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 oral dabigatran etexilate (DE) versus subcutaneous enoxaparin for the prevention of venous thromboembolism after total knee replacement and total hip replacement (THR) surgery. The authors concluded that, from the perspective of the UK National Health Service, DE was as effective and as safe as enoxaparin and was cost-saving, especially in THR patients. The study was based on valid methodology and was well presented, which makes the authors’ conclusions more robust.

Type of economic evaluation
Cost-effectiveness analysis, cost-utility analysis

Study objective
This economic evaluation examined the cost-effectiveness of oral dabigatran etexilate (DE) in comparison with subcutaneous low-molecular-weight heparin for the prevention of venous thromboembolism (VTE) after total knee replacement (TKR) and total hip replacement (THR) surgery.

Interventions
The two thromboprophylactic strategies were oral DE (220mg once daily) and subcutaneous enoxaparin (40mg once daily). These treatments were administered for 6 to 10 days for TKR surgery and for 28 to 35 days for THR surgery.

Location/setting
UK/secondary care.

Methods
Analytical approach:
This study was based on a decision-analytic model in the short-term, plus a Markov model with a lifetime horizon. The authors stated that the analysis was carried out from the perspective of the UK National Health Service (NHS).

Effectiveness data:
The clinical inputs were derived from both a systematic review of the literature and a selection of phase III randomised controlled trials (RCTs) of thromboprophylaxis. The data on the efficacy of the two prophylactic options came from head-to-head RCTs and the rates of long-term events came from longitudinal studies. The statistical procedure used to calculate the time-dependent probabilities was reported. The primary clinical endpoint was the probability of VTE events.

Monetary benefit and utility valuations:
The utility estimates came from published studies. The instruments used and the sources of preferences were reported for each set of data. Most of the estimates were obtained using the European Quality of life (EQ-5D) questionnaire.

Measure of benefit:
The summary benefit measures were quality-adjusted life-years (QALYs), life-years (LYs), and VTE events. All these benefits were estimated using the decision model framework and were discounted at 3.5% per annum.

Cost data:
The health service costs were those of drugs (acquisition and administration), nursing time for injection (during hospital stay and at the patient's home), and management of VTE and adverse events. The resource use for drugs was based on data derived from RCTs. Nursing time was derived from a published economic analysis. The costs and resource use consumption for VTE and adverse events came from multiple sources including NHS sources, published studies, and authors’ assumptions. The price year was 2008. Costs were in UK pounds sterling (£) and were discounted at 3.5% per annum.

Analysis of uncertainty:
Both a probabilistic and a deterministic approach were used to investigate the uncertainty in the findings. Probability distributions were assigned to the model inputs to generate confidence intervals around the incremental cost-effectiveness and cost-utility ratios. One-way sensitivity analysis was conducted on selected model inputs, such as the relative risk for DE versus enoxaparin, using data derived from alternative sources. Subgroup analyses by age, gender, and risk factors for VTE were performed and the extended use of DE was also investigated. A cost-minimisation analysis was carried out using a scenario that assumed equal effectiveness and safety of the two drugs.

Results
In TKR patients, the expected VTE events were 16.0% for DE and 16.3% for enoxaparin, the LYs were 10.261 for DE and 10.252 for enoxaparin, and the QALYs were 7.647 for DE and 7.639 for enoxaparin. In THR patients, the expected VTE events were 5.9% for DE and 6.1% for enoxaparin, the LYs were 11.242 for DE and 11.234 for enoxaparin, and the QALYs were 8.432 for DE and 8.426 for enoxaparin.

In TKR patients, the total costs were £589 for DE and £606 for enoxaparin and, in THR patients, they were £392 for DE and £493 for enoxaparin.

The incremental analysis showed that DE was dominant over enoxaparin, given the slight improvement in clinical benefits and the lower lifetime costs.

The results of the probabilistic analysis showed that, in TKR patients, DE was dominant over enoxaparin in about 66% of simulations and at the UK willingness-to-pay threshold of £20,000 per QALY, the probability of cost-effectiveness was 75%. In THR patients, DE was dominant in the majority of simulations and the probability of cost-effectiveness at the £20,000 threshold was 97%.

The results of the deterministic sensitivity analysis confirmed that these base-case findings were robust, except in some extreme scenarios, which showed similar efficacy and safety profiles for the two drugs. The cost-savings were greater in males than in females, and in patients at the highest risk for a recurrence of VTE.

Authors' conclusions
The authors concluded that, from the perspective of the UK NHS, DE was as effective and safe as enoxaparin and was cost-saving, especially in THR patients.

CRD commentary
Interventions:
Enoxaparin was selected as the relevant comparator because it was the most commonly used treatment for the prevention of VTE in the UK. It was also likely to be a valid comparator in other health care settings. The dosages and duration of therapy were clearly reported.

Effectiveness/benefits:
The authors selected RCTs from which to derive the data on the efficacy of the treatments. These studies were known to the authors and represented the most appropriate sources of data available, given the strengths of their design. Other clinical inputs were based on studies identified through a published literature review the details of which were not reported. The authors did provide extensive details on the derivation of the clinical inputs and their adaptation to the model. In general, the analysis of the clinical inputs appears to have been carried out satisfactorily. The benefit measures were appropriate for detecting the impact of the treatments on the patients' health. Both generic and disease-specific benefit measures were used and appropriate discounting of future benefits was performed.
Costs:
The economic approach was consistent with the guidelines of the National Institute for Health and Clinical Excellence. The categories of costs reflected the perspective of the third-party payer and were explicitly reported. They were broken down into individual items and the details on unit costs and resource quantities were presented separately. The sources of data were given and the derivation of costs was described. All other aspects of the cost study such as the price year, use of discounting, probability distributions, and assumptions were given. In general, the economic analysis was transparently reported.

Analysis and results:
The costs and benefits were appropriately combined using an incremental analysis, which indicated the superior economic and clinical profile of DE. The issue of uncertainty was appropriately addressed. The approaches used in the sensitivity analyses and the findings of both the base case and the sensitivity analysis were clearly reported. A detailed description of the results for subgroups was provided and the details of the decision model were well presented. The authors stated that the structure of the model was based on information derived from a systematic literature review. A justification for the time horizon was given. The authors noted that the costs associated with platelet monitoring and the utility benefits associated with the oral route were not modelled, and their inclusion might have further improved the cost-effectiveness of DE. They also noted that the analysis focused on the UK NHS structure, which might not be generalisable to other health systems.

Concluding remarks:
The study was based on valid methodology and was well presented. These points make the authors’ conclusions more robust.

Funding
Funded by Boehringer Ingelheim International GmbH.

Bibliographic details

PubMedID
19243718

DOI
10.1016/j.clinthera.2009.01.001

Other publications of related interest


Indexing Status
Subject indexing assigned by NLM

MeSH
Aged; Anticoagulants /administration & dosage /adverse effects /economics; Arthroplasty, Replacement, Hip /economics /methods; Arthroplasty, Replacement, Knee /economics /methods; Benzimidazoles /administration & dosage /adverse effects /economics; Clinical Trials, Phase III as Topic; Cost-Benefit Analysis; Dabigatran; Decision Trees; Drug Costs; Enoxaparin /administration & dosage /adverse effects /economics; Female; Great Britain; Hemorrhage /chemically induced; Humans; Longitudinal Studies; Male; Markov Chains; National Health Programs /economics; Pyridines /administration & dosage /adverse effects /economics; Venous Thromboembolism /prevention & control

AccessionNumber
22009101053

Date bibliographic record published
13/05/2009

Date abstract record published
22/07/2009