Cost-effectiveness of enoxaparin vs low-dose warfarin in the prevention of deep-vein thrombosis after total hip replacement surgery

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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
Enoxaparin sodium and low-dose warfarin sodium.

Type of intervention
Primary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
Study population was a hypothetical cohort of 10,000 patients undergoing total hip replacement surgery.

Setting
Hospital. The economic study was carried out in the USA.

Dates to which data relate
Effectiveness data were derived from studies published between 1982 and 1994. Resource data mainly related to the period 1990-1993. 1993 prices were used.

Source of effectiveness data
Data from the published literature produced the estimates of effectiveness.

Modelling
A decision tree was used in estimating costs and effectiveness.

Outcomes assessed in the review
Incidence of deep vein thrombosis (DVT); mortality during treatment of DVT; incidence of pulmonary embolism (PE); mortality during treatment of PE.

Study designs and other criteria for inclusion in the review
Randomised controlled trials. Studies were selected if they met the following criteria:

a) included only patients undergoing elective total hip replacement surgery;
b) used a placebo, low-dose warfarin or subcutaneous enoxaparin sodium;

c) started treatment no later than 24 hours after surgery and maintained it for at least 7 days;

d) used bilateral venography to confirm the presence of DVT.

Sources searched to identify primary studies
The search to establish the likelihood of DVT and other clinical events was described as a computerised literature search of English language sources only, discussions with experts, and reviews of citations from retrieved articles.

Criteria used to ensure the validity of primary studies
Not stated.

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

Number of primary studies included
To estimate the likelihood of DVT, 16 RCTs were used (6 trials that employed a placebo arm; 6 trials with a low-dose warfarin arm; and 4 trials with an enoxaparin arm).

Methods of combining primary studies
A pooled rate of DVT was calculated for placebo, low-dose warfarin, and enoxaparin by dividing the reported cases of DVT by the total number of patients randomised to each of these agents across trials. Other factors such as mortality during treatment of DVT, incidence of PE, and mortality during treatment of PE were taken directly from the literature, without justification.

Investigation of differences between primary studies
Where applicable, differences were not investigated.

Results of the review
The mean rate of DVT in cases of no prophylaxis was 52.8% (95% CI 48.3 to 57.3); if low-dose warfarin was administered, the mean rate was 22.5% (95% CI 19.2 to 25.8); if enoxaparin was administered, the mean rate was 13.6% (95% CI 10.9 to 16.3). The mortality during treatment of DVT was 0.25%. The incidence of PE in patients with undetected DVT was 20%. Finally, the mortality during treatment of PE was 2.5%.

Measure of benefits used in the economic analysis
’Lives Saved’ was the outcome measure estimated using a decision-analytic model.

Direct costs
Some costs and quantities (hospital days) were reported separately. The costs of prophylaxis, diagnosis and treatment were based on findings in the literature review and data from current clinical practices. Specifically drug costs were estimated from US quarterly average hospital purchasing prices for 1993. Laboratory costs were estimated using the American College of Pathologists’ relative value scale. Diagnostic costs were estimated using the American College of Radiologists’ relative value scale (no date stated). Staffing costs in diagnosis and general nursing costs were based on the Maryland hospital charge rate for 1993. Physician time was estimated using the Medicare Resource Based Relative Value Scale physician payment rate for 1992. Treatment costs were based on an 8 day duration period. Hospitalisation...
following confirmed DVT was estimated to be 7-15 days, which were estimated using data from the National Hospital Discharge Survey. Final costs were calculated using a decision tree.

**Currency**
US dollars ($).

**Sensitivity analysis**
The variables which were tested included the assumed risk of DVT among enoxaparin users (using the upper and lower bounds of the 95% confidence interval); sensitivity of B-mode ultrasonography; mortality rate for patients with undetected PE; mortality rate amongst DVT and PE treated cases; duration and cost of prophylaxis; costs of monitoring warfarin receivers; and the cost of treating DVT and PE. The method implies a one-way simple sensitivity analysis, but was not explicitly stated.

**Estimated benefits used in the economic analysis**
With no prophylaxis, there would be 259 deaths (per 10,000 patients); using warfarin there would be 149 fewer deaths (per 10,000 patients). The use of Enoxaparin would result in a further 43 fewer deaths (per 10,000).

**Cost results**
For a cohort of 10,000 patients, the total costs would be $5,327,000 if there was no prophylaxis; $3,759,000 if low-dose warfarin sodium was used; and $3,787,400 if enoxaparin sodium was used. The incremental cost of enoxaparin vs warfarin was $528,400.

**Synthesis of costs and benefits**
The incremental cost per life saved for enoxaparin vs warfarin was estimated to be $12,288.

**Authors' conclusions**
The authors concluded that enoxaparin is more costly than low-dose warfarin, but it would further reduce thromboembolic risk. Its cost-effectiveness in total hip replacement compares favourably with other accepted medical interventions.

**CRD Commentary**
1) The clinical effectiveness analysis approach comparing individual arms from different trials can produce bias. Moreover, issues of the comparability of patient groups was not addressed. The authors acknowledged that they had little information on the potential bias surrounding the multiple clinical trial data in their DVT data and that direct comparison would have been preferable.

2) The authors note that the costs of recurrent DVT, postphlebitic syndrome and chronic venous insufficiency were not included.

3) Treatment side-effects and risk factors were not mentioned.

**Implications of the study**
Further studies could be developed with a more thorough effectiveness analysis. A randomised control trial comparing these two methods of prophylaxis is desirable.

**Source of funding**
Supported by a research grant from Rhone-Poulenc Rorer Pharmaceuticals Inc, Collegeville, Pa.

**Bibliographic details**

**PubMedID**
7695464

**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Cost-Benefit Analysis; Decision Trees; Enoxaparin /economics /therapeutic use; Hip Prosthesis /adverse effects; Humans; Pulmonary Embolism /economics /prevention & control; Sensitivity and Specificity; Thrombosis /diagnosis /economics /etiology /prevention & control; Treatment Outcome; Warfarin /economics /therapeutic use

**AccessionNumber**
21995000566

**Date bibliographic record published**
25/03/1997

**Date abstract record published**
25/03/1997