**Cost-effectiveness of pravastatin therapy for survivors of myocardial infarction with average cholesterol levels**

*Tsevat J, Kuntz K M, Orav E J, Weinstein M C, Sacks F M, Goldman L*

---

**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**

The health technology under investigation was pravastatin therapy (PT). This is an aggressive cholesterol-lowering strategy for the treatment of patients who have already experienced coronary heart disease and are at high risk of having ischaemic events.

**Type of intervention**

Secondary prevention.

**Economic study type**

Cost-effectiveness analysis.

**Study population**

The study population comprised patients with average cholesterol levels who had already had MI. These patients were also at risk of fatal coronary events, nonfatal MI, revascularisation procedures such as coronary artery bypass grafting and angioplasty, and strokes.

**Setting**

The setting was the community. The economic study was carried out in the USA.

**Dates to which data relate**

The dates during which the effectiveness data were gathered were not reported. The costs were obtained for a period of 6 years. The price year was 1996.

**Source of effectiveness data**

The effectiveness data were derived from a single study on cholesterol and recurrent events (CARE) trial (see Other Publication of Related Interest no.1).

**Link between effectiveness and cost data**

The costing was undertaken prospectively on the same patient sample as that used in the effectiveness analysis.

**Study sample**

In total, 4,159 patients were enrolled in both arms of the CARE trial. The mean age of the patients was 59 (standard deviation = 9) years and 86% of the patients were men. The proportion of Caucasian patients was 93% in the PT arm and 92% in the placebo arm. The mean cholesterol level at study entry was 209 mg/dL for each group. No power calculations were used to determine sample size. The methods used to select the study sample were not reported.
Study design
Very few details of the CARE trial (see of Related Interest no.1) were reported. The authors stated only that a trained medical record coder assessed the costs, blinded to the treatment assignment.

Analysis of effectiveness
It was not stated whether the analysis of the clinical study was based on intention to treat or treatment completers only. The primary health outcomes were the utility values for the health states obtained through the Markov models. The patients were asked to rate their health on a scale that ranged from 0 (dead) to 100 (perfect health). The ratings were then transformed into health utilities using the McMaster power transformation (see of Related Interest no.2). The difference in health ratings between PT and placebo groups was tested for significance using a regression model. This used health rating as the dependent variable, whilst the independent variables were the group (PT or placebo) and the number of observations per patient. Years of life were discounted at 3% per annum.

Effectiveness results
The mean health ratings were approximately 1% higher in the PT group (77.8%) than in the placebo group (77%). The health utility was 0.968 for the PT group and 0.965 for the placebo group, (p<0.03).

Clinical conclusions
The utility value associated with the PT strategy was greater than that obtained in the placebo group.

Modelling
Two pairs of Markov models were used to derive survival rates and health-related quality of life data. One pair was based on all-cause mortality data from CARE (mortality models) and was used to calculate the quality-adjusted life-years (QALYs) gained with PT. The other pair of Markov models was based on recurrent event data from CARE (recurrent events models) and was used to simulate the primary end points of the trial. Overall, four models were estimated: mortality model 1, mortality model 2, recurrent events model 1 and recurrent events model 2.

Measure of benefits used in the economic analysis
QALYs were used to estimate the benefits of PT in comparison with the placebo strategy. The utility scores in the four models were defined using patients' values.

Direct costs
The costs were discounted at a rate of 3%. The quantities and costs were not reported separately. The cost estimates for the model were based on the actual resource utilisation of the patients in the trials, and were derived from medical records. The hospitalisation data were calculated using appropriate DRG (Diagnosis-Related Groups) reimbursement rates. The medication costs were based on the average wholesale price, reduced by 18.3% for brand names and 42.5% for generic formulations, with a dispensing cost of $5.47 per 1-month supply added.

The quantity/cost boundary adopted was not stated. The costs considered in the analysis were those for PT, other cardiac medications, hospitalisation, MI, unstable angina, revascularisation, and stroke. The costs were gathered during a 6-year time period and the price year was 1996. The costs of outpatient tests were excluded because they were assumed to be equal for both the PT and placebo strategies.

Statistical analysis of costs
No statistical analysis of costs was reported.
Indirect Costs
Indirect costs were not included.

Currency
US dollars ($).

Sensitivity analysis
Sensitivity analyses were used to examine the robustness of the results, since there was some uncertainty about the variability of some of the parameters. The following parameters were varied: survival rates, cost of PT, hospitalisation costs, and the difference in case-fatality rates between the PT and placebo groups.

Estimated benefits used in the economic analysis
The average discounted QALYs were:

- 13.62 for PT and 13.27 for the placebo when using mortality model 1;
- 13.92 for PT and 13.13 for the placebo when using mortality model 2;
- 12.99 for PT and 12.64 for the placebo when using recurrent events model 1; and
- 13.10 for PT and 12.55 for the placebo when using recurrent events model 2.

Cost results
The average discounted costs were:

- $53,177 for PT and $42,223 for the placebo when using mortality model 1;
- $54,359 for PT and $41,788 for the placebo when using mortality model 2;
- $48,734 for PT and $37,435 for the placebo when using recurrent events model 1; and
- $49,087 for PT and $37,224 for the placebo when using recurrent events model 2.

Synthesis of costs and benefits
The costs and benefits were combined by an incremental cost-utility analysis. The value of the incremental cost-utility ratio of PT was $31,000 with mortality model 1, $16,000 with mortality model 2, $32,000 with recurrent events model 1, and $22,000 with recurrent events model 2.

The sensitivity analyses showed that in mortality model 1, when changing the survival benefit of PT from 9 to 22% the incremental ratio dropped to $14,000 per QALY. The sensitivity analyses also demonstrated that if the annual cost of PT was less than $146 (it was $925 per year in the base-case), then PT was dominant, i.e. less costly and more effective.

The annual cost of PT would have to exceed $1,389 for the incremental ratio to exceed the threshold of $50,000 per QALY.

The cost-utility ratios were also calculated in sub-group analyses. The analysis showed that PT was associated with more QALYs in the case of patients older than 60 years.

Authors' conclusions
The study suggested that pravastatin therapy (PT) was a cost-effective strategy for survivors of MI with average...
cholesterol levels, especially older patients.

**CRD COMMENTARY - Selection of comparators**
The choice of placebo as the comparator was appropriate given that the study was a controlled trial.

**Validity of estimate of measure of effectiveness**
The effectiveness measure and the characteristics of the CARE trial were discussed in a different paper, thus only a few details were reported by the authors.

**Validity of estimate of measure of benefit**
The choice of the QALY as the benefit measure seemed appropriate since the use of PT as a secondary prevention strategy is likely to affect both survival length and quality of life.

**Validity of estimate of costs**
The study included all the categories of costs relevant to the analysis. However, the costs and quantities were not reported separately. The authors pointed out that the exclusion of outpatient costs could have biased the results of the analysis against the pravastatin strategy, because those patients administered placebo were likely to have more outpatient visits and tests.

**Other issues**
Although the authors stated that a societal perspective was adopted, only direct medical costs were included in the study. Productivity losses were not considered. The issue of generalisability to other settings was not addressed, although the authors made comparisons of their finding with those of other studies. The authors recognised that the sub-group analysis was not reliable because of the small sample size of certain sub-groups.

**Implications of the study**
The cost-effectiveness of PT compared favourably with other interventions given that the threshold of $50,000 per QALY was not reached. Since the procedure for calculating QALYs requires a complex technique, the authors suggested that future studies should focus on more reliable methods to model the outcomes from trials. In addition, the impact of these methods on the cost-effectiveness analysis results should be assessed. 1. Sacks FM, Pfeffer MA, Moye LA, et al. The effect of pravastatin on coronary events after myocardial infarction in patients with average cholesterol levels. New England Journal of Medicine 1996;335:1001-9. 2. Torrance GW, Feeny DH, Furlong WJ, et al. Multiattribute utility function for a comprehensive health status classification system: Health Utilities Index Mark 2. Medical Care 1996;34:702-22.

**Source of funding**
Supported by a grant from Bristol-Myers Squibb.

**Bibliographic details**

**PubMedID**
11320359

**DOI**
10.1067/mhj.2001.114805
Indexing Status
Subject indexing assigned by NLM

MeSH
Anticholesteremic Agents /economics /therapeutic use; Cholesterol, LDL /blood; Cost-Benefit Analysis; Female; Humans; Hypercholesterolemia /blood /complications /drug therapy /mortality; Male; Middle Aged; Myocardial Infarction /blood /etiology /mortality /prevention & control; Pravastatin /economics /therapeutic use; Quality of Life; Secondary Prevention; Sensitivity and Specificity; Survival Rate; United States /epidemiology

AccessionNumber
22001001050

Date bibliographic record published
31/03/2002

Date abstract record published
31/03/2002