Cost-effectiveness of cholesterol lowering: results from the Scandinavian Simvastatin Survival Study (4S)

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
Simvastatin 10, 20 or 40mg/day for the prevention of coronary events and death in patients with established coronary heart disease.

Type of intervention
Secondary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
Patients with prior myocardial infarction (MI) or angina pectoris. 81% of the study population were male and 51% were aged 60 or above.

Setting
The practice setting was clinical centres. The resource use data were drawn from five Scandinavian countries. Unit cost data came from Sweden.

Dates to which data relate
1993 cost data were used, inflated to 1995 figures. Effectiveness data was taken from the 4S trial, which covered the period from May 1988 to August 1994. Resources used comprised DRG-related hospitalization and drugs.

Source of effectiveness data
Effectiveness data was derived from the multi-centre Scandinavian Simvastatin Survival Study (4S), which was a randomised controlled trial.

Link between effectiveness and cost data
Costing was undertaken prospectively on the same patient sample as that used in the effectiveness study.

Study sample
4,444 patients with a history of angina pectoris or myocardial infarction who were eligible and consented, were randomly assigned to treatment with simvastatin 20mg or to placebo. Dosage was adjusted at routine visits on the basis of cholesterol level. The protocol specified 4,400 patients to achieve a study power of 95% to detect 30% reduction in total mortality. Treatment differences were assessed by log rank test and the groups were found to be well matched. Of those recruits who were not enrolled, 84% had cholesterol levels outside the required range and 15% were unwilling to
Study design
The 4S study was a double blind, randomized controlled trial based in five Scandinavian countries. There was a median follow-up of 5.4 years. 6% of both groups discontinued therapy.

Analysis of effectiveness
The analysis was based on intention to treat. The primary health outcomes used were deaths from coronary heart disease (CHD), revascularization procedures and acute cardiovascular events. Groups were well matched at baseline.

Effectiveness results
The trial demonstrated a 30% reduction in relative risk of mortality from any cause in CHD patients (RR=0.7; 95% CI: 0.58-0.83, p = 0.0003), due solely to a 42% reduction in coronary deaths. The relative risk of a major coronary event was 0.66 (95% CI: 0.59-0.75, p = 0.00001), and there was a 26% reduction in the rate of hospitalization for acute cardiovascular disease (p<0.0001), a 32% reduction in coronary revascularization procedures (p<0.00001), and a 34% reduction in the number of days spent in hospital with the above conditions (p<0.0001).

Clinical conclusions
Treatment with simvastatin improved survival in CHD patients with raised cholesterol levels.

Modelling
The life years saved up to 5.5 years were obtained from the trial data. Additional benefits beyond this period, and up to a total of 10 years, was based on actuarial data, disregarding future treatment effects.

Measure of benefits used in the economic analysis
The outcome measure used was life-years gained, discounted at 5% pa.

Direct costs
Resource use quantities on hospital admissions for acute cardiovascular events, revascularization procedures and use of simvastatin were collected prospectively in conjunction with the trial. Cost data came from Sweden, and was converted from 1993 to 1995 prices. Hospitalization costs were based on DRGs. Costs were discounted at 5% p.a. Simvastatin had little impact on the use of other cardiovascular medications, which were therefore not included in the analysis.

Statistical analysis of costs
There does not appear to have been a statistical analysis of costs.

Indirect Costs
These were not included in the analysis.

Currency
Swedish Kroner (SEK), converted to UK pounds sterling ( ).

Sensitivity analysis
A one way sensitivity analysis was carried out on 4 parameters: life expectancy at the end of the trial; life years gained.
estimated by the Weibull method; extra costs for monitoring and initiating the treatment; and the discount rate was varied for both costs and benefits.

**Estimated benefits used in the economic analysis**
The average gain in life expectancy during the trial was 0.054 years per patient, discounted at 5%. The total discounted gain in life expectancy from 5.5 years of simvastatin treatment was 0.24 life-years.

**Cost results**
The total net 5% discounted treatment cost per patient in the simvastatin arm over the 5.4 years was SEK 37,302 (3639). This was composed of SEK 21,100 (2059) drug costs and SEK 16,202 (1580) in hospitalization costs. This gives an incremental cost per patient in the simvastatin group of SEK 13,540 (1321). Costs and quantities were measured over the trial period.

**Synthesis of costs and benefits**
The incremental cost per discounted life-year saved was SEK 56,400 (5502), at 1995 prices. In the sensitivity analysis, cost per life-year saved ranged from SEK 37,600 (3668) to SEK 96,100 (9376).

**Authors’ conclusions**
The cost per life-year saved for simvastatin was well within the range normally considered to be cost-effective and was stable across a range of scenarios. The inclusion of indirect costs in the analysis would probably improve the cost-effectiveness of simvastatin.

**CRD COMMENTARY - Selection of comparators**
Comparing a new drug with placebo is sensible. However, the cost-effectiveness relative to other interventions is also needed.

**Validity of estimate of measure of effectiveness**
The clinical evidence comes from a large multi-centre RCT which is highly reliable.

**Validity of estimate of costs**
Resource quantities and costs were reported separately, and adequate details of the methodology used were supplied. No important cost items were omitted. In view of the quality of both the clinical evidence and the economic analysis, the results appear reliable.

**Other issues**
The clinical evidence was discussed with reference to other lipid-lowering therapy trials. The cost-effectiveness ratio of simvastatin was compared in a narrative way with the ratios of other cardiovascular interventions, taken from separate studies. The authors generalized their cost-effectiveness result to make international comparisons, but advise caution in their interpretation.

**Implications of the study**
Simvastatin should be considered for people with coronary heart disease.

**Source of funding**
None stated

**Bibliographic details**
lowering: results from the Scandinavian Simvastatin Survival Study (4S) European Heart Journal 1996; 17(7): 1001-1007

**Other publications of related interest**

**Indexing Status**
Subject indexing assigned by NLM

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