

# Economic Comparison of Rivaroxaban with Enoxaparin in the UK and Sweden

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## Introduction

- ◆ Venous thromboembolism (VTE) is the composite of deep vein thrombosis (DVT) and pulmonary embolism (PE)
- ◆ The risk of VTE is increased after total hip replacement (THR) and total knee replacement (TKR) surgery.<sup>1</sup> With more than 400,000 such procedures performed annually in the European Union the potential public health risk is sizeable<sup>2</sup>
- ◆ Rivaroxaban is an oral, direct Factor Xa inhibitor that received marketing approval in 2008 in the European Union and several other countries for the prevention of VTE after elective THR and TKR surgery
- ◆ Two randomized controlled trials relevant for the purposes of the economic analysis were conducted:
  - In RECORD1, after THR, 35 days' rivaroxaban reduced total VTE (composite of DVT, either symptomatic or asymptomatic detected by bilateral venography, non-fatal PE, and all-cause mortality) by 70% (relative risk reduction [RRR]) versus 35 days' enoxaparin (40 mg once daily)<sup>3</sup>
  - In RECORD3, after TKR, 14 days' rivaroxaban reduced total VTE by 49% (RRR) and symptomatic VTE by 66% (RRR) versus 14 days' enoxaparin (40 mg once daily)<sup>4</sup>
  - In both studies, the incidences of major bleeding were not significantly different between groups<sup>3,4</sup>
- ◆ Two further randomized controlled trials of rivaroxaban versus enoxaparin were excluded from the economic analysis – RECORD2<sup>5</sup> because the duration of enoxaparin was 12±2 days followed by placebo, and RECORD4<sup>6</sup> because the enoxaparin regimen (30 mg twice daily) is not used in the European setting

## Objective

- ◆ The aim of this analysis was to assess the cost-effectiveness of 35 days' rivaroxaban versus 35 days' enoxaparin for the prevention of VTE after THR and 14 days' rivaroxaban versus 14 days' enoxaparin after TKR in the UK and Sweden

## Methods

- ◆ An economic model was developed to assess the cost-effectiveness of rivaroxaban versus enoxaparin from the perspective of the national healthcare systems in Sweden and the UK – these countries have different health systems, but each produces reliable data, and the results demonstrate the generalizability of the analyses

- ◆ The analysis models the period from surgery up to 90 days after surgery (Figure 1), followed by recurrent VTE and post-thrombotic syndrome occurring from 90 days to 5 years after surgery (Figure 2)
- ◆ The probabilities of VTE and major bleeding during prophylaxis were derived from RECORD1 for THR<sup>3</sup> and RECORD3 for TKR.<sup>4</sup> The probability of untreated asymptomatic VTE becoming symptomatic in the period between the end of prophylaxis and 90 days after surgery was based on published clinical data<sup>7</sup>
- ◆ The costs of major bleeding are included in the results, but the non-significant difference between major bleeding with enoxaparin and rivaroxaban means that the costs attributed to major bleeding are also similar
- ◆ Estimated risks of recurrent VTE and post-thrombotic syndrome beyond the 90 days after surgery were based on published epidemiologic data<sup>8</sup>
- ◆ The costs of symptomatic VTE, major bleeding, and post-thrombotic syndrome (2008 values) were derived from published sources<sup>1,8-17</sup> and applied to the events in the model
- ◆ Existing therapy with subcutaneous enoxaparin incurs additional resources
  - A proportion of patients who are unwilling, or unable, to self-inject enoxaparin (8% in the UK,<sup>1</sup> 10% in Sweden<sup>14</sup>) receive daily outpatient nurse visits while receiving enoxaparin
  - In the UK, patients require full blood counts every second day to test for heparin-induced thrombocytopenia<sup>1</sup>
  - As an oral drug with no coagulation monitoring needs, rivaroxaban would not incur this resource use – enoxaparin is monitored for the occurrence of rare heparin-induced thrombocytopenia
- ◆ Rivaroxaban is administered after surgery, but the initial dose of enoxaparin is administered the day prior to surgery. In Sweden, research showed that 30% of patients in 80% of hospitals (24% in total) would save 1 day in hospital because they could be admitted on the day of surgery, rather than the day prior to surgery (Bayer data on file)
- ◆ Results were converted into euros using exchange rates from February 2009
- ◆ Quality-of-life weights associated with DVT<sup>15</sup> and long-term complications<sup>16</sup> were taken from a systematic literature review. These were adjusted depending on whether patients had undergone THR or TKR<sup>17</sup>
- ◆ Costs and outcomes beyond the first year were discounted at the rates suggested by relevant national reimbursement guidelines
- ◆ Probabilistic sensitivity analyses, where all variables in the model were varied simultaneously (to values reflecting their mean and coefficients of variation), were conducted to show the impact of variance on the model results

## Results

- ◆ After THR, 35 days' rivaroxaban produced per-patient savings ranging from approximately €4 in Sweden to €124 in the UK versus 35 days' enoxaparin. These cost savings were driven by the reduced number of symptomatic VTEs and savings associated with oral administration

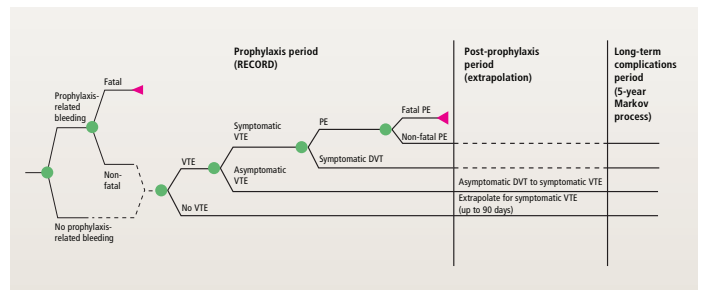


Figure 1. Prophylaxis and post-prophylaxis phases of the model. DVT, deep vein thrombosis; PE, pulmonary embolism; VTE, venous thromboembolism.

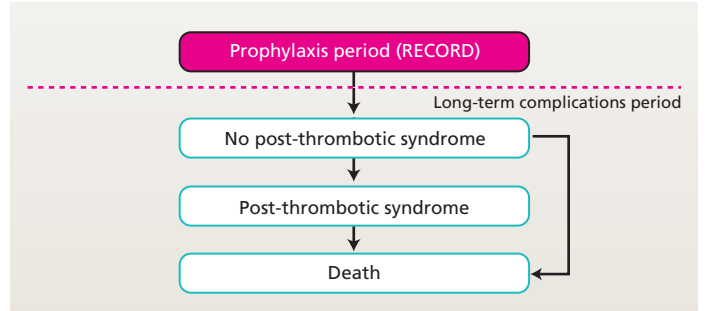


Figure 2. Long-term complications phase of the model. Note: recurrent venous thromboembolism is modeled as a transitory event.

- ◆ These cost savings were accompanied by improvements in health outcomes, as measured by quality-adjusted life years. The improved health outcomes and reduced costs associated with rivaroxaban after THR are shown in Table 1
- ◆ After TKR, 14 days' rivaroxaban produced per-patient savings ranging from €81 in Sweden to approximately €145 in the UK versus 14 days' enoxaparin. Again, these savings were driven by the reduced cost of managing symptomatic venous thromboembolic events. The reduced costs of oral administration also contributed to the cost savings in Sweden and the UK
- ◆ The substantial cost savings were accompanied by improved health outcomes, as demonstrated by the gain in quality-adjusted life years in each country (Table 2)
- ◆ The variation in the quality-adjusted life year results are due to different discount rates being used in different countries; whereas the quality-of-life weights used in Sweden reflected the Swedish population rather than the population in general
- ◆ Sensitivity analyses simultaneously varied key cost and clinical comparators to assess the robustness of the model to changes in the value of key variables
- ◆ In THR, rivaroxaban is cost saving and more effective in more than 60% of cases in Sweden and almost 100% of cases in the UK (Figure 3); in TKR, rivaroxaban is cost saving and more effective in 100% of cases (Figure 4)

Table 1. Cost-effectiveness of rivaroxaban versus enoxaparin after total hip replacement

	Rivaroxaban	Enoxaparin	Incremental
<b>UK cost-effectiveness analysis</b>			
Total costs	€330.45	€453.97	-€123.52
Quality-adjusted life years	3.5928	3.5887	0.0041
<b>Rivaroxaban saves €123.52 per patient and produces a gain of 0.0041 quality-adjusted life years per patient</b>			
<b>Sweden cost-effectiveness analysis</b>			
Total costs	€224.05	€228.25	-€4.20
Quality-adjusted life years	3.8673	3.8663	0.0009
<b>Rivaroxaban saves €4.20 per patient and produces a gain of 0.0009 quality-adjusted life years per patient</b>			

Table 2. Cost-effectiveness of rivaroxaban versus enoxaparin after total knee replacement

	Rivaroxaban	Enoxaparin	Incremental
<b>UK cost-effectiveness analysis</b>			
Total costs	€238.63	€383.18	-€144.55
Quality-adjusted life years	3.5342	3.5196	0.0146
<b>Rivaroxaban saves €144.55 per patient and produces a gain of 0.0146 quality-adjusted life years per patient</b>			
<b>Sweden cost-effectiveness analysis</b>			
Total costs	€135.29	€216.31	-€81.02
Quality-adjusted life years	3.8072	3.8043	0.0029
<b>Rivaroxaban saves €81.02 per patient and produces a gain of 0.0029 quality-adjusted life years per patient</b>			

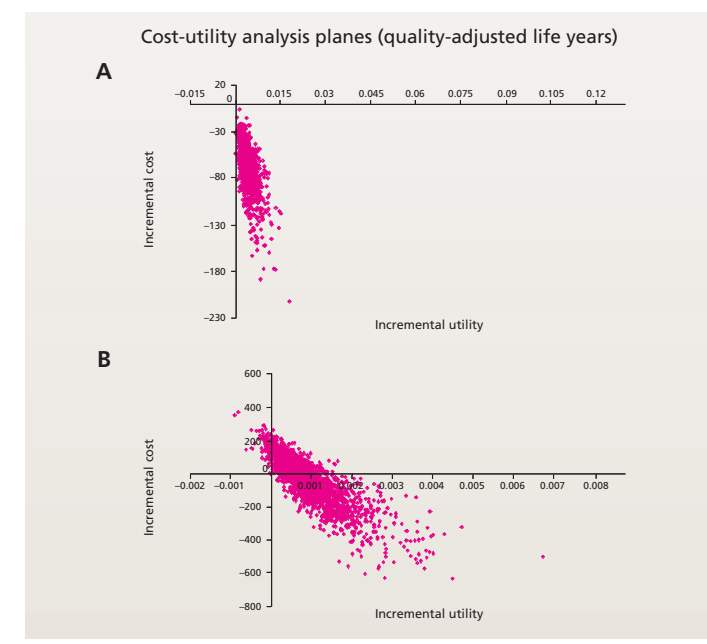


Figure 3. Plot of incremental cost versus incremental quality-adjusted life years: 35 days' rivaroxaban versus 35 days' enoxaparin after total hip replacement (RECORD1) in (A) the UK (£) and (B) Sweden (SEK).

## Conclusions

- ◆ By reducing venous thromboembolism and providing an oral alternative to subcutaneous enoxaparin, the use of rivaroxaban may result in healthcare cost savings and improved quality of life for patients in the European Union
- ◆ With possible savings of up to €145 per patient, and more than 400,000 procedures performed annually, the potential for savings to European Union healthcare systems is substantial
- ◆ Extensive sensitivity analyses show that these results are robust

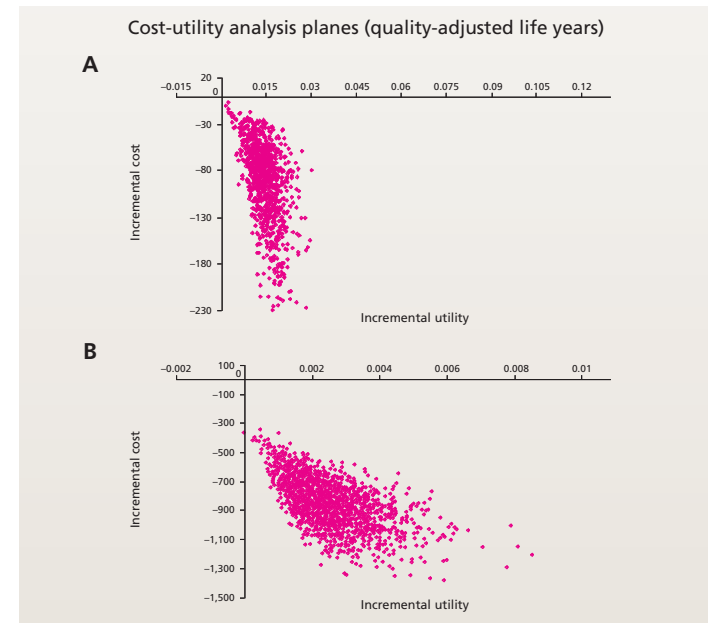


Figure 4. Plot of incremental cost versus incremental quality-adjusted life years: 14 days' rivaroxaban versus 14 days' enoxaparin after total knee replacement (RECORD3) in (A) the UK (£) and (B) Sweden (SEK).

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**Disclosure of conflict of interest**  
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