
Low-molecular weight heparin for deep vein thrombosis prophylaxis in hospitalized medical patients: results from a cost-effectiveness 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.

Health technology

The study examined low molecular weight heparin (LMWH) compared with unfractionated heparin (UFH) for deep vein thrombosis (DVT) prophylaxis in hospitalised patients.

Type of intervention

Primary prevention.

Economic study type

Cost-effectiveness analysis.

Study population

The target population comprised individuals hospitalised for acute medical diseases.

Setting

The setting was inpatient care. The economic study was carried out in the USA.

Dates to which data relate

The effectiveness data were drawn from studies published between 2000 and 2005. The resource use and costing data were drawn from studies published between 2002 and 2005. The price year used was 2004.

Source of effectiveness data

Model inputs included the frequency of DVT, major bleeds and heparin-induced thrombocytopenia (HIT) in patients receiving UFH thromboprophylaxis, and odds ratios for these end points if LMWH was given instead of UFH.

Modelling

A decision analytic model, which followed the recommendations of the Panel on Cost Effectiveness in Health and Medicine, was developed. A number of modelling assumptions were presented and fully justified. The authors sought to bias the model against the novel intervention (LMWH). A graphical depiction of the model was provided.

Sources searched to identify primary studies

The frequencies of DVT and major bleeding for both comparators were derived from randomised controlled trials (RCTs) comparing LMWH and UFH. The odds ratio for a reduction in HIT for LMWH was also derived from RCTs comparing LMWH and UFH. The incidence rate of HIT was derived from two prospective observational studies.

Methods used to judge relevance and validity, and for extracting data

The authors relied on a systematic review of published data to obtain estimates. A meta analysis provided the rates of DVT and major bleeding; the authors reviewed several databases to determine whether the study required updating, but no newer RCTs were found. Another meta analysis provided the odds ratio for reduction in HIT for LMWH, albeit drawn from mainly surgical populations. For the incidence of HIT, the authors pooled the results of two prospective observational studies in which the definition of HIT required clinical sequelae (i.e. they used a more conservative definition than that seen in clinical trials).

Measure of benefits used in the economic analysis

The measure of benefits used was the number of DVTs and associated complications prevented.

Direct costs

Direct health care costs were included. These comprised the costs of treating a DVT occurring in an inpatient, the costs of major bleeding and HIT, and drug acquisition costs. Direct pharmacy acquisition costs were used, that is, pharmacy administration charges were excluded. Cost-accounting studies provided non-drug cost estimates. All costs were indexed to 2004 US dollars. The costs were not discounted as the authors assumed the impact of outcomes occurred in the short term. Quantities were not reported.

Statistical analysis of costs

The costs were treated deterministically.

Indirect Costs

Productivity costs were not relevant to the perspective taken (i.e. third-party payer).

Currency

US dollar (\$).

Sensitivity analysis

For baseline rates of clinical events and odds ratios for LMWH, the authors used the 95% confidence intervals reported in the meta-analyses. The costs were adjusted by +/- 25%. The 95% confidence intervals for the cost-effectiveness estimates were computed using 10,000 Monte Carlo simulations. "Best-case" and "worst-case" scenarios were examined by setting all parameters to extreme values within the predetermined ranges. Threshold values were calculated for each individual variable to determine the point at which there were no cost-savings with LMWH.

Estimated benefits used in the economic analysis

In the base-case analysis of 1,000 patients, 20 DVTs, 10 severe bleeds and 14 cases of HIT were associated with the UFH strategy, while 17 DVTs, 5 severe bleeds and 1 case of HIT were associated with the LMWH strategy.

Cost results

The total DVT prevention-related costs were \$405,534 per 1,000 patients with the UFH strategy and \$315,929 with the LMWH strategy. This implied potential savings of \$89,465 from the adoption of LMWH.

Synthesis of costs and benefits

The LMWH strategy dominated UFH. Routine use of LMWH resulted in savings of approximately \$89 per patient.

The Monte Carlo simulation showed the 95% confidence interval ranged from savings of \$7 to \$373 per patient with

LMWH.

The lower rate of HIT accounted for much of the savings. In the univariate sensitivity analysis, the model was moderately sensitive to the baseline rate of HIT, the odds ratio of HIT with LMWH and the cost of HIT. The multivariate sensitivity analysis confirmed that LMWH dominated UFH.

"Worst-case" scenario modelling showed that LMWH remained dominant even when it increased the risk of DVT, had less effect on the rate of HIT, and was substantially more costly than UFH.

In the threshold analysis, it was discovered that LMWH would result in equivalent or greater costs to UFH only in the following scenarios:

the cost of HIT treatment fell to 15.3% of the original estimate;

LMWH costs were nearly doubled to \$39/day per patient;

LMWH increased the rate of DVT by 25% or more, relative to UFH;

LMWH decreased the rate of HIT by 26% or less, relative to UFH; or

the baseline rate of HIT with UFH decreased to 0.41% or less.

Authors' conclusions

Despite higher acquisition costs, low molecular weight heparins (LMWHs) for thromboprophylaxis in hospitalised patients resulted in cost-savings overall. These results were robust across a range of assumptions and despite uncertainty about several key inputs.

CRD COMMENTARY - Selection of comparators

Although no explicit justification was given for the use of UFH as the comparator, it appeared to represent current practice in the authors' setting. You should decide if UFH is relevant in your own setting.

Validity of estimate of measure of effectiveness

The sources of the model parameters were identified and justified. Where data were combined from two observational studies, the resulting value and confidence interval was provided. The authors used published meta-analyses of RCTs to inform the key model inputs, and described the databases they searched for new RCTs with which to update the meta-analyses (although none were found). The data sources used were studies high in the hierarchy of evidence quality, which implies a high internal validity.

Validity of estimate of measure of benefit

The authors selected the rates of DVT and complications as measures of benefit, but did not combine the outcomes into a single summary measure. Therefore, none of the outcomes captured in the model fully reflect the health benefits of the interventions. In addition, the results cannot easily be compared with those of other treatments or areas of therapy.

Validity of estimate of costs

The analysis of the costs was carried out from the perspective of a third-party payer. Appropriate direct costs were included in the analysis. It was unclear whether all the relevant cost types had been included as only aggregate costs of complications were reported. These were taken from published sources and inflated to 2004 levels. Discounting was considered unnecessary as short-term outcomes were considered. Drug administration costs were purposely excluded, with the intention of biasing the model against LMWH. It appears unlikely that any omissions would have affected the authors' conclusions. With the exception of a lack of resource use, which was not reported, the cost data were adequately presented.

Other issues

The authors compared, in detail, the results of their study with those of two other studies in the same population. They

found general agreement with one and criticised the other (which was not in agreement) on several counts. They also summarised the findings of other studies of LMWH in different populations. The authors addressed the issue of generalisability to different centres in the USA and suggested that their threshold analysis could provide guidance for settings other than that examined in this paper. The results were not presented selectively and comprehensive sensitivity analyses were performed.

The authors acknowledged several limitations to their study. First, the model assumptions could be incorrect. Second, other therapies not associated with HIT, such as direct thrombin inhibitors or pentasaccharides, were not examined. Third, the quality of the results depends directly on the quality of published data used to derive the inputs.

Implications of the study

The authors suggest that the savings shown across all the sensitivity analyses support the expanded use of LMWHs, and that clinicians and institutions should incorporate the observation of cost-savings into their treatment decisions. Further RCTs are required to establish conclusively the relative effectiveness of LMWH in DVT prevention. Accurate data about the frequency and cost of HIT are also currently unavailable in this population.

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