Cost effectiveness in Canada of eptifibatide treatment for acute coronary syndrome patients using PURSUIT subgroup analysis

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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
To evaluate the use of eptifibatide, a highly selective platelet glycoprotein IIb/IIa receptor inhibitor in the treatment of patients with acute coronary syndromes (ACS), including unstable angina and non-Q wave myocardial infarction (MI). The eptifibatide was administered as a bolus, 180 microgrammes/kg body weight followed by infusion of 2.0 microgrammes/kg/min until hospital discharge or for 72 hours. For patients who were undergoing percutaneous intervention the maximum infusion time was 96 hours. In addition, all patients in both groups were also given standard acetylsalicylic acid and heparin at the discretion of the treating physician.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients with ACS in hospital, with ischaemia-related chest pain of at least 10 minutes duration during the previous 24 hours, presence of transient ST segment elevation of more than 0.5 mm or ST segment depression (persistent or transient) of more than 0.05 mm, or T wave inversion of more than 1 mm within 12 hours of chest pain; or levels of serum creatinine kinase MB isoenzyme above the normal for the hospital setting.

Patients were excluded from the study if they had persistent ST segment elevation of more than 1 mm, history of bleeding, severe hypertension, renal failure, pregnancy or exposure to platelet glycoprotein IIb/IIIa receptor inhibitors or thrombolytic agents.

Setting
The setting was secondary care. The economic analysis was conducted in Canada.

Dates to which data relate
Patients were enrolled between 1995 and 1997. The dates of the cost data were 1995-1997. The price year was 1995.

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

Link between effectiveness and cost data
For the main part of the study, costs were calculated for the Canadian patients participating in the original large-scale multinational effectiveness study, and the effectiveness data were obtained from an earlier published paper (Mark, et
al), which used data on US patients enrolled in the same multinational trial (the PURSUIT trial). Costing was carried out retrospectively.

Study sample
The power calculations were reported in the original large-scale effectiveness paper. It was reported that a sample of 9,382 patients in two groups would provide the study with 80% power to detect a reduction of 20% (or an absolute difference of 1.7%) in 30-day incidence of death or non-fatal myocardial infarction.

The original PURSUIT study enrolled 10,948 patients, 4,722 to high-dose eptifibatide and 4,739 to placebo. The high dose eptifibatide group was referred to as the eptifibatide group as originally there had been 1,487 patients allocated to low-dose eptifibatide but their data were not used in the current study.

305 patients from Canada, 3,522 from the USA, 433 from Greece and 429 from the UK participated in the trial, with smaller numbers from 24 other countries also taking part.

Study design
The original large-scale study was a randomly controlled multi-centre multinational trial, (726 hospitals in 28 countries). The follow-up was 6 months.

Analysis of effectiveness
The analysis was based on intention to treat. The primary health outcomes used in the analysis were differences in mortality and non-fatal myocardial infarctions. The original large-scale study showed the characteristics of the two patient groups and, although they did not report a statistical test, the two groups appeared almost identical in terms of demographics and health status. However, none of these data were available for the patient subgroups that provided the information for this study.

Effectiveness results
The effectiveness results used in the study were:

6-month death or MI rate of 15.2% in the eptifibatide group and 18.95% in the placebo group, (p=0.004.)

The 6-month mortality rate was 4.00% in the eptifibatide group and 5.48% in the placebo group, (p=0.52).

A Cox proportional hazards model was used to estimate a life expectancy from the time of randomisation of 15.96 years for patients treated with eptifibatide and 15.85 years for patients in the placebo group.

Clinical conclusions
Eptifibatide increased life expectancy by 0.11 life years per patient.

Modelling
The Cox proportional hazards regression model was used to project survival beyond 6 months (details in Mark et al; see "Other Publications of Related Interest" below).

Measure of benefits used in the economic analysis
The measure of benefit used in the economic analysis was discounted life years gained.

Direct costs
Discounting was not carried out as the costs were estimated over a period of less than 2 years. Costs and quantities were measured and reported separately. The following costs were measured: hospital costs, (broken down into cardiac care unit and ward), each medical procedure carried out (catheterisation, percutaneous transluminal coronary angioplasty (PTCA), stent, atherectomy, coronary artery bypass graft (CABG), intra-arterial balloon pump (IABP), MRI, CT, pacemaker, groin bleed treatment, treadmill stress test, whole blood transfusion, interhospital transfer), all the medications apart from heparin and salicylic acid, (abciximab, streptokinase, t-PA, urokinase, epifibatide), and rehospitalisation (ward, catheterisation, PTCA, CABG). The estimation of the costs was based on actual data. Resource use data were derived from the Canadian patient records. The sources of the price data were 1995 Ontario Case Costing project, the 1992 Ontario Schedule of Benefits, the Ontario Ministry of Health. The price of epifibatide was the price at which it was supplied for the study. The price year used was 1995.

**Statistical analysis of costs**
No statistical analysis of costs was carried out.

**Indirect Costs**
No indirect costs were calculated.

**Currency**
Canadian dollars (Can$).

**Sensitivity analysis**
Sensitivity analysis was carried out with respect to the following variables: the discount rate was varied between 0 and 5%, the effect of adding cost data from other countries (USA, UK and Greece) on the cost-effectiveness ratio was calculated, the effect of varying the costs of PTCA and CABG was calculated. Finally the effect of equalising the length of hospital stay in the initial treatment for both groups of patients was calculated.

**Estimated benefits used in the economic analysis**
The benefit of epifibatide was 0.08 discounted years. Which equates to an additional eight years of life per one hundred patients treated with epifibatide.

**Cost results**
Total cost per patient receiving placebo was $10,265, and receiving epifibatide $10,691.

The marginal cost was $426.

Costs were calculated for 6 months after treatment began.

Costs of treating adverse effects were dealt with in the costing.

**Synthesis of costs and benefits**
The cost per discounted life year gained was $5,165.

The sensitivity analysis did not alter the authors' conclusions as to the cost-effectiveness of epifibatide. Using resource data from the UK and Greece reduced the cost per life year gained to $4,036. Adding data from the USA increased it to $6,830.

Using different costs (from a different Canadian source) for PTCA and CABG reduced the cost per discounted year saved to $4,805.
Equalising the initial length of hospital stay reduced the cost per discounted year saved to $2,582.

Authors’ conclusions
The authors concluded that the gain in life years caused by eptifibatide was obtained at a cost far lower than that accepted by many health care decision makers.

CRD COMMENTARY - Selection of comparators
The comparator, acetylsalicylic acid and heparin treatment, was implicitly justified by its description as being a 'standard treatment' for ACS. You should decide whether it represents current practise in your own setting.

Validity of estimate of measure of effectiveness
The study used a subset of the original effectiveness study that had shown that different countries had different experiences with eptifibatide. The internal validity of the PURSUIT trial is likely to be quite high. It is not clear, however, what the impact of using selected subgroup results will have on that overall internal validity. The country that showed the greatest improvement in patient outcomes was the USA, and the current study used only the effectiveness results from North America (US and Canada). The original multinational study showed that patients were representative of the study population, although, the US patients did show some differences from the other groups. The original multinational study showed comparability of the patients receiving the two kinds of treatment, but there were no data showing comparability within countries, between treatment groups. It was not clear that it was valid to use only the US data in the current study.

Validity of estimate of measure of benefit
The measure of benefit, discounted years gained, was derived almost directly from the measure of effectiveness, life years gained. Any weaknesses in the derivation of the measure of effectiveness would be present in the measure of benefit. Also, the paper did not justify the discounting of increases in life years gained.

Validity of estimate of costs
The economic analysis was conducted from the perspective of the Canadian health care system and, as such all relevant costs were included. In addition, costs and quantities were reported separately which will be helpful in reproducing the results in other settings. No statistical analyses of quantities or prices were carried out. Prices were taken from the authors’ setting using published sources. Sensitivity analysis was used to evaluate variations in the cost and resource use, thus increasing generalisability. The price year was reported which will aid any future reflation exercises.

Other issues
The authors made comparisons with other studies but did not directly address the issue of generalisability to other settings. The effectiveness data were derived from both the USA and Canada, as there were insufficient numbers when only Canadian patients were considered. Although the authors conducted sensitivity analysis it is not clear that their justification for which countries they chose to combine for each different scenario tested was in any way systematic.

The authors were aware of the issue of generalisability but did not deal with it in a systematic way. As their main results used cost data from Canada and effectiveness data from the USA, the generalisability of the results to other countries may be very limited. The original PURSUIT study showed considerable variation in effectiveness between countries: North America showed the greatest effectiveness and Eastern Europe a reduction in effectiveness. The study by Mark et al, showed that US cost data produced a much higher cost per life year gained ($16,491). However, the clear way in which the authors broke down the Canadian cost information will be very useful for decision makers in Canada and elsewhere.

Implications of the study
The authors are aware that a study using effectiveness data from Canadian patients would be superior to the current one. They are also aware that, as longer-term follow-up data in the PURSUIT trial become available, a better-informed study will be possible.

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**Other publications of related interest**


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