Impact of rosuvastatin use on costs and outcomes in patients at high risk for cardiovascular disease in US managed care and Medicare populations: a data analysis


Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
The study examined the use of rosuvastatin in patients at high risk of cardiovascular disease. The study compared two scenarios: the current scenario, in which the drug-utilisation mix did not include rosuvastatin; and a rosuvastatin scenario, in which a share of statin usage for treatment of high-risk patients was shifted to this drug, assuming an 11% dyslipidaemia market share for rosuvastatin for a commercial population and a 7% share for a Medicare population.

Type of intervention
Primary and secondary prevention.

Economic study type
Cost-effectiveness analysis

Study population
The study population comprised a cohort of patients with CHD, arthrosclerosis of peripheral and/or cerebral arteries, diabetes, and/or multiple other risk factors conferring a risk of at least 20% of suffering CHD or stroke within 10 years. Two sub-group analyses were undertaken: one comprising 1 million commercially insured patients, and another comprising 1 million Medicare enrolled patients (however, only those patients enrolled in Medicare with employer-sponsored health insurance were included).

Setting
The study setting was outpatient secondary care. The economic study was carried out in the USA.

Dates to which data relate
The effectiveness data were derived from studies published between 1997 and 2004. The price year was 2005.

Modelling
A Markov model was created to simulate the costs to the health plans of lipid-lowering treatment in high-risk patients. One-year transition cycles were used and the time horizon was 5 years.

Study designs and other criteria for inclusion in the review
The clinical and epidemiological data used in the economic model were:

the dose-specific efficacy of each drug (as measured by percentage changes in serum lipid concentrations);

the risk of drug-related adverse events;

the impact of serum levels (i.e. total cholesterol and high-density lipoprotein cholesterol) on cardiovascular risk; and

the mortality rates due to myocardial infarction, stroke and death from other causes.

Sources searched to identify primary studies
The dose-specific efficacy rates of each drug were derived from the data published in package inserts, as approved by
the Federal Drug Administration (FDA). The risk of drug-related adverse events was assumed to be 0 based on results from published studies. Cardiovascular risk prediction was based on data from the Framingham Heart Study, epidemiologic studies and the Heart Protection Study (a large randomised controlled trial). Mortality rates were derived from the published literature.

**Methods used to derive estimates of effectiveness**

A review of the literature was undertaken, but the methods used to identify the studies from which clinical and epidemiological data were obtained were not reported (i.e. the authors did not report the inclusion criteria for their study, the search strategy, the sources used to identify the studies, or the methods used to extract data from the studies).

**Measure of benefits used in the economic analysis**

The measure of benefits used was cardiovascular events avoided. This included acute myocardial infarction, other CHD events, coronary revascularisation, stroke and other cardiovascular events. Since the outcomes could be incurred over a 5-year period, discounting was relevant but was not performed.

**Direct costs**

The direct costs to the health insurance service were included in the analysis. The costs included were for lipid-modifying therapies, testing serum lipid levels, and health care (which included initial acute inpatient stay and subsequent transfers to other hospitals or skilled-nursing facilities) for acute myocardial infarction, other CHD events and stroke. The drug costs were estimated using average wholesale prices. All other costs were based on health care resource utilisation and expenditure data from the MarketScan Commercial Claims and Encounters database and the Medicare Supplemental database. Since the costs were incurred over a 5-year period, discounting was relevant and was appropriately performed using an annual rate of 3%. However, discounting was only undertaken for the sensitivity analysis. The study reported the total costs. The price year was 2005. The authors provided total cost estimates investigating the budget impact of rosuvastatin on a health insurance system.

**Statistical analysis of costs**

The costs were treated as point estimates (i.e. the data were deterministic).

**Indirect Costs**

The productivity costs were not included.

**Currency**

US dollars ($).

**Sensitivity analysis**

The authors undertook a series of one-way sensitivity analyses to explore the sensitivity of the model results to variation in particular input parameters. The authors varied the age of the population, the risk factors, drug efficacy, the market share of rosuvastatin and the costs of the drugs.

**Estimated benefits used in the economic analysis**

The number of cardiovascular events avoided over 5 years when the rosuvastatin scenario was compared with the current scenario (i.e. no rosuvastatin) was 36 for the commercial plan and 727 for the Medicare plan.

**Cost results**

Over the 5-year time horizon, the costs incurred in the current scenario were $299,140,000 in the commercial plan and $295,110,000 in the Medicare plan.

Over the 5-year time horizon, the costs incurred in the rosuvastatin scenario were $4,317,180,000 in the commercial plan and $4,282,860,000 in the Medicare plan.

**Synthesis of costs and benefits**

The costs and benefits were not combined as the rosuvastatin scenario was found to be dominant over the current scenario (i.e. it was less costly and more effective).
The results of the sensitivity analysis showed that rosuvastatin was still dominant when compared with the current scenario in all age group categories (ranging from age 35 to 44 years to over 75 years). The results also showed that, as the market share of rosuvastatin increased, more events per 1,000 patients were avoided and greater savings per patient were generated.

**Authors’ conclusions**
The authors concluded that increasing the use of rosuvastatin could result in a reduction in cardiovascular events and cost-savings.

**CRD COMMENTARY - Selection of comparators**
A justification was given for using a no rosuvastatin scenario as the comparator. It was closely representative of the current scenario of health care provision in the authors’ settings. You should decide if the comparator used represents current practice in your own setting.

**Validity of estimate of measure of effectiveness**
The parameters were derived from published research, but it was unclear from the study whether some synthesis of the results had taken place. The authors did not report any search methods or inclusion criteria. Cardiovascular risk prediction estimates were derived from large cohort studies, such as the Framingham Heart Study, and a large randomised controlled trial, the Heart Protection Study. It was unclear if data published in package inserts, although approved by the FDA, were the best source from which to derive efficacy rates. Data based on randomised controlled trials would have provided a better estimate than the pharmaceutical industry's own estimates.

**Validity of estimate of measure of benefit**
The estimation of health benefit (cardiovascular events avoided over 5 years) was derived appropriately using a Markov model. Although benefits could be incurred over 5 years, discounting was not performed by the authors even though it would have been appropriate to have done so. Furthermore, the one-dimensional measure of health benefit will make comparisons with other interventions more difficult, and might not capture all the other health benefits of the intervention (e.g. increased survival and/or quality of life).

**Validity of estimate of costs**
The analysis of the costs was performed from the perspective of the health insurance system paying for the treatment, in this case Medicare for those aged over 65 years, and for younger individuals the perspective of a commercial one. It would appear that all the relevant categories of cost were included in the analysis, as were all major relevant costs. Although the authors reported that the costs of drug-related adverse events were not included in the analysis, they reported that available evidence did not suggest that adverse-event rates differed significantly across statins. The sources of the resource use and unit costs were adequately reported. Discounting was relevant as the costs were incurred over 5 years. However, it was only performed in the sensitivity analysis. The price year was appropriately reported, which will assist future inflation exercises. The unit costs and the resource quantities were not reported separately, which will hamper the generalisability of the authors' results.

**Other issues**
The authors reported that the study was not directly comparable to published cost-effectiveness studies on lipid-lowering therapy, as they have been based on one of two analyses different to the one performed here: a short-term cost-eficacy study, which only evaluated the short-term cost of relative reduction in lipids; and long-term costs and gains in life-years or quality-adjusted life-years, which have not focused on the total budgetary and clinical impact on a health insurance’s membership. The authors investigated the effect of varying the age groups and risk factors, and presented the results of these variations in detail. They also undertook a limited sensitivity analysis by varying other model parameters. The authors do not appear to have presented their results selectively and their conclusions reflected the scope of the analysis.

The authors reported a number of further limitations to their study. First, the effects of rosuvastatin on cardiovascular morbidity and mortality have yet to be demonstrated in a randomised, placebo-controlled trial. Second, the assumption that one unit of lipid change led to the same amount of cardiovascular risk reduction, an assumption that was supported by results from the Heart Protection Study. Third, the efficacy data were derived from FDA-approved package inserts. Fourth, the overall cost estimates represented the national averages and did not take into account regional cost...
variations. Finally, the model did not include the beneficial effect that very high-intensity statin therapy can regress arteriosclerosis in patients with CHD.

Implications of the study
The authors concluded their article by reporting that rosuvastatin use may be considered to be a cost-effective means of preventing cardiovascular disease in high-risk patients for whom statins are recommended therapy.

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MeSH
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