Cost effectiveness of eptifibatide in acute coronary syndromes: an economic analysis of Western European patients enrolled in the PURSUIT trial


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 evaluated was eptifibatide (180 micro grammes per kilogram followed by infusion of 2 micrograms per kilogram per minute). The comparator was placebo.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients with acute coronary syndromes (unstable angina and myocardial infarction without persistent ST-segment elevation).

Setting
The setting was secondary care. The study was an international multi-centre study. This paper describes results from a sub-group of patients from Western European countries (France, Germany, Italy, The Netherlands, Spain and the UK).

Dates to which data relate
The dates to which the effectiveness data relate were not reported. This information may be available in the paper reporting the full clinical trial (see Other Publications of Related Interest). The dates relating to the resources used were also not reported. The unit costs were collected for the year 1996.

Source of effectiveness data
The effectiveness data were derived from a single study.

Link between effectiveness and cost data
The cost data were collected prospectively using the same sample of patients as for the effectiveness data.

Study sample
Power calculations to determine the sample size were not reported, and neither was the method of sample selection. This information may be available in the paper reporting the full clinical trial (see Other Publications of Related Interest). A total of 1,850 patients received eptifibatide and 1,847 patients received placebo.
Study design
The study was a multi-centre, randomised controlled trial that was conducted internationally. The authors did not report the method of randomisation, loss to follow-up or method to mask the assessors to treatment allocation. However, they did provide a reference to the paper describing the full clinical trial. The duration of follow-up was 6 months.

Analysis of effectiveness
The basis of the analysis of the study was intention to treat. The analysis included patients from the sub-group of Western European countries in the trial. Patients from other countries (n=5,764) were not included in the cost-effectiveness analysis reported in this paper. The primary clinical outcome for the trial was the composite of death and myocardial infarction at 30 days. A second outcome was years of life projected from the combined outcome at 6 months' follow-up. The comparability of the intervention and comparator groups was not reported. This information may be available in the paper reporting the full clinical trial.

Effectiveness results
For the sub-group analysis in this paper, there was an absolute 1% reduction (from 14.7 to 13.7%) in death or myocardial infarction at 30 days for eptifibatide-treated patients in comparison with placebo, (p=0.386). For the full study, the corresponding figures were 15.7% and 14.2%, (p=0.04). For the sub-group analysis, the 6-month outcomes showed no difference in mortality and a 1% absolute difference in myocardial infarction. For the full study, there was no difference in mortality and an absolute 1.4% reduction in nonfatal myocardial infarction.

Clinical conclusions
The authors concluded that routine eptifibatide use was associated with a reduction in the combined end point of death and myocardial infarction at 30 days.

Measure of benefits used in the economic analysis
Two measures of benefit were used in the cost-effectiveness analysis. These were the years of life saved, as calculated from the 6-month combined end point, and combined death and myocardial infarction at 30 days. The life-years saved were estimated for the trial patients using a Cox proportional hazards regression model and data from 8,169 non-trial patients with myocardial infarction or unstable angina and the trial data.

Direct costs
The resource quantities and the costs were reported separately. The direct costs to the hospital of index hospitalisation, subsequent hospitalisation, and major events were included in the analysis. The cost of index hospitalisation included intensive care/coronary care length of stay, regular ward length of stay, coronary arteriogram, percutaneous coronary intervention and coronary artery bypass graft surgery. The cost of subsequent hospitalisation included length of stay, coronary arteriogram, percutaneous coronary intervention and coronary artery bypass graft surgery. Major events were myocardial infarction, death or severe disabling stroke. The quantities and the costs were estimated from actual data. Discounting was not performed since the duration of the study was less than one year. The study reported the average costs. The price data referred to 1996.

Statistical analysis of costs
A statistical analysis of resource use was conducted. Mean values and confidence intervals (CIs) were reported.

Indirect Costs
The indirect costs were not included since they were not relevant to the perspective of the analysis.

Currency
Euros (Euro). Country-specific unit costs were converted to Euros using the exchange rates published in the Financial Times (6 July 1999) and confirmed in the Wall Street Journal (6 July 1999).

Sensitivity analysis
A sensitivity analysis of the benefits was performed. Life expectancy was discounted by 0, 3 and 6%. Sensitivity analyses were conducted on the mean resource use, assuming no difference in the length of stay between treatment arms. The cost-effectiveness ratio was also calculated using the average resource use consumption reported by countries with low and high coronary arteriography rates, to examine the impact of different coronary syndrome management patterns.

Estimated benefits used in the economic analysis
The eptifibatide patients in Western Europe had an absolute 1% lower rate of death and nonfatal myocardial infarction at 30 days than the placebo patients. For Western European countries, the survival model calculated life expectancy as 0.029 years (undiscounted), which translated into 2.9 additional life-years per 100 patients treated with eptifibatide. Survival was 0.022 years when discounted at 3% and 0.017 years when discounted at 6%.

Cost results
The mean cost per patient at 6 months for eptifibatide-treated patients was Euro 10,228 (95% CI: 9,640 - 10,928) in France, Euro 10,513 (95% CI: 9,973 - 11,129) in Germany, Euro 6,120 (95% CI: 5,839 - 6,412) in Italy, Euro 10,470 (95% CI: 9,898 - 11,108) in The Netherlands, Euro 7,040 (95% CI: 6,699 - 7,425) in Spain, and Euro 9,624 (95% CI: 9,122 - 10,187) in the UK. The corresponding cost for placebo-treated patients was Euro 9,999 (95% CI: 9,320 - 10,700) in France, Euro 10,247 (95% CI: 9,634 - 10,862) in Germany, Euro 5,776 (95% CI: 5,485 - 6,074) in Italy, Euro 10,258 (95% CI: 9,615 - 10,903) in The Netherlands, Euro 6,641 (95% CI: 6,268 - 7,017) in Spain, and Euro 9,338 (95% CI: 8,775 - 9,903) in the UK.

Synthesis of costs and benefits
The costs and benefits (years of life saved) were combined in a cost-effectiveness analysis, and an incremental analysis was performed. The cost per death or myocardial infarction avoided was Euro 27,690 in France, Euro 36,329 in Germany, Euro 37,431 in Italy, Euro 28,991 in The Netherlands, Euro 43,792 in Spain, and Euro 35,015 in the UK. The cost per year of life saved (discounted at 0%) was Euro 7,908 in France, Euro 9,184 in Germany, Euro 11,289 in Italy, Euro 7,285 in The Netherlands, Euro 13,742 in Spain, and Euro 9,846 in the UK.

For a discount rate of 3%, the cost per year of life saved was Euro 10,424 in France, Euro 12,107 in Germany, Euro 15,593 in Italy, Euro 9,603 in The Netherlands, Euro 18,115 in Spain, and Euro 12,979 in the UK. The corresponding costs for a discount rate of 6% were Euro 13,490 (France), Euro 15,667 (Germany), Euro 20,179 (Italy), Euro 12,428 (The Netherlands), Euro 23,443 (Spain) and Euro 16,796 (UK), respectively.

When the differences in length of stay were excluded, the cost per year of life saved (3% discount) was Euro 7,937 in France, Euro 10,089 in Germany, Euro 15,638 in Italy, Euro 8,033 in The Netherlands, Euro 16,732 in Spain, and Euro 11,930 in the UK.

When a low coronary arteriography rate was considered, the cost per year of life saved (3% discount) was Euro 6,689 in France, Euro 3,940 in Germany, Euro 7,117 in Italy, Euro 4,209 in The Netherlands, Euro 10,079 in Spain, and Euro 3,329 in the UK. When a high coronary arteriography rate was considered, the corresponding costs (3% discount) were Euro 18,215 (France), Euro 18,895 (Germany), Euro 17,089 (Italy), Euro 24,099 (The Netherlands), Euro 23,689 (Spain) and Euro 19,926 (UK), respectively.

Authors' conclusions
The addition of eptifibatide to the usual treatment for unstable angina or myocardial infarction without persistent ST-segment elevation is economically attractive compared with other treatment strategies in routine clinical use.
CRD COMMENTARY - Selection of comparators
The authors did not justify their choice of the comparator and did not describe current routine practice. However, this information may be available in the paper presenting the results of the full clinical trial.

Validity of estimate of measure of effectiveness
The source of the effectiveness data was a single study. The analysis used a randomised controlled trial, which was appropriate. The study sample was representative of the study population, but the authors did not report whether the intervention and control groups were comparable at analysis. They also did not report a full statistical analysis of the effect data. This information may be available in the paper presenting the full results of the clinical study.

The authors used a sub-group of patients enrolled in the clinical trial to assess the effectiveness in a Western European setting. This sub-group included all patients enrolled in Western European countries, which meant that the same group of patients was used for both the effectiveness and cost analysis. The authors compared the baseline characteristics of the sub-group from Western Europe (n=3,697) to patients from other countries (n=5,764), and found statistically significant differences between them. These factors suggest that the sub-group analysis was appropriate. However, since the sample size for the Western European patients was smaller, there may have been insufficient power to detect statistically significant differences. The authors presented a summary of the results of the full trial sample, which indicated statistically significant differences in outcomes that were not found in the Western European group. A post hoc power calculation for the sub-group analysis would have been useful.

Validity of estimate of measure of benefit
The combined measure of death and myocardial health was derived from a single measure of effectiveness. The measure of years of life saved was obtained from a single measure effectiveness measure (projection of data using Cox proportional hazards regression methodology). These choices of estimate were justified. However, the model was developed from data on non-trial patients in the United States between 1971 and 1994, and then used to project survival from the trial data. The authors did not report whether differences in health care practice between the USA and Western European countries, or changes in health care practice over a 20-year time period, would affect the validity and accuracy of the model for the analysis.

Validity of estimate of costs
All the categories of cost relevant to the perspective adopted were included in the analysis. For each category of cost, all of the relevant costs were included in the analysis. The costs and the quantities were reported separately. Resource use was taken from a single study. A statistical analysis of the quantities was performed. Country-specific unit costs were estimated for each resource item. Resource use was averaged for each trial arm, rather than per country. This was justified by the small sample sizes in some countries. The authors tested the impact of practice differences between countries in the sensitivity analysis. A statistical analysis of the prices was not performed. Appropriate currency conversions were performed. Charges were not used to proxy prices. The date to which the prices related was reported.

Other issues
The authors did not directly compare their findings with those from other studies of antiplatelet therapies, but they noted that the intervention evaluated was a new therapeutic agent. The authors did, however, compare their results with studies examining other selected health care interventions. The issue of generalisability to other settings was addressed. The authors did not present their results selectivity. The study enrolled patients with acute coronary syndromes without persistent ST-segment elevation and this was reflected in the authors' conclusions. The authors reported a number of limitations to their study. For example, although attempts were made to standardise the costing methods, the estimates of unit costs for the major health resources varied widely among the six countries. This was primarily because of differences in accounting practice and the availability of cost information.

Implications of the study
The authors stated that the PURSUIT study was the largest randomised trial of a glycoprotein IIb/IIIa platelet inhibitor. The trial was international and multi-centred, and had broad inclusion criteria. This makes the results more relevant to the generality of patients with acute coronary syndromes.

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