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
Lipid lowering with simvastatin in patients with diabetes.

Type of intervention
Primary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
Diabetic and non-diabetic patients with coronary disease.

Setting
Community. The study was carried out in Sweden.

Dates to which data relate
Effectiveness and resource use data were collected from the Scandinavian Simvastatin Survival Study (4S) published in 1999. Cost data were derived from 1995-1997 sources. 1995-1997 prices were used.

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

Link between effectiveness and cost data
The costing was undertaken prospectively alongside the effectiveness study and on the same patient sample.

Study sample
The 4S study included 4,444 men and women aged 35-70 years with a prior MI or angina or both. Patients were randomised to treatment with simvastatin 20 to 40 mg or placebo, and the drug was titrated to reach a total cholesterol concentration of 5 mmol/l. Two subgroups were defined using clinical history: non-diabetic patients (n=4,242) and diabetic patients (n=202). Three subgroups were defined using the ADA criteria: non-fasting glucose (NFG) patients (n=3,237), impaired fasting glucose (IFG) patients (n=678), and diabetic patients (n=483).

Study design
This was a prospective, double-blind, randomised and placebo controlled study, carried out at 94 centres in Denmark, Finland, Iceland, Norway and Sweden. Patients were followed up for 5.5 years. Any loss to follow-up was not reported.
Analysis of effectiveness
The analysis of the clinical study was based on intention to treat. The primary health outcomes used were the number of hospitalisations and the mean survival time. At analysis, the groups were shown to be comparable in terms of demographic characteristics.

Effectiveness results
The gain in survival probability (simvastatin - placebo) was significant (p<0.05) except for the diabetic subgroup based on the ADA criteria. IFG patients who received placebo had a survival probability between that of NFG and diabetic patients. Among those who received simvastatin, IFG patients had the highest survival probability. For all subgroups, patients treated with simvastatin had a longer projected survival time than patients who received placebo. A similar survival time was projected for diabetic patients treated with simvastatin with the two classification schemes. For patients receiving placebo, a longer survival time was projected for the diabetic patients defined by ADA. Simvastatin reduced the number of hospitalisations in all subgroups by 23 to 40%. With the ADA classification, simvastatin yielded the greatest gains in survival time among the IFG group.

Clinical conclusions
For all subgroups, patients treated with simvastatin had a longer projected survival time than patients who received placebo.

Modelling
No modelling was undertaken.

Measure of benefits used in the economic analysis
The number of life years gained was used as the measure of benefits. The survival time during the first 5.5 years of the trial was estimated by the area under the Kaplan Meier survival curve. Life expectancy beyond 5.5 years was based on the estimated Kaplan Meier survival probability at 5.5 years and an average remaining life expectancy for the survivors. Benefits were discounted at an annual rate of 3%.

Direct costs
Direct costs were discounted at an annual rate of 3%. Quantities and costs were not reported separately. Direct costs included costs of the intervention (costs of hospitalisation, simvastatin) minus savings from a reduction in the costs of hospitalisation for CHD. The quantity/cost boundary adopted was that of the health service. The estimation of quantities and costs was based on actual data. Direct costs were estimated using costs from Sweden and other European countries. 1995-1997 prices were used.

Statistical analysis of costs
Not reported.

Indirect Costs
Not reported.

Currency
Swedish kroner (SEK) and Euros (ECU).

Sensitivity analysis
Sensitivity analysis was performed on mean survival time.

**Estimated benefits used in the economic analysis**
See the Effectiveness Results section above.

**Cost results**
When comparing the intervention costs for simvastatin with the savings in costs due to fewer hospitalisations, the proportion of intervention costs offset was highest in the diabetes group (67% based on classification by clinical history and 76% based on ADA).

**Synthesis of costs and benefits**
Cost per life year gained were calculated. In Sweden, cost-effectiveness ranged from 1,554 ECU for the diabetic subgroup (based on clinical history) to 7,345 ECU for the NFG subgroup (based on ADA criteria). The cost per life year gained was lower for the diabetic subgroups than for the non-diabetic subgroups. The cost-effectiveness of simvastatin in the IFG group was lower than that for the NFG and diabetic subgroups. In the other evaluated countries, intervention with simvastatin showed a favourable cost-effectiveness ratio independent of differences in local health care unit costs. At a threshold of 200,000 SEK per life year gained, the probability that intervention with simvastatin would be cost-effective ranged from 0.75 to 0.98 for the various subgroups. These results were not affected by varying the mean survival time.

**Authors’ conclusions**
For all subgroups in the diabetic classification schemes, treatment with simvastatin resulted in estimates of cost per life year gained that were well within the range generally considered to be cost-effective.

**CRD COMMENTARY - Selection of comparators**
The rationale for the choice of the comparator was clear. You, as a user of this database, should verify whether this health technology is relevant to your setting.

**Validity of estimate of measure of benefit**
A relevant measure of benefits was used although some of the subgroups suffered from a small sample size. The authors had to make assumptions about mean survival time. For instance, they assumed that among patients with heart disease, those with diabetes have a shorter life expectancy than those who are non-diabetic. However, a good feature of the study was that uncertainty surrounding these assumptions was tested in the sensitivity analysis.

**Validity of estimate of costs**
Only direct costs incurred by the health service were considered. Indirect costs such as those related to lost productivity were not included. No attempt was made to correct for potential price changes over time. Costs associated with added life years were not considered. Estimates of cost-effectiveness were based on 4S resource utilisation and local unit costs in 10 European countries. However, the authors acknowledged that resource utilisation may also vary across European countries.

**Other issues**
Adequate comparisons with other relevant studies were made. The generalisability of the results to other settings or countries was discussed. The authors do not appear to have presented their results selectively. The study enrolled diabetic and non-diabetic patients with cardiovascular disease and this was reflected in the authors’ conclusions.
Implications of the study
Based on the Scandinavian Simvastatin Survival Study, simvastatin therapy provides good value for money in both diabetic and non-diabetic patients with cardiovascular disease.

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None stated.

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