Cost-effectiveness of rivaroxaban versus heparins for prevention of venous thromboembolism after total hip or knee surgery in Sweden
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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 assessed the cost-effectiveness of rivaroxaban versus two low-molecular-weight heparin (LMWH) treatments (enoxaparin and dalteparin) for the prevention of venous thromboembolism, after total hip or knee replacement. The authors concluded that rivaroxaban was a cost-effective alternative to 14 days of LMWH, over five years, in Sweden. The methods were valid and transparent, which supports the authors’ conclusions.

Type of economic evaluation
Cost-effectiveness analysis, cost-utility analysis

Study objective
This study assessed the cost-effectiveness of rivaroxaban versus two low-molecular weight heparin (LMWH) treatments, enoxaparin or dalteparin, for the prevention of venous thromboembolism, after total hip replacement or total knee replacement.

Interventions
The interventions were rivaroxaban 10mg daily, enoxaparin 40mg daily, or dalteparin 5,000 units daily. For hip replacement patients, rivaroxaban was given for 35 days or either LMWH was given for 14 days. For knee replacement patients, all treatments lasted 14 days.

Location/setting
Sweden/hospital.

Methods
Analytical approach:
The analysis was based on a decision model of the progress of patients after surgery for a period of five years. The model had three parts: prophylaxis, after prophylaxis, and long-term complications. The first two parts were decision trees, and the third part was a Markov model. The perspective was not explicitly stated.

Effectiveness data:
Most of the clinical data were from a selection of relevant studies. A key input was the incidence of venous thromboembolism in patients receiving prophylaxis. This input was based on evidence from two phase III randomised trials of rivaroxaban versus enoxaparin. The patients’ characteristics were also based on these trials. A literature review found no clinical trial of the efficacy of dalteparin compared with rivaroxaban or enoxaparin. On the basis of two retrospective studies and one pilot study comparing dalteparin with enoxaparin, they were assumed to be clinically equivalent. Published sources were used for the other inputs. The mortality estimates were from Swedish life tables.

Monetary benefit and utility valuations:
The utility values were from published sources, including a Finnish study that supplied the baseline health state for patients without complications after surgery.

Measure of benefit:
Quality-adjusted life-years (QALYs) and avoided symptomatic venous thromboembolisms were the summary benefit measures. An annual discount rate of 3% was applied.
Cost data:
The economic analysis included the costs of drugs (acquisition and administration), treatment of bleeding, diagnosis of venous thromboembolism, in-patient and out-patient treatment of deep vein thrombosis or pulmonary embolism, and management of long-term complications, such as recurrent venous thromboembolism or post-thrombotic syndrome. The resource quantities were from published studies or Swedish clinics. The costs were from various sources, including official price lists, Swedish studies, and cost studies performed in other countries. For example, UK NHS reference prices were used because of a lack of reliable Swedish data for the diagnosis of chronic thromboembolic pulmonary hypertension. All costs were presented in Swedish kronor (SEK). The price year was 2008 and a 3% annual discount rate was applied.

Analysis of uncertainty:
One-way sensitivity analyses were carried out to examine how robust the findings were to variations in the model inputs, using published or assumed ranges of values. A probabilistic sensitivity analysis was carried out, using Monte Carlo simulation, with statistical distributions fitted to all the model inputs.

Results
Total hip replacement: The expected costs were SEK 2,432 with rivaroxaban, SEK 2,313 with enoxaparin, and SEK 2,288 with dalteparin. The QALYs were 3.8671 with rivaroxaban, 3.8630 with enoxaparin, and 3.8630 with dalteparin. The symptomatic venous thromboembolism was 0.0079 with rivaroxaban, 0.0381 with enoxaparin, and 0.0381 with dalteparin.

The incremental cost per QALY gained with rivaroxaban was SEK 29,378 over enoxaparin, and SEK 35,436 over dalteparin. The incremental cost per symptomatic venous thromboembolism avoided with rivaroxaban was SEK 3,929 over enoxaparin, and SEK 4,739 over dalteparin.

Total knee replacement: The expected costs were SEK 1,457 with rivaroxaban, SEK 2,329 with enoxaparin, and SEK 2,336 with dalteparin. The QALYs were 3.8072 with rivaroxaban, 3.8043 with enoxaparin, and 3.8043 with dalteparin. The symptomatic venous thromboembolism was 0.0143 with rivaroxaban, 0.0362 with enoxaparin, and 0.0362 with dalteparin.

Rivaroxaban was dominant, as it was more effective and less costly than either comparator.

Sensitivity analysis: The efficacy of rivaroxaban and its lower cost due to oral administration were key drivers after hip replacement, while the cost of prophylaxis was the most influential input after knee replacement. Variations of other inputs did not substantially alter the base-case results.

Rivaroxaban was dominant in 30% of simulations for hip replacement, and all simulations for knee replacement.

Authors' conclusions
The authors concluded that rivaroxaban was a cost-effective alternative to 14 days of LMWH, over five years, for prophylaxis against venous thromboembolism, after total hip or knee replacement, in Sweden.

CRD commentary
Interventions:
The rationale for the selection of the comparators was clear. Rivaroxaban was a new prophylactic treatment, and its cost-effectiveness in Sweden had not been evaluated against either enoxaparin or dalteparin. These were the two most common preventive treatments following orthopaedic surgery.

Effectiveness/benefits:
The sources for the clinical inputs appear to have been the most relevant to the authors' context. The treatment effect for rivaroxaban versus enoxaparin was based on two clinical trials that followed Swedish treatment guidelines. No clinical trials were available for dalteparin, and studies with less reliable methods were used. Local sources were selected for other inputs. The sensitivity analysis showed that variations in the key clinical parameters did not alter the conclusions. Both benefit measures were appropriate for capturing the impact of the disease on the patients' health. QALYs allow comparisons to be made with the benefits of other health care interventions. The sources for the utility
values were reported, but the instruments used to elicit the patient preferences were not.

Costs:
The perspective was not stated, but only the direct medical costs appear to have been included suggesting a health care payer viewpoint. The unit costs were reported for some items, while other costs were presented as category totals. Key information was given on the data sources and they appear to have been relevant to Sweden. The authors justified the need for costs from other countries due to a lack of reliable Swedish sources. The impact of variations in the key cost estimates was tested in the sensitivity analyses. The price year, currency conversions, and discounting were appropriately reported.

Analysis and results:
The results were clearly reported for both models. An incremental approach was used to synthesise the costs and benefits of the alternative strategies. A clear description and diagrams of the modules of the decision model were provided. The uncertainty was investigated, using valid approaches, and the methods and results were clearly reported. The statistical distributions for the model parameters and their values were reported in detail. The authors acknowledged some limitations of their analysis due to the need for assumptions and the use of some differing secondary sources, but these were extensively tested in the sensitivity analyses. The transferability of the results was not explicitly addressed, but the findings might be similar for countries with the same relative drug costs.

Concluding remarks:
The methods were valid and transparent, which supports the authors’ conclusions.

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