Cost effectiveness of simvastatin treatment to lower cholesterol levels in patients with coronary heart disease

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
Using simvastatin (Zocor, Merck) for reducing cholesterol levels in patients with coronary heart disease (CHD).

Type of intervention
Secondary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
Patients 35 to 70 years of age with total cholesterol levels of 5.50 to 8.00 mmol

Setting
Hospital. The economic study was carried out in Sweden.

Dates to which data relate
The effectiveness and resource use data were obtained from a study published in 1994. The prices used were those prevailing in 1995.

Source of effectiveness data
Effectiveness data were derived from a single study.

Link between effectiveness and cost data
The costing was undertaken retrospectively on the same patient sample as that used in the effectiveness analysis.

Study sample
No power calculations were reported. The total number of patients included was 4444. There were 2221 patients in the intervention group, and 2223 in the comparator.

Study design
Randomised controlled trial, carried out in 94 clinical centres. The median duration of follow up was 5.4 years. No loss to follow up was reported.
Analysis of effectiveness
It was not explicitly stated whether the analysis was based on intention to treat or on treatment completers only. The primary health outcomes used were annual risk reduction for coronary events (only for the first coronary event, not subsequent ones), and the proportion of fatal coronary events among all coronary events. 'Coronary event' was defined as including death from a coronary cause, a definite or probable hospital-verified nonfatal acute myocardial infarction, resuscitation after cardiac arrest, definite silent myocardial infarction, myocardial revascularization, and admission to the hospital for acute CHD when there was no diagnosis of myocardial infarction.

Effectiveness results
The annual risk reduction for first coronary event was 27% for the first five years. Thereafter, the annual risk was assumed to be equivalent to the risk if there had been no treatment. The proportion of fatal coronary events among all coronary events for the age group 35 to 64 years old was 7.7% for men and 2.2% for women. The corresponding value for the group aged 65 years or older was 14.4% and 5.7%, respectively.

Clinical conclusions
Not reported.

Modelling
A Markov model was used to estimate cost and benefits. The model dealt with the uncertainty in the occurrence of a cardiovascular event or death from a non-coronary cause. The probabilities for the model were calculated from hazard functions estimated from Poisson models for the placebo group.

Measure of benefits used in the economic analysis
The benefits were expressed in terms of life-years gained. A Markov model was used to deal with the uncertainty in health status after initiation of treatment and, by doing so, to translate clinical outcomes (i.e. annual risk reduction with intervention for first coronary event) to an estimate of effectiveness in terms of life-years gained. Benefits from intervention were assumed to last for a period of 5 years.

Direct costs
Costs were discounted. Cost items were reported separately and were analysed on a cost per year basis (i.e. cost of the first, second etc., year after a coronary event). The costs measured were operating costs (drug) and cost of complications (associated with coronary event occurrence). The boundary adopted was that of the health care system. The resource quantities were based on actual data published in 1994. The broad (unit) costs estimates were based on the official retail price of the drug in Sweden from published sources of 1994 and 1995, and for hospitalisation costs, from actual costs of hospitalisation for patients in various diagnosis-related groups at 4 hospitals in Sweden with patient-based cost accounting systems. The prices used were those prevailing in 1995. Costs associated with physician visits and laboratory tests were excluded as they were assumed to be common. Costs avoided were considered for a period of 5 years only.

Indirect Costs
Costs were discounted and were analysed on a cost per year basis. The costs measured were those associated with productivity losses. The boundary used was the ‘patient’. The resource quantities were based on actual quantities published in 1994 (estimates based on work status assessed every 6 months). The unit cost used was the average annual cost for the labour of a full-time Swedish worker in 1995. Costs avoided were considered for a period of 5 years only.

Currency
US dollars ($). The original figures were collected in Swedish Kroner (SEK) and the conversion rate used was $1= SEK7.30 (1995 rate).
Sensitivity analysis
The parameters explored in the sensitivity analysis were as follows: relative risk of coronary events (confidence interval (CI), using lower and upper bounds), average risk of death from non-coronary causes (using Swedish values for different ages instead of the risk of death obtained by the hazard function and, in another case, increasing and decreasing the annual risk of death by 50%), costs associated with morbidity after a nonfatal coronary event (raised and lowered by 50%), cost of intervention (i.e. drug therapy, with the US price case considered), discount rate (from 0 to 10%), inclusion of cost of follow-up, inclusion of both the cost of follow-up and screening. One-way simple sensitivity analysis was carried out.

Estimated benefits used in the economic analysis
The years of life gained with intervention (discounted at an annual rate of 5%), relative to the comparator, for a 59-year-old patient with CHD and a pre-treatment total cholesterol level of 261 mg per decilitre were estimated to be 0.28 (if female), and 0.16 (if male).

Cost results
The costs were discounted at a 5% annual rate. The expected incremental costs of the intervention relative to the comparator, without indirect costs, were $1,524 for a 59-year-old man with CHD and pre-treatment total cholesterol level of 261 mg per decilitre. For a woman with the same characteristics the figure would be $1,685. The corresponding figures, when indirect costs were included, were $459 and $809, respectively.

Synthesis of costs and benefits
The synthesis of costs and benefits was expressed in terms of incremental discounted costs per discounted life-year gained with the intervention. The prices used were those of 1995 and the discount rate for costs and benefits used was 5%. The expected figures for a 59-year-old man (woman) with CHD and pre-treatment total cholesterol level of 261 mg per decilitre were $5,400 ($10,500), without indirect costs, and $1,600 ($5,100), with indirect costs considered. The cost-effectiveness ratio decreased with increasing cholesterol levels and with age. The overall incremental discounted cost per discounted year of life gained ranged from $3,800 to $27,400 in the various groups of patients when indirect costs were excluded from the analysis. With indirect costs included, 35-year-old patients, both men and women, had negative figures (discounted savings associated with the intervention). When only direct costs were considered, sensitivity analyses resulted in ranges, for men, from $3,000 to $12,000, and from $4,500 to $21,800, for women. When both direct and indirect costs are considered, the ranges were from savings to $9,300 and from $100 to $18,500, for men and women, respectively.

Authors’ conclusions
Simvastatin is a cost-effective (5-years) therapy for both male and female patients with CHD at the ages and pre-treatment cholesterol levels investigated in the study.

CRD COMMENTARY - Selection of comparators
The reason for the choice of the comparator is clear.

Validity of estimate of measure of benefit
The estimate of benefit measure used in the analysis is likely to be internally valid. Quality of life effects were excluded.

Validity of estimate of costs
The resource quantities were reported in a rather highly aggregated manner. Adequate details of cost estimation were reported. The cost data were not comprehensive or gathered prospectively. Costs of outpatient diagnosis and treatment
were excluded.

**Other issues**
The issue of generalisability was only partially addressed in the sensitivity analysis (inclusion of prices prevailing in the US).

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