Low-molecular-weight heparin versus unfractionated heparin for prophylaxis of venous thromboembolism in medicine patients: a pharmacoeconomic analysis

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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.

CRD summary
This study assessed the cost-effectiveness of low-dose unfractionated heparin versus low-molecular weight heparin (LMWH) for the prevention of venous thromboembolism, in patients hospitalised for non-surgical treatment. The authors concluded that LMWH was a cost-effective alternative to unfractionated heparin, in Canada, especially for patients with a history of deep vein thrombosis. The methods were clearly described and the cost-effectiveness framework was valid. The authors’ conclusions are robust.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
This study assessed the cost-effectiveness of low-dose unfractionated heparin, versus low-molecular weight heparin (LMWH) for the prevention of venous thromboembolism (VTE) in patients hospitalised for non-surgical treatment.

Interventions
The two preventive strategies were LMWH (enoxaparin 40mg subcutaneously, once daily) and unfractionated heparin (5,000 units subcutaneously, twice daily). Either treatment was initiated on the first day in hospital and continued for seven days.

Location/setting
Canada/hospital.

Methods
Analytical approach:
The analysis was based on a probabilistic decision-analytic model. The time horizon was the length of hospital stay, which was an average of seven days. The authors stated that the analysis was carried out from an institutional perspective.

Effectiveness data:
The clinical data were from a selection of relevant studies. The probabilities of deep vein thrombosis and major bleeding while on LMWH or unfractionated heparin were the key inputs. These data were from a published meta-analysis of nine clinical trials. The remaining data were from published economic evaluations, meta-analyses, and diagnostic studies.

Monetary benefit and utility valuations:
Not considered.

Measure of benefit:
The summary benefit measures were the number of uncomplicated deep vein thromboses and a combined measure of untoward events, which included pulmonary embolism, major bleeding, and death.

Cost data:
The economic analysis included the direct medical costs incurred during initial hospitalisation, which were drugs,
diagnostic tests, and the treatment of major bleeding or VTE (deep vein thrombosis or pulmonary embolism). The drug costs used their official prices at the Vancouver General Hospital in-patient pharmacy. The cost of major bleeding was from published pharmacoeconomic analyses conducted in Canada. The remaining costs were based on official rates in the province of British Columbia. All costs were in Canadian dollars (CAD) and the price year was 2009.

Analysis of uncertainty:

One-way sensitivity analyses were carried on the acquisition costs of LMWH and unfractionated heparin, the cost of managing a pulmonary embolism and major bleed, the rate of deep vein thrombosis, the probability of progression to pulmonary embolism without treatment, and the length of stay for complicated or uncomplicated deep vein thrombosis. The ranges of values were from published sources or were assigned by the authors. An alternative scenario included the nursing and pharmacy labour costs. Subgroup analyses were carried out, using published data, for patients older than 75 years, and for those with a history of deep vein thrombosis, chronic respiratory disease, pneumonia, heart failure, or malignancy. A probabilistic sensitivity analysis was carried out, using a Monte Carlo simulation and predetermined probability distributions for each type of model input. Cost-effectiveness acceptability curves were plotted.

Results

The rates of deep vein thrombosis were 0.024 with unfractionated heparin and 0.021 with LMWH. The rates of untoward events were 0.0115 with unfractionated heparin and 0.0102 with LMWH. The hospital costs were CAD 5,302 with unfractionated heparin and CAD 5,310 with LMWH.

The incremental cost per deep vein thrombosis averted with LMWH, over unfractionated heparin, was CAD 2,046. The incremental cost per untoward event averted was CAD 6,832.

These results were not substantially altered in the sensitivity analyses. The incremental cost per deep vein thrombosis avoided ranged from CAD 228 to CAD 6,809. The incremental cost per untoward event averted ranged from CAD 761 to CAD 22,740.

In the subgroup analyses, the highest cost-effectiveness ratios were observed for patients with heart failure, while LMWH was dominant for patients with a history of deep vein thrombosis, as it was more effective and cheaper.

At a willingness to pay threshold of CAD 50,000 per untoward event avoided, LMWH was cost-effective in 76% of simulations. It was dominant in 33% of simulations and unfractionated heparin was dominant in 13% of simulations.

Authors' conclusions

The authors concluded that LMWH was a cost-effective alternative to unfractionated heparin for the prevention of VTE in hospitalised non-surgical patients, in Canada, especially for those with a history of deep vein thrombosis.

CRD commentary

Interventions:
The selection of the comparators was appropriate as low-dose unfractionated heparin and LMWH were the two drugs most commonly used to prevent venous thromboembolism. Their dosages were reported.

Effectiveness/benefits:
No systematic search was reported to identify the relevant data sources. The efficacy of treatments was from a published meta-analysis of clinical trials, which should have been valid given the design of clinical trials and the process of meta-analysis. The other sources were not described, making it difficult to fully assess the validity of the clinical inputs. Extensive sensitivity analyses were carried out on these model inputs. Two disease-specific benefit measures were used. They captured the direct impact of the disease on the patients' health but did not allow comparisons to be made with the benefits of other health care interventions. The authors acknowledged that quality-adjusted life-years could have provided more relevant information, but they were not feasible given the very short time horizon of seven days.

Costs:
Only those costs relevant to the hospital stay were analysed, in accordance with the institutional perspective stated. The sources of data were representative of the Canadian context and the authors' institutions. The costs of major bleeding
varied substantially in the published studies and these were varied in the sensitivity analysis. The resource quantities and unit costs were generally not reported separately and the costs were presented as category totals. The price year was reported, allowing reflation exercises. The distributions assigned to the costs in the probabilistic sensitivity analysis were provided.

Analysis and results:
The costs and benefits of the two preventive approaches were clearly reported and were appropriately synthesised, using an incremental approach. The uncertainty was investigated using both deterministic and probabilistic sensitivity analyses, and their methods and results were clearly described and discussed. The subgroup analyses provided further valuable information. The authors stated that the incremental cost per untoward event averted with LMWH was likely to be cost-effective, given the severity of the events averted, but no formal thresholds were available. Other published studies had found that LMWH was dominant or cost-neutral, and generally safer. The authors acknowledged some limitations of their analysis, such as the short time horizon and the restricted perspective. The analysis appears to have been specific to Canada and might not be transferable to other settings, unless the relative prices of drugs and other costs are the same.

Concluding remarks:
The methods were clearly described and the cost-effectiveness framework was valid. The authors’ conclusions are robust.

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