Cost effectiveness of HMG-CoA reductase inhibitor (statin) treatment related to the risk of coronary heart disease and cost of drug treatment

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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

Hydroxymethyl glutaryl coenzyme A (HMG-CoA) reductase inhibitor (statin) treatment in subgroups of the population at different levels of coronary heart disease (CHD) risk.

Type of intervention

Primary and secondary prevention.

Economic study type

Cost-effectiveness analysis.

Study population

Four groups of hypothetical patients at different levels of CHD risk: CHD risk of 4.5% per year (secondary prevention), primary prevention at CHD risk of 3%, 2% and 1.5% per year. CHD is defined as definite, plus probable, or suspected fatal and non-fatal coronary events, excluding silent myocardial infarction.

Setting

Primary care. The economic study was conducted at the University of Sheffield, UK.

Dates to which data relate

The effectiveness data relate to studies published between 1994 and 1996. The drug prices used were based on 1997 data and the costs of prevented events (CHD diagnosis, hospital admission, percutaneous trasluminal coronary angioplasty (PTCA) and coronary artery bypass graft (CABG)) were based on 1991 data (which was reflated). The price year appears to have been 1997.

Source of effectiveness data

All parameters used in the effectiveness analysis were based on a review of two completed studies for CHD risks of 4.5% and 1.5%. The effectiveness data for CHD risk of 2% and 3% were modelled based on the two studies assuming a linear relationship between all cause mortality and annual CHD risk (for CHD risks between 1.5% and 4.5%).

Modelling

Extrapolations of effectiveness data beyond the timescale in the original trials (5.4 years Scandinavian Simvastatin Survival Study (4S) trial and 4.9 years West of Scotland Coronary Prevention Study (WOSCOPS) trial), as well as interpolation of the effectiveness for the 3% and 2% CHD risk groups, were performed. Mortality of the patients with CHD risks of 2% and 3% was calculated based on data for the ratio of coronary deaths to coronary events of 0.25 and non-coronary mortality from the WOSCOPS trial. A modelling of survival of the cohorts (1.5%, 2%, 3% and 4.5% CHD risks) on statin treatment and on placebo (life table method) provided estimates of the life years gained, events

avoided and costs.

Outcomes assessed in the review
The outcomes assessed were the annual all cause mortality at any age for individuals with the specified CHD risk (4%, 3.5%, 2 % and 1.5%) on statin and on placebo, and the effectiveness in terms of relative risk of statin treatment for the four CHD risk groups.

Study designs and other criteria for inclusion in the review
Recent controlled trials evaluating statin treatment provided data for this study.

Sources searched to identify primary studies
The article did not specify whether a search of the literature was performed.

Criteria used to ensure the validity of primary studies
The criteria for ensuring validity of the analysis were not reported.

Methods used to judge relevance and validity, and for extracting data
The methods used to judge the relevance and validity of the reviewed evidence were not reported.

Number of primary studies included
Four primary studies were included in the review.

Methods of combining primary studies
Two principal studies provided data for different CHD risks (4.5%, 1.5%) for the study duration. Extrapolation of the results to life long duration was performed. The outcomes for CHD risk of 3% and 2% were estimated by linear interpolation based on the results of the primary studies reviewed.

Investigation of differences between primary studies
The studies analysed the outcomes of statin treatment for different CHD risks (4.5% and 1.5% respectively). The average age of the participants in both studies differed (58 and 55 years respectively) as well as the duration of the two studies (5.4 and 4.9 years respectively).

Results of the review
The survival curves for placebo and statin treated patients from the 4S and WOSCOPS trials were used to calculate the life years gained. The relative risks for all cause mortality of 0.66 (4S) and 0.78 (WOSCOPS) were employed to calculate the relative risk for all cause mortality for the different risk groups. The mortality of men on placebo was 1.74 times that of the same age group in the UK general population (4.5% CHD risk, 4S trial) and 0.87 (1.5% annual CHD risk, WOSCOPS trial).

Measure of benefits used in the economic analysis
The benefit measures were the number of life-year gained and the reduction of myocardial infarction, CABG and angioplasty. These were estimated for cohorts of patients on statin treatment compared with cohorts on placebo. The estimates were based on the extrapolated mortality data from the reviewed studies for CHD risks of 4% and 1.5% assuming the same mortality relative risks. Interpolation of the results from these studies, assuming a linear relationship between CHD risk and relative risk for all cause mortality, provided estimates of the benefits for CHD risks of 2% and

3%. The authors also reported the number needed to treat (NNT) to prevent one CHD event.

Direct costs

Direct drug costs were estimated based on the survival analysis data and assuming treatment with the drug simvastatin. The simvastatin dose was taken from the 4S trial (27.4 mg daily). The simvastatin cost of 1.52 per day (555 per year) was taken from the British National Formulary (March 1997). The drug costs and potential savings were discounted at 6% per year, as recommended by the UK Treasury (for public expenditure). Unit costs per drug and type of savings, as well as total costs, were reported. The number of potential events avoided was reported but the quantities of prevented health events were not stated. Costs relating to these elements were taken from hospital records from Newcastle-upon-Tyne in 1991, which were inflated by 28% according to data from the UK Audit Commission. The price year appears to have been 1997, but this was not clear from the paper.

Statistical analysis of costs

No statistical analysis of costs was performed.

Indirect Costs

No indirect costs were evaluated in the study.

Currency

UK pounds sterling ().

Sensitivity analysis

A series of one and two-way sensitivity analyses was performed:

for a statin treatment employing the drug pravastatin (WOSCOPS and CARE trials) (40mg daily), at a cost of 2.22 per day (811 per year) was performed;

a best case scenario of life-long treatment and life-long effect, and a worst case scenario for 5 years treatment and effect;

analysis of the effect of inclusion of cost savings for health interventions based on 1991 cost data from Newcastle-upon-Tyne inflated by 28% (Audit commission) in order to reflect the rise of costs. The updated costs were 5,500 per CABG, 3,517 per PTCA, 1,887 per admission for myocardial infarction and 1,471 per admission for other CHD diagnosis;

no discounting of costs and benefits;

relative mortality risks for CHD risks of 2% equal to 0.66 (4S) and for CHD of 3% equal to 0.78 (WOSCOPS) instead of using interpolated relative risks; and

annual costs of drug varied from 100 to 800.

Estimated benefits used in the economic analysis

Life-long duration of relative mortality risks was assumed for the main results and a sensitivity analysis for 5-year effects was performed. The benefits were discounted at 6% per year. No separate reporting of these benefits was provided in the article. The NNT to prevent one CHD event for each group would be: 4.5% = 13; 3% = 20; 2% = 30; 1.5% = 40.

Cost results

The costs were discounted at 6% per year.

The annual cost of implementing treatment fully for the four risk groups in England would be:

4.5% = 549 million (5.1% of the UK population affected);

3% = 885 million (8.2% of the UK population affected);

2% = 1,712 million (15.8% of the UK population affected);

1.5% = 2,673 million (24.7% of UK population affected).

Synthesis of costs and benefits
The costs for statin treatment of CHD risks per life year gained were:

4.5% = 5,100 (3,200 to 8,200 in sensitivity analysis);

3% = 8,200 (4,500 to 15,800);

2% = 10,700 (5,500 to 22,100);

and 1.5% = 12,500 (6,100 to 26,800).

The results were sensitive to the timescale of treatment and the cost-effectiveness ratios increased with decreasing length of treatment and effect, from life-long to 5-year:

4.5% = 8,200;

3.0% = 15,800;

2.0% = 22,100;

and 1.5% = 26,800.

The treatment with pravastatin was relatively less cost-effective than the treatment with simvastatin:

4.5% = 7,400;

3.0% = 12,000;

2.0% = 15,600;

and 1.5% = 18,200.

If the possible savings in health care costs were taken into account the cost-effectiveness of statin treatment for all CHD risks improves:

4.5% = 4,300;

3.0% = 7,500;

2.0% = 10,100;

and 1.5% = 12,500.

The cost-effectiveness results were sensitive to the drug costs and, for costs less than 300 per year, the treatment of CHD risk of 1.5% per year was becoming cost-effective.

Authors' conclusions

At current prices the statin treatment for secondary prevention and for primary prevention at a CHD event risk 3% per year, is as cost-effective as many treatments in wide use. The implementation into practice should take into account the number of treatments needed in the country and would make necessary improvement of measurement of CHD risk. The first priority should be given to those who already have overt vascular disease.

CRD COMMENTARY - Selection of comparators

The use of placebo as a comparator is justified when the "do nothing" alternative is the usual practice.

Validity of estimate of measure of benefit

The estimates of the measure of benefits were extracted from two studies or were modelled from them. Insufficient detail of the method of selection of the studies included was given. The generalisability of the results from these studies (in particular the 4S Scandinavian study to an UK setting) was not addressed but may be relevant. No detail of the estimates of the volume of prevented health care interventions (myocardial infarctions, CABG, angioplasty) for different CHD risks was given.

Validity of estimate of costs

Only the drug costs and the costs of major health events prevented were analysed. A broader cost perspective, including the costs for CHD risk assessment, primary care costs, and laboratory costs would be more informative. Cost estimates were based on a 100% compliance rate even though, in the source trials, this fell to 70% after five years, which is recommended in the literature but which produces a conservative estimate. A good feature of the cost results was that total costs of implementation in England were given, which explicitly provides policy makers with the cost implications associated with the intervention.

Other issues

The cost-effectiveness results of this study were appropriately compared with other studies of primary and secondary prevention of CHD. The implications of the study for the UK population were stated and a discussion of the most effective implementation was provided. The study implicitly examined the process of generalisability by utilising the results of trials conducted outside the UK, which were used in conjunction with UK costs and therefore cost-effectiveness.

Implications of the study

Secondary CHD prevention and primary prevention at a CHD event risk of 3% are cost-effective interventions. As the cost of statin falls, primary CHD prevention becomes more cost-effective but the large volume of treatment required remains a major problem. The authors recommend that the first priority is to treat those already diagnosed with vascular disease as they can easily be identified. For primary prevention, decisions should not be based on levels of cholesterol or lipid fractions alone, nor on intuitive assessment of CHD risk. The authors advocate the use of the Sheffield table (details given in the paper) which identifies those suitable for statin treatment.

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None stated.

Bibliographic details

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Other publications of related interest

Scandinavian Simvastatin Survival Study group. Randomised trial of cholesterol lowering in 4444 patients with coronary heart disease: the Scandinavian simvastatin survival study (4S). Lancet 1994;344:1383-9.

Shepherd J, Cobbe SM, Ford I, et al for the West of Scotland Coronary Prevention Study Group. Prevention of Coronary heart disease with pravastatin in men with hypercholesterolemia. New England Journal of Medicine 1995;333:1301-7.

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Subject indexing assigned by NLM

MeSH

Coronary Disease /economics /prevention & control; Cost-Benefit Analysis; Drug Costs; Humans; Hydroxymethylglutaryl-CoA Reductase Inhibitors /economics /therapeutic use; Hypolipidemic Agents /economics /therapeutic use; Life Tables; Male; Middle Aged; Risk Assessment; Simvastatin /economics /therapeutic use

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