

Cost-Effectiveness of Rivaroxaban for Prevention of Deep Vein Thrombosis and Pulmonary Embolism after Total Hip or Knee Replacement in US Patients

Louis M Kwong¹, Aurea Duran², Alex Diamantopoulos², Nishan Sengupta³, Michael Lees⁴

¹Harbor-UCLA Medical Center, Torrance, CA, USA; ²IMS Health, London, UK; ³Johnson & Johnson, CA, USA; ⁴Bayer HealthCare, Uxbridge, UK

Introduction

- The RECORD program compared rivaroxaban 10 mg once daily with subcutaneous enoxaparin 40 mg once daily (RECORD1, 2, and 3) or 30 mg every 12 hours (q12h; used in North America – RECORD4)¹⁻⁴
 - The primary outcome in all four studies was the composite of symptomatic or asymptomatic deep vein thrombosis (DVT; detected by mandatory, bilateral venography), non-fatal pulmonary embolism (PE), and all-cause mortality
- RECORD1 compared rivaroxaban with enoxaparin over 35 days in patients who underwent elective total hip replacement (THR).¹ RECORD2 compared long-term prophylaxis (35 days) with rivaroxaban with short-term prophylaxis (10–14 days followed by placebo) with enoxaparin in patients who underwent THR²
- RECORD3 compared rivaroxaban with enoxaparin as venous thromboembolism (VTE) prophylaxis over 10–14 days in patients who underwent elective total knee replacement (TKR).³ RECORD4 compared rivaroxaban with the more widely used enoxaparin regimen in North America (30 mg q12h) in patients who underwent elective TKR⁴
 - The incidence of the primary endpoint observed across these studies is shown in Figure 1
- The major bleeding rates observed with these two drugs across the RECORD studies were as follows:
 - In RECORD1, major bleeding rates were 0.3% and 0.1% for rivaroxaban and enoxaparin, respectively ($p=0.18$).¹ In RECORD2, major bleeding rates were similar (0.1%) between the two study groups²
 - In RECORD3, major bleeding rates were 0.6% and 0.5% for rivaroxaban and enoxaparin, respectively ($p=0.77$).³ In RECORD4, major bleeding rates were 0.7% and 0.3% for rivaroxaban and enoxaparin, respectively ($p=0.11$)⁴

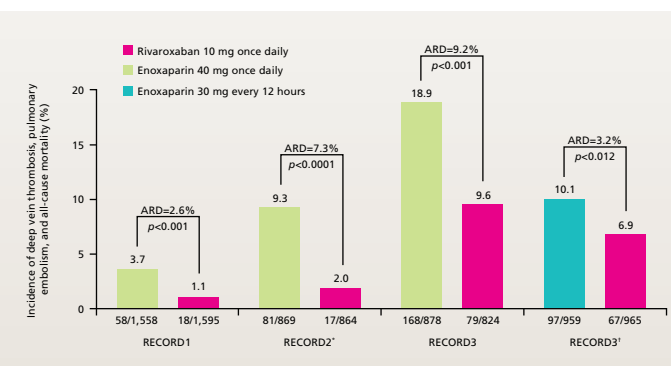


Figure 1. Incidence of the primary endpoint (any deep vein thrombosis, pulmonary embolism, and all-cause mortality) in the RECORD1–4 studies.¹⁻⁴ *RECORD2 compared extended prophylaxis with rivaroxaban against short-term prophylaxis with enoxaparin plus placebo. †RECORD4 compared rivaroxaban with the more widely used enoxaparin regimen in North America (30 mg every 12 hours). ARD, absolute risk difference.

Objective

- To demonstrate the cost-effectiveness of rivaroxaban after elective THR and TKR from the perspective of the US payer

Methods

- Economic decision models (Figure 2) were developed based on the efficacy and safety parameters from individual RECORD studies. Separate models were necessary because of the different treatment durations and doses with enoxaparin. The models followed patients for up to 1 year after THR or TKR surgery

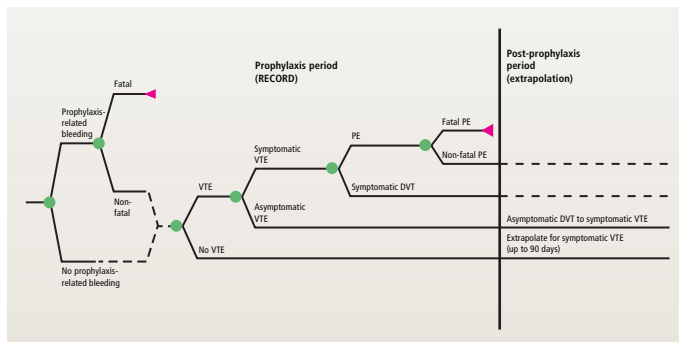


Figure 2. Economic decision models. DVT, deep vein thrombosis; PE, pulmonary embolism; VTE, venous thromboembolism.

- The clinical efficacy (DVT, non-fatal PE, and symptomatic venous thromboembolic events) and safety profiles of both drugs were obtained from the published RECORD studies,¹⁻⁴ whereas the incidence of VTE up to 90 days after surgery was extrapolated based on epidemiologic data⁵
 - The incidence of recurrent VTE and post-thrombotic syndrome beyond this period was based on clinical data derived from a prospective long-term follow-up study⁶
- Treatment costs for symptomatic VTE and major bleeding were taken from published data on managed care in the US,^{7,8} with all costs being inflated to 2007 dollars (Table 1). For costing purposes, the duration of hospitalization for THR (3 days) and TKR (4 days) was obtained from a published US orthopaedic registry⁹

Table 1. Selected costs related to venous thromboembolism and pulmonary embolism.^{9,10}

Event	Cost (\$)
Bleeding (prophylaxis related)	
Major bleeding (fatal or non-fatal)	3,828
Costs related to venous thromboembolism	
Treating deep vein thrombosis during hospitalization	11,676
Treating pulmonary embolism during hospitalization	16,538
Treating deep vein thrombosis post-discharge	8,180
Treating pulmonary embolism post-discharge	16,538
Treatment of recurrent venous thromboembolism	13,980

All costs in the model are inflated to 2007 dollars. Costs are per event.

- Because major bleeding requires physician visits and potentially an emergency room visit or hospitalization, which are costly, the economic models only included major bleeding costs
- It was conservatively assumed that no incremental nurse time or home visit costs were associated with subcutaneous enoxaparin injection in the primary analyses
- Additional analyses (sensitivity analysis) included incremental costs associated with home healthcare nurse visits to administer enoxaparin injections, based on other studies¹⁰ and clinical experience of VTE in the US
- Probabilistic sensitivity analysis (PSA) was performed to assess variations of treatment costs and significant and non-significant trial endpoints (including symptomatic events and major bleeding) and its impact on cost-effectiveness
 - PSA addresses the uncertainty around all observed variables (efficacy, safety from clinical trials, cost variables from published literature) used in the economic model and several simulations ran simultaneously using different values within the 95% confidence interval or a predefined range for treatment cost
- The duration of prophylaxis with rivaroxaban was assumed to be 35 days for THR patients and 14 days for TKR patients. As rivaroxaban is not yet available in the US, the analysis assumed similar daily drug acquisition costs to enoxaparin 40 mg once daily in the US

Results

- The 1-year analysis based on RECORD1 showed that rivaroxaban resulted in an average cost saving of \$82 and a reduction of six symptomatic events, both per 1,000 patients undergoing THR (Table 2)

Table 2. Cost savings based on the 1-year economic model[†]

	Oral rivaroxaban (10 mg once daily)	Subcutaneous enoxaparin (40 mg once daily)	Incremental
RECORD1	For 35 days	For 35 days	
Cost	\$894.86	\$977.14	-\$82.29
Symptomatic venous thromboembolic events [†]	0.0049	0.0107	-
Symptomatic venous thromboembolic events avoided [†]	-	-	-0.0058
RECORD2	For 35 days	For 10–14 days	
Cost	\$901.53	\$752.62 [‡]	\$148.91
Symptomatic venous thromboembolic events [†]	0.0065	0.0316	-0.0250
Incremental cost-effectiveness ratio	\$5,944.67 per symptomatic event avoided		
RECORD3	For 10–14 days	For 14 days	
Cost	\$482.46	\$767.02	-\$284.57
Symptomatic venous thromboembolic events [†]	0.0118	0.0300	-
Symptomatic venous thromboembolic events avoided [†]	-	-	0.0181
RECORD4	For 10–14 days	For 14 days	
Cost	\$501.50	\$792.93	-\$291.43
Symptomatic venous thromboembolic events [†]	0.0110	0.0126	-
Symptomatic venous thromboembolic events avoided [†]	-	-	0.0016

[†]It is conservatively assumed that there are no administrative or nursing monitoring costs relevant to the subcutaneous administration of enoxaparin.

[‡]Events per 1,000 patients undergoing total hip replacement.

[§]Based on 12 days' enoxaparin 40 mg acquisition costs.

- RECORD2 showed that long-term prophylaxis with rivaroxaban was associated with an incremental cost per symptomatic venous thromboembolic event avoided of \$5,945 (Table 2)
- Similar analysis based on RECORD3 demonstrated that rivaroxaban resulted in an average cost saving of \$285 and a reduction of 18 symptomatic events, both per 1,000 patients undergoing TKR (Table 2)
- RECORD4 versus enoxaparin (North American regimen of 30 mg q12h) demonstrated that rivaroxaban was associated with an average cost saving of \$291 and a reduction of 1.6 events, both per 1,000 patients undergoing TKR (Table 2)
 - These improvements were driven primarily by the reduced costs of hospitalization for symptomatic events
- Sensitivity analyses, including the costs associated with home nursing time (for the administration of subcutaneous enoxaparin in patients unable to self-inject) or training patients to self-administer subcutaneous enoxaparin, showed potential for more cost savings if patients receive oral rivaroxaban (Tables 3 and 4)
 - Published data suggest that home nursing visits for prophylaxis after hospital discharge cost \$100 for a course of enoxaparin¹⁰
- PSA based on RECORD2 suggested that rivaroxaban might be a cost-effective treatment option in 80% of cases (Figure 3) and that it might save costs in the remaining 20% of cases

Table 3. Cost savings including one-time home healthcare nursing costs related to injection

	Oral rivaroxaban (10 mg once daily)	Subcutaneous enoxaparin (40 mg once daily)	Incremental
RECORD3			
Cost	\$482.46	\$867.02	-\$384.56
Symptomatic venous thromboembolic events [†]	0.0118	0.0300	-
Symptomatic venous thromboembolic events avoided [†]	-	-	0.0181
RECORD4			
Cost	\$501.50	\$892.93	-\$391.43
Symptomatic venous thromboembolic events [†]	0.0110	0.0126	-
Symptomatic venous thromboembolic events avoided [†]	-	-	0.0016

[†]Events per 1,000 patients undergoing total hip replacement.

Table 4. Cost savings including nursing costs

	Oral rivaroxaban (10 mg once daily)	Subcutaneous enoxaparin (40 mg once daily)	Incremental
RECORD1			
Cost	\$894.78	\$1,076.82	-\$182.05
Symptomatic venous thromboembolic events [†]	0.0049	0.0107	-
Symptomatic venous thromboembolic events avoided [†]	-	-	0.0058
RECORD2			
Cost	\$901.35	\$851.70	\$49.65
Symptomatic venous thromboembolic events [†]	0.0065	0.0316	-
Incremental cost-effectiveness ratio	\$1,981 per symptomatic venous thromboembolic event avoided		

[†]Events per 1,000 patients undergoing total hip replacement.

Conclusions

- Despite the clinical benefits of extended prophylaxis for up to 5 weeks with enoxaparin, and its recommendations in the guidelines,¹¹ its use is limited in current clinical practice in the US for total hip replacement surgery⁹
- This analysis demonstrates that oral rivaroxaban has the potential to be cost-effective based on its superior efficacy over enoxaparin in US patients undergoing total hip replacement or total knee replacement surgery
- With more than 300,000 US patients undergoing total knee replacement surgery and 150,000 US patients undergoing total hip replacement surgery annually, the potential economic impact from an effective and cost-effective oral prophylaxis for venous thromboembolism may be very important
- PSA based on RECORD4, which used the North American regimen of enoxaparin (30 mg q12h in TKR), suggested rivaroxaban might be a cost-effective treatment option in 41% of cases and that it might save costs in the remaining 59% of cases
- PSA based on RECORD1 as well as RECORD3 suggested rivaroxaban is cost-effective in all scenarios

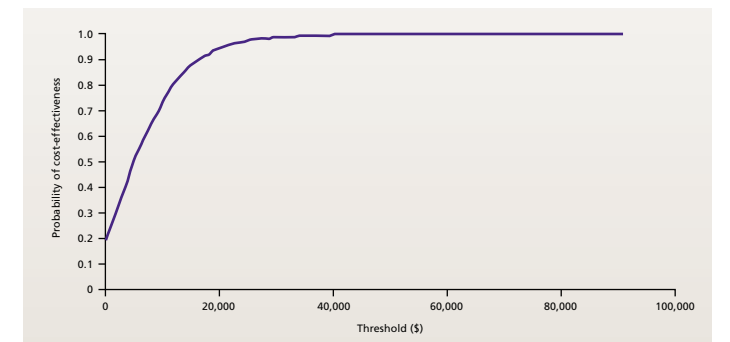


Figure 3. Probabilistic sensitivity analysis for RECORD2. Cost-effectiveness acceptability curve: 35 days' rivaroxaban versus 12 days' enoxaparin.

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Disclosure of conflict of interest

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