Cost-effectiveness analysis of antithrombotic therapy in nonurgent percutaneous coronary intervention

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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 authors assessed three percutaneous coronary interventions (PCIs):

- bivalirudin with a provisional glycoprotein (GP) IIb-IIIa inhibitor;
- unfractionated heparin (UFH) with eptifibatide; and
- UFH with abciximab.

Type of intervention
Treatment to relieve coronary narrowing in patients with atherosclerotic heart disease.

Economic study type
Cost-effectiveness analysis.

Study population
The target population was selected to match individuals from the REPLACE-2 trial (Lincoff et al. 2003, see 'Other Publications of Related Interest' below for bibliographic details). The inclusion criteria specified patients older than 21 years who were undergoing PCI as an elective procedure. Patients were excluded if the PCI indication included reperfusion for acute myocardial infarction.

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

Dates to which data relate
The effectiveness evidence referred to studies published between 1998 and 2003. The resource use data was determined using the decision model. A price year was not reported.

Source of effectiveness data
The effectiveness data were derived from a review and synthesis of published studies.

Modelling
A decision analysis model was used to estimate and combine clinical and cost outcomes.

Outcomes assessed in the review
The outcomes were probabilities for input into the decision model. Specifically, the authors estimated the probabilities of myocardial infarction, urgent revascularisation, major bleeding, minor bleeding and thrombocytopenia, and the success rate.

Study designs and other criteria for inclusion in the review
The authors used REPLACE-2 (Lincoff et al. 2003) as a reference trial, searching for studies that were comparable in their patient characteristics, design, specific drug dosing and administration methods.

Sources searched to identify primary studies
The authors searched PubMed/MEDLINE between January 1966 and July 2005.

Criteria used to ensure the validity of primary studies
The authors ensured the comparability of the included studies by using REPLACE-2 as a reference trial and selecting other studies with comparable characteristics that evaluated abciximab or eptifibatide in patients undergoing elective intervention.

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

Number of primary studies included
Four primary studies were used in the review.

Methods of combining primary studies
The data were combined using weighted point estimates, with weights based on the number of participants in each study.

Investigation of differences between primary studies
The studies were compared in a narrative, with the authors reporting that rates for patients with histories of hypertension, diabetes mellitus, myocardial infarction, coronary artery bypass grafting and PCI were all similar. In addition, all of the trials excluded patients with active or recent bleeding history, in each trial more than 95% of patients received stents, and thienopyridine pre-treatment and aspirin was given to everyone.

Results of the review
The probabilities observed were as follows.

The probability of myocardial infarction was 7.0 (range: 6.0 to 7.6) for bivalirudin, 5.9 (range: 5.4 to 6.2) for eptifibatide and 5.5 (range: 4.5 to 6.2) for abciximab.

The probability of urgent revascularisation was 1.2 (range: 0.8 to 1.6) for bivalirudin, 1.2 (range: 0.6 to 1.6) for eptifibatide and 0.9 (range: 0.7 to 1.3) for abciximab.

The probability of major bleeding was 0.6 (range: 0.5 to 0.8) for bivalirudin, 0.94 (range: 0.9 to 1.0) for eptifibatide and 0.9 (range: 0.7 to 1.5) for abciximab.

The probability of minor bleeding was 1.3 (range: 1.1 to 1.4) for bivalirudin, 2.9 (range: 2.8 to 3.0) for eptifibatide and 3.7 (range: 2.9 to 4.3) for abciximab.
The probability of thrombocytopenia was 0.7 (range: 0.3 to 0.9) for bivalirudin, 1.1 (range: 0.2 to 1.7) for eptifibatide and 2.1 (range: 1.7 to 2.4) for abciximab.

The success rate was 89.2 (range: 87.7 to 91.3) with bivalirudin, 88.0 (range: 86.5 to 90.1) with eptifibatide and 86.9 (range: 84.3 to 89.5) with abciximab.

Methods used to derive estimates of effectiveness
The authors made some assumptions to support their decision model.

Estimates of effectiveness and key assumptions
The authors assumed that 85% of patients in each arm had stents during PCI, a similar percentage of patients in each arm had multiple stents, and all complications were mutually exclusive.

Measure of benefits used in the economic analysis
The authors used the percentage of efficacy for each of the three treatments as the summary measure of health benefit. No further details were given.

Direct costs
The economic analysis was carried out from the perspective of the academic medical centre. The cost of each treatment strategy was estimated as the sum of the acquisition cost of treatment and the cost of treating potential complications. Drug acquisition costs were obtained from the wholesale purchasing database used by the Virginia Commonwealth University Medical Centre's Department of Pharmacy (Richmond, VA) and combined with specified dosages. The authors specifically did not include any institutional discounts to preserve the applicability of the analysis to other settings. The costs for complications were estimated by assigning diagnosis-related groups to each outcome. The cost of physician services was included in the cost of complications by using a Current Procedural Terminology code to approximate hospital payments. The quantities were determined via the decision model. Discounting was not required given the very short time horizon of the study. A price year was not reported.

Statistical analysis of costs
The costs were treated deterministically.

Indirect Costs
The indirect costs were not estimated and were not relevant to the perspective adopted.

Currency
US dollars ($).

Sensitivity analysis
Several one-way and multiple-way sensitivity analyses were carried out. These analyses explored the impact of differences in the probabilities of complications and acquisition and complication costs. Ranges for probabilities were determined from the literature, while those for costs were determined by using different sources for the cost estimates.

Estimated benefits used in the economic analysis
The authors did not report the exact efficacy of each treatment strategy. However, they did report that UFH plus eptifibatide was 1.2% less effective than bivalirudin and that UFH plus abciximab was 2.3% less effective than bivalirudin.
Cost results
Although the authors reported a breakdown of the cost components, they did not report a total expected cost of each treatment strategy. However, they did report that UFH plus eptifibatide was $74 more expensive than bivalirudin and that UFH plus abciximab was $777 more expensive than bivalirudin.

Synthesis of costs and benefits
In the base-case analysis, bivalirudin was reported to dominate the other treatment strategies (offered greater benefit for less cost).

Bivalirudin dominated the other strategies in the majority of sensitivity analyses. Dominance was lost in several situations: a higher body weight requiring two vials of bivalirudin, use of 24% provisional eptifibatide (wholesaler purchasing cost), and highest rates of major and minor bleeding and thrombocytopenia for bivalirudin.

Authors' conclusions
Bivalirudin is a cost-effective antithrombotic treatment option, from an institutional perspective, for use in patients undergoing non-urgent percutaneous coronary intervention (PCI).

CRD COMMENTARY - Selection of comparators
The authors compared three PCIs, justifying their choice of the comparators by explaining the background, current treatment guidelines and challenges to current practice.

Validity of estimate of measure of effectiveness
Although the authors did not state explicitly that a systematic review of the literature was carried out, their search strategy and imposition of criteria to define which studies were included meant that, in practice, a systematic review was carried out. The authors clearly reported the sources searched to identify the literature and were very specific about the characteristics defining the patients who would be included. The effectiveness estimates were combined using weighted averages that reflected the number of patients in any given study. Overall, the authors went to great lengths to ensure the validity of the data included in their review. Where assumptions were made, these were discussed explicitly and their implications were explored in both sensitivity analyses and a narrative.

Validity of estimate of measure of benefit
The authors used efficacy as a summary measure of health benefit, but gave few details as to how this was estimated or what, for instance, 10% efficacy meant in practice (i.e. 10% of patients treated successfully or 10% fewer complications). The analysis would have benefited from greater explanation in this area and the reporting of total efficacy for each arm rather than just incremental efficacy.

Validity of estimate of costs
The authors estimated costs from an institutional perspective. The elements included in the analysis (i.e. costs of drug acquisition and treatment complications, and physician-related expenses) reflected that perspective. It was not evident that overheads and capital-related costs were taken into account, and this might be a subject for further work. The authors did not undertake a statistical analysis of the costs, thus it was not possible to assess whether the costs were statistically different between the treatment strategies. However, the authors carried out extensive sensitivity analyses, which showed the primary results to be robust to changes in the underlying parameters. A detailed breakdown separating the unit costs from the quantities was reported. This enables the reader to understand the results in greater depth and see independently the main influences on total cost. In reporting the results, the analysis would have benefited from reporting the total costs of each treatment strategy as well as the incremental costs.
Other issues
The authors were able to compare their own results with those obtained from alternative studies, and concluded that the results agreed. They were also able to discuss differences in methodology between these studies that may explain slight differences between the results. The issue of generalisability was considered at length with the inclusion of extensive sensitivity analyses. In addition, to maintain applicability to other institutions, wholesale costs without institutional discounts were used. The conclusions drawn were an accurate reflection of the results presented and related well to the scope of the study. Several limitations were considered, such as differences in definitions between the studies included in the effectiveness review. There was a useful discussion of attempts made to understand and, where possible, reduce the impact of these limitations.

Implications of the study
The authors did not make any recommendations for policy, citing the recent Food and Drug Administration approval of bivalirudin therapy, but suggested others might use these results to introduce more cost-effective decision-making.

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Other publications of related interest

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MeSH
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