Subcutaneous low-molecular-weight heparin vs warfarin for prophylaxis of deep vein thrombosis after hip or knee implantation


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
Subcutaneous low-molecular-weight heparin versus warfarin for prophylaxis of deep vein thrombosis after hip or knee implantation.

Type of intervention
Secondary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
Adult patients undergoing elective hip and knee replacement surgery.

Setting
Hospital. The economic study was conducted in Canada and USA.

Dates to which data relate
Effectiveness and resource use data were obtained from a study published in 1993. The fiscal year was 1992.

Source of effectiveness data
Effectiveness data were derived from a single study.

Link between effectiveness and cost data
The cost-effectiveness analysis summarised in the report was planned prior to the performance of the clinical trial and the costs used were part of the original planning, also carried out prior to performance of the original trial. It can, therefore, be concluded that costing was prospectively planned for in producing the cost-effectiveness article.

Study sample
Power calculations were not reported as being used to determine the sample size. A consecutive series of 1,436 patients aged 18 years and older who underwent elective hip or knee replacement surgery (795 and 641 patients respectively) were included in the study. These patients were randomly allocated to receive either postoperative warfarin (n=721) or low-molecular-weight heparin prophylaxis (n=715).

Study design
This was a multicentre, randomised, double-blind clinical trial. The duration of follow-up was 14 days or until discharge. The exact rate of loss to follow up was not reported.

**Analysis of effectiveness**

The principle used in the analysis of effectiveness was treatment completers only. The main health outcomes used in the analysis were the frequency of proximal vein thrombosis (venous thrombosis in the popliteal, superficial femoral, common femoral, external iliac, and common iliac veins with or without calf vein thrombosis) and occurrence of deep vein thrombosis (proximal and/or calf deep vein thrombosis). Major bleeding complications were also considered in the analysis. The groups were comparable in terms of clinical characteristics at entry.

**Effectiveness results**

Deep vein thrombosis was recorded in 37% of warfarin patients (231 out of 617 patients), and in 31% of subcutaneous low-molecular-weight heparin patients (185 out of 590 patients), (p = 0.03). Proximal vein thrombosis occurred in 8% of warfarin patients and in 6% of subcutaneous low-molecular-weight heparin patients. Major bleeding complications occurred in 1% of warfarin patients and 3% of low-molecular-weight heparin patients.

**Clinical conclusions**

The decision to use low-molecular-weight heparin or warfarin prophylaxis is a complex trade-off. Warfarin use is more complex but is associated with fewer major bleeding complications than low-molecular-weight heparin. Low-molecular-weight heparin is more effective.

**Measure of benefits used in the economic analysis**

No summary benefit measure was identified in the economic analysis, and only separate clinical outcomes were reported.

**Direct costs**

Discounting of costs was not required due to the short follow-up period considered in the study. Quantities were not fully reported separately from the costs but cost items were reported separately. Direct health service costs were considered such as the costs of each prophylactic approach, comprising the cost of administering the active drug plus the cost of diagnosis and treatment of complications associated with each prophylactic alternative. The perspective adopted in the cost analysis was that of a third-party payer (the Provincial Ministry of Health in Canada and the insurance company in the USA). The cost data were obtained from a hospital in Canada and another in the USA. The date of the price data was 1992. The cost analysis did not include the costs of placebo or venography.

**Indirect Costs**

Not considered.

**Currency**

US dollars ($) and Canadian (Can$) dollars.

**Sensitivity analysis**

Multiple sensitivity analyses were performed, mainly on the cost variables. Threshold analysis was conducted on the costs of the US tinzaparin.

**Estimated benefits used in the economic analysis**

Not applicable.
Cost results
In Canada, the total cost per 100 patients was Can$11,598 for the warfarin group and Can$9,197 for the low-molecular-weight heparin group (a saving of Can$2,401 for the latter). In the USA, the total cost per 100 patients was $20,876 for the warfarin group and $25,594 for the low-molecular-weight heparin group (an increase of $4,718 for the latter).

Synthesis of costs and benefits
Prophylaxis with low-molecular-weight heparin is equally, or more, effective than the warfarin prophylaxis, with associated lower or higher costs, depending on the country where it is performed. The most sensitive parameters were the cost of the drug, the cost of monitoring the patient's international normalised ratio, and the costs associated with major bleeding complications.

Authors' conclusions
Prophylaxis with low-molecular-weight heparin is equally, or more, effective than warfarin prophylaxis. The results are health care system dependent. In Canada, low-molecular-weight heparin prophylaxis (tinzaparin) is less costly because it avoids the need for international normalised ratio monitoring. In the USA, the drug cost for low-molecular-weight heparin will likely be the principal determinant of relative cost-effectiveness.

CRD COMMENTARY - Selection of comparators
The reason for the choice of the comparator is clear.

Validity of estimate of measure of benefit
The effectiveness results are likely to be internally valid due to the use of a randomised design. In view of the lack of a summary benefit measure in the economic analysis, the study may be regarded as a cost-consequences study.

Validity of estimate of costs
Quantities were not reported systematically separately from the costs. Adequate details of the methods of cost estimation were given.

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Other publications of related interest


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