A cost analysis of fondaparinux versus enoxaparin in total knee arthroplasty
Spruill W J, Wade W E, Leslie R B

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 (2.5 mg daily) and enoxaparin (30 mg twice daily), both administered subcutaneously, as prophylaxis for deep vein thrombosis (DVT) in patients undergoing total knee arthroplasty.

Type of intervention
Primary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised a hypothetical cohort of 1,000 patients undergoing total knee arthroplasty.

Setting
The study setting was secondary care. The economic study was carried out at the College of Pharmacy, University of Georgia, USA.

Dates to which data relate
The effectiveness data were derived from a single study carried out in 2001. The resource use data were derived from a review of studies published between 1995 and 2000. The price year was 2002.

Source of effectiveness data
The effectiveness data were derived from a single study (Bauer et al., see Other Publications of Related Interest), supplemented with authors' assumptions based on the literature.

Link between effectiveness and cost data
The cost analysis was based on a hypothetical cohort of 1,000 patients. The patients providing the effectiveness data provided the cost data for drug prophylaxis. The other costs were derived from the literature.

Study sample
The authors only provided brief details on the study by Bauer et al., (see Other Publications of Related Interest). All reported details of this study are given here. The study randomly assigned patients to either fondaparinux or enoxaparin. It would appear that each arm in the study consisted of 372 patients. The enoxaparin arm was comprised 43% men and 57% women, whereas the fondaparinux arm comprised 39% men and 61% women. The average age in both groups was 67.5 years.
Study design
The study of Bauer et al. was a randomised controlled trial (RCT). The authors did not provide any details on the length of follow-up and loss to follow-up in this study.

Analysis of effectiveness
The authors did not report whether the study was conducted on an intention to treat basis or for treatment completers only. The outcome measures in the study of Bauer et al. included venous thromboembolism (VTE) up to day 11 after surgery, and major bleeding. VTE was detected by mandatory bilateral venography, or documented symptomatic DVT or pulmonary embolism (PE). Major bleeding was defined as overt bleeding with a bleeding index of 2 or more. Other bleeds were also assessed in the analysis. There was no analysis of the comparability of the different patient groups.

Effectiveness results
A total of 21.3% of patients suffered a distal DVT in the enoxaparin group, compared with 9.4% of patients in the fondaparinux group.

Similarly, more patients (5.4%) suffered a proximal DVT in the enoxaparin group than in the fondaparinux group (2.4%).

A total of 0.8% of patients suffered a nonfatal PE in the enoxaparin group, compared with 0.2% of patients in the fondaparinux group.

No patients suffered a major bleed in the enoxaparin group, compared with 1.7% of patients in the fondaparinux group.

A total of 0.2% of patients suffered a major bleed leading to reoperation in the enoxaparin group, compared with 0.4% of patients in the fondaparinux group.

A total of 3.7% patients suffered other bleeds in the enoxaparin group, compared with 2.7% of patients in the fondaparinux group.

Bauer et al. reported an overall 55.2% risk reduction in VTEs (including both distal and proximal DVTs) with the use of fondaparinux in comparison with enoxaparin.

Clinical conclusions
The authors concluded that the use of fondaparinux was more effective in preventing DVT.

Methods used to derive estimates of effectiveness
The authors supplemented the effectiveness data from Bauer et al. with their own assumptions, which were based on published literature.

Estimates of effectiveness and key assumptions
Based on literature estimates, which reported a mortality rate of 0.2% to 0.7% secondary to PE, the rate of fatal PEs in the absence of prophylaxis in total knee arthroplasty patients was assumed to be 0.5%.

Measure of benefits used in the economic analysis
The benefits used were the number of additional VTE events avoided, and the number of deaths averted and life-years gained using prophylaxis over no prophylaxis. The number of deaths averted was calculated by assuming an average fatal PE rate of 0.5% for patients receiving no prophylaxis in the hypothetical cohort of 1,000 patients. The life-years gained were derived by multiplying the number of deaths by the gender-adjusted average life expectancy for this hypothetical cohort, which was derived from 1997 life tables.
Direct costs
The costs and resource use were not reported separately. The direct costs included were those to the hospital. These were for physician visits, therapeutic monitoring requirements, extended hospitalisations, complications, drug prophylaxis, diagnosis of VTEs and drug treatment. The cost information was derived from the literature: MEDLINE was searched for articles evaluating the costs associated with VTE prophylaxis and treatment, and seven studies were identified. The costs of the prophylactic agents, enoxaparin and fondaparinux, were obtained from the average wholesale price. It would appear that the costs were incurred during a short time, hence discounting would appear not to have been relevant. If this assumption is true, then discounting was appropriately not performed by the authors. The authors reported the total costs for the 1,000 patients. The costs were adjusted at 5% annually until the year 2002.

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

Indirect Costs
The indirect costs were not included.

Currency
US dollars ($).

Sensitivity analysis
Sensitivity analyses combined with an analysis of extremes were performed to determine the robustness of the incremental cost-effectiveness calculations. The variables evaluated in these analyses included 1 standard deviation of the mean costs of treating proximal DVT, nonfatal PE and major bleeding events.

Estimated benefits used in the economic analysis
In the hypothetical cohort of 1,000 patients, the total number of VTEs was 62 in the enoxaparin group versus 26 in the fondaparinux group. This represents a total of 36 VTEs avoided by the use of fondaparinux.

A total of 5 deaths were averted when using enoxaparin or fondaparinux over no prophylaxis.

The gender-adjusted average life expectancy was 16.36 years for the enoxaparin arm and 16.48 years for the fondaparinux arm.

Cost results
For the hypothetical cohort of 1,000 patients, the total cost was $444,717.71 in the enoxaparin group versus $405,789.69 in the fondaparinux group.

Synthesis of costs and benefits
The costs and benefits were combined using an incremental cost-effectiveness ratio, which represents the additional cost per VTE avoided by the use of fondaparinux over enoxaparin. This analysis indicated that fondaparinux was associated with cost-savings of $1,081.33 per VTE avoided in comparison with enoxaparin.

The costs and benefits were also combined by dividing the cost of providing prophylaxis to 1,000 patients by the number of patients expected to die if they did not receive prophylaxis. Therefore, the cost per death averted was $88,943.54 in the enoxaparin group and $81,157.94 in the fondaparinux group.

Finally, the costs and benefits were combined by dividing the cost per death averted by the adjusted life expectancy for both groups. When compared with no prophylaxis, the cost per life-year gained was $5,437 for enoxaparin and $4,925 for fondaparinux.
for fondaparinux.

The results of the sensitivity analysis showed that fondaparinux produced cost-savings over enoxaparin in both worst- and best-case scenarios. It was also demonstrated that if the cost of enoxaparin was reduced by 25%, any cost-savings attained by fondaparinux would disappear.

Authors’ conclusions
The lower incidence of prophylaxis failures observed with fondaparinux, compared with enoxaparin, offers an opportunity for cost-savings.

CRD COMMENTARY - Selection of comparators
Although no explicit justification was given for using enoxaparin as the comparator, it would appear to represent current practice in the authors’ setting. You should decide if the comparator represents current practice in your own setting.

Validity of estimate of measure of effectiveness
The estimates of the measure of effectiveness were derived from an RCT. This was appropriate for the study question, as well-conducted RCTs are considered the ‘gold’ standard study design when comparing different health interventions. However, the authors only provided brief details of this RCT, so the internal validity of this study cannot be assessed without looking at the study in further detail (Bauer et al., see Other Publications of Related Interest). For example, it was unclear whether the study sample was representative of the study population as the method of sample selection was not reported. In addition, there was no assessment of the patients at baseline in order to determine the comparability of the patient groups. The validity of the effectiveness analysis was limited as no statistical analysis was performed, and no sensitivity analysis on health outcomes was carried out.

Validity of estimate of measure of benefit
The estimation of benefits was derived by applying the effectiveness estimates to a hypothetical cohort of 1,000 patients. The life-years gained were obtained using estimates from other studies, while life expectancy was derived from life tables for each arm in the study. However, it was unclear how the authors derived different life expectancies for enoxaparin and fondaparinux.

Validity of estimate of costs
All the categories of cost relevant to the perspective adopted were included, and no relevant costs appear to have been omitted. Although the costs and the quantities were not reported separately, the authors provided unit costs for each prevention and treatment component, which will increase the generalisability to other settings. A review of the literature was undertaken, using MEDLINE, to find relevant costs for the study. Seven studies were included. A sensitivity analysis of the costs was performed by considering the best- and worst-case scenarios, and this enhances the interpretation of the results. The authors did not explicitly report the time period during which the costs were incurred, although it appears to have been less than one year. Hence, discounting was not relevant. The price year was appropriately reported, which will aid any possible inflation exercises.

Other issues
The authors did not make any appropriate comparisons of their findings with those from other studies. The issue of generalisability to other settings was partially addressed in the sensitivity analysis. The authors do not appear to have presented their results selectively and their conclusions reflected the scope of the analysis. The authors did not report any limitations of their study.

Implications of the study
The authors made no recommendations. However, on viewing their results, the authors appear to recommend the use of fondaparinux for this patient population.

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None stated.

**Bibliographic details**

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**Other publications of related interest**


**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
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