthier choices among the population. The role of these population interventions for reducing CVD (primary prevention) compared with targeted “high risk” approaches has been much debated.

5.1. Advantages and disadvantages of high-risk and population strategies

Early studies by Rose identified two principal strategies for CHD primary prevention: the ’high-risk’ approach, which seeks to target individuals thought to be at highest risk of disease on the basis of risk factor levels, and the population approach, which seeks to reduce incidence in the entire population [30]. A summary of key advantages of each approach is summarised in Table 2.

The high risk prevention strategy ignores the large group of individuals considered to be at low to moderate risk; the majority of events/deaths occur among those at low to moderate risk because this category encompasses most of the population. The population approach shifts the risk distribution for the entire population towards the low to moderate end of the spectrum, thereby potentially imparting greater reductions in events compared with that seen with the high risk approach; in addition, the population approach has the added theoretical benefit of fewer high risk patients to treat.

Table 2
Summary of advantages and disadvantages of the high-risk approach and population approach for CHD primary prevention

Strategy	Advantages	Disadvantages
High-risk approach	• Intervention more appropriate to the individual • Motivation (patient and physician) may be higher • Cost effective use of resources • Risk/benefit ratio favourable	• Large effort to identify high-risk individuals • Does not eliminate underlying cause • Limited potential to the individual and population • Behaviourally inappropriate (deviating from the cultural norm)
Population approach	• Addresses the underlying cause of the disease • Behaviourally appropriate • Large potential to impact the population	• Poor motivation of individual and physician • Risk/benefit ratio not as favourable as high-risk approach • Small benefit for the individual (known as the prevention paradox)

5.2. Evidence base for primary prevention

The large evidence base for primary prevention (i.e., reducing CVD risk) comes from a compilation of 141 review/meta-analyses [31] that addressed risk factor reduction (such as cholesterol reduction, smoking cessation, BP reduction, weigh loss, physical activity promotion). The interventions analysed tended to be focussed on changing the behaviour of individuals rather than whole populations and were dominated by pharmaceutical intervention in high risk patients.

Several gaps in the evidence base were identified, particularly with respect to policy interventions in whole populations. These include, for example: (1) Changes to the built environment (new parks, walking/cycle routes) on physical activity; (2) The impact of legislation or financial incentives (such as parking fees) on physical activity; (3) The effect of legislation or regulations banning advertising of junk foods to children; (4) The influence of interventions with suppliers (such as the food industry) to improve labelling and promote healthier foods. Interventions that may be very effective in reducing risk in whole populations have been under-evaluated, compared with "high risk" approaches.

5.3. Statistical modelling of benefits of high risk versus population approaches

A validated statistical model (IMPACT) [32,33] has been used to assess the progressive decline in CHD mortality (CHD mortality in men from 1968 to 2003 in a variety of Western countries show a substantial downward trend) and estimate the effectiveness of potential whole population/high risk interventions. The model incorporated major population risk factors for CHD (smoking, high BP, elevated total cholesterol, obesity, diabetes, and physical inactivity) and all the usual medical and surgical treatments for CHD.

In an analysis focussing on England and Wales over the period 1981 to 2000, CHD mortality rates fell by 62% in men and by 45% in women 25 to 84 years old [32]. As shown in Fig. 5, there were 68,230 fewer deaths in 2000 than expected from baseline mortality rates in 1981. The fall in mortality was mainly due to a net reduction in population risk factors (−58%) and improved efficacy and uptake of treatments (−42% reduction). The improvements in certain major risk factors (e.g., smoking, serum total cholesterol, and BP), was, however, offset by adverse trends for some other risk factors, including a worsening of obesity, diabetes mellitus, and physical activity.

The theoretical impact of population and high-risk strategies for the primary prevention of CVD [34] was compared in the British Regional Heart Study, a prospective study of CVD based in one General Practice in each of 24 British towns (Fig. 6). Participants (aged 40–59 years) were enrolled in 1978–1980 and were followed for all-cause mortality and for CV morbidity. In the high-risk approach, aggressive pharmacological treatment (statins, beta-blockers, ACE-inhibitors and aspirin) in individuals with a 10-year Framingham event risk of ≥30% (estimated to be approximately 6% of the population) would theoretically reduce CVD deaths by 11% (34% in individuals with a 10-year Framingham event risk of ≥20% [26% of population]). On the other hand, modest reductions in the population distributions of serum total cholesterol and systolic BP led to higher theoretical reductions in CVD (a 5% reduction in both cholesterol levels and BP in the population would result in a 26% fewer CHD deaths; a 10% reduction would result in 45% fewer CHD deaths).

5.4. Conclusions

Some good evidence exists to guide population-based policy for CHD prevention but large gaps in the evidence base exist particularly with respect to physical activity and

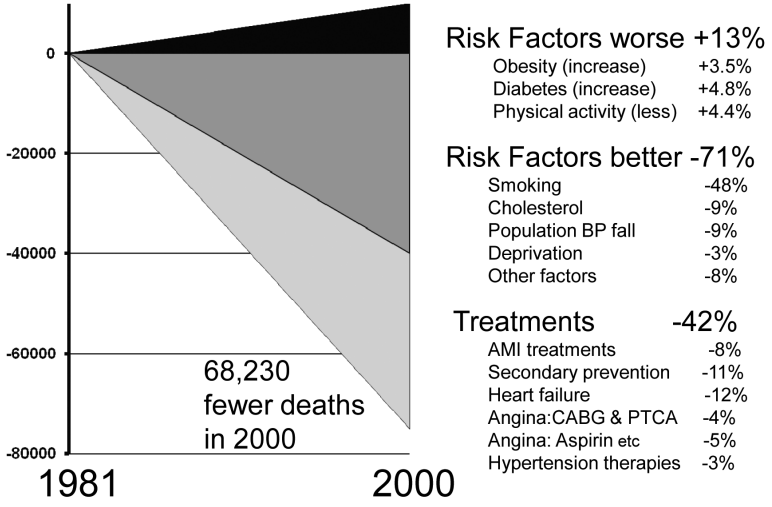


Fig. 5. Use of the IMPACT mortality model to explain the fall in coronary heart disease deaths in England & Wales 1981–2000. Reproduced with permission from Lippincott Williams & Wilkins © [32].

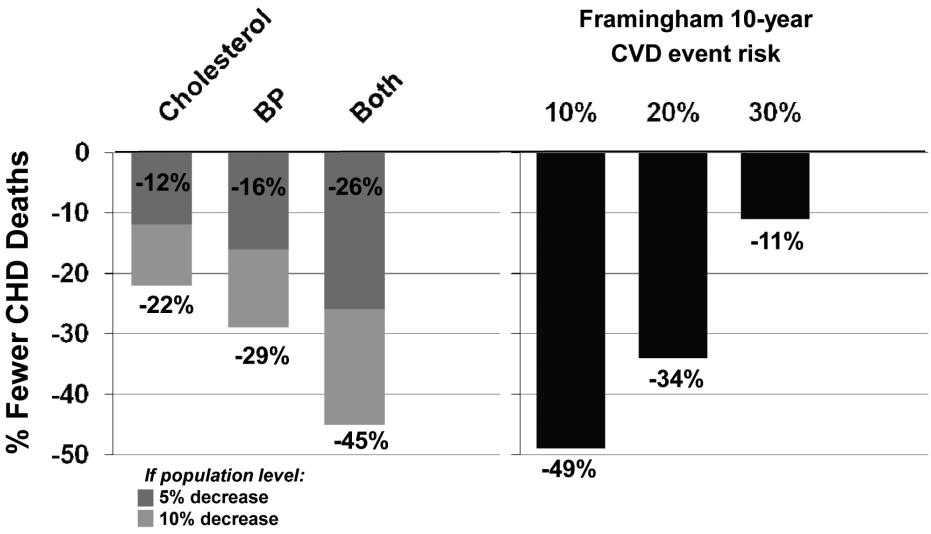


Fig. 6. Results from the British Regional Heart Study comparing the impact of modest population-wide and high-risk strategies on CHD risk. Data extracted from Emberson et al. [34].

fiscal and legislative policy. Modelling studies have an important role to play to help assess effective methods to reduce CVD risk but also need to take advantage of natural experiments (such as impact of a congestion charge in inner London on physical activity) to evaluate effectiveness and costs of hard-to-measure interventions. Targeting high-risk individuals (while effective) need to be complemented with population approaches that take into account not only mortality but also life years gained.

6. Cost-effectiveness of lipid-lowering therapy

[Lindgren P.]

The introduction of statins led to increased interest in economic aspects of lipid-lowering therapy. Since statins were perceived as effective but potentially very costly, a need existed to assess the economic consequences of this class of drug. Initially this was achieved through prediction models (such as using Framingham risk equations) but the completion of end-point trials (starting with the Scandinavian Simvastatin Survival Study (4S)) led to economic evaluations based on large trial populations.

6.1. Cost-effectiveness of statin therapy: evaluation of major trials

The objective of an economic evaluation is to assess the cost per unit of health gained for an intervention, and this can be achieved in two ways: (1) Within the trial setting, often estimating the cost of an event avoided; and (2) Using a model to predict the long-term outcome, estimating the cost per life-year or quality adjusted life year (QALY) gained.

A cost-effective evaluation of major statin trials has involved either analysis of the cost per QALY (reflects long-term cost-effectiveness) or cost per event during the trial period (short-term cost-effectiveness) (summarised in Fig. 7). A clear cost-effectiveness pattern emerges in terms of prevention – the higher the absolute risk in the population, the more cost-effective statin therapy becomes, given similar relative risk reductions. The Incremental Decrease in End-points through Aggressive Lipid-lowering Trial (IDEAL), a secondary prevention study comparing high-dose atorvastatin vs. simvastatin, shows a higher cost per QALY because the protocol used an active comparator not placebo, and, thus, the absolute risk in the comparator arm was lower.

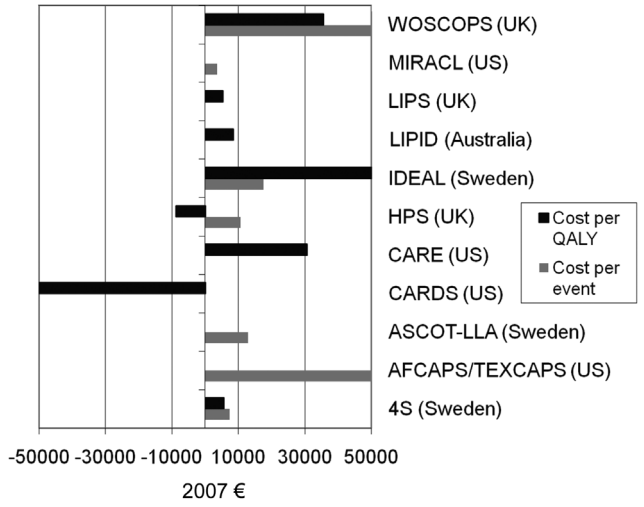


Fig. 7. Cost effectiveness of statins according to analysis of major trials.

The Heart Protection Study (HPS) has been analyzed in two separate studies: one study using cost per QALY and one using cost per event. The cost-per-event-avoided model revealed expenditure to prevent an event while the cost per QALY revealed cost reduction. This outcome occurred

because the statins became generic during the second study trial, leading to lower drug costs. The inclusion of generic costs after patent expiration was also a contributing factor behind the large savings reported in the Collaborative Atorvastatin Diabetes Study (CARDS).

6.2. Impact of generic statins on cost-effectiveness

The introduction of generic statins following the expiration of the patents for pravastatin and simvastatin in 2006 led to a reduction in statin prices. In 4S, for example, 40 mg simvastatin cost 14.91 SEK per tablet compared with 0.56 SEK or 4% of its original price. The availability of generic statins thus impacts the interpretation of previously performed health economic studies. The re-analysis of the earlier statin trials using generic prices now universally report savings rather than having to pay for a given unit of health (Fig. 8).

6.3. Ways to improve cost-effectiveness of statin in CVD management

The introduction of generic statins and the subsequent price cuts have the potential to free up resources within the field of CVD risk management. This allows us to use the resources to improve risk management; the key question is, however, "What is the most cost-effective way to do this?" There are two potential strategies to consider in this regard: (1) Treat high-risk patients more intensively; or (2) Expand the number of treated patients by improving adherence, identifying untreated patients at high risk, or treating patients at low risk.

6.3.1. Treating high-risk patients intensively

Treating high-risk patients more intensively could be achieved either by uptitrating the statin doses or by adding ezetimibe. Accordingly, this would result in the following additional effects on LDL-C levels: (1) A 6 to 9% reduction for uptitrating statin (according National Institute for Health and Clinical Excellence (NICE) guidance [35]); (2) A 23% decrease over 5 years (according to a 2007 meta-analysis of the cholesterol-lowering effect of ezetimibe added to ongoing statin therapy) [36]; and (3) A 1 mmol/L reduction in LDL-C reduces non-fatal MI and CHD death by 23% over 5 years, according to a meta-analysis of clinical trials [24].

The cost-effectiveness of treating high-risk patients more intensively according to NICE guidance were as follows:

- Ezetimibe + statin vs. titration: £ 24,000 to £ 43,000 per QALY
- Ezetimibe as monotherapy: £ 24,000 per QALY
- Ezetimibe + rosuvastatin vs. rosuvastatin alone: £ 19,000 to £ 33,000 per QALY
- Ezetimibe + simvastatin vs. atorvastatin: £ 1500 to £ 4000.

Cost effectiveness was also estimated using a Markov health economic model [37]. The analysis was based on registry data (applying LDL-C reduction and relative risk of events linked to LDL-C reduction) and estimated direct costs for a cohort of 1,000 hypothetical male patients aged 55 years. Ezetimibe + statin therapy was estimated to prevent 43 nonfatal MIs, 7 nonfatal strokes, and 26 CV deaths over a lifetime (vs. doubling the statin dose). The events avoided would provide a mean of 134 QALYs. With a mean incremental cost of £ 3,693,000, the lifetime discounted cost per QALY was £ 27,475 (£ 32,000 for men aged 75 years).

6.3.2. Expanding patient base

The cost-effectiveness of expanding the patient base has not been evaluated in any formal studies conducted so far. Given the low cost of statins, the important cost drivers would be the cost of screening the patients and regular management (physician visits). For this type of analysis, opportunistic identification and subsequent treatment of patients already being regularly followed may be one viable option; for example, in the Anglo-Scandinavian Cardiac Outcomes Trial-Lipid-Lowering Arm (ASCOT-LLA), patients were already being treated for hypertension [38].

The cost-effectiveness of improving adherence was determined in a retrospective cohort observational study of patients continuously enrolled in medical and prescription benefit plans (1997 to 1999) [39]. Patients with specific chronic diseases were identified based on claims for outpatient, emergency room, or inpatient services during the initial 12 months of the study. Then, an integrated, disease-specific analysis was performed that included administrative claims data, medical and drug utilisation. With respect to diabetes and hypercholesterolaemia, improved medication adherence was associated with lower disease-related medical costs. The attenuated medical costs more than compensated for the rise in medication-associated costs, thereby resulting in reduced overall health care costs.

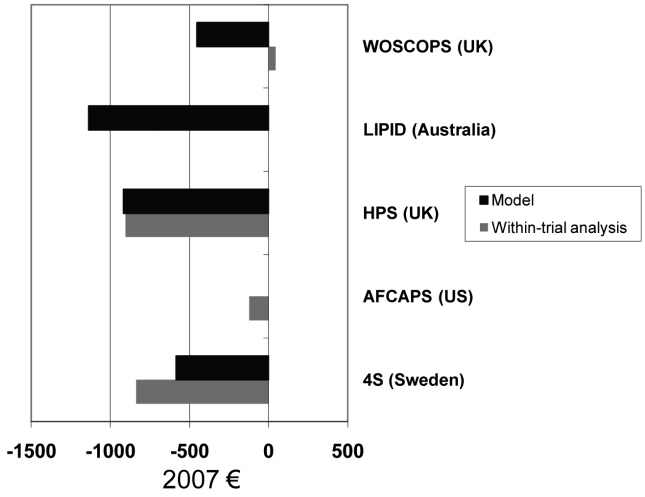


Fig. 8. Cost savings in major trials using generic prices.

6.4. Conclusions

The cost of statin treatment fell following the introduction of generics. Reinterpretation of previously published cost-effectiveness data indicate that statin therapy would be cost saving in the studied risk groups. If freed-up resources were used to treat more intensively, studies indicate that ezetimibe would provide good value. The cost-effectiveness of expanding the number of treated patients is largely unknown. The optimum trade-off between more intensive management compared with an expanded patient base needs to be investigated more fully.

7. Better lipid-lowering therapy improves long-term financial health care sustainability: a simulation model

[Atella V.]

Despite improvements in drug treatments and medical care over the last 25 years, CVD currently represents a major health care issue in terms of both health and economic aspects and is expected to be a growing concern for the future. Hospitalisation forecasts in Italy (based on Ministry of Health data) show that the number of patients at risk of hospitalisation for CVD due to high cholesterol levels is anticipated to increase by more than 50% over the next 30 years (assuming technology remains constant) (Fig. 9). The key question is "How can this projected pattern be changed through better drug treatment of cholesterol levels?"

7.1. Economic analysis using the health search database

To estimate empirically the aggregate potential savings that could be obtained in Italy by reducing CVD hospitalisation rates through improved lipid-lowering (statin) treatment in both primary and secondary prevention, an economic analysis of Italian primary care data from the Health Search Database (a longitudinal observational database set up by the Italian College of General Practitioners) was conducted over the period 2001 to 2006.

As of December 31st 2006, the database contained information collected by 796 GPs for a total of 1,532,357 patients, 15,727,442 diagnoses, 108,441,541 diagnostic tests, and 77,276,255 prescriptions. The database collects patient information, which is linked to drug prescriptions, and medical diagnoses, hospital administrations, and causes of death. To study the clinical and economical effects of statin treatment, a subsample of patients was used. This subgroup involved a total of 11,868 patients who were aged 39–70 years and who received a statin prescription during 2001 to 2006.

Based on available data, the analysis projected that about 5% of the Italian population were affected by high cholesterol levels (about 3 million individuals). Among those, approximately 47% were considered at risk of under treatment. In terms of expenditure, approximately 30% of patients used statins in a nonoptimal way, resulting in an estimated cumulative cost of € 977.8 million (at 2005 prices). A projected estimation shows that it would cost approximately € 435.3 million at constant 2005 prices (annual expenditure for statins) to bring all patients to full compliance.

7.2. Potential savings through improved lipid lowering

The potential savings associated with bringing all patients into full compliance with statin therapy were estimated by multiplying the total unit cost (direct + indirect costs) of a CV event by the number of potentially avoidable events through improved drug therapy in each region. Figure 10 shows the projected shifts in hospitalisation rates at the national level from 2007 until 2050 and the potential gains in terms of hospitalisations that can be achieved under the assumption of a fully compliant at-risk population. The number of hospitalisations increases until 2040 and declines thereafter, exclusively reflecting changes to the demographic structure of the Italian population.

Overall, the analysis shows that better compliance with drug treatment (and, thus, more effective primary and secondary prevention) may save a significant amount of

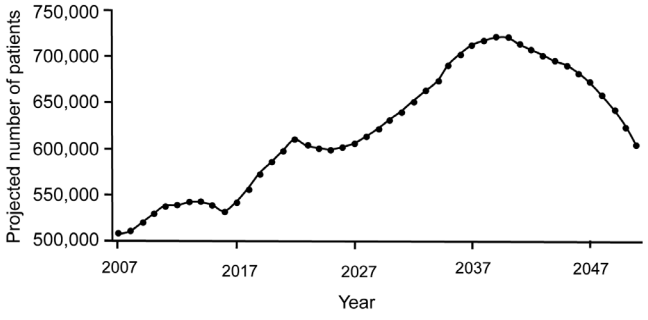


Fig. 9. Projected number of patients at risk of hospitalisation for CVD due to high levels of cholesterol. This number is forecasted to increase by more than 50% over the next 30 years. Calculation based on RGS and Ministry of Health data.

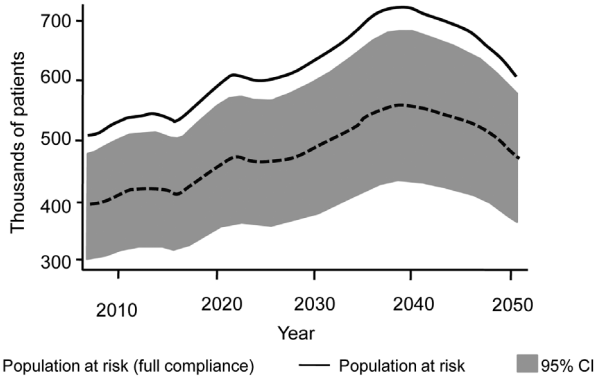


Fig. 10. Potential gain in terms of hospitalisation reduction under the assumption of a fully compliant population at risk.

Table 3
Projected aggregate savings at the national level

Savings	Year				
	2010	2020	2030	2040	2050
Change in CVD hospital admissions	−118464	−131094	−140985	−160083	−138705
Change in direct costs (million €)	−2265	−2503	−2687	−3051	−2641
Change in indirect costs (million €)	−1024	−1130	−1212	−1376	−1190
Total (million €)	−3289	−3633	−3899	−4427	−3831

money in both the short and the long term by reducing direct and indirect costs. Estimates of the potential yearly savings are relatively large, ranging from € 3289 million by 2010 and € 4427 million by 2040 (Table 3). The cost savings estimate is conservative since it does not take into account reduced cost of generic statins. The long-term saving profiles were very different across the 20 Italian regions (e.g., Trentino saving more than Liguria), suggesting the need to implement different regional health policies in the future.

7.3. Conclusions

The Health Search Database represents an important source of information to produce patient-level analyses. The results provide a country-wide picture of an important phenomenon such as the under treatment of patients suffering from hypercholesterolaemia. The simulation appears to suggest the existence of large potential savings resulting from better management of patients with high cholesterol. At 2005 prices, the estimates of potential savings range from € 2.9 billion in 2012 to € 4 billion in 2040.

8. Barriers and incentives to CVD prevention

[Hobbs F.D.R.]

This section serves to identify the spectrum of barriers to implementing CVD prevention (including those strategies pertaining to lipid management) as well consider potential incentives to overcome these barriers.

8.1. Barriers to better CVD prevention

Multiple barriers to better CVD prevention are evident and are summarised in Table 4.

Table 4
Summary of barriers to implementing CVD prevention

- Difficulty in making an accurate CVD risk estimation
- Limitations of CVD risk prediction tools
- Lack of public awareness of cholesterol as a CHD risk factor
- Failure to implement guidelines on CVD prevention
- Failure to achieve guideline-recommended LDL-C levels
- Low rates of adherence with lipid-lowering therapies

8.1.1. Difficulty in making an accurate CVD risk estimation

A key barrier to CVD prevention is the difficulty in making an accurate CVD risk estimation in clinical settings, particularly in the high-risk patient population. This includes, for example, the difficulty in identifying overall CVD risk on the basis of multiple risk factors and the tendency of physicians to underestimate patient CV risk on the basis of a simple clinical impression. According to a Swedish study comparing actual with perceived 10-year risk of coronary events for hypercholesterolaemic patients, GPs systematically under-estimated risk in several patient profiles across a range or coronary risk. Greater effort is needed to communicate the advantages and difficulties involved in multiple risk assessment [40].

8.1.2. Limitations of CVD risk prediction tools

Another important barrier relates to the limitations of CVD risk prediction tools, such as underutilisation of current CVD risk calculators, especially in primary care (only 13% of physicians always use risk charts to assess a patient's risk of developing CHD) [41]. Risk calculators tend to be too complicated for a busy practice. In addition, health care practitioners can be overwhelmed by the abundance of available algorithms including, for example, NCEP ATP III, Framingham, United Kingdom Prospective Diabetes Study (UKPDS) Risk Engine for patients with type 2 diabetes, Systematic Coronary Risk Evaluation (SCORE), Heart SCORE, Prospective Cardiovascular Münster (PROCAM) equation, British Hypertension Society (BHS), NZ Chart, Pocock Risk Score, Sheffield tables, Q-risk, all of which have some limitations. For example, using the Framingham score, an overestimation of risk occurs in the European population (CVD risk in 10-year scores benefits the elderly and underestimates the risk in younger patients). A lifetime attributed risk is needed to determine the order in which patients are treated.

8.1.3. Lack of public awareness of cholesterol as a CHD risk factor

According to a survey of 5104 members of the public in five countries (France, Germany, Italy, Sweden and the UK) [41], only 45% of the public correctly identified CHD as the leading cause of death in their country, and only 51% were aware that high cholesterol increases CHD risk (Fig. 11). Approximately half of the general public reported they had never discussed their cholesterol levels with a physician

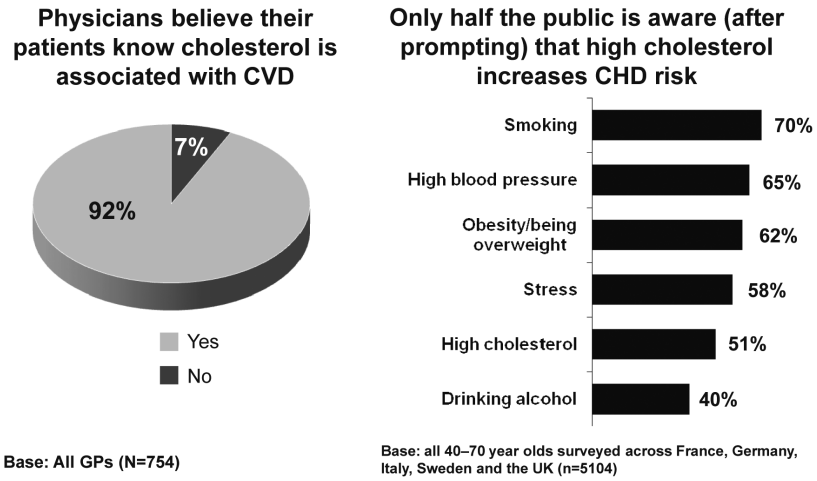


Fig. 11. Lack of public awareness of cholesterol as a CHD risk factor [41].

and only 33% knew what their target level was. Despite this, 92% of physicians believed their patients knew that cholesterol is associated with CVD.

A more recent global survey of patients' understanding of cholesterol management (The Heart study) [42], conducted in 1547 patients being treated for high cholesterol in 10 countries, showed that, overall, 74% of patients could not state MI as a consequence of high cholesterol and 19% could not identify any consequence of high cholesterol. These surveys highlight the disconnect between what the general public actually knows about cholesterol and what physicians think they know.

8.1.4. Failure to implement guidelines on CVD prevention

An additional barrier is a failure to implement guideline recommendations on lipid management and CVD prevention effectively [43]. This includes, for example, a failure to treat all risk factors to explicit targets (lipid-lowering drugs either not prescribed and/or taken, as shown in the National Health and Nutrition Examination Survey [NHANES] 1999–2000) or a failure to recognise dyslipidaemia. Despite the availability of effective lipid-lowering medications, numerous studies show that at-risk patients are often failing to reach the treatment goals recommended in guidelines.

The first European Action on Secondary Prevention through Intervention to Reduce Events (EUROASPIRE) survey [44], conducted among patients with established CHD followed up in specialist clinics, revealed a sizeable potential for CVD risk reduction. A subsequent EUROASPIRE survey [45] showed promising improvements in lipid management but many heart disease patients still had cholesterol and BP levels exceeding the recommended European targets, continued to smoke, and remained overweight. The most recent survey (EUROASPIRE III) [46] also suggests that primary-prevention patients are under treated to an even greater extent than coronary patients as well as not adhering to lifestyles that promote CV health. Approximately 75% of these patients had total cholesterol and LDL-C levels above the ESC guideline-recommended values [47].

8.1.5. Low rates of adherence with lipid-lowering therapy

[Catapano A.L.]

Many patients who begin statin therapy have low rates of adherence and, thus, experience no or limited CV benefit attributable to effective lipid lowering. A recent study showed that elderly patients with and without recent ACS have low rates of adherence to statins: 2-year adherence rates were only 40.1% for patients with ACS, 36.1% for patients with chronic CAD, and 25.4% in patients with no coronary disease (primary prevention) [48]. Similarly, a retrospective cohort study of 34,501 individuals (65 years and older beginning statin treatment) showed a substantial decline in persistence with statin therapy over time, particularly over the first 6 months of therapy [49]. Nonwhite race, lower income, older age, less CV morbidity at initiation of therapy, depression, dementia, and occurrence of CHD events after starting treatment were all identified as predictors of poor long-term persistence.

Adherence to statin therapy may also impact survival, according to results from a recent study evaluating the relationship between drug adherence and mortality in survivors of acute MI [50]. The risk of mortality was greatest for patients with low adherence to statin therapy, compared with high-adherence counterparts (24% vs. 16%, $P = 0.001$) and was intermediary for patients who had intermediate adherence (20%, $P = 0.03$). According to the West of Scotland Coronary Prevention (WOSCOP) study, patients taking 75% or more of their prescribed lipid-lowering medication reduced their risk of death from any cause by 33% compared with those who took less than 75% of their medication, and there was also a significantly reduced need for revascularisation procedures.

8.2. Potential incentives to overcome barriers

[Hobbs F.D.R.]

A number of incentives and implementation strategies have been shown to improve outcomes in CVD prevention, including government endorsement of guidelines, targeted financial incentives, structured care, audit, and feedback, and educational activities. Government endorsement of guidelines (via national health policy) may help to reduce the burden of CVD and to change physician and patient behaviour. The implementation of CVD prevention guidelines can be made more effective, particularly in high-risk patients already identified, by a number of means (Table 5) [43]. Several examples exist (meningococcal vaccination and cervical cytology targets) demonstrating that public health policy and government policy can influence clinical practice rapidly.

Targeted financial incentives can improve CVD risk management in primary care, as evidenced by the introduction of the Quality Outcomes Framework (QOF) in the UK in 2004. This scheme involves relating performance with pay; 25% of the income in the primary care setting comes from a complex set of initiatives in chronic disease management, practice organisation, patient experience, and additional services. Over half of the clinical indicators relate to vascular disease. Evidence of the impact of systematic quality improvement initiatives on quality of care in the National Health Service (NHS) comes from longitudinal cohort studies. Substantial improvements were seen in quality of care for three major chronic diseases (CHD, asthma, and type 2 diabetes) between 1998 and 2003 [51]. Substantial improvements were also seen in the percentage of patients reaching total cholesterol (<5 mmol/L) or BP <150/90 mmHg) targets. Quality of care between 2003 and 2005, following the introduction of QOF financial incentives, resulted in a further increase (approximately 20%) [52].

Structured care, audit, and feedback are also potentially important considerations in overcoming barriers to CVD prevention, but their effectiveness is small and should not be relied upon in isolation. In addition, educational interventions (such as lectures, conferences, continuing medical education (CME), and education outreach) can be useful, but there is limited evidence that these activities change actual clinical practice; instead, they tend to enhance knowledge rather than change behaviour.

Table 5
Suggested ways to improve implementation of CVD prevention guidelines

- Harmonise guidelines and focus on common areas of consensus rather than state-of-the-art science
- Remove the boundary between primary and secondary prevention and focus on total (global) risk
- Help policy makers understand the different components of CVD
- Include professional societies from different specialties in guideline development/implementation to increase ownership
- Increase nurse involvement, especially during the first 6 months after initiating statin therapy (especially valuable in improving compliance and adherence to therapy)

9. Overcoming barriers to proper lipid management: lessons from Italy

[Vanuzzo D.]

Overcoming barriers to proper lipid management in country-specific health organisations will require revising the legislative and administrative policy objectives at the EU, national, and regional levels. Examples of these new objectives could be: (1) To implement national and regional cholesterol performance measures and incentives for primary care physicians to screen high risk patients and achieve cholesterol target levels in these patients; (2) To identify and eliminate legislative and administrative barriers to providing optimal lipid care to high-risk patients at the EU, national, and regional levels of government and health care systems; and (3) To introduce a policy action devoted to apparently health people.

Italy may provide a useful example of the types of changes needed. The Italian health system is structured into multiple layers, headed by the Ministry of Health (responsible for main strategies), followed by regional health systems (responsible for planning and organisation), and health units (responsible for implementation and monitoring).

9.1. National CVD prevention plan

A national prevention plan relevant to CVD was developed over the period 2005–2008 and includes several key components such as assessment of CVD risk, development of a CV risk observatory, and prevention of recurrent events:

Assessment of CVD risk. This encompasses the use of risk score software (www.cuore.iss.it in English) (Fig. 12) to provide users with the tools needed to assess the likelihood that a person will experience a major CVD event (MI, stroke) over 10 years, knowing the values for certain risk factors. The software advises physicians to consider dyslipidaemia as a diagnosis in cases of high cholesterol levels. This is important since dyslipidaemias are considered chronic diseases and, if certified by a public lipid clinic, allow complete reimbursement of many blood assays, noninvasive procedures, and lipid-lowering therapies. From these activities, a patient registry could be foreseen to actively search for dyslipidaemias in various Italian regions. GPs were also trained in assessing CVD risk using this programme.

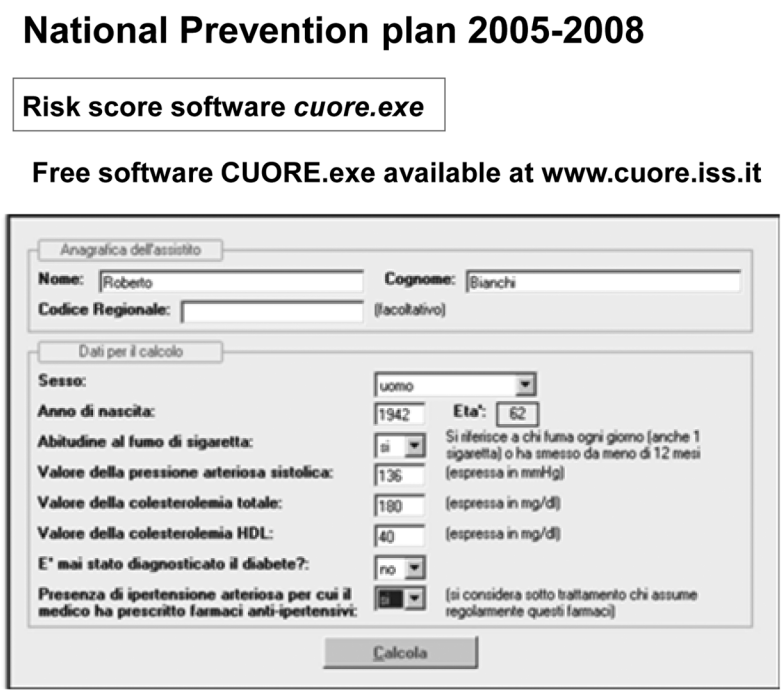


Fig. 12. Risk score software provides users with tools to assess the likelihood that a person will experience a major CVD event (MI, stroke) over 10 years when values for certain risk factors are known.

Development of a CV risk observatory (cuore-iss.cineca.it). This web-based tool enables physicians to monitor CV risk, perform a quality control assessment of data collection, use data analysis in an easy and fast way, and assess a patient's risk and compare it to patients in other regions and at national level. The observatory also benefits the National Institute of Health and Ministry of Health by providing a platform for data analysis of CVD risk at national level and by providing support for health policy makers.

The prevention of recurrent events. This is achieved through the use of a hospital discharge letter and disease management of heart failure (for patients with CHD) and through organisation of stroke units (for patients with stroke).

9.2. Population level CVD prevention

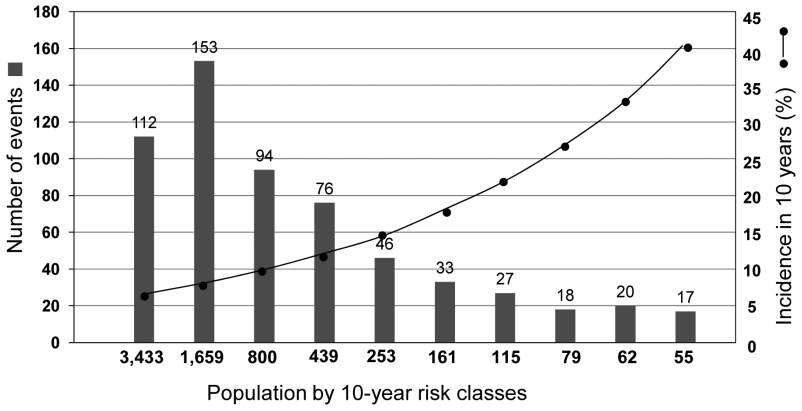
A programme was also recently launched by the Ministry of Health with aim of improving the health status of the population according to WHO multidisciplinary interventions. The programme focuses on making healthy choices easy options for individuals and is in line with the EHHC (launched in Milan, 15 November, 2007) stating the every child born in the new millennium has the right to live until the age of at least 65 without suffering from avoidable CVD.

9.3. Monitoring of CVD outcomes using registries

The monitoring of CVD in Italy through an Italian registry of coronary and cerebrovascular events provides common tools to assess the outcome benefits of various prevention strategies [53]. For example, the Osservatorio Epidemiologico Cardiovascolare, a Health Examination Survey conducted in Italy from 1998 to 2002 [53], allowed monitoring of intermediate outcomes of various risk factors such as BP, cholesterol, smoking, BMI, and obesity. As noted by Stamler [54] in a 2007 editorial, "A key strategic challenge – and opportunity – for medical care and public health is to achieve a progressive steady increase in the proportion of the population at low risk. This is essential for the conquest (i.e., ending) of the CVD epidemic" (Fig. 13) [55].

9.4. Conclusions

In Italy, close cooperation among the Ministry of Health, the National Drug Governance Agency, The National Institute of Health, the Federation of Cardiologists, the Heart Foundations, and the College of General Practitioners represents a step forward for sustainable disease prevention strategies, according to European recommendations. Lifestyle intervention is costly and time consuming, and lifestyle advice should be incorporated in the treatment of a disease or part of rehabilitation. Life style recommendations should go hand in hand with drug treatment. Health professionals should be role models for their patients and/or health services, and for other workplaces. Training health professionals should be included in local plans to satisfy local needs, including active dyslipidaemia search. A specific plan should be developed for familial dyslipidaemias, including regional and national registries, benefits for the



A key strategic challenge—and opportunity—for medical care and public health is to achieve a progressive steady increase in the proportion of the population at low risk. This is essential for the conquest (i.e., ending) of the CVD epidemic."

Jeremiah Stamler

Fig. 13. CVD events and incidence by 10-year risk classes in men ages 35 to 69 in Italy. Reproduced with permission [55].

relatives of dyslipidaemic patients (e.g. lipid assessment and access to a lipid clinic free of charge), educational courses for physicians, proper communication with the affected people and the public opinion.

10. Strategies and interventions to improve CV prevention: the Italian experience

[Volpe M.]

CVD is expected to have a substantial clinical and socioeconomic impact in Italy in the next few years, potentially threatening the sustainability of the entire national health care system [9]. To enhance the level of attention on interventional strategies for improving CV prevention in Italy, consensus document or White Paper was developed [9].

10.1. Scope and objectives of the 2008 White Paper

The White Paper represents the collaborative work of several scientific societies in Italy with the goal of rapidly promoting strategies and interventions to better prevent CVD. The White Paper proposes both general and specific interventions, addresses decision-makers, stakeholders, institutions, citizens, physicians, health care workers, organisations and industries, and is aimed at reducing the incidence of CVD and its impact on the health care system in the short to medium term (3 to 10 years) as well as long term. The objectives of the document were to:

- Support health-policy initiatives and interventions in national, regional, and local plans for CVD prevention.
- Increase awareness of physicians, health care operators, and citizens about the relationship between CVD risk factors and major CVD events (mostly MI and ischemic stroke) and about ways to reduce this risk.
- Promote the development of more effective interventions for control of CVD risk.

10.2. Interventions to reduce CVD burden in Italy

Suggested specific interventions to achieve the White Paper objectives were wide ranging (Table 6) and should serve as a starting point for promoting the implementation of integrated strategies for effective CVD prevention.

10.3. Conclusions

Action to reduce CVD burden should ideally be a three-pronged attack: (1) integrate strategies for reducing incidence of major CV events in the short-term; (2) improve the use of tools for total (global) CV risk estimation; (3) provide useful and updated information for the development of national or local databases for monitoring CV disease trends. In addition, initiatives to educate the population on CVD prevention should be considered via various media tools (such as web casts), involvement of journalists, employers serving as health coaches, and making yearly cholesterol and BP measurements mandatory to obtain government documents such as a driver's licence.

It is critical that the medical community embraces and acts on the new total risk management strategy. Failure to replace the current treatment paradigm (based on addressing single risk factors) with a more comprehensive approach will result in missed opportunities to reverse the current epidemic of CV diseases.

11. Speaker Panel discussion

After reviewing the facts about CVD and barriers to achieving widespread improvements in lipid control and CVD prevention, the panel members, under the direction

Table 6
Suggested interventions to reduce CVD burden in Italy

1. Sustain and support health policies designed to promote or improve prevention of CVD in Italy
2. Support and implement initiatives to quit smoking
3. Identify training and educational strategies aimed at preventing CVD
4. Increase awareness of the importance of medical management of total (global) CV risk
5. Use detection of potential indicators of high CVD risk (such as family history, high BP, cholesterol levels, or other modifiable risk factors) as a starting point to perform a total CV risk stratification
6. Assess the total (global) CV risk and project an estimate of CV risk over time
7. Discuss the importance of CV risk assessment and prevention of CV benefits with patients
8. Start diagnostic and therapeutic interventions early
9. Promote the use of recommendations for CV prevention, which should be simple, integrated, and shared by the various scientific societies
10. Promote the role of general practitioners
11. Provide cultural and scientific support to multidisciplinary professional activities of all health professionals involved in preventing CVD
12. Identify and support initiatives by industries or public and private associations, which may have an impact on CVD prevention
13. Develop documents for CV prevention
14. Harmonise and sanitise the initiatives and policies in terms of CV prevention in association with the EU
15. Identify annual or periodic objectives that are clearly specified, realistic, and achievable using criteria of verification the attained results

Extracted from Volpe [9].

of the meeting co-chairmen (see layout of the Session, page 21), identified and discussed several aspirational and achievable goals or targets that could potentially improve the health of all nations within the EU. These key issues are summarised in Table 7 and described below.

- Evaluate the economic burden of disease by incorporating indirect costs due to CVD and informal costs linked to patients' relatives. Economic models predicting substantial health care cost savings with more effective lipid control and use of statins need to be bolstered by actual documented (not theoretical) savings in the real world. While evidence from Scotland (population approximately 5 million) indicates that implementation of total cholesterol targets of <5 mmol/L translates into prevention of 22,000 CHD events over 4 years, the cost of achieving this target is high (€ 90 million) and even higher (€ 400 million) for more aggressive targets (4 mmol/L). Effective means to communicate these cost-effective benefits to policy makers need to be identified and acted upon.

Table 7
Aspirational and achievable goals to improve the health of all nations within the EU

- Evaluate the economic burden of CVD by including indirect costs and informal costs linked to patients' relatives
- Focus attention on stroke prevention as well as CHD
- Consider joint government initiatives
- Re-evaluate farming policy and food subsidies related to unhealthy foods
- Increase funding of primary prevention strategies
- Evaluate potential impact of financial incentives to patients
- Assess the impact of further reducing statin costs
- Improve patient adherence/persistence with lipid-lowering therapies
- Improve public awareness of CVD
- Coordinate the knowledge and efforts of health economists, medical professionals, and biologists to change public policy on CVD prevention

- Focus attention on stroke prevention in addition to premature CHD. The US has successfully achieved an amalgamation of stroke and CHD prevention strategies by focusing on both cholesterol and BP lowering but Europe is lagging behind in this regard. The population tends to be more concerned about experiencing a non-fatal stroke than an MI; this public concern could be leveraged to bring about broader changes in health care prevention policy.
- Consider joint government initiatives. Since a large part of total CVD cost extends beyond health care and impacts the whole of society, a preventative strategy should perhaps be considered which includes joint initiatives with ministries of health and other departments such as the department responsible for labour and social welfare.
- Critically re-evaluate farming policy and food subsidies that drive the population to eat unhealthy foods.
- Increase funding of primary prevention strategies at the general practice level. Most financial health care resources in Europe are spent on secondary CVD prevention in patients with established disease, particularly with respect to in-patient care in hospitals; a more comprehensive approach to primary prevention should involve not only population strategies but also additional funding of strategies at the general practice level, which are currently inadequately funded with only 5% of the total CVD budget.
- Evaluate potential impact of financial incentives to patients. Consideration and evaluation should also be given to paying patients to make certain lifestyle choices (such as smoking cessation) or adherence to drug therapies as well as financial incentives to physicians to improve CVD risk management.
- Determine the impact of further reducing the cost of statins. Reduced cost of statins could potentially shift the emphasis on CVD prevention cost-effectiveness away from the targeted high-risk group to a larger

proportion of the entire population. However, poor adherence of patients to statin therapy would still need to be addressed.
- Improve patient adherence/persistence with existing lipid-lowering therapies to provide substantial health and economic gains.
- Improve public awareness of CVD and dispel widely held public misconceptions. This potentially could shift the CVD risk profile of the population towards the lower risk categories.
- Coordinate and better disseminate the knowledge and efforts of different disciplines (health economists, medical professionals, and biologists) to leverage change in public policy to focus on CVD prevention in a more concerted way (currently lacking in the European environment).

12. Concluding remarks

[Graham I.M.]

The key priorities to improve the health of all nations within the EU with respect to lipid lowering and CVD prevention should include the following:
- All policy recommendations should fall within the general context of the EHHC.
- Multidisciplinary implementation groups that include politicians, educators, as well as physicians, need to be convened and empowered.
- The general public health issues of obesity and fat balance within Europe urgently need addressing.
- Equity of access of health care services should be improved to enfranchise the poor and deprived and empower them to take the necessary positive steps to lower their lipids and their total (global) CV risk.
- The radically altered cost/benefit profile of statins needs to be acknowledged and integrated as a central component of any CVD prevention strategy moving forward.

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Layout of the Session (Saturday, 25 October, 2008)

BRIDGING SCIENCE AND HEALTH POLICY IN CARDIOVASCULAR DISEASE: FOCUS ON LIPID MANAGEMENT

The Facts

Chairs: DA Wood (London, UK) – AL Catapano (Milan, Italy) – M Volpe (Rome, Italy)

Introductory remarks
DA Wood (London, UK)

The economic burden of cardiovascular disease in the European Union
J Leal (Oxford, UK)

Cardiovascular risk reduction in whole populations: achievements and challenges
J Critchley, F Young, DR Whiting, NC Unwin, S Capewell (Newcastle-upon-Tyne and Liverpool, UK)

Cardiovascular prevention: A call-to-action to reduce disease burden
M Volpe (Rome, Italy)

The Barriers

Chairs: DA Wood (London, UK) – AL Catapano (Milan, Italy) – M Volpe (Rome, Italy)

Clinical evidence in lipid management
AL Catapano (Milan, Italy)

Barriers and incentives to improving CVD prevention
R Hobbs (Birmingham, UK)

Panel discussion with the following discussants:
AL Catapano (Milan, Italy) – J Critchley (Newcastle-upon-Tyne, UK) – R. Hobbs (Birmingham, UK) – J Leal (Oxford, UK) – R Paoletti (Milan, Italy) – M Volpe (Rome, Italy) – DA Wood (London, UK)

Q & A from the floor

The Policy

Chairs: A Brady (Glasgow, UK) – IM Graham (Dublin, Ireland)

Cost-effectiveness of lipid-lowering – implications of the changing economic landscape
P Lindgren (Stockholm, Sweden)

Can better drug treatment improve long-run financial sustainability of the NHS in Italy? The case of statins
V Atella, F Bellotti, F D'Amico (Rome, Italy)

Setting legislative and administrative policy objectives at European, national, and regional levels
D Vanuzzo (Udine, Italy)

Panel discussion with the following discussants:
V Atella (Rome, Italy) – A Brady (Glasgow, UK) – IM Graham (Dublin, Ireland) – P Lindgren (Stockholm, Sweden) – D Vanuzzo (Udine, Italy)

Q & A from the floor

Summing Up
IM Graham (Dublin, Ireland)

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Atherosclerosis Supplements 10 (2009) 22–28

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The Lorenzini Foundation in a changing scenario of patient management

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Abstract

The loss of life, disability, and economic burden attributed to cardiovascular disease (CVD) in Europe has created an urgent need for all stakeholders in CVD prevention to partner together to address the barriers in local health policy and produce effective programs in individual and population risk reduction and rational use of health services. Countries have a legal and moral obligation to achieve the highest standard of CV health care for citizens and to improve national health care systems accordingly. As part of a vision for future potential opportunities in CVD prevention, the Lorenzini Foundation would like to raise awareness of several key areas among the European authorities: Integration of interventions aimed at several risk factors within an individual country's health care system; implementation of a comprehensive approach combining policy development, capacity building, partnership and information support at all levels; promotion of transversal health policies, including coordinated action outside of the health sector to address major determinants of ill health; a combination of health policy and high-risk strategies to link health promotion, public health services, primary care, and hospital care; and, finally, reduction in ethnic, cultural, socioeconomic, and gender inequalities to multiple risk factor management among and within countries through use of cost-effective medications and medical technologies.

Keywords: Non-communicable diseases; Cardiovascular disease; Risk factors; Health policy; Health services; Prevention; Lipids

1. Introduction – defining the needs

The 7th International Symposium on "Multiple Risk Factors in Cardiovascular Diseases: Prevention and Intervention – Health Policy" held in Venice, Italy, on 22–25 October, 2008, reviewed a plethora of concepts on how best to proceed with programs dedicated to reduce the loss of life, disability, and economic burden of CVD. In particular, the Symposium stressed the necessity to actively tackle the structural barriers in local health policy and produce effective programs in individual risk reduction, population risk reduction, and rational use of health services. It was clear from the Symposium that an urgent need exists for all of the stakeholders in CVD prevention to partner together to disseminate throughout Europe the substantial body of evidence-based knowledge on the clinical and socioeconomic benefits of multiple risk management. In addition, the Symposium also revealed that many barriers to better CVD prevention remain to be overcome and that, with respect to the relatively more efficient health systems in Europe, coordination of different health services is critical to optimise the treatment and to prevent CVD and, indeed, NCD in general.

2. Critical issues in the continuity of medical care

In its broadest sense, continuity of medical care encompasses policies that help to create more coherent patient-centred care within and across care settings over time, thereby making health care systems more responsive to patient's individual needs and ensuring appropriate care in acute and chronic settings [1]. According to a recent health policy report in the New England Journal of Medicine [2], several key domains of care coordination exist: (A) Among providers (this includes, for example, general practitioners (GPs) and specialists; GPs and emergency departments; GPs and hospital-based physicians; GPs and health districts plans; physicians and source of diag-

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nostic data; physicians and regulatory requirements) and (B) Between providers and patients and their families (this includes, for example, GPs and patients and their families; hospitals and patients and their families; health districts, municipalities and patients and their families). Clearly, the number of coordination relationships can be extensive in the typical health care scenario of three provider organisations involving multiple caregivers and patients and their family members [2].

It is widely acknowledged that the principal barriers to continuity of care exist between the hospital and home. In fact, transitions from one health care setting to another often parallel transitions in health status and can be associated with intentional as well as unintentional changes in patient care. For example, hospitalisation may put patients at increased risk of discontinuity of medications used in the community setting. Hospital safety programs should thus focus attention on medication therapy discontinuities at times of transition to ensure continuity of care in relation to drug therapy [3]. Additional barriers to the continuity of care also exist between the local health services and patients, particularly with respect to procedural rules, methodologies, and technical support.

Improvements in the structure of health care systems to reduce costs is especially important for patients who are chronically ill [1]. A 2007 report from the Directorate for Employment, Labour, and Social Affairs Health Committee comprehensively reviewed care coordination practices in EU and other countries and attempted to identify problems currently impeding better coordination [1]. The report noted that targeted programmes (e.g., disease and case management aimed at specific illnesses or populations) appeared to have a positive impact on the quality of care but had inconsistent cost-saving benefits. The report also revealed that continuity of care could be improved through better information transfer (e.g., more widespread use of information and communications technology (ICT)) and by fine-tuning existing health care systems through better organised ambulatory care to patient-centred integration of health and long-term care.

Many of these issues were raised, discussed, and further elaborated upon during the Session entitled: “From Hospital to Home: Continuity of Care in Internal Medicine”, and key findings are summarised in Table 1. Adequately exploring and defining these issues as well as formulating and applying effective, practical solutions is a challenge for the future and will necessitate the development and implementation of effective procedural tools as well as a retooling of health organisation and structure.

3. Critical issues in health policy strategies

Many health care systems in Europe are universal, although differences do exist among countries and among regions within individual countries. In the Session entitled “From Hospital to Home: Health Policy Strategies”, the main domains reviewed and discussed were:

1. Primary and secondary care (including, for example, life and economic burdens, pathways, performances, and outcomes)
2. Strategy of integration of competences (including, for example, system development, quality assurance, objectives, key players, procedures, tools, and monitoring), and
3. Alliances, programmes and projects.

With respect to primary and secondary care, a restructuring of the local regional health plans is required, particularly in terms of the relationship between hospitals and the community. A key priority in this restructuring is to improve the efficiency and efficacy of the health care systems, thereby increasing the appropriate use of resources. A principal driving force in this modernisation process is the economic viability of the plans, as assessed by a number

Table 1
Summary of key issues relating to continuity of care raised during the Session entitled “From Hospital to Home: Continuity of Care in Internal Medicine” discussed by B. Maisch (Marburg, Germany), G. Vescovo (Vicenza, Italy), C. Cricelli (Florence, Italy), R. Nardi (Bologna, Italy), G. Baggio (Padua, Italy), S.D. Anker (Berlin, Germany) and A. Rosenberg (Uppsala, Sweden)

- Continuity of care across all settings and over the natural history of disease
- Medical, social, and housing service coordination via collaborative teams
- The home as the centre of health care delivery and social supports
- Matching patient goals with processes of care
- Shared responsibility among university hospital, municipality, and primary care and focussing on comprehensive, patient-centred approach involving integration, cooperation, collaboration, and effective communication
- Clinical, social, and political programs for elderly, frail patients:
  - To better integrate hospital/community care and facilitate early discharge of elderly patients from hospital after an acute event
  - To plan continuum of care in the community for chronic conditions
- Evidence-based clinical practices across multiple disciplines to improve the quality and cost-effectiveness of care for patients with chronic conditions
- Patient assessment using biomarkers (especially in heart failure)
- Integrated, cost effective approach to patient lifestyle changes between GPs and specialist centres
- Electronic referral, referral agreements, and efficiency in information exchange among specialists
- Video discharge conference to increase the effectiveness and quality of the discharge procedure by connecting the patient, patient’s relatives, staff from the university hospital, primary care, and representatives from the municipality

of accounting items such as costs associated with hospitalisation, outpatient care, pharmacotherapy, home care support, work-days lost, and social costs. Since the efficient management of CVD involves integration among all players at the national, regional and local levels, inside and outside the health care sector, proper funding is important and "silo budget" thinking should be avoided. Saving money in one specific area could increase costs in another area – for example, rapid discharge of patients may decrease hospital costs but can also increase costs in the community [4,5]. Thus, funding for specific types of health care, allocation of specific budgets for pharmaceuticals or service types, and cost containment measures aimed at specific resources or services should be discouraged [6]. Instead, emphasis should be placed on overall allocations of health care expenditure based on population-based budgeting, assessment of value based on technology assessment and analysis of cost effectiveness, allocation of resources for specific disease programs rather than types of services, and development of disease-based practice guidelines and related monitoring of care provision [6].

It is clear that more efforts in identifying bench marking and best practices are needed to evaluate the strategies of integration in terms systems development, quality assurance, and performance. During the Session, several possible approaches were identified to aid in this process:

- Identification of main problems
- Comprehensive analysis
- List of recommended interventions
- Governed competence distribution among providers
- Clinical governance and budget balance
- Quality assurance and medical performance evaluation
- Optimised approach to ICT and e-health
- Emergency regional networks
- GPs and specialists alliance
- Personalised pathways for diagnosis, treatment and prevention
- Health promotion, training, education
- Partnership with academia, basic research, NGOs
- Partnership with industry research and development
- Continuous quality control and quality improvement.

Several models of successful health care modernisations were presented during the Session, including those from several European regions: Lombardy (L. Bresciani, Milan, Italy), Friuli Venezia Giulia (D. Vanuzzo, Udine, Italy), Veneto (L. Bertinato, Venice, Italy) and the Andalusia region (J.L. Rocha Castilla, Seville, Spain). The Lombardy model is based on a health care network with three levels of delivery [7] as described by the Lombardy Health Ministry, L. Bresciani: the 1st level comprising prevention strategies, general practitioners, community health measures, and pharmacies; the 2nd level including specialist care, first and second level diagnostics, and general hospital care/treatment; and the 3rd level encompassing medium and high-technology hospital care. The Lombardy plan involves moving medicine closer to the patient by shifting 1st and 2nd level diagnostic and treatment procedures to a more local level while leaving complex technologies within accredited hospitals. In addition, the plan includes improved quality of emergency care systems, involvement of professionals, local governments, and voluntary and charitable associations in planning and implementation, and use of latest technologies (e.g., ICT, e-health, telemedicine, and telediagnostics).

The integrated approach to managing chronic diseases (including CVD) in Andalusia, also involved re-designing the clinical systems across primary care, secondary care, acute care, and community care. As with the Lombardy Region Plan, the goal is integrate and manage health care closer to the patient. The intention of this process reengineering is to provide the right care at the right time with the right provider, the first time and every time.

The Veneto region of Italy is actively engaged in hospital reform not only with respect to utilisation of restructuring tools involved with purchasing, payment systems, and contracting but also in terms of benchmarking health care systems as a way of improving the quality of hospitals and health services. In particular, acute MI patients benefit from a new cardiac care cycle strategy as part of the overall health system. The main components of the cardiac care cycle focus on (1) coordinated and effective health care addressing the needs of both patients and caregivers, (2) faster hospital arrival times, (3) better monitoring of bio-chemical and ECG signals sent from ambulances to destination hospitals, (4) shorter stays in hospital, (5) encouraging caregivers to promote healthier lifestyles, and (6) effective management of long-term conditions in partnership with GPs and territorial health units. This programme has markedly improved cardiac care as evidenced by increased numbers of live patients arriving with acute MI in hospitals, rapid initiation of reperfusion therapy upon arrival, and better follow-up treatment after discharge.

In the Friuli Venezia Giulia region, a steering committee is developing and implementing an integrated training programme in CVD prevention and health promotion among general practitioners, cardiologists, and public health doctors. Part of this programme involves the development of a unique website dedicated to CV risk evaluation and monitoring, including promoting healthy lifestyles.

A recent trend presented and discussed during the Session entitled "From Hospital to Home: Continuity of Care in Internal Medicine" is the use of remote patient monitoring and telemedicine. This type of clinical monitoring is now gaining acceptance because of recent developments in information technology, decreased costs of mobile communications, and demonstration of effectiveness compared to nurse telephone support. In the Trans-European Network-Home-Care Management System Study (TEN-HMS), telemedical support of ambulatory patients with heart failure resulted in survival benefits and reduced length of hospitalisation compared to usual nurse-led care [8]. To overcome problems of earlier systems (such as availability

during office hours only and a lack of physician screening leading to limited decision making), third generation systems [9] are being now being developed and tested. In one system in Germany, discussed by S.D. Anker (Berlin, Germany), physicians and nurses at a telemedicine centre in Berlin make clinical decisions 24 hours per day/7 days per week based on incoming data, the patient's history, current treatment, and direct patient contact. The system can be programmed to permit transfer of a variety of patient clinical data, including ECG, body weight, arterial oxy-haemoglobin saturation, and cardiac and infection biomarkers. The system is currently undergoing extensive clinical trial testing in Germany using the primary endpoint of total mortality and secondary endpoints of CV mortality rate, overall non-elective hospitalisation, CV hospitalisation, plasma level of N-terminal prohormone brain natriuretic peptide (NT-proBNP), and quality of life, and cost effectiveness. If the results are positive, tele-home-care networks will essentially put the emergency room into the home of the patient.

The application of information technology is also proving useful in the discharge conference for hospitalised patients. For example, in Sweden, as described by A. Rosenberg (Uppsala, Sweden), a video discharge conference uses telemedicine to increase the effectiveness and quality of the discharge procedure by helping to connect the patient, the patient's relatives, staff from the university hospital, primary care, and representatives from the municipality.

4. Potentially rewarding avenues for CVD prevention

In terms of the much broader framework of CVD prevention, the Lorenzini Foundation has been actively engaged in identifying several key areas where decisive action may be expected to be especially advantageous not only for the individual citizen but also for society as a whole. These areas are summarised below:

- Collection, analysis and evaluation of reliable epidemiological data from different countries, including life and economic burdens, risk factors, life style, public health structure and organisation, and policy plans. The absence of adequate methods for assessment impacts the financing not only of health care systems but also preventive public health measures [10,11].
- Identification and elimination of inequalities in access to health systems among European countries. This includes, for example, the rights to health, rights to medicines, per capita expenditures in medicines, total government spending on health (in relation to gross domestic product and to military expenditures), national health plans, and health indicators such as life expectancy [12].
- Validation and context-specific qualification of the use of biomarkers. This includes their integration in the clinical decision-making process and their application to risk stratification [13].
- Multiple risk factor approach in the diagnosis, prevention, and treatment of CVD, emphasising the use of integrated protocols and coordinated clinical management by different medical specialties.
- Public awareness and recognition of the multiple risk factor concept (hypercholesterolaemia, hypertension, smoking, obesity/overweight, malnutrition, diabetes, sedentarity, air pollution) by citizens of all ages, by institutions, and by health care workers [14].
- Gender differences in the pathophysiology and management of CVD [15].
- Translation of harmonised international and national guidelines for primary and secondary prevention [16,17].
- The boundary between primary and secondary CVD prevention, with a focus on the level of global risk [17].
- Ethnic, cultural, socioeconomic, and behavioural differences (e.g., food, smoking, air pollution) among citizens in various countries [16,18,19].
- Inertia of governmental action and reaction to CVD.
- Budget constraints limiting the use of effective drugs in primary care [20].
- Patient compliance with prescribed therapies [21–23].
- Effectiveness of education programs on CVD prevention [24,25].
- Mapping national plans, policies and measures that impact cardiovascular health promotion and CVD prevention (in progress by European Heart Network).
- Variations in policies, resources and outcomes information, consumer rights choice, access (including waiting times), and prevention procedures (including medication) in all fields of health care [26].
- A stronger commitment to disseminate the European Heart Health Charter (EHHC) by the European and national political institutions and decision makers [27].
- Differences among European countries in managing high-risk individuals in primary-prevention programs (as demonstrated by EUROASPIRE I, II, and III surveys). Too few high-risk patients follow the European guidelines for the prevention of CVD and more than 80% never have received any advice or direction about the importance of following a heart-healthy lifestyle program [28–30].
- Empowerment of consumers and patients to take active roles in their own health from the perspective of both disease prevention and disease management, as promulgated by the American Heart Association (AHA). As an organisation committed to "building healthier lives free of CVD and stroke", the AHA should be encouraged to continue identifying opportunities to further empower consumers and patients using the latest developments in evidence-based care, consumer research, and technologies, such as the PHR (Partnering to Reduce Risks and Improve Cardiovascular Outcomes). The multiple-target and multiple-tools approach by AHA deserves careful consideration in the European setting [31].

5. Potential opportunities to overcome barriers to multiple risk factor management

To help reduce the barriers to effective and comprehensive multiple risk factor management of CVD within Europe, the economic and health authorities of the EU are ideally positioned to contemplate a unified European CV health strategy. Under the leadership of the EU, countries could be encouraged to develop comprehensive national health plans consistent with defined criteria, including adequate budget allocations for all proposed activities. These health plans could, for example:

- Propose general and specific interventions addressed to decision-makers, institutions, citizens, physicians, health care workers, scientific societies, organisations, and industries aimed at reducing the CVD loss of life, disability, and economic burden in the EU;
- Standardise approaches within health economic systems to evaluate the burden of CVD in European countries;
- Promote more effective and gender-, ethnic-, and socioeconomic-appropriate interventions for CVD prevention at the national, regional, and local levels;
- Reduce ethnic, cultural, socioeconomic, and gender inequalities to multiple risk management among and within countries through use of cost-effective medicines and medical technologies. The radically altered cost/benefit profile of statins needs to be acknowledged and integrated as a central component of any CVD prevention strategy moving forward;
- Increase the awareness of physicians, health care providers, and citizens about the relationship between multiple risk factors and major CVD events (mostly MI and ischemic stroke) and ways to reduce this risk;
- Maintain and regularly update a global data record on CVD multiple risk management;
- Lead the process to establish a European standard in achieving CVD burden reduction;
- Support health worker alliances in projects, coordinated among specialties and directed to CVD primary prevention with international benchmark assessments;
- Assure that rights to CV health are properly incorporated in health systems planning, with equal access by all citizens independent of their ethnic and socioeconomic status;
- Disseminate information and deliver effective educational programs to citizens (regardless of their age) on personal life style changes to reduce multiple risk factors (hypercholesterolemia, hypertension, smoking, obesity/overweight, malnutrition, diabetes, sedentarity, air pollution). Available evidence shows that major chronic diseases (CVD, cancer, COPD, and diabetes) result from a few lifestyle-related behaviours (eating an unhealthy diet, reduced physical activity, tobacco use, and alcohol abuse) [32];
- Support activities of civil society organisations that can be aligned with the comprehensive national health plans;
- Provide assistance to national governments to conduct an impact assessment of CV health-rights;
- Actively promote knowledge sharing among clinical and academic experts with respect to CV health and CV health-rights protection in health care systems;
- Monitor the programs and identify criteria and plans for accountability, especially with respect to returns on investment for various interventions.

6. Final comments

The new European Guidelines on Cardiovascular Disease Prevention in Clinical Practice, as put forth by the 4th Joint Task Force of the European Society of Cardiology and other societies [33,34] has already outlined programs emphasising the increased responsibilities of general practitioners and cardiovascular nurses, stressing the importance of total risk estimation, and offering practical, useable advice on CVD management. The recent launch of the Heart Health Charter (EHHC) in Bruxelles in June, 2007, by the EU Commission in collaboration with the European Society of Cardiology (ESC) and the European Heart Network (EHN), and their affiliates, complements and supports these efforts [27].

It is the belief of the Lorenzini Foundation that countries have a legal and moral obligation to achieve the highest attainable standard of CV health care for their citizens and to improve national health care systems accordingly. Action to reduce CVD burden should ideally be led by European authorities in a three-pronged attack to: (1) integrate strategies for reducing the incidence of major CV events in the short term; (2) improve the use of tools for global CV risk estimation; and (3) provide useful and updated information for the development of national or local databases for monitoring CV disease trends. In parallel, European authorities should also consider actively educating the population on CVD prevention using several methods. This could include, for example, the use of media tools (e.g., web casts), journalists, employers as health coaches, and making yearly cholesterol and BP measurements mandatory to obtain government documents (e.g., driver's licence). Providing a reduction in the cost of health insurance for non-smokers would also provide a positive incentive to the individual as well as reduce the overall costs of health insurance.

The Lorenzini Foundation would also like to suggest that the European authorities, along with the medical community, promote the new total risk management strategy. A failure to replace the current treatment paradigm (based on limited intervention from authorities and focused on treating single risk factors by the medical community) with a more comprehensive and integrated approach involving all stakeholders will likely result in missed opportunities to reverse the current burgeoning epidemic of CVD. Since a small number of risk factors are common to several major

NCDs, a concerted and sustained effort to reduce these risk factors could also potentially exert a major impact on public health. This concept emphasises health promotion and disease prevention through existing health care systems and the active participation both of communities and of individuals [26].

Finally, as part of a vision for future potential opportunities in CVD prevention, the Lorenzini Foundation would like to raise awareness of several key areas among the European authorities: Integration of interventions aimed at several risk factors within an individual country's health care system; Implementation of a comprehensive approach combining policy development, capacity building, partnership and information support at all levels; Promotion of transversal health policies, including coordinated action by several sectors to address major determinants of ill health that fall outside the purview of the health sector; and a combination of health policy and high-risk strategies to link health promotion, public health services, primary care, and hospital care; and, finally, reduction in ethnic, cultural, socioeconomic, and gender inequalities to multiple risk factor management among and within countries through use of cost-effective medications and medical technologies.

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Layout of the Sessions (Friday, October 24, 2008)

FROM HOSPITAL TO HOME: CONTINUITY OF CARE IN INTERNAL MEDICINE

Chairs: B Maisch (Marburg, Germany) – G Vescovo (Vicenza, Italy)

Continuity of Care in the Multiple Risk Diseases: Introduction
C Cricelli (Florence, Italy)

Metabolic Syndrome and Disease Management
R Nardi (Bologna, Italy)

A Model of Continuity of Care for the Polypathological Frail Old People
G Baggio, C Destro, M Bussolotto, MC Corti (Padua, Italy)

Care for Heart Failure Patients Using Novel Cardiovascular Biomarkers
SD Anker (Berlin, Germany)

Continuity of Care: Discharge Conference; A Transferable Tool?
A Rosenberg (Uppsala, Sweden)

General Discussion

Organized in collaboration with the Italian Federation of Internal Medicine (FADOI)

FROM HOSPITAL TO HOME: HEALTH POLICY STRATEGIES

Chairs: L Bresciani (Milan, Italy) – R Paoletti (Milan, Italy)

Opening Remarks
R Paoletti (Milan, Italy)

Primary and Secondary Care: Scenario and Numbers: Pathways, Performances, Outcomes, Economic Burden
P Lindgren (Stockholm, Sweden)

Primary and Secondary Care: Strategy of Integration of Competences: System Development, Quality Assurance, Objectives, Actors, Procedures, Tools and Monitoring
L Bresciani (Milan, Italy)

ALLIANCES, PROGRAMMES, AND PROJECTS

The Partnership for the Heart – Alliances, Programmes, and Projects – Interdisciplinary Alliances in CV Continuity of Care
SD Anker (Berlin, Germany)

The Experience of Andalusia: An Integrated Approach for Cardiovascular Diseases
JL Rocha Castilla (Seville, Spain)

The Experience Called "Hearty People"
D Vanuzzo (Udine, Italy)

The Cardiac Care Cycle Strategy in the Veneto Region
L Bertinato (Venice, Italy)

General Discussion

Concluding Remarks
L Bresciani (Milan, Italy)

Organized in collaboration with the Health Council of the Lombardy Region

Appendix A: Diet as a risk factor for CVD

A. Peracino, R. Paoletti

Giovanni Lorenzini Medical Science Foundation, Milan, Italy, and Houston, Texas, USA

Although not presented at the symposium, diet is recognized to represent a major modifiable risk factor for CVD [1]. A recent case-controlled study (INTERHEART) involving subjects from 52 countries clearly demonstrated that an unhealthy diet increases the risk of an acute MI globally, accounting for approximately 30% of the population-attributable risk. The study suggests that the risk of acute MI in all geographic regions of the world can be attenuated by reducing the intake of fried foods and increasing the consumption of fruits and vegetables [1].

1. Cardiovascular impact of the Mediterranean diet

One of the healthiest dietary models is the Mediterranean diet (characterised by the types of foods typically eaten by various populations bordering the Mediterranean sea) [2]. This diet is characteristically rich in fruits, vegetables, bread, cereals, potatoes, beans, nuts, seeds, olive oil (as an important fat source), dairy products, and fish, along with and low to moderate amounts of poultry, a little red meat, and modest consumption of red wine with meals [3].

Robust clinical evidence exists indicating that the Mediterranean diet may be cardioprotective, positively impacting the clinical progression of CHD, reducing the risk of CHD (by 8% to 45%), and attenuating the CV complications after a MI [4–6]. The Mediterranean diet may also confer other health benefits including weight loss, favourable effects on glycaemic control, and a reduction in risk of developing metabolic syndrome [7,8].

2. Cost-effectiveness of the Mediterranean diet

The Mediterranean diet may also represent a cost-effective option to prevent CVD. Evidence of cost effectiveness of this dietary pattern comes from the Lyon Diet Heart Study, a randomised secondary prevention trial comparing the Mediterranean-type diet with a Western diet on the rate of CV complications following a first MI [4]. After 4 years of follow up, the Mediterranean diet group experienced significant reductions in the composite outcomes of cardiac death and nonfatal MI (14 vs. 44 events in the Western-type diet group, $P = 0.0001$) or cardiac death, nonfatal MI plus unstable angina, stroke, heart failure, pulmonary or peripheral embolism (27 vs. 90 events, $P = 0.0001$). The Mediterranean diet did not impact the usual relationships between major traditional risk factors such as high cholesterol and BP and event recurrence.

The Mediterranean diet (vs. Western diet) was estimated to cost AU$ 1013 (US$ 703, € 579) per QALY gained per person. The study revealed a mean gain in life years of 0.31/person and a gain in QALY of 0.40/person [9]. Thus, as the authors noted, "The Mediterranean diet is highly cost-effective for persons after a first MI and represents an exceptional return on investment" [9].

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Acknowledgements

The articles in this supplement were based on presentations and discussions at three expert panel meetings organised by the Giovanni Lorenzini Medical Science Foundation, Milan, Italy and Houston, TX, USA, held during the 7th International Symposium on Multiple Risk Factors in Cardiovascular Diseases: Prevention and Intervention – Health Policy (Venice, Italy, October 22–25, 2008). The authors wish to thank Jan S. Redfern, PhD, Redfern Strategic Medical Communications, Goshen, NY, USA, for writing and editorial assistance, and Andrea Peracino, MD, PhD, Vice President of the Giovanni Lorenzini Medical Science Foundation, for coordinating the project.

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