

# Epidemiology of Dyslipidemia and Economic Burden on the Healthcare System

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## Abstract

A literature review was undertaken to describe trends in the prevalence of dyslipidemia and the associated medical costs. The search focused on recent trials showing effects of treatment on strokes and in patients with diabetes mellitus (DM). Online databases were searched for recent studies analyzing prevalence and/or cost of dyslipidemia, stroke, and DM. More than 43 000 papers have been written on dyslipidemia, with 700 considering costs and more than 100 focusing on the costs of dyslipidemia alongside stroke or DM. Findings in almost every case point toward high costs associated with dyslipidemia and cost-effective therapeutic options for treatment. The findings indicate that dyslipidemia is widespread and imposes substantial costs on the healthcare system. Treatment of elevated cholesterol and mixed lipid disorders using statins may relieve some of the burden, as recently noted for patients with DM and stroke.

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Research over the past 4 decades has consistently shown the burden of dyslipidemia to be very high in terms of morbidity, mortality, and medical costs. Dyslipidemia is an important major risk factor for coronary heart disease (CHD), which is the leading cause of death in the United States. The World Health Organization estimates that dyslipidemia is associated with more than half of global cases of ischemic heart disease and more than 4 million deaths per year.<sup>1</sup>

Dyslipidemia is a broad term that refers to a number of lipid disorders. Most (80%) lipid disorders are related to diet and lifestyle, although familial disorders (20%) are important as well. The basic categories of dyslipidemias include: elevated low-density lipoprotein cholesterol (LDL-C), low high-density lipoprotein cholesterol (HDL-C), excess lipoprotein(a), hypertriglyceridemia, atherogenic dyslipidemia, and mixed lipid disorders.<sup>2</sup> Most patients with CHD have mixed dyslipidemia (eg, elevated LDL-C and low HDL-C), which is also commonly seen in patients with diabetes mellitus (DM).

The literature on the epidemiology and economics of dyslipidemia is extensive. Quite literally, tens of thousands of papers (more than 43 000 listed on Medline alone) have been written on dyslipidemia, with more than 700 considering costs and more than 100 considering the costs of dyslipidemia alongside stroke or DM. This review searched online databases for recent studies analyzing prevalence and/or cost of dyslipidemia, with a focus on analyses related to stroke and DM. Admittedly, not all 43 000 papers on dyslipidemia were examined, nor even all 700 considering costs, but the review found very consistent themes of high costs associated with dyslipidemia and many cost-effective therapeutic options for treatment. This review highlights a few key reports and studies that demonstrate these themes.

The American Heart Association estimates that more than 100 million Americans—one third of all Americans—have total cholesterol levels in excess of 200 mg/dL, which is considered a moderately high level, and more than 34 million adult Americans have levels greater than 240 mg/dL, which is considered a high level necessitating treatment.<sup>3</sup> The total cost associated with cardiovascular diseases and stroke in the United States—many of which are related to dyslipidemia—is estimated to exceed \$400 billion in 2006.<sup>4</sup> Total costs

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include medical services (direct costs) as well as lost wages (indirect costs). While the healthcare system is only associated with the direct costs, these are nearly two thirds of total costs. Costs of cardiovascular disease and stroke vary widely around the world, but in every instance, costs are substantial.<sup>5</sup>

Closely related to dyslipidemia is DM. Persons with DM have average LDL-C levels in excess of 140 mg/dL, and most require drug therapy.<sup>6</sup> Nearly 1 in 10 Americans may suffer from DM at some level. In 2002, the direct and indirect costs of DM were estimated at \$132 billion, with direct medical care costs again comprising two thirds of the total.<sup>7</sup> Worldwide, the number of persons with DM is approaching 200 million, accounting for 1.1 million deaths per year in 2005.<sup>8</sup> More than three quarters of persons with DM have some form of cardiovascular disease or stroke, which is an important source of mortality and costs. All told, DM care may be related to as much as \$1 of every \$5 spent on healthcare in the United States.<sup>7</sup>

The relationship between dyslipidemia, cardiovascular disease, and stroke appears to be clear and direct. A number of trials have demonstrated the efficacy of 3-hydroxymethyl-3-glutaryl coenzyme A (HMG-CoA) reductase inhibitor (statin) treatment for both secondary and primary prevention. However, the magnitude of the effect of treatment with statins appears to be larger than would be expected, given the changes in levels of cholesterol.<sup>9</sup> Therefore, recent studies have explored the association between cardiovascular events and statin use in persons with typical dyslipidemia. The Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT) randomized 10 305 patients with hypertension and  $\geq 3$  additional cardiovascular risk factors but without previous history of CHD to either atorvastatin (10 mg) or placebo.<sup>10</sup> The investigators had planned follow-up for an average of 5 years, but the lipid component of the trial was discontinued nearly 2 years early because of significantly better clinical outcomes in the atorvastatin group. The primary end point—nonfatal myocardial infarction and fatal CHD—was 36% lower in the treatment group and strokes were 27% lower.

The cost-effectiveness of lipid lowering in ASCOT was subjected to analysis of the cost of therapy versus the cost of reduced events.<sup>11</sup> It should be noted that this was a Scandinavian/UK

study and the pharmacoeconomic analysis was conducted using US costs extrapolated over the life of the trial. The results were that patients treated with atorvastatin had additional costs of just over \$400, which translated to \$12 000 per event avoided. Even with dramatic rates of efficacy, treatment with medications yielding fewer events still costs more than nontreatment. This raises the question, Is this additional expense worthwhile? Would people or insurance companies be willing to trade the disability and burden to the patient associated with stroke and the impact on the caregiver, for \$12 000? Although it is difficult to make the extrapolation to costs per life-years saved and societies' willingness to pay for life-years saved, these results suggest that statin treatment for patients at risk for cardiovascular disease and stroke is cost-effective.

The relationship between dyslipidemia and DM is slightly less clear, as large numbers of persons with DM have otherwise unimpressive cholesterol levels. A Markov model based on the Scandinavian Simvastatin Survival Study (4S) results and usual medical services costs indicated that treating patients with DM but without cardiovascular disease might be quite cost-effective (<\$25 000 per life-year saved).<sup>12</sup>

To investigate the statin-DM relationship directly, the Collaborative Atorvastatin Diabetes Study (CARDS) was conducted.<sup>13</sup> Nearly 3000 patients with type 2 DM,  $\geq 1$  additional risk factor but without CHD, and normal LDL-C levels were randomized to atorvastatin (10 mg) or placebo. Like ASCOT, CARDS was stopped 2 years early because of improved clinical outcomes in the treated group. Atorvastatin reduced the number of major cardiovascular events by 37% and the rate of stroke by 48%. Although there are a host of reasons to be cautious about the application of carefully controlled clinical trial data to daily practice, the CARDS results suggest the importance of addressing lipid levels, and certainly dyslipidemia, in patients with DM.

Numerous cost-effectiveness studies of treatment of dyslipidemia among patients with DM have been conducted. Although results suggesting cost-effective use of statins are numerous, so are the flaws (or potential flaws) in study designs, owing mostly to the absence of long-term study data.<sup>14</sup> A population-based study found that of patients having at

least 1 cholesterol measurement and a statin prescription, slightly more than one third achieved their LDL-C goal.<sup>15</sup> Among those who achieved their goal, there was a clear trend toward lower costs for inpatient, cardiovascular-related care. The application of pharmacoeconomic analysis to CARDS, as was done with ASCOT, may help to provide clinical trial-based data to supplement findings from observational studies.

In aggregate, beyond stroke and DM, treatment of dyslipidemia has engendered substantial debate with regard to cost-effectiveness. Much of the debate surrounds risk of cardiovascular events. A review of studies found that cost-effectiveness ratios ranged from net savings (certain very-high-risk categories) to \$490 000 per life-year saved (certain very-low-risk categories).<sup>16</sup> At average values of \$15 000 to \$20 000 per life-year saved (based on average 10-year risk), treatment is quite cost-effective. Of course, depending on the study population and criteria employed for making claims, there will be continued debate over aggregate cost-effectiveness and the relative cost-effectiveness of competing treatments.<sup>17,18</sup>

### **Awareness, Adherence to Lipid Treatment Recommendations**

Information on high cholesterol and its consequences has not been lost on the healthcare system and the American public. Behavioral Risk Factor Surveillance System data show that cholesterol screening has increased from 67% in 1991 to 73% in 2003.<sup>19</sup> Awareness of high blood cholesterol among persons screened increased from one quarter in 1991 to nearly one third in 2003. The good news on cholesterol attention and awareness is that between 1988 to 1994 and 1999 to 2002, the mean total cholesterol and LDL-C levels of adults actually decreased (by 1% and 3%, respectively).<sup>20</sup> Similarly, total cholesterol levels decreased 8% among patients with DM.

The Third Report of the National Cholesterol Education Panel (NCEP) suggested that the primary approach to LDL-C lowering is making lifestyle changes, but many adults at higher risk will likely need medication to control their dyslipidemia.<sup>21</sup> Medications for dyslipidemia, specifically statins, are among the most popular drugs sold in the world. With more than \$13 billion in annual spending,

atorvastatin has been the highest selling product in the United States for the past 5 years.<sup>22</sup> The discouraging news is the missed opportunity to make an even larger dent in the burden of dyslipidemia. Even at this very high level of spending, only about one third of patients being treated are achieving their NCEP goals. Only two thirds of patients whose test results indicated high blood cholesterol or who were taking a cholesterol-lowering medication reported being informed that they had high cholesterol. Furthermore, fewer than half of those persons who qualify for any kind of treatment for dyslipidemia are receiving it—fewer than half even among those persons diagnosed with CHD.

Lack of treatment to NCEP goals has at least 2 sources: insufficient prescribing and insufficient consumption. Sadly, there remain clear patterns and disparities in screening and prescribing of treatment for dyslipidemia.<sup>19,23</sup> Women and persons in various age and demographic categories are not prescribed treatment at the same rate as middle-aged white men, even accounting for risk differences. The issues surrounding disparities are larger than just dyslipidemia treatment.

Similarly, issues surrounding treatment adherence are also larger than just dyslipidemia treatment, but they may be more directly manageable. Although the pharmacoeconomic impact of nonadherence has not been widely examined, it is clear that less than full adherence is associated with lower treatment costs but worse health outcomes.<sup>24</sup> One study in a managed care organization found 3 key factors associated with adherence to statin therapy: days' supply, number of concomitant medications, and cost-sharing.<sup>25</sup> Another managed care study found that in addition to demographic factors, level of copayment is a significant factor in adherence with statin therapy.<sup>26</sup> Strategies for improving adherence may include providing 90-day supplies (rather than 30-day supplies), careful attention to the number of medications prescribed, and lowering copayments for selected medications for selected patients.<sup>27,28</sup>

### **Conclusion**

As ample evidence indicates, dyslipidemia is widespread and imposes substantial costs on individuals and the healthcare system. Treatment of elevated LDL-C levels and mixed lipid disorders using statins may relieve some of the burden, as recently

noted for patients with DM and stroke. Continued research is needed on the issue of cost-effectiveness of therapeutic options in general, and for certain categories of patients and individual therapies. Promoting the use of cost-effective therapies for certain patients may require more than just making therapies available. Behavioral and societal change may be required, as well as health benefit plan design change to encourage use of appropriate therapies.

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