Cost effectiveness of a low-molecular-weight heparin in prolonged prophylaxis against deep vein thrombosis after total hip replacement

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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
Low molecular weight heparin (LMWH) in prolonged prophylaxis against deep vein thrombosis (DVT) after total hip replacement.

Type of intervention
Primary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
Patients who have undergone total hip replacement.

Setting
The setting of the efficacy studies was hospital and community, in France. The economic analysis was also carried out in France.

Dates to which data relate
Efficacy and resource use data were derived from studies published in 1987, 1994, 1995 and 1996. The prices used were from prices published in 1997, except for the cost of a hospital day, which was from 1995.

Source of effectiveness data
Effectiveness data was derived from a synthesis of previously published studies.

Modelling
A decision analysis model was used in estimating benefits and costs. The purpose of using this model was to integrate the estimates of outcomes and costs from multiple studies.

Outcomes assessed in the review
The outcomes used in this study were the incidence of DVT or pulmonary embolism (PE), and death.

Study designs and other criteria for inclusion in the review
Single centre, double-blind, placebo controlled, randomized trials, using enoxaparin 40mg once daily during hospitalization and for 3 weeks after discharge were included. The studies also required that patients not have evidence
(symptoms or venography) of a DVT at the time of randomization (= discharge). Additional studies were used to identify mean probabilities for outcomes in the model. These studies were not described.

Sources searched to identify primary studies
The source or method of search was not stated.

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
Two studies were included in the review, however an additional four studies were used to estimate probabilities in the model.

Methods of combining primary studies
The studies were combined by narrative method using the decision analysis model.

Investigation of differences between primary studies
The two studies differed in the duration of LMWH therapy prior to randomization (7 versus 14 days), the proof that there was no DVT at discharge (symptoms versus venography), and the duration of follow-up (30 versus 35 days). No further discussion of these differences was offered.

Results of the review
Based on a hypothetical cohort of 100,000 patients, prolonged prophylaxis with LMWH prevented from 601 to 783 deaths and 16,012 to 21,222 DVT/PEs. Further, the authorsestimated that, based on standard practice in France, only 3,623 to 4,812 of these DVT/PEs would have been diagnosed and treated (because venography used in the studies is not used as first line in standard practice).

Measure of benefits used in the economic analysis
The benefits used in the economic study were the incidence of DVT or PE diagnosed by venography, DVT/PEs diagnosed under standard practices in France, and life-years saved. A decision analysis model was used to estimate life-years saved, and DVT/PEs diagnosed under standard practices in France. Valuations of DVT/PE diagnosed by venography were estimated by direct measurement (venography by study clinicians) in the two studies reviewed. Valuations of DVT/PE diagnosed under standard practices in France and life-years saved were estimated based on the authors’ assumptions.

Direct costs
The direct costs included in the model were costs for duplex scan and venography for DVT, 3 days hospitalization for diagnosis of PE, treatment costs for DVT and PE, and LMWH prophylaxis (enoxaparin, 1 platelet count per week, and visiting nurse administered injections daily). Discounting was unnecessary due to the short duration of therapy. Not all costs and quantities were reported separately. The boundary assumed was that of the health service. Estimation of quantities was based on the studies reviewed. The DVT/PE rates were taken, as a range, directly from the two main studies reviewed. All other probabilities in the model were taken from the average of the 4 other studies reviewed. Estimation of costs was based on actual data from published sources in France. These sources were the VIDAL index.
for drug costs, the National Diagnostic Related Group Cost Study, and the French National Sickness Fund. In addition, the authors and 'four experts' estimated the quantity of duplex scans and venography used in a standard practice situation. The resource use estimates were obtained from the studies published in 1987, 1994, 1995 and 1996. 1997 published prices were used, except for the cost of a hospital day, which was from 1995. Median and incremental costs were reported. The costs of adverse effects were excluded because the two main trials reported a low incidence, and mild effects. In order to account for uncertainty around the cost data, a Monte Carlo simulation was used to create a distribution. The distribution for the cost of enoxaparin was set between 100 and 125%, to account for unforeseen costs associated with this therapy.

**Statistical analysis of costs**
Costs were treated stochastically, in that median values, and the 5% and 95% centile were reported. Statistical analysis was not reported.

**Currency**
French Francs (FF). Results were also reported in US dollars in the discussion.

**Sensitivity analysis**
A simple one-way sensitivity analysis was carried out on the variability in cost and efficacy data.

**Estimated benefits used in the economic analysis**
Based on a hypothetical cohort of 100,000 patients, prolonged prophylaxis with LMWH prevented from 601 to 783 deaths and 16,012 to 21,222 DVT/PEs. Further, the authors estimated that based on standard practice in France, only 3,623 to 4,812 of these DVT/PEs would have been diagnosed and treated (because venography used in the studies is not used as first line in standard practice).

**Cost results**
The average cost of prolonging prophylaxis with LMWH was FF1,118 to FF1,300 per patient.

**Synthesis of costs and benefits**
Costs and benefits were combined in terms of cost per life-year saved. An incremental cost-effectiveness analysis was performed in cost per death avoided, cost per DVT/PE avoided (by venography) and cost per DVT/PE diagnosed in standard practice. The median cost per year of life saved was between FF11,158 and FF34,590. The median cost of each potential death avoided was between FF139,480 and FF216,188. The median cost per DVT/PE avoided under study setting was FF5,286 to FF8,031. The median cost per DVT/PE avoided under standard practices was FF23,532 to FF35,268. All of these ranges were based on the median of the distribution created by the Monte Carlo simulation. Cost per year of life saved was sensitive to the cost of enoxaparin, incidence of PE, mortality rate from PE, and the rate of DVT's diagnosed by venography. No comment was made on the significance of these findings.

**Authors' conclusions**
Despite uncertainties over cost and effectiveness data, this study strongly suggests that prolonged LMWH (enoxaparin) anticoagulation prophylaxis during hospitalization and for 3 weeks after hospital discharge in patients undergoing elective hip replacement is not only more effective in routine practice, but is also cost effective when compared with short LMWH (enoxaparin) prophylaxis given only during the hospitalization period. Further clinical and economic studies are needed to demonstrate the potential interest of other anticoagulant therapies in this indication.

**CRD COMMENTARY - Selection of comparators**
The authors justified the selection of placebo as the comparator in that the two studies used in the review also chose...
placebo as the comparator. They state that previous studies using oral anticoagulants have not shown an effect in prolonged anticoagulation after hip replacement, at least using the old method of monitoring oral anticoagulation. However, the authors point out that recent studies hint that there may be an effect under the new methods of monitoring oral anticoagulation. The choice of unfractionated heparin as a comparator was not discussed.

Validity of estimate of measure of benefit
The estimation of benefits was derived from a model combining a variety of results from published studies. The review was not systematic and so results may be biased. A more reliable assessment of the relative benefits would come from a randomized controlled trial.

Validity of estimate of costs
A weekly platelet count and daily injections given in the home by a nurse are included as costs. It is questionable that either of these two resources would be utilized to the degree assumed in this study, as neither are considered standard procedures. The costs included for diagnosing a PE are not fully included. The hospitalization costs are included, but not the additional costs of performing and interpreting the required tests.

Other issues
Costs for treatment of DVT/PE are given in terms of the total DRG in France. The actual treatment was not described, and therefore these estimates are not generalizable to other settings or countries.

Implications of the study
A randomized, controlled trial is needed to confirm these results. Comparison to other therapies needs to be considered.

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