Cost-effectiveness of pravastatin in secondary prevention of coronary artery disease
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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
Cholesterol lowering using pravastatin in people with Coronary Artery Disease (CAD).

Type of intervention
Secondary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
Male patients (n=445, mean age of 60 years) with CAD and moderately elevated serum low-density lipoprotein cholesterol.

Setting
The practice setting was the secondary care sector and the trials were multi-centred within the USA. The economic study was based on American data.

Dates to which data relate
Effectiveness data were extracted from two studies published in 1992 and 1993. The cost of drug therapy and the dispensing fee were based on average US prices in 1995. Other resource costs were derived from the medical literature and were adjusted to 1995 prices.

Source of effectiveness data
Two previously completed, placebo-controlled plaque regression studies were reviewed and the data extracted were pooled.

Modelling
To estimate costs and effects, decision analysis was used. In order to determine the survival curve and the average remaining years of life for each age cohort of patients who had a nonfatal myocardial infarction (MI), life-table analysis was used. Life years saved were estimated using the Markov process. The Framingham Study was used to estimate the annual morbidity and mortality rates for non-fatal MI patients beyond the period covered by the PLAC trials. Life-table analysis was undertaken to estimate the average remaining years of life and the survival curve for each cohort of patients who had experienced nonfatal MI whilst participating in the PLAC studies.

Outcomes assessed in the review
The key outcome assessed was non-fatal MIs.
Study designs and other criteria for inclusion in the review
Data from two placebo-controlled plaque regression RCTs (PLAC I and PLAC II). These studies covered a three year period. To extend the length of follow-up so that mortality and morbidity rates for nonfatal MI patients might be observed, results were extrapolated using the Framingham Study.

Sources searched to identify primary studies
Not stated.

Criteria used to ensure the validity of primary studies
Not stated.

Methods used to judge relevance and validity, and for extracting data
Not stated.

Number of primary studies included
Two placebo-controlled plaque regression studies (PLAC I and II) including 445 men with CAD.

Methods of combining primary studies
Pooled statistical analysis of clinical end points for the two PLAC trials.

Investigation of differences between primary studies
As the PLAC I and PLAC II trials were found to have similar inclusion criteria, baseline risk factors and baseline demographics, results were pooled.

Results of the review
Analysis of the two PLAC studies revealed that over the three year study period, fewer men in the pravastatin group had nonfatal MIs (9 vs 20, p<0.05). No statistically significant difference was found in all-cause mortality.

Measure of benefits used in the economic analysis
The outcome measure used was estimated life-years saved. This was derived from the non-fatal MI rate using the Markov model to extrapolate the results from the short to the long term.

Direct costs
The following direct costs were measured; drug costs, the dispensing fee, hospitalization costs and diagnostic intervention costs associated with myocardial infarction and its complications, physician fees and post-myocardial infarction and subsequent event follow-up costs. The daily weighted average dose per patient was derived from the PLAC studies. Probabilities relating to hospitalization costs of myocardial infarction and possible subsequent events were based on a literature review. The frequency of service post-myocardial infarction was based on expert medical opinion. Estimation of subsequent events was based on the Framingham data. Costs were discounted at the rate of 5% per year. Quantities were reported separately from costs. The price date was 1995.

Statistical analysis of costs
No statistical analysis of costs.
Indirect Costs
Not included

Currency
US dollars ($).

Sensitivity analysis
A sensitivity analysis was carried out on the hospitalization cost of myocardial rates, morbidity and mortality variations and the effects on utilization over a ten year period, the variation in the post-MI annual cardiovascular disease mortality rate and finally the impact of the observed risk reduction on non-fat myocardial infarction for men in the pravastatin arm of the PLAC studies.

Estimated benefits used in the economic analysis
The average discounted gain in life expectancy with pravastatin ranged from 0.11 to 0.21 years per patient over a ten year period in men with CAD with one and three or more additional risk factors respectively.

Cost results
The estimated net incremental costs associated with therapy initiation and annual follow-up were $298.50 (for men with one additional risk factor) and $163 (for men with three or more additional risk factors). Additional to this, incremental dispensing costs amounted to $17.80 per year.

Synthesis of costs and benefits
The incremental cost per life year saved with pravastatin in secondary prevention of CAD varied from $12,665 to $7,124 for male CAD patients with one and three of more additional risk factors respectively. Cost-effectiveness varied by 16% as hospital costs of myocardial infarction were varied by +/- 25%. The cost per life year saved decreased by 24% over the additional seven years projected for patients on pravastatin therapy. As the annual post-MI cardiovascular disease mortality rate was reduced from 3.4 to 2%, the cost-effectiveness ratio increased from $12,665 to $20,101 per life year saved. The range of cost per life year gained varied from $77,267 for male CAD patients with one additional risk factor to $3,068 for those with three or more additional risk factors.

Authors' conclusions
Pravastatin therapy in secondary prevention of CAD was cost-effective and was estimated to cost between $7,124 and $12,665 per life year saved depending on the patient's risk profile. Comparison with other major medical interventions for cardiovascular disease such as percutaneous transluminal coronary angioplasty, hydrochlorothiazide for the treatment of systemic hypertension, coronary artery bypass surgery and heart transplantation revealed that the use of pravastatin was a cost-effective intervention for reducing cardiovascular disease.

CRD COMMENTARY - Selection of comparators
The comparator is the placebo. This is an appropriate comparator given that no cholesterol lowering drug is the usual alternative.

Validity of estimate of measure of effectiveness
Data used were taken from well controlled studies and comprehensive use was made of such data. The data on mortality benefit were not taken from the trials but extrapolated from MIs only which, though strongly associated with future mortality, may be biased.

Validity of estimate of costs
Resource quantities were reported separately from costs. However, it is not clear how accurate the methods of
estimation were. Cost savings were not taken from the trial but from models and reviews the validity of which is unclear.

**Other issues**
The search strategy was not stated. The Framingham heart study was conducted eight years before the Ashraf et al study. As the author suggests, the Framingham study does not reflect current advances in reperfusion therapy.

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Bristol-Myers Squibb (NJ).

**Bibliographic details**

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**Other publications of related interest**


**Indexing Status**
Subject indexing assigned by NLM

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