Minimizing costs for treating deep vein thrombosis: the role for fondaparinux

Shorr A F, Jackson W L, Moores L K, Warkentin T E

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 compared the use of fondaparinux with the low molecular weight heparin (LMWH) enoxaparin in the treatment of deep vein thrombosis (DVT).

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised a hypothetical cohort of 1,000 DVT patients. The authors assumed that the patients had essentially normal renal function and that outcomes were discrete. The authors also assumed that patients could not suffer from multiple complications (e.g. bleeding and DVT recurrence).

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

Dates to which data relate
The effectiveness and cost data were derived from studies published between 1999 and 2005. The price year was 2005.

Source of effectiveness data
The effectiveness data included in the model were the rates of recurrence, major bleeding and heparin-induced thrombocytopenia associated with enoxaparin and fondaparinux.

Modelling
A decision tree model was created to capture the central issues in acute DVT treatment and to examine the cost-effectiveness of fondaparinux for DVT therapy compared with enoxaparin. The model was based on various assumptions on efficacy, drug dosing and costs, which were all reported in the current study but are too numerous to be reported here. However, the authors reported that their model was biased against fondaparinux.

Sources searched to identify primary studies
The rate of DVT recurrence with enoxaparin and the odds ratio for recurrence with fondaparinux were drawn from a double-blind, randomised controlled trial (RCT) comparing these two treatments directly. Major bleeding rates were derived from two VTE treatment trials of fondaparinux. For rates of heparin-induced thrombocytopenia (HIT), the authors derived information from a study comparing multiple LMWHs, and extracted the information only for patients
given enoxaparin. The rates of HIT for patients treated with fondaparinux were based on authors’ assumptions.

Methods used to judge relevance and validity, and for extracting data
The authors did not report whether a systematic review of the literature was undertaken. They also did not report the search methods or inclusion criteria used to identify relevant studies. However, they did report that the risk for major bleeding and HIT rates were derived by pooling studies using meta-analytic techniques.

Measure of benefits used in the economic analysis
The authors made a major assumption. Specifically, as clinical data suggested that fondaparinux and LMWH had similar outcomes for some end points, the authors assumed that fondaparinux and LMWH enoxaparin had similar outcomes (such as quality of life, morbidities and mortality) and no summary measure of benefit was derived. Therefore, only the costs were included in the economic analysis. Consequently, a cost-minimisation study was undertaken.

Direct costs
The direct costs to a large third-party payer were included in the analysis. These comprised the cost of enoxaparin and fondaparinux, the cost of DVT recurrence, the cost of major bleeding and the cost per case of HIT. Acquisition costs were obtained in order to derive the costs of fondaparinux and enoxaparin. The costs of clinical outcomes were derived from earlier cost-effectiveness analyses in DVT treatment. Since the costs were incurred during a short time, discounting was not relevant and was therefore not performed. All costs were adjusted to 2005 prices using the Consumer Price Index. The average costs were reported in the study. The authors reported that their model was biased against fondaparinux and that some relevant costs associated with enoxaparin (e.g. pharmacy administration and wastage costs) were excluded from the analysis.

Statistical analysis of costs
The costs were treated as point estimates (i.e. the data were deterministic).

Indirect Costs
The productivity costs were not included in the analysis.

Currency
US dollars ($).

Sensitivity analysis
The authors undertook a series of one-way sensitivity analyses. Clinical event rates were varied using the 95% confidence intervals (CIs) reported in the literature, while the rate of HIT with fondaparinux was increased to 50%. As 95% CIs were not available for the costs, these were varied by 25% in each direction. In addition, 10,000 Monte Carlo simulations were performed in order to compute 95% CIs for the incremental cost-effectiveness of fondaparinux. In this analysis each parameter was varied over a specified range. Best- and worst-case scenarios were also evaluated.

Estimated benefits used in the economic analysis
The authors reported that clinical data suggested that, for some end points, fondaparinux and LMWH had similar outcomes. Therefore no summary of benefit was derived and, in effect, a cost-minimisation study was undertaken.

Cost results
The average cost of treating patients was $769 per patient with enoxaparin compared with $472 per patient with
fondaparinux.

The sensitivity analysis showed that the results of the model were mildly sensitive to the costs of the agents. The Monte Carlo simulations showed that the 95% CIs around point estimates of average savings with fondaparinux were $48 to $401 per patient, and that in 99.1% of simulations there were savings with fondaparinux.

**Synthesis of costs and benefits**
The costs and benefits were not combined as the authors performed a cost-minimisation analysis.

**Authors’ conclusions**
Fondaparinux represented a financially attractive option for deep vein thrombosis (DVT) treatment for third-party payers, managed care organisations and hospitals.

**CRD COMMENTARY - Selection of comparators**
A justification was given for using a LMWH treatment, in this case enoxaparin, as the comparator: over the last decade, it has evolved as an important tool in the management of DVT. You should determine if the comparator used represents current practice in your own setting.

**Validity of estimate of measure of effectiveness**
The parameters were derived from published research and authors’ assumptions. In some instances the study results were combined using meta-analytic methods, which were clearly reported in the study. However, the authors did not report whether a systematic review was undertaken to identify the health and economic outcomes, nor did they report any of the search methods or inclusion criteria used in the review of the literature.

**Validity of estimate of measure of benefit**
No summary of benefit was derived and, in effect, a cost-minimisation study was undertaken. Although the authors reported that there were more recurrences and more cases of HIT with enoxaparin than with fondaparinux, they assumed that fondaparinux and LMWH had similar outcomes for some end points (i.e. the main outcomes such as mortality or quality of life). However they did not provide any justification for the choice of assumptions.

**Validity of estimate of costs**
The analysis of the costs was performed from the perspective of the third-party payer. All the categories of costs relevant to this perspective appear to have been included in the analysis. However, the authors reported that some costs associated with enoxaparin treatment (e.g. pharmacy preparation time and disposal) were not included in the analysis. Such omissions will therefore bias the results of the model against fondaparinux. The costs were derived from published sources. Appropriate sensitivity analyses were undertaken, with the ranges used to vary costs appearing to be wide.

The costs were incurred during a short time, therefore discounting was not relevant and was appropriately not performed. The price year was reported, which will aid any possible inflation exercises. However, the costs were adjusted using the Consumer Price Index, which might not reflect the specific medical care inflation, which is generally higher than overall inflation. The costs and the quantities were not reported separately, which will limit the generalisability of the authors' results.

**Other issues**
The authors compared their findings with those from other studies that had examined the cost-effectiveness of fondaparinux in orthopaedic prophylaxis. These studies also concluded that the use of fondaparinux was associated with cost-savings. The issue of generalisability to other settings was partly addressed in the sensitivity analysis. The authors do not appear to have presented their results selectively and their conclusions reflected the scope of the
The authors reported a number of further limitations to their study. First, in some instances there was little published research with which to populate the model. Second, the outcomes were assumed to be discrete and the authors did not use a Markov model in which patients could make transitions between multiple health states. Third, the authors assumed there was no renal failure in the population. Fourth, the authors presumed that the costs of major bleeding were similar for fondaparinux and enoxaparin, which will not always be the case as protamine can be used as an antidote for bleeding with LMWHs. Finally, the results might not apply outside of the USA as the costs of the treatments may vary widely.

**Implications of the study**

The authors reported that greater use of fondaparinux could yield substantial cost-savings without compromising clinical outcomes or patient safety.

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**Bibliographic details**


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**Other publications of related interest**

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**Indexing Status**

Subject indexing assigned by NLM

**MeSH**

Body Weight; Costs and Cost Analysis; Enoxaparin /adverse effects /economics /therapeutic use; Hemorrhage; Heparin, Low-Molecular-Weight /adverse effects /economics /therapeutic use; Humans; Models, Economic; Polysaccharides /adverse effects /economics /therapeutic use; Recurrence; Thrombosis /chemically induced; Venous Thrombosis /drug therapy /economics