Cost-effectiveness of bivalirudin versus heparin plus glycoprotein IIb/IIIa inhibitor in the treatment of non-ST-segment elevation acute coronary syndromes

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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.

CRD summary
This study examined the cost-effectiveness of bivalirudin compared with heparin plus glycoprotein IIb/IIIa inhibitor in thienopyridine-treated patients with non-ST-segment elevation acute coronary syndrome and medium-to-high risk of major cardiovascular events, who were undergoing early or urgent invasive management. The authors concluded that bivalirudin was likely to be cost-effective from the perspective of the UK NHS compared with conventional heparin plus glycoprotein inhibitor. The methods were valid and transparent, which should ensure the validity of the authors’ conclusions.

Type of economic evaluation
Cost-utility analysis

Study objective
This study examined the cost-effectiveness of bivalirudin versus heparin plus glycoprotein IIb/IIIa inhibitor in thienopyridine-treated patients with non-ST-segment elevation acute coronary syndrome, with a medium-to-high risk of major cardiovascular events, who were undergoing early or urgent invasive management.

Interventions
Bivalirudin was compared against heparin plus acute coronary syndrome.

Location/setting
UK/hospital.

Methods
Analytical approach:
The analysis was based on a decision-analytic model of the costs and benefits, for the first year, with a Markov model, for the lifetime horizon. The authors stated that the analysis was carried out from the perspective of the UK NHS.

Effectiveness data:
The clinical evidence came mainly from two sources; the Acute Catheterization and Urgent Intervention Triage Strategy (ACUITY) trial and the Global Registry of Acute Coronary Events (GRACE). The treatment effect for bivalirudin and heparin plus glycoprotein IIb/IIIa inhibitor and the consequent event rates, which were the key inputs for the model, were from the ACUITY trial, which was a large, multicentre, prospective, randomised, open-label, parallel-group, phase III trial. Additional data for heparin plus glycoprotein IIb/IIIa inhibitor were from UK patients in the GRACE, which was a large-scale, multinational, observational study of acute coronary syndrome patients recruited from 1999 to 2007. Patients with similar characteristics in the ACUITY trial and the GRACE were considered. The two analyses were carried out separately. Additional calculations for long-term survival were based on the Nottingham Heart Attack Register.

Monetary benefit and utility valuations:
The utility values were from a study of 229 consecutive myocardial infarction survivors, from a UK centre. The European Quality of Life (EQ-5D) instrument was used, with UK tariffs derived using the time trade-off method.

Measure of benefit:
Quality-adjusted life-years (QALYs) were the summary benefit measure and were discounted at an annual rate of 3.5%.

Cost data:
The economic analysis included the drugs, hospitalisations, events and procedures (angiography, coronary artery bypass graft, and percutaneous coronary interventions), and long-term annual cardiovascular treatment for one-year survivors. The resource use data were from the two main clinical sources, wherever possible. The costs were from UK sources, such as NHS reference costs and the British National Formulary. They were in UK pounds sterling (£) and referred to 2007 to 2008 prices. A 3.5% annual discount rate was applied.

Analysis of uncertainty:
A deterministic sensitivity analysis was undertaken on the major inputs for the model, using published confidence intervals for the clinical inputs, interquartile ranges for the costs, and ±25% for the survival and utility scores. A probabilistic analysis was carried out, considering conventional distributions of probability for the model inputs. Several alternative scenarios, reflecting UK medical practice, were considered.

Results
Using data from the ACUITY trial, bivalirudin led to a gain of 0.025 QALYs at an additional cost of £250 over heparin plus glycoprotein IIb/IIIa inhibitor. The incremental cost per QALY gained was £9,906.

Using data from the GRACE, bivalirudin led to a gain of 0.034 QALYs at an additional cost of £423 over heparin plus glycoprotein IIb/IIIa inhibitor. The incremental cost per QALY gained was £12,276.

The sensitivity analyses confirmed that the base-case findings were robust; the incremental cost-utility ratios remained below the commonly used threshold of £20,000 per QALY in almost all cases. In the probabilistic sensitivity analysis it was found that the probability of being below this threshold was 72.1% in the ACUITY trial analysis and 67.0% in the GRACE analysis.

The use of alternative data using UK medical practice, rather than data from the ACUITY trial or the GRACE, did not alter the conclusions; the cost-effectiveness of bivalirudin remained close to £15,000 per QALY or less.

Authors' conclusions
The authors concluded that bivalirudin was likely to be cost-effective from the perspective of the UK NHS, compared with conventional heparin plus glycoprotein IIb/IIIa inhibitor.

CRD commentary
Interventions:
The selection of the comparators was appropriate as the intervention (bivalirudin) was compared with the usual practice (heparin plus a glycoprotein IIb/IIIa inhibitor) in the authors' setting, as well as in other health care systems.

Effectiveness/benefits:
The clinical data were mainly taken from two sources; a large multicentre, prospective, randomised, clinical trial and UK patients in a large-scale, multinational, observational study. These two sources were used for alternative analyses to ensure high internal validity with the trial data and external validity with the observational data. The relative risk with bivalirudin compared with heparin plus glycoprotein IIb/IIIa inhibitor was from the clinical trial for both analyses, but the baseline risk for heparin plus glycoprotein IIb/IIIa inhibitor differed between them. This increases the validity of the analysis. Similar patient populations were selected from the two studies. Long-term projections for the clinical events were from a well-known UK cohort study. QALYs were a valid benefit measure because they take account of the impact of the disease on both survival and quality of life, and they allow comparisons to be made with other diseases. The sources for the utility weights were reported and the instrument used (EQ-5D) was appropriate, as were the standard tariffs for the UK.

Costs:
The cost categories were an accurate reflection of the perspective. The resource use and unit costs were reported separately for most items. As in the clinical analysis, the resource use was from the clinical trial or the observational study for each analysis. Detailed estimates are likely to have been made in both studies. The authors also considered
alternative scenarios that better reflected UK medical practice. This did not have a substantial impact on the cost-effectiveness results. The costs were varied both in a deterministic and a probabilistic sensitivity analysis. Other details, such as the price year and discount rate, were reported. In general, the economic analysis was conducted in a satisfactory way.

Analysis and results:
The results were extensively presented. An incremental approach was appropriately used to synthesise the costs and benefits of the alternative strategies. The uncertainty was satisfactorily investigated, using various approaches, and the methods were clearly presented and the results were reported and discussed. The decision model was clearly presented and depicted. Standard discount rates were used, according to England and Wales guidelines. The analysis might be transferred to settings with a similar cost structure.

Concluding remarks:
The methods were valid and transparent, which should ensure the validity of the authors' conclusions.

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