Pharmacoeconomic analysis of 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitor therapy for the secondary prevention of coronary heart 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
The use of 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitor (pravastatin) therapy for the secondary prevention of coronary heart disease (CHD) was examined. The dosage studied was 10 mg/day.

Type of intervention
Secondary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised CHD patients with a serum total cholesterol concentration of between 180 and 219 mg/dL and diagnosed as having coronary strictures of 50 to 90% by coronary angiography (CAG). The patients agreed to participate in the trial after reading a leaflet describing it. New cases of myocardial infarction (MI) and cerebral apoplexy were not included.

Setting
The setting was secondary care. The economic study was conducted at Osaka Medical Center for Health Science and Promotion, Sankyo Co. Ltd, Tokyo and Osaka Medical Center for Cancer and Cardiovascular Diseases, Japan.

Dates to which data relate
The effectiveness and resource data related to a period between September 1991 and March 1995. The price year was not stated.

Source of effectiveness data
The effectiveness data were derived from a single study, which was reported in the parent clinical study of this economic evaluation (Sato et al., see 'Other Publications of Related Interest' for bibliographic details).

Link between effectiveness and cost data
The cost data for the single study were collected retrospectively from the same sample as that used in the effectiveness analysis.

Study sample
Power calculations were not used to determine the sample size. The study sample comprised 54 patients in the pravastatin group and 66 patients in the no pravastatin group (who did not receive any cholesterol-lowering drugs). The
age range was 20 and 69 years. No further details were provided, although they may be available in the parent clinical study (Sato et al., see Other Publications of Related Interest).

Study design
This was an open-labelled randomised controlled trial carried out in a single centre. The patients were randomly assigned to either the pravastatin group or the no pravastatin group, although the specific randomisation methods used were not reported. The duration of follow-up was two years. No loss to follow-up was reported. Further details may be available in the parent clinical trial (Sato et al., see Other Publications of Related Interest).

Analysis of effectiveness
The analysis of effectiveness was conducted on an intention to treat. The clinical effectiveness outcomes assessed were:

- the suppression of disease progression observed by CAG,
- the occurrence of events (e.g. percutaneous transluminal coronary angioplasty (PTCA), MI, cerebral apoplexy, heart failure leading to death), and
- the recurrence rate.

The comparability of the patients was not reported in the present study, but it might have been described in the parent clinical study (Sato et al., see Other Publications of Related Interest).

Effectiveness results
In terms of the suppression of disease progression, the pravastatin group was reported to be significantly better than the no pravastatin group (no specific data provided).

There were 2 events during the follow-up period in the pravastatin group versus 8 in the no pravastatin group, but this difference was found to be statistically non significant.

The disease recurrence rate was 3.7% in the pravastatin group and 9.1% in the no pravastatin group (details of statistical significance were not reported).

Clinical conclusions
The pravastatin group showed better results than the no pravastatin group for the suppression of disease progression and the disease recurrence rate.

Measure of benefits used in the economic analysis
The measure of benefit used was the occurrence of events and the recurrence rate. In terms of the number of event occurrences, no differences were found between the pravastatin and no pravastatin groups. Consequently, a cost-minimisation analysis was carried out. The recurrence rate was used to calculate the estimated cost per event-free year in a further cost-effectiveness analysis.

Direct costs
The direct costs included in the cost-minimisation analysis were for pravastatin, the treatment of side effects and events (including hospitalisation). In the cost-effectiveness analysis, such costs were for pravastatin and the treatment of side effects (including hospitalisation). Discounting was not carried out in the main analysis, although discount rates of 3 and 5% were used in the sensitivity analyses. The costs and the quantities were not reported separately. The costs were estimated using actual data from the single study. The price year was not stated.
Statistical analysis of costs
The cost data were not treated stochastically.

Indirect Costs
No indirect costs were included.

Currency
Japanese yen (Y).

Sensitivity analysis
One-way sensitivity analyses were carried out for the cost-minimisation analysis. The parameters investigated were the discount rate (3% and 5%), medication compliance, pravastatin costs (maximum and minimum costs during the study), event treatment (PTCA) costs (25 percentile and 75 percentile) and potential events (MI and heart failure leading to death and PTCA, and MI and heart failure leading to death and PTCA and cerebral apoplexy). One-way sensitivity analyses were also conducted for the cost-effectiveness analysis. The parameters investigated were the discount rates (3% and 5%), medication compliance and pravastatin costs (maximum and minimum costs during the study).

Estimated benefits used in the economic analysis
In the cost-effectiveness analysis, the disease recurrence rate was 3.7% for the pravastatin group and 9.1% for the no pravastatin group.

Cost results
The total costs (for pravastatin, treatments of side effects and events) for two years was Y182,532 per patient in the pravastatin group and Y224,444 per patient in the no pravastatin group.

Sensitivity analyses for the cost-minimisation analysis showed that the costs for the no pravastatin group were consistently higher than those for the pravastatin group.

The mean total medical costs were Y729,849 in the pravastatin group (based on 30 out of 54 patients whose hospitalisation fees could be followed-up) and Y989,606 in the no pravastatin group (40 out of 66 patients).

The expected costs before a case occurs were Y152,364/person in the pravastatin group and Y3,223/person in the no pravastatin group.

Synthesis of costs and benefits
The estimated cost per event-free year was Y2,766,994 and the number-needed-to-treat to prevent one case was 19.

Authors' conclusions
"Pravastatin therapy in normocholesterolaemic patients with coronary sclerosis seems to have an excellent pharmacoeconomic profile."

CRD COMMENTARY - Selection of comparators
The rationale for the choice of the comparator was clearly given. The no pravastatin group enabled the clinical effectiveness and cost of the intervention to be assessed. You should decide if this would be an acceptable approach in your own setting.
Validity of estimate of measure of effectiveness
The effectiveness data were derived from a randomised controlled trial and, therefore, the data should have high validity. However, the present paper did not provide sufficient details for an objective assessment of the strengths and weaknesses of the methods used. The study, by its nature, was open-labelled and, therefore, blinding was not possible. This introduces the potential for bias. Issues regarding the comparability of the patients at baseline, power calculations to assure an adequate sample size, and statistical analyses might have been addressed in parent clinical study. The reader should consult this study for further details (Sato et al., see ‘Other Publications of Related Interest’ for bibliographic details).

Validity of estimate of measure of benefit
The authors employed two measures of health benefit in the economic analyses, occurrence of events and the recurrence rate. As event occurrence showed no differences between the groups, the authors performed a cost-minimisation analysis. A difference in effect was observed for the recurrence rate, and this was used to derive a cost-effectiveness ratio. It would thus be possible to regard this study as a cost-consequences analysis in which the costs and all clinical outcomes were reported separately, rather than dividing the analyses into discrete sections.

Validity of estimate of costs
All the relevant costs appear to have been included for the chosen perspective (including costs of side effects of the drugs). In addition, the cost data were derived from actual patients participating in the study, which enhances the validity of the findings. The impact of different discounting rates was assessed in the sensitivity analyses. However, the cost analysis had several limitations that would limit its generalisability to other settings. More specifically, the costs and the quantities were not reported separately, and the price year was not given.

Other issues
Comparisons were made with other studies and similar results were found, for example, in the Scandinavian Simvastatin Survival Study (recurrence suppression study) and the West of Scotland Coronary Prevention Study. The authors clearly covered the issue of generalisability, indicating that the results of the present study (which were relevant for a Japanese population) were consistent with those from other countries. In terms of limitations of the study, the authors cited four factors. First, the follow-up period of 2 years was rather short and shorter than the 5 years of other analyses. Second, the number of patient events in the present study was very small and, in order to derive a more reliable estimate, larger study samples would be necessary. Third, the indirect costs associated with outpatient visits for other treatments in pravastatin patients should be considered. Finally, the present study was limited to only one hospital, thus generalisability might be improved by using several different settings, although the sensitivity analysis on costs limits the impact of this limitation.

Implications of the study
The findings of the present study supported the use of pravastatin in the secondary prevention of coronary events in patients with moderately high levels of cholesterol. In terms of future research, the authors called for a large-scale clinical trial with a longer follow-up period, to validate and/or enhance the reliability of the present study.

Source of funding
None stated.

Bibliographic details
Other publications of related interest

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Subject indexing assigned by NLM

MeSH
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