Statin cost-effectiveness in the United States for people at different vascular risk levels
Heart Protection Study Collaborative Group

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.

CRD summary
The objective was to assess the cost-effectiveness of prescribing generic simvastatin in the USA for people at different risk levels for vascular disease. The authors concluded that treatment with generic simvastatin was cost-effective for a wider US population than that recommended by clinical guidelines at the time. The methods were good and they and the results were reported in detail. The conclusions of the authors appear to be appropriate.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
The objective was to assess the cost-effectiveness of prescribing generic simvastatin in the USA for people at different risk levels for vascular disease.

Interventions
The authors evaluated generic simvastatin for people, with different levels of vascular risk. The risk levels were 12%, 18%, 22%, 28%, and 42% for a major vascular event (MVE) within five years; the combined data for all these patients was also analysed. The use of simvastatin was compared with no simvastatin and the analysis was also subdivided into four age groups (40 to 49 years, 50 to 59 years, 60 to 69 years, and 70 years or older).

Location/setting
USA/out-patient care.

Methods
Analytical approach:
A published decision analytic Markov model that was designed to assess the lifetime cost-effectiveness of simvastatin in the UK was modified to a US setting (Heart Protection Study Group. 2006, see 'Other Publications of Related Interest' below for bibliographic details). This model was used to extrapolate the results from the Heart Protection Study (HPS, Heart Protection Study Group. 2002, see 'Other Publications of Related Interest' below for bibliographic details), which had an average follow-up of five years, to the lifetime of the patient. A within-in trial analysis was also conducted using the five-year data. The authors reported that a US health care payer perspective was adopted.

Effectiveness data:
The majority of the effectiveness and other clinical data were from the HPS, a randomised controlled trial of more than 20,000 participants, who received either simvastatin or placebo, carried out in the UK. Other sources, such as US life tables, were used to extrapolate the baseline risk beyond the end of the trial. The main effectiveness measure was the rate of MVEs, such as stroke and myocardial infarction.

Monetary benefit and utility valuations:
Not relevant.

Measure of benefit:
For the within-trial analysis, the measure of benefit was the number of vascular deaths avoided. For the lifetime analysis, the measure of benefit was life-years gained. Future benefits were discounted at an annual rate of 3%.

Cost data:
The direct costs analysed were those relating to hospitalisations due to major vascular events, hospitalisations due to other causes, and simvastatin. The costs of hospitalisations due to other causes were not included in the within-trial analysis, but were included in the lifetime extrapolation. The hospitalisation resource use was from the HPS. These hospitalisations had a UK National Health Service Read code that was translated into International Classification of Diseases 9th Revision Clinical Modification (ICD-9) codes. These codes with length of stay information were translated into US diagnosis-related group (DRG) data. The hospitalisation costs included physician fees, which were from Medicare schedules. All costs were inflated to 2006 prices using the medical care component of the Consumer Price Index. They were reported in US dollars ($) and discounted at an annual rate of 3%.

Analysis of uncertainty:
The uncertainty in the estimates of outcomes, costs, and costs per life-year gained was assessed by non-parametric bootstrapping of the event and cost equations used in the model. A series of one-way sensitivity analyses were also undertaken, by varying the cost of simvastatin and the costs of hospitalisations.

Results
For the within-trial analysis, over five years, the estimated additional costs with simvastatin ranged from savings of $38 per patient with a risk of 42% to a cost of $859 for patients with a risk of 12%. The estimated vascular deaths avoided by prescribing simvastatin, per 1,000 patients, ranged from four for patients with a risk of 12% to 30 for those with a 42% risk. Compared with placebo, prescribing simvastatin was associated with an incremental cost-effectiveness ratio ranging from net savings of $1,300 (95% CI -15,600 to 13,200) per vascular death avoided, for patients with a risk of 42% to a cost of $216,500 (95% CI 123,700 to 460,000) per vascular death avoided for patients with a risk of 12%.

For the lifetime extrapolation, the life-years gained with simvastatin ranged from 0.47 (95% CI 0.26 to 0.68) for patients aged 70 or older with a 12% risk to 1.33 (95% CI 0.76 to 1.89) for patients aged 40 to 49 years with a 42% risk. Regardless of age, and MVE risk, the lifetime use of simvastatin increased the lifetime costs. In all cases, compared with placebo, simvastatin was associated with an incremental cost-effectiveness ratio of less than $11,000 per life-year gained.

Authors' conclusions
The authors concluded that treatment with generic simvastatin was cost-effective for a wider US population than that recommended by clinical guidelines at the time.

CRD commentary
Interventions:
The interventions were reported clearly and in detail.

Effectiveness/benefits:
Most of the outcome and effectiveness parameters were from a randomised controlled trial, with over 20,000 participants, which makes it very likely that the results were both internally and externally valid. The HPS also had a long follow-up, averaging five years, and published data, such as life-tables, were used to extrapolate these baseline risks to the lifetime of the patient. The methods used to extrapolate the relative treatment effect beyond the end of the trial were reported in another published study.

Costs:
The perspective was explicitly reported to be that of the US health care payer. Only the costs of simvastatin and hospitalisations were analysed, with other health care costs omitted from the analysis, but it is unlikely that the inclusion of costs, such as primary or out-patient care, would have altered the conclusions. The hospitalisation costs were based on UK patients and the reasons for hospital admission and length of stay were translated into US DRG codes to produce US costs. The methods used to obtain the costs were reported in detail. The price year, time horizon, discount rate, and currency used were all reported.

Analysis and results:
The costs and outcomes from the HPS were extrapolated, using a published Markov model that was modified to the US...
setting. No diagram of the model was given. The parameter uncertainty was assessed using non-parametric
bootstrapping, and a series of one-way analyses were performed. The 95% confidence intervals were presented for the
incremental cost-effectiveness ratios. The main limitation of the study according to the authors was that the treatment
patterns in the USA differ from those in the UK, with more invasive interventions being performed in the USA, which
would have an impact on the cost results.

Concluding remarks:
The methods were good and they and the results were reported in detail. The conclusions of the authors appear to be
appropriate.

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Other publications of related interest
Heart Protection Study Collaborative Group. Lifetime cost effectiveness of simvastatin in a range of risk groups and
age groups derived from a randomised trial of 20,536 people. BMJ 2006; 333: 1145-1148.

Heart Protection Study Collaborative Group. MRC/BHF Heart Protection Study of cholesterol lowering with

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Subject indexing assigned by NLM

MeSH
Adult; Age Distribution; Aged; Cardiovascular Diseases /drug therapy /epidemiology /prevention & control; Cost-
Benefit Analysis; Drug Costs; Female; Hospitalization /statistics & numerical data; Humans; Hydroxymethylglutaryl-
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