A practical cost analysis of bivalirudin

Compton A

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 use of bivalirudin, an antithrombotic agent aimed to reduce both ischaemic and haemorrhagic complications associated with percutaneous coronary intervention (PCI), was examined. Two different dosages were considered. One was a 0.75 mg/kg bolus followed by 1.75 mg/kg per hour infusion for the duration of the procedure, the other was a 1 mg/kg bolus plus 2.5 mg/kg per hour infusion for 4 hours.

Type of intervention
Secondary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients who had undergone PCI. Since the analysis was carried using patient data from three different clinical trials, the results of each evaluation apply to different patient populations.

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

Dates to which data relate
The effectiveness data came from studies published from 2001 to 2002. The costs were estimated from studies published between 1993 and 1998. The price year was not explicitly reported.

Source of effectiveness data
The effectiveness evidence was derived from published studies.

Outcomes assessed in the review
The outcomes assessed from the literature were the rates of death, myocardial infarction (MI) and major haemorrhage (MH) with bivalirudin or heparin.

Study designs and other criteria for inclusion in the review
It was not stated whether a systematic review of the literature was undertaken to identify the primary studies. Only randomised clinical trials (RCTs) were considered. Details on the design (randomisation and blinding) of the primary studies were reported. However, there was limited information on the patients' characteristics, with the exception of the BAT study. The BAT study was used to carry out a sub-group analysis of patients at high-risk, such as those who had experienced an MI, had moderate-to-severe renal impairment, or were either women or elders (age =/> 65 years).
Sources searched to identify primary studies
Not stated.

Criteria used to ensure the validity of primary studies
The validity of the primary studies was ensured by the selection of RCTs. Most of them were also double-blinded.

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

Number of primary studies included
Three primary studies provided clinical data.

Methods of combining primary studies
The primary studies were not combined since data extracted from each RCT were used for a different analysis.

Investigation of differences between primary studies
Not relevant.

Results of the review
In the BAT study:

the rate of death was 0.2% with bivalirudin and 0.2% with heparin,

the rate of MI was 3.3% with bivalirudin and 4.2% with heparin, and

the rate of MH was 3.5% with bivalirudin and 9.3% with heparin.

In the sub-group of patients who had experienced an MI in the BAT study:

the rate of death was 0% with bivalirudin and 0.5% with heparin,

the rate of MI was 3% with bivalirudin and 5.6% with heparin, and

the rate of MH was 2.4% with bivalirudin and 11.8% with heparin

Thus, the risk reduction for bleeding due to the use of bivalirudin was 9.4%. The sub-group analysis showed that the risk reduction for bleeding due to the use of bivalirudin was 6.7% in patients with renal impairment, 10.2% among women and 7.7% in elderly patients.

In the CACHET study:

the rate of death was 0% with bivalirudin and 0% with heparin,

the rate of MI was 2.1% with bivalirudin and 1.6% with heparin, and

the rate of MH was 1.4% with bivalirudin and 6.3% with heparin.

In the REPLACE-1 study, the rates of death, MI and MH were, respectively:
0%, 5.6% and 3.5% with bivalirudin plus glycoprotein IIb/IIIa inhibitors;

0.5%, 6.1% and 4.2% with heparin plus platelet glycoprotein IIb/IIIa inhibitors;

0%, 3.2% and 0% with bivalirudin; and

0.7%, 2.7% and 1.4% with heparin.

Measure of benefits used in the economic analysis
The summary benefit measure used was the rate of reduction in bleeding events. This was estimated directly from the effectiveness analysis and was used only in the sub-group analysis. The number-needed-to-treat (NNT) to prevent a bleeding episode was calculated only for the sub-group analysis.

Direct costs
The perspective adopted in the study was unclear, although it could have been that of the hospital. The health services included in the economic evaluation were cardiac catheterisation laboratory costs, non-procedural hospital costs, physician costs, complication costs and drug costs. The laboratory costs included procedures, disposable equipment, overheads, depreciation for the cardiac catheterisation laboratory, and non-physician personnel. The unit costs were presented separately from the quantities of resources used only for some cost items. The costs were estimated from the HCRI study, which considered a database of 3,271 procedures in which detailed resource use was collected on all patients, with costs determined by cost-accounting methods. The costs of complications were estimated using a multivariate analysis. Other costs were estimated from a Medicare cost report. Cost-to-charge ratios were also used to derive actual treatment costs. The drug costs came from average wholesale prices. The price year was not explicitly stated, but the costs were assessed in 2000 and 2001. Discounting was not relevant given the short timeframe of the analysis.

Statistical analysis of costs
The costs were treated deterministically.

Indirect Costs
The indirect costs were not considered in the economic evaluation.

Currency
US dollars ($).

Sensitivity analysis
Sensitivity analyses were not carried out.

Estimated benefits used in the economic analysis
The NNT to prevent a bleeding episode was 10.6 for patients with a recent MI, 15 among patients with renal impairment, 10 among women, and 13 for elderly patients. The reduction in bleeding events has been reported already.

Cost results
In the BAT study, the mean reduction in costs of complications per patient (including MI, transfusion costs and repeat PCI) was $636 with bivalirudin over heparin when considering the overall cohort, and $1,175 when only patients who had experienced MI were considered. The estimated cost of bivalirudin in this trial was $1,340.
In the CACHET study, the mean reduction in the costs of complications per patient with bivalirudin was $1,394.

In the REPLACE study, the mean reduction in the costs of complications per patient with bivalirudin ranged from $295 to $386, although complications were quite infrequent.

The estimated cost of bivalirudin cost in these two trials was $335.

**Synthesis of costs and benefits**
The costs and benefits were combined using a cost-effectiveness ratio only for some sub-groups of patients. Using BAT data, the incremental cost to prevent one bleed with bivalirudin was $7,537 among patients who had experienced a MI, which was lower than the costs of treating one bleeding episode ($8,098). However, if higher dosages of bivalirudin were used, then the increased drug costs ($10,050) would not be completely offset by the prevention of bleeding.

The incremental cost to prevent one bleed with bivalirudin was $5,025 in the sub-group of patients with renal impairment, $3,350 in the sub-group of women and $4,355 in the sub-group of elderly.

Thus, the cost of a bleed could be as low as $5,025 for patients with renal impairment, $3,350 for women and $4,355 for the elderly in order for the hospital to break even.

**Authors' conclusions**
The use of bivalirudin led to a reduction in costs associated with complications, which almost completely offset the acquisition price of bivalirudin in patients who had undergone a percutaneous coronary intervention (PCI). The cost-savings were very sensitive to drug dosages.

**CRD COMMENTARY - Selection of comparators**
The rationale for the selection of the comparator (heparin) was clear and appropriate as it is commonly considered as a reference strategy for patients undergoing PCI. You should decide whether it is a valid comparator in your own setting.

**Validity of estimate of measure of effectiveness**
The effectiveness evidence came from published clinical trials. These were not combined since each study provided clinical data for a specific analysis. In effect, separate cost analyses were carried out using data extracted from each trial. Some details of the design and number of patients included in the trials were reported. The use of RCTs to provide evidence ensured the robustness of the primary sources. The trials appear to have been identified selectively rather than through a review of the literature.

**Validity of estimate of measure of benefit**
The summary benefit measure (i.e. haemorrhages avoided) was specific to the disease considered in the study and is not comparable with the benefits of other health care interventions. The impact of the interventions on quality of life was not addressed. In effect, the number of bleeding avoided was used to assess the cost-savings.

**Validity of estimate of costs**
The perspective adopted in the study might have been that of the hospital, although it was not stated clearly. The unit costs were reported for some costs, although most of the costs were presented as macro-categories. A detailed breakdown of the cost items was not reported. The source of the costs was reported, with the authors stating that the costs of complications were derived from a reliable dataset. Further, such a database gathered data from several centres, thus taking data variability into consideration. The price year was not explicitly reported, which reduces the possibility of performing reflation exercises in other time periods. The costs were treated deterministically and were specific to the study setting.
Other issues
The authors reported the cost-savings of bivalirudin estimated in other economic evaluations of the BAT study, and stated that similar results were obtained. The limitations of the published studies were noted. The issue of the generalisability of the study results to other settings was not addressed and sensitivity analyses were not performed. However, the analysis was performed in different patient populations (corresponding to each trial and sub-groups), which partially enhances the external validity of the study.

Implications of the study
The study results suggested that bivalirudin might be a cost-effective preventive strategy for patients who had undergone PCI, but drug dosage would appear to be a strong cost-driver. The authors stated that the ongoing REPLACE-2 trial would show whether bivalirudin could decrease the administration of provisional glycoprotein IIb/IIIa inhibitors, which might have important implications from a budgetary perspective.

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None stated.

Bibliographic details

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Other publications of related interest


Indexing Status
Subject indexing assigned by NLM

MeSH
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