Extended dalteparin prophylaxis for venous thromboembolic events: cost-utility analysis in patients undergoing major orthopedic surgery

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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 examined the cost-effectiveness of dalteparin compared with warfarin as deep vein thrombosis prophylaxis in patients undergoing major orthopaedic surgery; total hip replacement, total knee replacement, or hip fracture surgery. The authors concluded that dalteparin for 10 days was cost-effective. The extended dalteparin therapy was acceptable value for money and reducing the duration of therapy to 28 days after surgery was more cost-effective. The study was well conducted and presented and the authors’ conclusions appear to be valid.

Type of economic evaluation
Cost-utility analysis

Study objective
This study examined the cost-effectiveness of dalteparin in comparison with warfarin as deep vein thrombosis (DVT) prophylaxis in patients undergoing major orthopaedic surgery, such as total hip replacement, total knee replacement, or hip fracture surgery.

Interventions
Dalteparin for 10 days or 35 days (extended) was compared with warfarin for 10 days. Dalteparin was given at a dosage of 5,000 international units per day. Warfarin was given with a target international normalised ratio of between two and three.

Location/setting
Canada/hospital.

Methods
Analytical approach:
The analysis was based on a decision analytic model and the time horizon was three months. The authors stated that the perspective of the Canadian provincial health care system was adopted.

Effectiveness data:
The clinical evidence came from a review of the literature in commonly used electronic databases. The key inclusion criteria were reported. Randomised controlled trial (RCT) data were supplemented with data from published systematic reviews and meta-analyses. The rates of major bleeding and symptomatic DVT were the key clinical inputs. These were taken from a pivotal RCT (the North American FRAGMIN Trial, NAFT) for total hip replacement patients and from two meta-analyses of RCTs for total knee replacement and hip fracture surgery patients. Some assumptions were also needed.

Monetary benefit and utility valuations:
The utility values were estimated from a random sample of 24 Canadian people using the time trade-off technique.

Measure of benefit:
Quality-adjusted life-years (QALYs) were the summary benefit measure.

Cost data:
The economic analysis included the costs of thromboprophylaxis regimens (supplies, pharmacy mark-up, and dispensing fee), international normalised ratio monitoring, and diagnosis and treatment of clinical DVT and major bleeding events. The analysis covered the time as an in-patient and after discharge. The data sources included a survey of three clinicians from large Canadian hospitals (for the costs associated with DVT episodes), a community pharmacy, the University Health Network in Toronto, various Health Authorities, and other published sources. All costs were in Canadian dollars (CAD) and the price year was 2007.

Analysis of uncertainty:
The issue of uncertainty was investigated in a one-way sensitivity analysis that used ranges of values based on both published sources and expert opinion. An alternative scenario was considered that assumed an additional need for a home-care visit by a nurse, for a proportion of patients on the extended dalteparin regimen. Shorter durations of dalteparin were also considered.

Results
In total hip replacement patients, the mean cost per patient was CAD 331 with dalteparin for 10 days, CAD 576 with dalteparin for 35 days, and CAD 295 with warfarin (10 days). The QALYs were 0.244 with dalteparin for 10 days, 0.207 with dalteparin for 35 days, and 0.200 with warfarin.

In comparison with warfarin, the incremental cost per QALY gained was CAD 800 with dalteparin for 10 days and CAD 40,100 with dalteparin for 35 days. In total knee replacement patients, the incremental cost per QALY was CAD 500 with dalteparin for 10 days and CAD 46,500 with dalteparin for 35 days and, in hip fracture surgery patients, it was CAD 400 with dalteparin for 10 days and CAD 31,200 with dalteparin for 35 days.

The sensitivity analysis showed that the base case findings were robust for dalteparin for 10 days, which was generally more effective and, in some instances, less expensive (at a reduced duration of treatment of seven days) than warfarin. The extended regimen of dalteparin provided the most value for money in the 28-day protocol with an incremental cost per QALY lower than CAD 35,000 for all cases. If home visits by a nurse for dalteparin injections were assumed for 10% of patients, the incremental cost per QALY was under CAD 68,000.

Authors' conclusions
The authors concluded that dalteparin for 10 days was a cost-effective alternative to conventional warfarin prophylaxis. The extended dalteparin protocol was acceptable value for money and reducing the duration of therapy to 28 days after surgery was more cost-effective.

CRD commentary
Interventions:
The rationale for the selection of the comparators was clear. The alternative prophylactic strategies appear to have been appropriately selected and might be transferable to other settings. The treatment duration was in accordance with international guidelines.

Effectiveness/benefits:
The method used to identify the relevant sources of data was appropriate as it was a literature review. The inclusion criteria were designed to select the most valid sources of evidence. The key details of these data sources were reported, which enhances the validity of the clinical analysis. The method used to derive the utility values and then calculate the QALYs was extensively described and was in accordance with Canadian guidelines. The sample of people used to elicit the preferences was described in detail. QALYs were an appropriate benefit measure because of the impact of the disease on the quality of life.

Costs:
The economic analysis was satisfactorily carried out. The categories of costs were consistent with the viewpoint of the study. Extensive details of the unit costs, quantities of resources used, price year, and data sources were presented, improving the transparency of the economic analysis.

Analysis and results:
Both average and incremental cost-utility ratios were calculated from the costs and benefits, which were clearly reported. The issue of uncertainty was assessed using a deterministic approach, which focused on the changes in the individual model inputs that were considered to be the key drivers of the analysis. The authors noted that some data for both total knee replacement and hip fracture surgery patients were derived from epidemiological studies rather than RCTs, and these estimates might not be as reliable as those for total hip replacement patients. The costs were from large medical centres across Canada and they might not be representative of other medical institutions.

Concluding remarks:
The study was well conducted and presented and the authors’ conclusions appear to be valid.

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