

# Economic impact of venous thromboprophylaxis with rivaroxaban after major orthopaedic surgery

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## Introduction

Thromboprophylactic regimens based on rivaroxaban – a novel, oral, direct Factor Xa inhibitor in advanced clinical development for the prevention of venous thromboembolism (VTE) after major orthopaedic surgery – were compared with subcutaneous (s.c.) enoxaparin (40 mg once daily) regimens in phase III randomized clinical trials following total hip replacement (RECORD1 and RECORD2),<sup>1,2</sup> or total knee replacement (RECORD3).<sup>3</sup> The three study designs are shown in Figure 1. Bleeding rates were similar in both treatment groups. In addition to the clinical benefits associated with reducing symptomatic VTE, significant economic benefits can be achieved because fewer healthcare resources may be required with rivaroxaban.

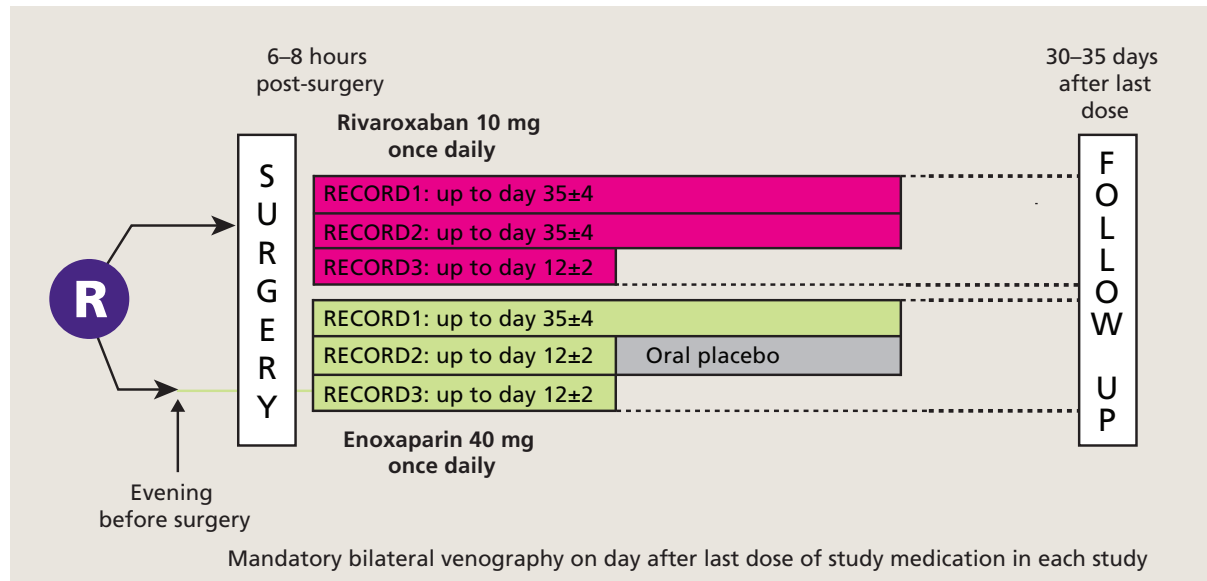


Figure 1. RECORD1–3 study designs. RECORD1 and RECORD2: total hip replacement; RECORD3: total knee replacement.

## Objectives

- An economic analysis was performed to assess the impact on non-drug healthcare costs in the US and UK associated with rivaroxaban regimens, compared with enoxaparin regimens, following total hip replacement and total knee replacement. This analysis incorporated the impact of differences in symptomatic VTE, and in monitoring and administration requirements between the regimens

## Methods

Data on the occurrence of symptomatic VTE (including deep vein thrombosis and pulmonary embolism) in patients given oral rivaroxaban or s.c. enoxaparin in the RECORD studies were used. These analyses were based on the safety population who underwent surgery. The impact of oral versus s.c. administration and reduced monitoring requirements was based on published studies in the UK<sup>4</sup> and the US.<sup>5</sup>

### Assumptions and costs included in the analysis

- For the UK only, it was assumed that full blood counts (FBCs) were undertaken every 3 days up to 15 days in patients receiving enoxaparin to monitor for heparin-induced thrombocytopenia<sup>6</sup>
- For costing purposes, the duration of hospitalization was assumed to be 5 days
- For the US and the UK, it was conservatively assumed that nurses would require 3 minutes per day to administer s.c. enoxaparin and train patients to self-inject for outpatient use
- Nursing times for s.c. administration of enoxaparin were taken from UK national guidelines.<sup>4</sup> The daily wages for US and UK nurses were estimated from published sources<sup>4,7</sup>
- Costs associated with symptomatic VTE, derived from published sources in the US<sup>8</sup> and the 2007 NICE Guidelines in the UK,<sup>4</sup> were used to estimate utilization of healthcare resources (Table 1)

Table 1. Weighted unit costs applied to healthcare resources utilization

	US	UK
Symptomatic venous thromboembolism*	\$10,724	£905
Full blood count (enoxaparin only) – cost per test	\$0	£4.04
Cost of administration and training (enoxaparin only) – cost per day	\$2.10	£1.05

\*Weighted unit costs per symptomatic venous thromboembolism for the year following surgery were calculated from incidence rates for symptomatic deep vein thrombosis and pulmonary embolism across all three RECORD trials. Costs for administration and training incurred during inpatient care for major orthopaedic surgery.

- Because rates of both major and non-major bleeding were similar in both treatment groups, it was assumed, for the purposes of analysis, that these rates were the same for both rivaroxaban and enoxaparin

### Costs excluded from the analysis

- Asymptomatic events costs were excluded from the analysis due to lack of evidence of their impact on healthcare resources use
- Costs associated with community nurse administration of s.c. enoxaparin in patients discharged from hospital unable to self-inject were excluded because of variations in the provision of such services between countries
- Indirect and long-term post-thrombotic event costs were excluded
- Acquisition costs for rivaroxaban and enoxaparin were excluded because the price of rivaroxaban has not yet been established

## Results

- Weighted unit costs per symptomatic VTE event were calculated from incidence rates across all three RECORD trials
- Applying these weighted unit costs to the incidence of symptomatic VTE in RECORD3, an incidence of 2.0% with enoxaparin and 0.7% with rivaroxaban (Figure 2) resulted in estimated costs for VTE management in the year following surgery of:
  - \$214.48 for enoxaparin and \$75.07 for rivaroxaban in the US, pro-rated per patient undergoing surgery
  - £18.10 for enoxaparin and £6.34 for rivaroxaban in the UK, pro-rated per patient undergoing surgery

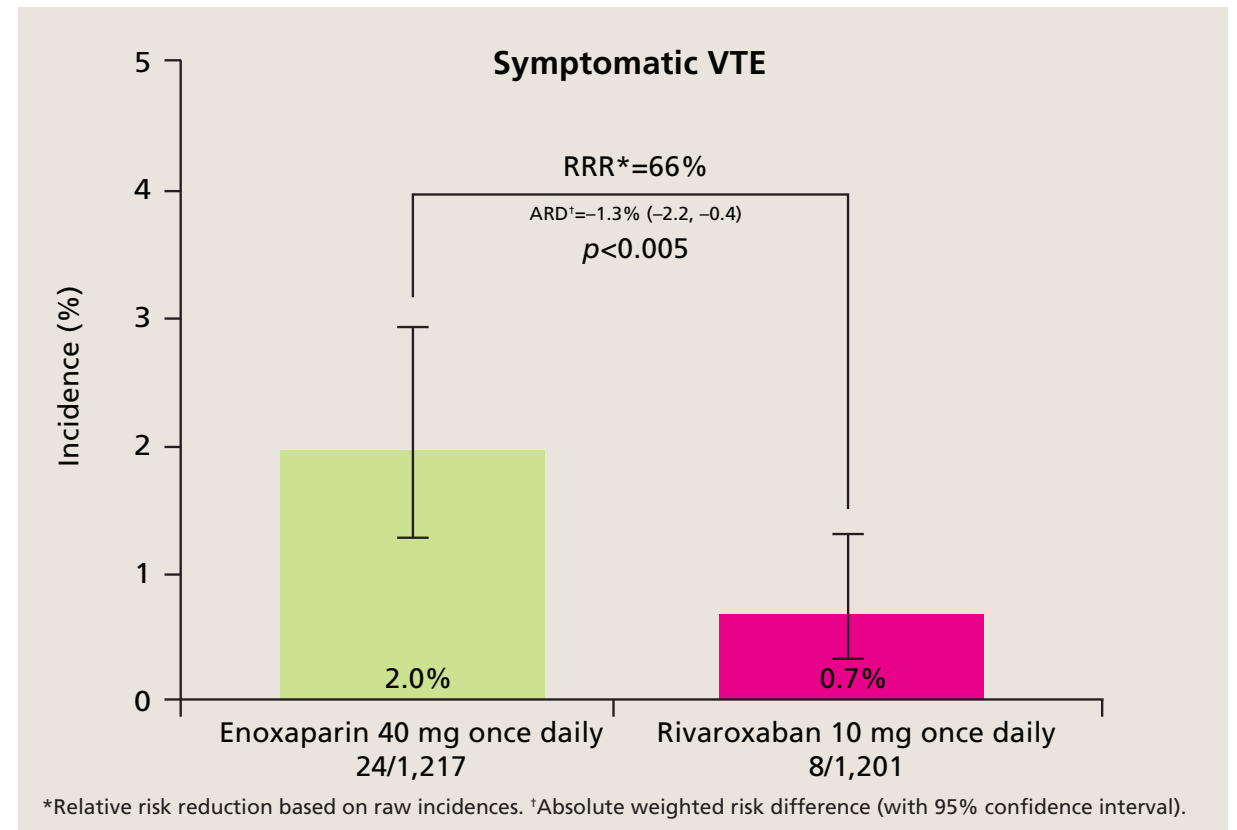


Figure 2. RECORD3 reduction in symptomatic venous thromboembolism (VTE) in the safety population (all patients randomized excluding those who did not undergo surgery; n=2,418).

- Costs for monitoring and training also differed between the US and UK, primarily due to the measurement of FBC in enoxaparin subjects; costs per admission for surgery were:
  - \$10.50 for enoxaparin and \$0 for rivaroxaban in the US
  - £25 for enoxaparin and £0 for rivaroxaban in the UK
- Therefore, the total pro-rated savings per patient for the year following surgery attainable with rivaroxaban from RECORD3 are \$149.91 in the US and £36.76 in the UK, based on the combined cost savings for both VTE management and monitoring and training
- Similarly, using the same cost estimates but the observed incidences of symptomatic VTE for RECORD1, RECORD2 and including RECORD3 yielded pro-rated savings per patient of \$31.95 to \$149.91 in the US and £26.81 to £36.76 in the UK (Table 2)

Table 2. Calculated costs of venous thromboembolism for year following surgery

		Enoxaparin	Rivaroxaban	Difference
RECORD1	US	\$64.12	\$32.17	\$31.95
	UK	£29.52	£2.71	£26.81
RECORD2	US	\$139.19	\$21.45	\$117.74
	UK	£35.86	£1.81	£34.05
RECORD3	US	\$224.98	\$75.07	\$149.91
	UK	£43.10	£6.34	£36.76

Based on weighted unit costs and observed symptomatic events from each trial (symptomatic venous thromboembolism was not significantly different between enoxaparin and rivaroxaban in RECORD1). RECORD2 compared extended prophylaxis with rivaroxaban (35±4 days) with short-term enoxaparin (12±2 days). Analyses were based on incidence of symptomatic events for the entire medication period for each study.

- Oral, once-daily dosing may enhance compliance and adherence to guideline-recommended treatment, and may reduce VTE events in the long term. The current model did not include this and may underestimate the actual savings from treatment with rivaroxaban

## Conclusions

- The impressive efficacy of oral rivaroxaban may be associated with marked per-patient reductions in healthcare costs following major orthopaedic surgery, and significant cost savings for healthcare services
- With over 650,000 patients in the US<sup>8</sup> and over 140,000 patients in England and Wales<sup>9</sup> undergoing hip and knee replacement annually, the potential cost savings with rivaroxaban are significant
- Based on these phase III data, rivaroxaban may be considered an appropriate oral agent for hospital-to-home VTE prophylaxis

## References and disclosures

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