Costs of dyslipidemia

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Dyslipidemia has been recognized as an important risk-factor for the development of cardiovascular disease. The current, available therapies of dyslipidemia, their effectiveness, costs, cost-effectiveness and healthcare implications are discussed. At the present time, the lipid-lowering therapies are dominated by statins. Despite a variety of assumptions regarding modeling cardiovascular disease risks and costs, statin therapy is generally cost-effective for secondary prevention and for primary prevention in individuals with additional risk-factors. The costs of drug therapy and the absolute risk of developing future cardiovasular events are the dominant factors determining the cost-effectiveness. When developing clinical guidelines, the cost-effectiveness and proportion of the population to be treated must be considered as well as the total population costs of treatment.

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As the leading cause of death in developed countries, cardiovascular disease (CVD) is associated with substantial healthcare costs. For example, in the USA alone, the total costs of CVD have been estimated at US$329 billion, in the year 2002 [1]. The direct health costs related to CVD treatment were US$199 billion (or 61% of the total costs). They included hospital, physician and related professional services, medications and other healthcare costs. The indirect costs relating to lost productivity from morbidity and premature mortality were US$130 billion.

Dyslipidemia has long been recognized as an important risk-factor for the future development of CVD (coronary heart disease [CHD] and stroke). It is also a modifiable risk-factor as increasingly demonstrated by the number of successful randomized clinical trials [2–9]. The results of these trials have recently lowered the threshold for initiating lipid therapy and also reduced the targets for lipid control. The number of individuals eligible for lipid therapy will grow in the coming years. There is therefore, increasing interest in identifying those individuals at high-risk of future CVD, events such that the benefits of lipid therapy can be targeted towards those who will benefit the most.

The current available therapies of dyslipidemia, their effectiveness, costs and cost-effectiveness among different CVD risk populations, and healthcare implications based on results of economic evaluations are discussed.

Available pharmacological therapies for dyslipidemia

Currently, there are four major classes of drugs available to lower cholesterol. They include 3-Hydroxy-3-Methylglutaryl (HMG) Coenzyme A (CoA) reductase inhibitors (statins), bile acid sequestrants (resins), nicotinic acid and fibric acid derivatives (fibrates).

HMG CoA reductase inhibitors

Statins include drugs, such as lovastatin (Mevacor®, Ranbaxy Laboratories Ltd, New Delhi, India), pravastatin (Pravachol®, Bristol-Meyers Squibb, NY, USA), simvastatin (Zocor®, Merck & Co, NY, USA), fluvastatin (Lescol®, Novartis Pharmaceuticals Corp., NJ, USA) and atorvastatin (Liptor®, Pfizer Inc., NY, USA). They are the most effective class of drugs to reduce total cholesterol especially low-density lipoproteins (LDL). Recent clinical trial results have demonstrated that they can significantly reduce CHD events and stroke, total mortality and the need for revascularization procedures [10].

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A meta-analysis of five major randomized, placebo-controlled, double-blind trials of 30,817 participants followed up on average for 5.4 years, revealed that statins reduced total cholesterol, LDL and triglyceride levels by 20, 28 and 13%, respectively, while high-density lipoprotein (HDL) was increased by an average of 5% [11]. Overall, statin therapies reduced the risk of major coronary events by 31% and all-cause mortality by 21%. In the three trials: the Scandinavian Simvastatin Survival Study (4S), the Cholesterol and Recurrent Events Trial (CARE) and the Long-term Intervention with Pravastatin in Ischemic Disease (LIPID) conducted among 17,617 patients with a history of CHD (secondary prevention) statin therapies were associated with a 34% risk-reduction in major coronary events [2,4,5,11]. In two trials: the West of Scotland Coronary Prevention Study (WOSCOPS) and the Air Force Texas Coronary Atherosclerosis Prevention Study (AFCAPS/TexCAPS) among 13,200 healthy participants (primary prevention) a 30% risk-reduction was observed [3,6,11].

A more recently published trial among 20,536 UK adults, the Medical Research Council (MRC)/British Heart Foundation (BHF) Heart Protection Study, demonstrated a 24% reduction in major vascular events, including coronary events, ischemic strokes, coronary and peripheral revascularizations among a wide range of high-risk individuals irrespective of their initial cholesterol levels [7]. Moreover, the study results suggest cholesterol lowering may be beneficial at much lower thresholds than previously thought.

Bile acid sequestrants

Resins include drugs such as cholestyramine (Prevalite®, Bristol-Myers Squibb, NY, USA), colestipol (Colestid®, Pharmacia & Upjohn, NJ, USA) and colesevelam (Welchol®, GelTex Pharmaceuticals, MA, USA). They reduce LDL by 15–30% and increase HDL by 3–5% [10]. In the Lipid Research Clinics Coronary Primary Prevention Trial, therapy with cholestyramine reduced the risk of CHD by 19% [12,13]. Resins are often used in combination with statins to further reduce the LDL. They remain unabsorbed in their passage through the gastrointestinal track and lack systemic toxicity. These drugs are relatively inexpensive compared with statins but are not popular with patients and their physicians despite their proven safety records. Their major disadvantages are their bulk as they lack convenience of administration and are believed to frequently cause various gastrointestinal symptoms.

Nicotinic acid

Nicotinic acid includes crystalline and time-release preparations and long-acting Niaspan® (Kos Pharmaceuticals, Inc., FL, USA) . This class of lipid-lowering drug favorably modifies lipids and lipoproteins and is especially effective in raising HDL levels by 15–35% [10]. Several clinical trials demonstrated the effectiveness of nicotinic acid in reducing the risk of CHD and progression of atherosclerosis. In combination with statins, the results have been particularly impressive [14].

Nicotinic acid therapy can be accompanied by a number of side effects including gastrointestinal symptoms, flushing of the skin and other complications, such as hepatotoxicity, hyperuricemia and hyperglycemia, especially at higher doses. Since many patients cannot tolerate higher doses, nicotinic acid is typically not used to lower LDL level alone. Instead, it is usually used in combination with other drugs such as statins.

Crystalline preparations of nicotinic acid are available without a prescription and are relatively inexpensive. The time-release preparations are designed to minimize cutaneous flushing. Niaspan is a proprietary extended-release formulation of nicotinic acid that also reduces skin flushing. It also appears to reduce the risk of hepatotoxicity.

Fibric acid derivatives

Fibric acid derivatives include drugs, such as gemfibrozil (Lopid®, Pfizer Inc., NY, USA), fenofibrate (Tricor®, Allergan, MA, USA) and clofibrate (Atromid-S®, AstraZeneca, London, UK). The fibrates are often used for lowering triglycerides, typically by 25–50% [10]. They also lower LDL and raise HDL. In the past there has been some concern about the safety of fibrates due to increased rates of nonCHD death [15]. In the Helsinki Heart Study of a primary prevention, gemfibrozil reduced 37% fatal and nonfatal myocardial infarction (MI) with no change in total mortality [16].

In the recent Veterans Administration HDL Intervention Trial (VA-HIT), a secondary prevention trial, gemfibrozil significantly reduced the risk of CHD and stroke with no increased risk of nonCHD mortality [17]. In the Diabetes Atherosclerosis Intervention Study (DAIS), micronized fenofibrate significantly reduced the cholesterol concentrations and the angiographic progression of CVD among Type 2 diabetic patients [9]. However, the trial was not powered to examine clinical end-points.

Overall, the results of clinical trials of fibrate therapy showed substantial reductions in CVD risk. There are no major side effects associated with fibrates other than various gastrointestinal complaints and increased risk of cholesterol gallstones and myopathy. In combination with statins, there is an important risk of myositis and rhabdomyolisis. There is no consistent data to suggest that fibrates constitute a cost-effective therapy.

Lipid-owering market

Currently the lipid-lowering market is dominated by statins. In a recent USA survey of over 48,000 patients with established CVD, most patients (84%) who received dyslipidemia treatment were prescribed statins [18]. Approximately 13% received fibrates, 8% niacin and 3% resins, some of them in combination with statins. Consequently, in the USA alone, over 8 million people are currently being treated with statins (4.5 million people on atorvastatin, two million on simvastatin, one million on pravastatin, 0.5 million on fluvastatin and negligible number on lovastatin) [19]. In a UK survey of 3689 patients in primary care practices, 88% of patients who were prescribed lipid-lowering drugs were on statins [20].

Cholesterol lowering drugs, especially statins, constitute one of the most dynamic segments of the total prescription drug market in the world. In terms of retail expenditure by therapeutic category, cholesterol-lowering drugs rank second after antiulcer agents and accounted for 5% of the worlds US$364 billion drug market in 2001 [21]. Cholesterol-lowering drugs have experienced a 22% increase in world sales since the year 2000, compared with 14% for antiulcer drugs. In the USA, dyslipidemia drugs account for 6.4% (US$10 billion) of the US$155 billion drug market in 2001 [22]. In Europe, cholesterol-lowering drugs constitute the second largest drug expenditures after antiulcer agents, with US$3.8 billion in sales or 4.6% of the total European market [21]. In the UK alone, US$0.7 billion is spent, representing 5.8% of total UK drug market. Since the year 2000, sales of dyslipidemia drugs have increased 22% in the USA, 19% in Europe and 28% in the UK [21,22].

Costs of dyslipidemia

The costs included in a cost-effectiveness analysis of dyslipidemia can be divided into two major components: direct and indirect costs. Direct medical costs included all medical costs related to a disease (hospitalization, outpatient services, medication, rehabilitation). Dyslipidemia therapy postpones the onset of CVD and in some cases reduces the need for surgical interventions. A calculation of the direct costs in a cost-effectiveness analysis of cholesterol reduction includes the costs of therapy and any CVD-related costs that may be avoided because of lipid therapy. The latter constitutes a cost–saving of a therapy.

In primary prevention, the costs of therapy usually include the costs of medications, outpatient physician visits, and laboratory tests. In secondary prevention the costs of therapy are only the incremental (additional) costs in terms of additional visits, tests and medication after the usual expenditures related to CVD management are subtracted.

The indirect costs of the CVD include productivity loses due to premature mortality and morbidity costs. In most cases they are calculated using the human capital approach based on the patient's work status and average wage rate provided by labor statistics.

Annual treatment costs of dyslipidemia

Patients receiving diet therapy alone or niacin incur much lower treatment costs than those on statin therapies. For example, Prosser and colleagues estimated (1997) that the costs of step one diet therapy in primary prevention at US$108 per patient per year as opposed to statin therapy (including outpatient physician visits and laboratory tests) of US$1318 in primary prevention, and US$1329 in secondary prevention per patient per year [23]. Costs of statin medications alone were calculated at US$1189 per patient per year and constituted 90% of total annual treatment costs. The annual costs of niacin were calculated at US$163 per patient. Patients taking niacin were assumed to have an annual discontinuation rate of 27% whereas patients receiving statins had only a 6% discontinuation rate. Tsevat and colleagues calculated (1996) the annual costs of 40 mg pravastatin at US$925 [24]. They also calculated the costs of other cardiac medications for patients in secondary prevention at US$1295.

Johannesson and colleagues in their cost-effectiveness analysis of the 4S trial estimated (1995) the annual costs of simvastatin using data from Sweden at US$604 [25]. In Canada, the annual cost of simvastatin was estimated at US$667 in 1996 [26]. In a seven-country comparison of cost-effectiveness, annual simvastatin costs were highest in the USA and Germany, US$1027 and 882 [27]. The costs for Canada, France and the UK were in the range of US$600–700 with the lowest costs of US$367 in Spain.

Costs of treating CVD

Hospital costs of treating MI range from US$9000–13,000 [23,28]. The costs of surgical intervention, such as Percutaneous Transluminal Coronary Angioplasty (PTCA) and Coronary Artery Bypass Graft (CABG) vary from US$18,000–36,000. Ganz and colleagues estimated the hospital cost for MI between US$3000–7000 and the costs of stroke at US$4500 [29]. Institutional care costs after stroke have been estimated between US$20,000 and over 60,000. In one cost-effectiveness analysis, Tsevat and colleagues estimated the hospital costs of MI between US$5087–6521, and stroke between US$2530–3913 [24].

Based on Swedish data, Johanesson and colleagues estimated the hospital costs of MI between US$1800–3800, and CABG between US$12,100–16,000, in 1995 [25]. In Canada, the hospital costs of MI and CABG were estimated at US$5272–12,315 in 1996 [26].

Results of recent cost-effectiveness studies

Cost-effectiveness analysis is a widely used method for estimating the value of a health care intervention in clinical decision-making. The goal is to determine the cost-effectiveness ratio (CER), or the dollar cost per unit improvement in health obtained by a specific intervention in comparison with a well-defined alternative. The CER is defined as the difference in costs between two interventions, divided by the difference in effectiveness, usually defined as years of life saved (YOLS) or quality-adjusted life years (QALY). The QALY gives less weight to years of life that are spent in pain, impaired health or diminished function even if there is no effect on the duration of survival itself.

Johanesson and colleagues estimated the short-term cost-effectiveness of simvastatin treatment based directly on the results of 4S trial [25]. In the 4S trial patients with pre-existing heart disease had a 30% reduction of overall mortality. Costs were defined as net costs of the intervention minus reduced treatment costs due to the decrease in morbidity from coronary causes. The benefits were reported in YOLS. Their analysis also included the indirect costs related to lost productivity due to coronary events. Both costs and benefits were discounted at 5% per year to account for different timing of the events.

Table 1. Summary of the recent cost-effectiveness analyses in dyslipidemia.

Target population	Costs characteristics (US$)	Drug costs/year
Secondary prevention Age 35–70 years Chol. 5.5–8.0 mmol/l	4S and Swedish resource use 5% discount rate in 1995 US$	Simvastatin US$604
Secondary prevention Age 40–70 years LDL/HDL ratio 3.5–5.0	Canadian resource use 3% discount rate in 1996 US$	Simvastatin US$667
Secondary prevention Age 35–84 years Chol. ≥ 4.1mmol/l	USA resource use 3% discount rate in 1997 US$	Simvastatin US$1189
Secondary prevention Elderly age 75–85 years Chol. < 6.2 mmol/l LDL 3.0–4.5 mmol/l	USA resource use 3% discount rate in 1998 US$	Pravastatin US$1237
Secondary prevention Age ≤ 75 Chol. < 6.2 mmol/l LDL 3.0–4.5 mmol/l	CARE and USA resource use 3% discount rate in 1996 US$	Pravastatin US$925
Primary prevention Aged 35–84 years Chol. ≥ 4.1 mmol/l	USA resource use 3% discount rate in 1997 US$	Simvastatin US$1189
Primary prevention among diabetics Age 40–70 years LDL/HDL ratio 3.5–5.0	Canadian resource use 3% discount rate in 1996 US$	Simvastatin US$667

4S: Scandinavian Simvastatin Survival Study; CARE: Cholesterol and Recurrent Events Trial; CHD: Coronary heart disease; Chol.: Cholesterol; HDL: High-density lipoprotein; LDL: Low-denisty lipoprotein.

Overall, the costs per YOLS ranged from US$3800–27,400 when only direct costs were included. When indirect costs associated with morbidity were also incorporated, treatment led to a cost-savings as the reduction in morbidity costs from coronary causes exceeded the costs of the intervention among men and women aged 35 years of age. The costs per YOLS dropped, ranging from US$1200–13,300 in the older groups of patients. These results were conservative because the authors did not include the impact of simvastatin on the incidence of stroke which was reduced by 30% [2,30].

Grover and colleagues forecast the long-term benefits and cost-effectiveness of statins in the secondary prevention of CVD based on the results of the 4S trial [2,26]. This study included the impact of statins on the incidence of stroke. It also provided life-long estimates beyond the results of 4S trial using the Cardiovascular Life Expectancy Model [31]. This study was notable as the model forecasts were also validated against the observed results of clinical trials including the results of primary prevention lipid trials, such as the Lipid Research Clinics Coronary Primary Prevention Trial, the Helsinki Heart Study and the WOSCOPS [3,13,31,32]. In secondary prevention the accuracy of the model was tested against studies including the Program on the Surgical Control of Hyperlipidemias, the 4S and the CARE trials and hypertension trials including Systolic Hypertension in the Elderly Program, the Metoprolol Atherosclerosis Prevention in Hypertensives and the Multiple Risk Factor Intervention Trial [2,4,33–36].

The authors concluded that simvastatin therapy in the secondary prevention of CHD and stroke with a LDL/HDL ratio greater than 3.5 for patients with and without additional risk-factors, was cost-effective with the estimates ranging from US$4419 to 21,719 per YOLS [26]. Among individuals with no additional risk-factors, the costs per year of life gained were estimated to be between US$5424 and 21,719 and among high-risk patients below US$10,000 per YOLS. If the effects of lipid modification on the risk of stroke were ignored, the costs per YOLS increase substantially, by as much as 100%.

The Cardiovascular Life Expectancy Model has also been used to estimate the cost-effectiveness of treating dyslipidemia in diabetic patients in primary prevention [37]. The CER among diabetic patients with CVD were consistently lower than those among nondiabetic CVD individuals, in the range

Table 1. Summary of the recent cost–effectiveness analyses in dyslipidemia.

Effectiveness	Cost-effectiveness (US$/YOLS or US$/QALY)		Ref.
27% reduction in CHD based on 4S trial	Direct costs only All ages Direct and indirect costs Age = 35 years Age > 35 years	 3800–27,400/YOLS Saves money and lives 1200–13,300/YOLS	[25]
35% decrease in LDL 8% increase in HDL based on 4S trial	Direct costs only Low-risk age 40–70 years High-risk age 40–70 years	 5400–21,700/YOLS 4400–8500/YOLS	[26]
25% decrease in total chol 35% decrease in LDL 8% increase in HDL based on 4S trial	Direct costs only Low-risk age 35–84 years High-risk age 35–84 years	 < 50,000/QALY < 10,000/QALY	[23]
33% reduction in CHD 40% reduction in stroke based on CARE trial	Direct costs only Age 75–84 years	 18,800/QALY	[29]
Mortality and recurrent event models based on CARE trial	Direct costs only All ages LDL < 3.2 mmol/l LDL 3.2–3.9 mmol/l LDL > 3.9 mmol/l	 13,000–37,000/QALY More expensive and less effective 16,000–18,000/QALY 7900–20,000/QALY	[24]
25% decrease in total chol 35% decrease in LDL 8% increase in HDL based on 4S trial	Direct costs only LDL 4.2–4.9 mmol/ LDL > 4.9 mmol/l	 77,000–1,400,000/QALY 54,000–560,000/QALY	[23]
35% decrease in LDL 8% increase in HDL based on 4S trial	Direct costs among diabetics LDL 5.46 mmol/l LDL 3.85 mmol/l	 4200–20,000/YOLS 5000–32,000/YOLS	[37]

CHD: Coronary heart disease; HDL: High-density lipoprotein; LDL: Low-density lipoprotein; QALYs: Quality-adjusted life years; YOLS: Years of life saved.

of US$4000 to 8000, indicating that the presence of diabetes identifies a subgroup among whom the secondary prevention is particularly cost-effective. The CERs associated with primary prevention among diabetic patients were also substantially lower than among nondiabetic patients and ranged from US$4000 to 40,000 across wide pretreatment lipid levels and other risk-factors.

Prosser and colleagues conducted a cost-effectiveness analysis of primary and secondary prevention with cholesterol-lowering therapies based on calculations of CHD risk from the Framingham Heart Study [23]. Men and women aged between 35 and 84 years with LDL-cholesterol levels of 4.1 mmol/l or greater were divided into 240 risk subgroups according to age, sex, diastolic blood pressure, smoking, LDL- and HDL-cholesterol levels. The effectiveness of statins in primary prevention was based on results from studies of pravastatin, the effectiveness of secondary prevention was taken from the 4S trial.

CERs for primary prevention with statins varied widely according to the presence of other risk-factors, from US$54,000–420,000 per QALY for men and from US$62,000–1,400,000 per QALY for women. Primary therapy with statins did not reach a CER of US$50,000 per QALY in any of the 240 risk subgroups and only a quarter of the risk subgroups reached the threshold of US$100,000 per QALY. Niacin for primary prevention had an estimated CE ratio of less than US$100,000 per QALY for most risk subgroups.

CERs for secondary prevention with statins were less than US$50,000 per QALY for all subgroups and approximately US$10,000 per QALY or less for most high-risk subgroups. As expected, CERs became more favorable with increasing number of risk-factors and with advancing age. They were also more favorable among men than women. The authors concluded that statins are generally cost-effective when used for secondary prevention but only sometimes when used for primary prevention [23]. Thus, in a low-risk population, a preventive intervention would be cost-effective only if it is clinically effective, but very inexpensive [10]. Consequently, at current drug costs, treatment with cholesterol-lowering drugs should be targeted to patients who have an elevated risk for CVD on the basis of both the lipid profile and other risk-factors.

Ganz and colleagues evaluated the cost-effectiveness of statin therapy among elderly patients (75–84 years of age) with a history of MI by extrapolating results from the CARE trial with pravastatin treatment (40 mg daily) and available epidemiologic

data [4,29]. In this analysis not only CHD but also stroke were explicitly modeled. They found that if the risk reductions found in published trials prevail in older patients, statin therapy would increase mean life expectancy by 4 months [29]. The base case CER compared with usual care was estimated at US$18,800 (1998) per QALY. Since costs of statins represent the majority of the treatment costs, sensitivity analysis showed that a given decrease in drug costs resulted in a proportional decrease in CER. Similar results were reported by Prossner and colleagues [23].

Higher rates of stroke and reinfarctions led to more favorable CERs because a greater absolute number of events would be prevented by statin therapy. Overall, statin therapy at its current price appears to be cost-effective among older patients in secondary prevention. Moreover, inclusion of stroke costs, especially expensive poststroke institutional care made the costs per QALY more favorable.

Tsevat and colleagues assessed the cost-effectiveness of pravastatin therapy (40 mg daily) in survivors of MI with average cholesterol levels (the mean cholesterol level of 5.4 mmol/l and mean LDL of 3.6 mmol/l) by extrapolating effectiveness data from the CARE trial [4,24]. The eligibility criteria for the CARE trial included a total cholesterol level of less than 6.2 mmol/l and a LDL between 3.0 and 4.5 mmol/l. The survival model was based directly on the data from the CARE trial and extrapolated beyond the trial end-points using USA life tables and the Framingham risk equations. The life expectancies were adjusted by health-related quality of life data from the CARE study. The overall adherence rate of pravastatin therapy was calculated at 91.2% based directly on the data from the CARE trial. All costs including CHD events, stroke and revascularization procedures (PTCA and CABG) were calculated over the entire life of the patient.

Assuming a persistent survival benefit of 9% with pravastatin therapy, costs per QALY were estimated between US$13,000 and 32,000. In a sensitivity analysis with survival benefit extended to 22% (taken from the LIPID study of pravastatin), the incremental CER dropped to US$14,000 per QALY from the base case of US$31,000 [5].

Public health implications of economic analyses

Despite a variety of assumptions regarding modeling CVD risks and costs, the findings of all the recent cost-effectiveness studies are consistent. Statin therapy is generally cost-effective for secondary prevention and for primary prevention in individuals with additional risk-factors.

From the population perspective, prevention of CVD through diet modification, exercise, weight and smoking reduction might be most attractive [23,38]. These approaches are safe, incur few direct medical costs and offer benefits beyond CVD reduction. By comparison, pharmacological interventions because of their costs, are cost-effective only for high-risk individuals. The introduction of relatively safe and efficacious statins makes clinical interventions relatively attractive. However, the costs of drug therapy and the absolute risk of developing future CVD events are the dominant factors determining the cost-effectiveness of the clinical approach to cholesterol reduction.

Some current guidelines for cholesterol-lowering treatment base their recommendations on the absolute risk of coronary disease [39–41]. In the Sheffield table for primary prevention, lipid-lowering treatment was recommended if the 1-year risk of CHD exceeded 3% [39,40]. In the recommendations by the European Society of Cardiology, treatment was recommended if the 10-year risk of CHD exceeded 20% [41]. In the USA, the recent ATP III recommendations were based predominantly on LDL levels and on global risk assessment complemented by 10-year risk calculations using the Framingham risk scoring system [10].

Researchers in the UK evaluated the healthcare policy implications of targeting statin treatment for populations at different CHD risk levels [42]. Given a CHD risk of 4.5% per year (the risk observed among the participants of 4S trial), 5.1% of the total UK adult population (4.8% in secondary prevention and 0.3% in high-risk primary prevention) would need to be treated with statin. With the estimated costs at this risk level, of only US$9000 per YOLS, this translates into 16% of total UK expenditures on prescription drugs to be spent on statins.

Full implementation of statin treatment at an annual CHD event risk of 1.5% (equivalent to the WOSCOPS risk level) would result in 25% of the UK adult population receiving statins. This would consume almost 90% of the current UK expenditure on drugs. Despite a favorable CER (US$21,000 per YOLS), the full implementation of this policy seems to be unlikely. If the costs of statins would fall from the current US$900 to less than 500, statin treatment of those with a CHD event risk of 1.5% would become cost-effective (below US$7000) and viable from a health policy perspective.

Similarly, in the USA according to the new National Cholesterol Education Program [NCEP] ATP III guidelines, 36 million Americans requiring primary prevention alone would be eligible for lipid-lowering drug treatment, a 140% increase since the ATP II [43]. The economic implications of these new guidelines primarily remain to be addressed. Given the annual costs of statins estimated at US$1000, one could imagine additional drug expenditures of US$36 billion required of the US healthcare system.

Goldman and colleagues estimated the population wide effect of full implementation of the ATP II guidelines. In their results they concluded that primary prevention would only yield about half of the benefits of secondary prevention despite requiring nearly twice as many person-years of treatment [44]. The projected increase in QALY per year of treatment for secondary prevention was 3- to 12-fold higher than for primary prevention.

When developing guidelines, one must consider not only cost-effectiveness but also the proportion of the population to be treated, as well as the total population costs of treatment. Primary prevention is therefore, constrained by total drug costs. As patents on initial statins expire and competition intensifies, it is likely that costs of cholesterol-lowering drugs will decline substantially and statin therapy will become more affordable for primary prevention. At the same

Key issues

- At the present time there are four major classes of drugs available to lower cholesterol. They include 3-Hydroxy-3-Methylglutaryl Coenzyme A (HMG CoA) reductase inhibitors (statins), bile acid sequestrants (resins), nicotinic acid and fibric acid derivatives (fibrates). Currently, the lipid-lowering therapies are dominated by statins.
- Dyslipidemia therapy postpones the onset of cardiovascular disease (CVD) and in some cases reduces the need for surgical interventions. A calculation of the direct costs in a cost-effectiveness analysis of cholesterol reduction includes the costs of therapy and any CVD related costs that may be avoided because of lipid therapy. The latter constitutes a cost–saving of a therapy.
- In the cost-effectiveness analyses, the costs of statin therapy range from US$600 to over 1000 per patient per year and appear to constitute 90% of total annual outpatient management costs, including physician visits and laboratory tests. Hospital costs of treating a myocardial infarction (MI) range from US$2000 to over 13,000. The costs of surgical intervention, such as coronary ar tery bypass graft (CABG) can vary from US$12,000 to over 36,000.
- Despite a variety of assumptions regarding modeling CVD risks and costs, statin therapy is generally cost-effective for secondary prevention, with the cost-effectiveness ratios (CER) generally below US$50,000. Among high-risk patients with CVD, the CERs are usually below US$20,000. In primary prevention, statin therapy appears to be cost-effective only among individuals with additional risk factors.
- In a low-risk population, a preventive intervention would be cost-effective only if it is clinically effective but very inexpensive. Consequently, at current drug costs, treatment with cholesterol-lowering drugs in primary prevention should be targeted to patients who have an elevated risk for CVD on the basis of both the lipid profile and other risk-factors.
- The introduction of relatively safe and efficacious statins makes clinical interventions relatively attractive. However, the costs of drug therapy and the absolute risk of developing CVD events are the dominant factors determining the cost-effectiveness of the clinical approach to cholesterol reduction.
- When developing guidelines, one must consider not only cost-effectiveness but also the proportion of the population to be treated as well as the total population costs of treatment. As competition intensifies, it is likely that costs of the cholesterol lowering drugs will decline substantially and statin therapy will become more affordable for primary prevention.

time, more accurate identification of high-risk individuals, based on global cardiovascular risk assessment will be needed to select individuals who are most likely to benefit.

Expert opinion

At the present time, lipid-lowering therapies are dominated by statins. Given the current costs of statins, lipid-lowering therapy is generally cost-effective for secondary prevention. In primary prevention, lipid-lowering therapy appears to be cost-effective only among individuals with additional risk factors.

Five-year view

When developing public health policy, one must consider not only cost-effectiveness but also the proportion of the population to be treated as well as the total population costs of treatment. As competition intensifies, it is likely that costs of statins will decline, so that lipid-lowering therapy in primary prevention will generally become more affordable. At the same time, more accurate identification of high-risk individuals, based on global cardiovascular risk assessment will be adopted in treatment guidelines to select individuals who are most likely to benefit from therapy.

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