Pharmacoeconomic model of enoxaparin versus heparin for prevention of 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
Enoxaparin and heparin in prevention of deep vein thrombosis after total hip replacement.

Type of intervention
Primary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
Patients undergoing total hip replacement.

Setting
Managed care. The economic study was carried out in the USA.

Dates to which data relate
The analysis of effectiveness was based on 3 earlier studies published between 1988-1994. Unit cost data were for 1992-93. Resource use data were derived primarily from a study published in 1993.

Source of effectiveness data
The evidence for outcome event probabilities was based on a review of 3 clinical trials.

Modelling
A decision tree model was used to evaluate the benefits and expected costs associated with each of the strategies while considering the possible outcomes after prophylaxis (proximal and distal DVT -separately for symptomatic and asymptomatic cases - and no DVT).

Outcomes assessed in the review
The outcomes assessed in the review were the probability of proximal DVT, distal DVT, pulmonary embolism, and major bleeding after a DVT prophylaxis with enoxaparin and heparin.

Study designs and other criteria for inclusion in the review
The review included randomized controlled trials comparing enoxaparin with heparin. Included studies used bilateral venography to assess DVT outcomes and had identical criteria for assessing major bleeding.
Sources searched to identify primary studies
Not stated.

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

Methods used to judge relevance and validity, and for extracting data
Summary statistics were extracted from the primary studies.

Number of primary studies included
Three (3) randomized controlled trials.

Methods of combining primary studies
No combination was performed.

Investigation of differences between primary studies
The authors discussed the differences in primary studies with respect to the dosing of the tested drugs.

Results of the review
The probability of a proximal DVT event ranged from 0.021 to 0.075 after enoxaparin and from 0.048 to 0.185 after heparin prophylaxis. The probabilities of a distal DVT event ranged from 0.021 to 0.140 (enoxaparin) and from 0.053 to 0.167 (heparin). The probability of pulmonary embolism after enoxaparin was found to be zero in all 3 studies but ranged 0.080 to 0.200 after heparin treatment. The probability of major bleeding ranged from 0.017 to 0.040 (enoxaparin) and from 0.000 to 0.060 (heparin). In one of the studies, the difference in probability of proximal DVT between the two drugs was statistically significant at level p=0.014. In all other comparisons p>0.14.

Measure of benefits used in the economic analysis
The measure of benefits used in the economic analysis was the number of DVT events avoided. No valuation of health outcomes was carried out, i.e. distal DVT and proximal DVT were given equal weight. The benefits were calculated using a model.

Direct costs
Direct resource costs and quantities were reported for alternative DVT prophylaxis, and for the possible outcome events after prophylaxis. Resource use patterns and unit costs for treatments were obtained from published studies which reflected the treatment practice in the USA. Medication cost for both prophylactic regimens were based on average wholesale prices, and did not include time costs of administering the drugs and costs of ancillary supplies. Only costs incurred to the hospital were included. Cost estimates correspond to the 1992-93 price level.

Currency
US dollars($).

Sensitivity analysis
One-way simple sensitivity analysis was carried out on length of hospitalization for symptomatic proximal and symptomatic distal DVT, on cost per day of hospitalization, and on duration (shortening) of the prophylactic therapy.
Estimated benefits used in the economic analysis
The number of DVT events avoided per 1,000 patients ranged from 384 to 479 for enoxaparin and from 346 to 449 for heparin depending on the study used to obtain the estimates for event probabilities (using each one of the studies in turn led to the higher benefits so defined, being associated with enoxaparin in all three instances). Incremental gains of enoxaparin compared to heparin ranged from 22 to 89 additional events prevented per 1,000 patients.

Cost results
The total expected costs from the two prophylactic regimens ranged from $3,336 to $3,380 for enoxaparin and from $3,292 to $3,330 for heparin. The cost estimates for the alternative "no prophylactic therapy" was not reported. The costs of adverse effects (major bleeding) were taken into account in costing the interventions.

Synthesis of costs and benefits
The cost per DVT event avoided (at 1992-93 prices) compared to a no-treatment alternative was reported for both drug regimens, and results of an incremental analysis were provided. Average cost per DVT event avoided ranged from $6,976 to $8,804 for enoxaparin and from $7,356 to $9,508 for heparin. The incremental cost per DVT event avoided by switching from heparin to enoxaparin ranged from $494 to $2,273 depending on the source of the effect measure. The sensitivity analysis showed the enoxaparin to have a lower average cost-effectiveness ratio than heparin over all the parameters/ranges investigated.

Authors' conclusions
A model of enoxaparin versus heparin DVT prophylaxis after total hip replacement in the US treatment environment showed that enoxaparin was more costly than heparin in overall expected treatment costs but more cost-effective in the avoidance of DVT.

CRD COMMENTARY - Selection of comparators
A justification was given for the comparators used. The comparators chosen, subcutaneous enoxaparin and subcutaneous heparin, were both frequently used alternatives for the prevention of DVT in the United States. You, as a user of this database, should consider whether these are widely used health technologies in your setting.

Validity of estimate of measure of benefit
Benefit measures were obtained from three randomized controlled trials. Primary studies used therapy durations ranging from 7 to 14 days, while the duration in standard practice was reported to be from 4 to 7 days. The cost-effectiveness model was based on the costs of 7 days' therapy, but no adjustments were made for the treatment effect estimates obtained from studies that used a longer duration of intervention. In sensitivity analysis only the effect of shorter (4 days) duration on treatment costs was evaluated, even though the authors noted that the duration of therapy has a large impact on the costs and cost-effectiveness ratios of both drugs. However, enoxaparin was found to be more cost-effective than heparin in all the sensitivity analyses conducted.

Validity of estimate of costs
Resource quantities included in the model were reported separately from the costs and in adequate detail. While the main outcome measures were estimated by comparing drug therapies to a no-treatment alternative, the costs that would have occurred in the absence of prophylaxis were not reported. Hence, it is not clear whether these costs were deducted from treatment costs after active therapies. Considering the remarkable decrease in DVT event rates due to prophylactic therapy, one could have expected consequent savings from expected DVT treatment costs.

Other issues
The main conclusion, that enoxaparin was more cost-effective than heparin, was justified. However, the levels of
average cost-effectiveness ratios may be subject to uncertainty due to the issues raised above, and hence direct comparisons with studies conducted elsewhere should be done with care. The authors did not compare their results with results from other similar studies mentioned in the discussion. Standard treatment practices and unit costs appropriate to the US managed care setting may not be generalisable to other countries or settings.

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