The role of risk stratification in the decision to provide upstream versus selective glycoprotein IIb/IIIa inhibitors for acute coronary syndromes: a cost-effectiveness 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
The study investigated two treatment options for acute coronary syndromes (ACS).

Option 1 was upstream small molecule. This represented a strategy in which a small glycoprotein (GP) IIb/IIIa inhibitor was given upstream to all patients upon presentation with ACS and continued during percutaneous coronary intervention (PCI) for those patients receiving PCI.

Option 2 was selective abciximab. This represented a strategy in which no GP IIb/IIIa inhibitor was given upon presentation, and abciximab was selectively given only to patients ultimately undergoing PCI.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis and cost-utility analysis.

Study population
The study population comprised a hypothetical cohort of 100,000 patients presenting with unstable angina and non-ST-segment elevation myocardial infarction (MI) ACS.

Setting
The study setting was outpatient and inpatient secondary care. The economic study was carried out in the USA.

Dates to which data relate
The effectiveness data were derived from studies published between 1996 and 2004. The cost data were derived from studies published between 1996 and 2003. The price year was 2002.

Source of effectiveness data
The clinical data included the probability of PCI and coronary artery bypass grafting (CABG). The clinical data for abciximab and molecule GP IIb/IIIa included the probability of bleeds, MI and death. Also included were the life expectancy of patients with ACS who did not require PCI or CABG and for those who suffered a nonfatal MI without or having received PCI.

Modelling
An analytic decision tree model was used to examine two strategies for the medical treatment of ACS.
Sources searched to identify primary studies
The probabilities of PCI and CABG were obtained from the invasive arm of a contemporary trial of invasive and conservative treatment of ACS. Relative risks and odds ratios from randomised controlled trials of GP IIb/IIIa inhibitors in ACS patients were used to derive other probabilities. Major bleeding rates were derived from pooled estimates of bleeding rates in randomised controlled trials of ACS. The life expectancy of patients was derived from vital statistics data or from Kaplan-Meier estimates from published studies.

Methods used to judge relevance and validity, and for extracting data
A review of the literature was conducted to derive the effectiveness and epidemiological data needed to populate the model. However, the methods of the review were not reported. The effectiveness and epidemiological data were derived from published studies. When necessary, the authors pooled estimates from different studies in order to derive a single measure of effectiveness.

Measure of benefits used in the economic analysis
The authors stated that the main measure of benefit was the life-years (LYs). However, they also calculated the quality-adjusted life-years (QALYs) gained. The authors did not report the methods used to convert LYs into QALYs gained, although they referenced the source used to derive the utilities. Discounting was relevant, as lifetime outcomes were estimated, and was appropriately performed at an annual rate of 3%.

Direct costs
The direct costs to the health care service were included in the analysis. These comprised the costs of abciximab and small molecule GP IIb/IIIa inhibitor, and the costs of procedures and hospital stay. The 30-day and 6-month costs of procedures and hospital stay were derived from a published trial, whereas the costs incurred after 6 months were derived from projections for a typical 60-year-old MI patient from the Cholesterol And Recurrent Events trial population (Tsevat et al. 2001, see ‘Other Publications of Related Interest’ below for bibliographic details). The authors assumed the number of abciximab vials used per patient and derived the unit cost for each vial from published sources. The costs of GP IIb/IIIa inhibitor were derived from results from a published trial. Since the costs could be incurred over the lifetime of the patient, discounting was relevant and was appropriately performed at an annual rate of 3%. The price year was 2002. The study reported the average costs. The costs and the quantities were not reported separately.

Statistical analysis of costs
The costs were treated as point estimates (i.e. the data were deterministic).

Indirect Costs
Productivity costs were not included in the analysis.

Currency
US dollars ($).

Sensitivity analysis
The authors performed a series of one-way sensitivity analyses to assess the stability of the model's predictions. All parameters in the tree were varied across a range defined either by clinical plausibility or by the 95% confidence intervals of the variable.

Estimated benefits used in the economic analysis
The discounted LYs per 100,000 patients were 1,564,000 for the strategy of selective use of abciximab and 1,568,000 for the strategy of upstream use of small molecule GP IIb/IIIa inhibitor. Consequently, the discounted LYs gained by
using the upstream GP IIb/IIIa inhibitor strategy were 4,000 for every 100,000 patients.

The discounted QALYs gained per patient were 14.76 for the selective use of abciximab and 14.80 for the upstream use of small molecule GP IIb/IIIa inhibitor.

Cost results
The discounted lifetime cost per patient was $81,124 for the strategy of selective use of abciximab and $81,844 for the strategy of upstream use of small molecule GP IIb/IIIa inhibitor. Consequently, the incremental discounted costs incurred by using the upstream GP IIb/IIIa inhibitor strategy were $72,000,000 for every 100,000 patients.

Synthesis of costs and benefits
The costs and benefits were combined using an incremental cost-effectiveness ratio (i.e. the additional cost per LY gained). When compared with selective use of abciximab, a strategy of upstream use of small molecule GP IIb/IIIa inhibitor generated an additional cost of $18,000 for every LY and QALY gained.

The results of the sensitivity analysis showed that, for patients with low TIMI risk scores (i.e. 0 to 2), the additional cost per LY gained was $58,300 when the small molecule GP IIb/IIIa inhibitor strategy was compared with selective use of abciximab. The results also showed that, the higher the risk, the more cost-effective the GP IIb/IIIa inhibitor strategy became. So, the additional cost per LY gained was $24,730 for those at moderate risk (scores 3 to 4), and $14,444 per LY gained for those at high risk (scores 5 to 7). The results of the sensitivity analysis also showed the superiority of the upstream GP IIb/IIIa inhibitor strategy over the majority of scenarios.

Authors' conclusions
The upstream use of small molecule glycoprotein (GP) IIb/IIIa inhibition in patients with acute coronary syndromes (ACS) with moderate or high risk from cardiovascular events was cost-effective and should be considered for these subsets of patients.

CRD COMMENTARY - Selection of comparators
A justification was given for using a strategy based on selective use of abciximab as the comparator, namely that trials had shown that abciximab was superior to GP IIb/IIIa inhibitor during PCI. You should decide if the comparator used represents current treatment in your own setting.

Validity of estimate of measure of effectiveness
The parameters used in the model were derived from published research, mainly randomised controlled trials, which are the 'gold' standard study design when comparing health care interventions, potentially having one of the greatest levels of internal validity. In some instances some synthesis of the study results was carried out. However, the authors provided very few details of the methods used in their review of the literature review; for example, they did not report any search methods or inclusion criteria.

Validity of estimate of measure of benefit
The estimation of health benefits (LYs and QALYs gained) was derived appropriately using a decision analytic tree model. The health benefits were appropriately discounted. The authors did not report how LYs were transformed into QALYs gained and used as a primary outcome measure (LYs gained).

Validity of estimate of costs
Though not explicitly stated, the perspective of a health care service appears to have been adopted. Given this perspective, it appears that all the relevant cost categories and costs have been included in the analysis. The sources from which the costs were derived were reported. Since the costs could be incurred over the lifetime of the patient, discounting was necessary and was appropriately performed. The unit costs and the resource quantities were not
reported separately, which will limit the generalisability of the authors' results. However, the price year was reported, which will aid future inflation exercises.

**Other issues**
The authors reported that no study had investigated the cost-effectiveness of GP IIb/IIIa inhibition compared with abciximab by taking into account the benefits in ACS patients and in patients undergoing PCI. The issue of generalisability to other settings was partially addressed in the sensitivity analyses. The authors do not appear to have presented their results selectively and their conclusions reflected the scope of the study.

The authors reported a number of further limitations to their study. First, the model did not fully account for variable patient presentation; randomised controlled trials might not represent the full spectrum of ACS patients. Second, the study did not examine the potential benefits of novel antiplatelet therapies including clopidogrel, which might reduce the risk of the ACS patient. Third, the authors did not directly take the timing of PCI into consideration. Finally, the cost analysis did not account for the incremental costs of drug-eluting stent use, which would increase the overall costs of both strategies but not the incremental cost.

**Implications of the study**
The authors recommended the use of small molecule GP IIb/IIIa inhibition in ACS patients at moderate or high risk from cardiovascular events.

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None stated.

**Bibliographic details**

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**Other publications of related interest**
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**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Angina, Unstable /drug therapy /economics /therapy; Angioplasty, Balloon, Coronary; Antibodies, Monoclonal /administration & dosage /economics; Cost-Benefit Analysis; Decision Support Techniques; Drug Costs; Humans; Immunoglobulin Fab Fragments /administration & dosage /economics; Life Expectancy; Myocardial Infarction /drug therapy /economics /therapy; Peptides /administration & dosage /economics; Platelet Aggregation Inhibitors /administration & dosage /economics; Platelet Glycoprotein GPIIb-IIIa Complex /antagonists & inhibitors; Quality-Adjusted Life Years; Risk Assessment; Risk Factors; Tyrosine /administration & dosage /analogs & derivatives /economics

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