Cost and outcomes associated with rivaroxaban vs enoxaparin for the prevention of postsurgical venous thromboembolism from a US payer's perspective

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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 rivaroxaban versus enoxaparin for the prevention of venous thromboembolism after surgery in patients undergoing total hip or knee replacement. The authors concluded that rivaroxaban provided value for money, from the perspective of the US health care payer. The methods were valid and clearly reported as were the results and the authors’ conclusions appear to be robust.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
This study examined the cost-effectiveness of rivaroxaban versus enoxaparin for the prevention of venous thromboembolism after surgery in patients undergoing total hip or knee replacement.

Interventions
Oral rivaroxaban 10mg once daily was compared with subcutaneous enoxaparin 40mg once daily.

Three comparisons were carried out: extended prophylaxis (35 days) for both rivaroxaban and enoxaparin in hip replacement patients; extended prophylaxis rivaroxaban compared with short prophylaxis (10 to 14 days) enoxaparin in hip replacement patients; and short prophylaxis for both drugs in knee replacement patients.

Location/setting
USA/hospital.

Methods
Analytical approach:
This economic evaluation was based on a decision model with two periods: the prophylaxis period, which was up to 35 days for hip replacement or 10 to 14 days for knee replacement, and the post-prophylaxis period, which continued up to 90 days after surgery. The authors stated that they took the perspective of the US payer.

Effectiveness data:
The clinical inputs were from phase III clinical trials of rivaroxaban that formed part of the REgulation of Coagulation in ORthopaedic surgery to prevent Deep vein thrombosis and pulmonary embolism (RECORD) programme, which included over 12,500 patients. RECORD1 had 4,541 patients and compared extended rivaroxaban therapy with extended enoxaparin therapy in hip replacement patients. RECORD2 had 2,509 patients and compared extended rivaroxaban therapy with short enoxaparin therapy in hip replacement patients. RECORD3 had 2,531 knee replacement patients who received short therapy with either drug. The primary endpoint was the rate of total venous thromboembolism, defined as a composite of any deep vein thrombosis (DVT), non-fatal pulmonary embolism, or death. The main analysis assumed that the two treatments were equally effective for those endpoints where the trials did not find statistically significant differences between them.

Monetary benefit and utility valuations:
Not considered.
Measure of benefit:
The number of symptomatic events was the summary benefit measure.

Cost data:
The economic analysis included the costs of prophylaxis and treatment for venous thromboembolism. The quantities of resources were mainly from published studies, including the RECORD trials and other economic analyses conducted in the USA. Medicare reimbursement rates were used to estimate the costs of diagnosing venous thromboembolism or pulmonary embolism. All costs were in US $ and the price year was 2010.

Analysis of uncertainty:
Various one-way sensitivity analyses were carried out on selected inputs. The results of RECORD1 and RECORD2 were pooled, and data from RECORD4 were included with those of RECORD3 for the knee replacement population. A probabilistic sensitivity analysis was carried out using 95% confidence intervals from the clinical trials or published ranges of values.

Results
The main analysis considered only the prophylaxis period.

With extended prophylaxis for all hip patients, the expected costs were $346 with rivaroxaban and $1,041 with enoxaparin. The number of symptomatic events was 2.7 with rivaroxaban and 2.7 with enoxaparin. Rivaroxaban was as effective as enoxaparin, but reduced the costs by $695. The most influential inputs were the relative cost of enoxaparin and the high relative risk of symptomatic venous thromboembolism events with enoxaparin.

With extended rivaroxaban and short enoxaparin for hip patients, the expected costs were $319 with rivaroxaban and $563 with enoxaparin. The number of symptomatic events was 2.5 with rivaroxaban and 12.4 with enoxaparin. Rivaroxaban was dominant as it was more effective and less expensive. Influential inputs were the rate of symptomatic venous thromboembolism events with enoxaparin, the time horizon, and the costs of the two therapies.

With short prophylaxis for knee patients, the expected costs were $243 with rivaroxaban and $654 with enoxaparin. The number of symptomatic events was 6.7 with rivaroxaban and 19.7 with enoxaparin. Rivaroxaban was again dominant. Influential inputs were the rates of venous thromboembolism events and the costs of the therapies.

Overall, the base-case findings were robust. When a longer time horizon was considered (up to 90 days after surgery) the results were more favourable to rivaroxaban. The probabilistic sensitivity analysis showed a positive correlation between improved effectiveness for rivaroxaban and greater cost-savings.

Authors' conclusions
The authors concluded that rivaroxaban provided value for money, compared with enoxaparin, from the perspective of the US health care payer.

CRD commentary
Interventions:
The authors justified their selection of the comparators, which are likely to be appropriate for other settings.

Effectiveness/benefits:
The clinical inputs were form selected trials, which were valid because they directly compared the two treatments and had robust methods. Only the number of patients involved and the main results of these trials were reported. The authors stated that the trials had large samples, but few events (as pulmonary embolism or death) were found and this might be the reason for no statistically significant differences between the treatments for these outcomes. Extensive sensitivity analysis was conducted pooling the trial data and varying the key model inputs. A disease-specific benefit measure was used, as it was the natural outcome for prophylaxis, but it does not allow comparisons with the benefits of other health care interventions.

Costs:
Only the direct costs of prophylaxis and treatment for venous thromboembolism were analysed in accordance with the
payer perspective. The unit costs and quantities of resources were presented separately for most items, which increases the ability to replicate the analysis. The sources for the resource use were both the pivotal clinical trials and some published studies that were likely to be relevant to the USA. Other typical US sources, as Medicare, were used. The costs were varied in the sensitivity analysis. The price year was reported and this will allow reflation exercises.

Analysis and results:
The results were clearly presented. An incremental analysis was appropriately used to combine the costs and benefits of the two strategies. The uncertainty was satisfactorily investigated in deterministic and probabilistic analyses, and the methods and results were clearly reported. The key details of the decision model were reported. The time horizon was appropriate, as the authors pointed out that evidence had shown that patients remained at risk of venous thromboembolism for a period of three months. The authors presented the strengths and limitations of their analysis, some of which have been mentioned. In general, conservative assumptions against rivaroxaban were made. The results appear to be specific to the US setting and it is unclear whether they could be transferred to other settings.

Concluding remarks:
The methods were valid and clearly reported as were the results. The authors’ conclusions appear to be robust.

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