

Cost-Effectiveness of Rivaroxaban versus Enoxaparin for Thromboprophylaxis after Total Hip Replacement in Canada

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Introduction

- ◆ Venous thromboembolism (VTE; the composite of deep vein thrombosis [DVT] and pulmonary embolism [PE]) is the outcome of a clot, which forms within a vein and then travels through the blood vessels to a different site
- ◆ Total hip replacement (THR) surgery is an important risk factor for VTE¹
- ◆ With more than 28,000 THRs being performed in Canada annually, the potential public health risk is sizeable²
- ◆ Rivaroxaban is a novel, once-daily, direct inhibitor of Factor Xa that received marketing approval in the European Union and Canada in September 2008 for the prevention of VTE in adult patients undergoing elective THR and total knee replacement surgery. Unlike existing low molecular weight heparins such as enoxaparin, rivaroxaban is administered orally
- ◆ In two pivotal randomized controlled trials in patients undergoing THR, rivaroxaban reduced total VTE (composite of any DVT, non-fatal PE, and all-cause mortality) by 70% versus enoxaparin (both 35 days),³ whereas 35 days' rivaroxaban reduced total VTE by 79% and symptomatic VTE by 80% versus 14 days' enoxaparin followed by placebo.⁴ There were similar rates of major bleeding between rivaroxaban and enoxaparin in each study

Objective

- ◆ This study assesses the cost-effectiveness of rivaroxaban versus enoxaparin for the prevention of VTE after THR in Canada from a public payer's perspective over a 5-year time period based upon an economic model

Methods

- ◆ An economic model assessed the cost-effectiveness of rivaroxaban versus enoxaparin from the Canadian Ministry of Health perspective. The analysis initially models the period from surgery to up to 90 days after surgery (Figure 1), followed by long-term complications such as recurrent VTE and post-thrombotic syndrome (PTS) from 90 days to 5 years after surgery (Figure 2)

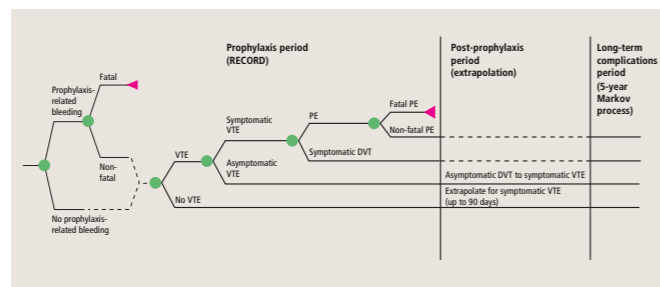


Figure 1. Prophylaxis and post-prophylaxis phases of the model. DVT, deep vein thrombosis; PE, pulmonary embolism; VTE, venous thromboembolism.

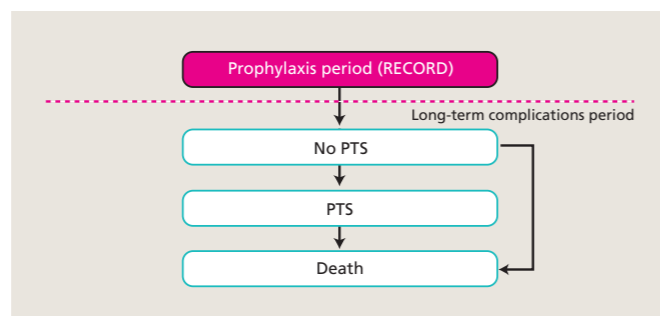


Figure 2. Long-term complications phase of the model. Note: recurrent venous thromboembolism is modeled as a transitory event. PTS, post-thrombotic syndrome.

- ◆ Event probabilities during prophylaxis were derived from RECORD1 and 2 data. The probability of asymptomatic events developing into symptomatic events after prophylaxis was based on published clinical data.⁵ The estimated risks of recurrent VTE and PTS beyond the initial 90 days after surgery were based on epidemiologic data⁶
- ◆ Resource consumption and associated costs of symptomatic events (2007 Canadian dollars [C\$]) were derived from published sources⁷⁻¹³ (Table 1)
- ◆ Previous research has shown that 19% of Canadian patients require daily nurse visits to inject subcutaneous enoxaparin.¹² It was assumed that reduced nursing time associated with oral administration in the inpatient setting with rivaroxaban did not lead to any cost offsets. This is a conservative analysis as it underestimates the benefit of oral administration
- ◆ Utilities (quality of life weights) associated with DVT and PE¹⁴ and long-term complications¹⁵ were taken from a systematic literature review. Utilities were adjusted for the fact that patients had undergone THR¹⁶
- ◆ Costs and outcomes beyond the first year were discounted at 5% per annum. Probabilistic sensitivity analyses were conducted. Event probabilities and utilities used a beta distribution, whereas costs used either a normal or gamma distribution

Table 1. Resource use and cost inputs for the economic model

	Resource use	Cost (C\$)	Source
Rivaroxaban	10 mg per day	9.92 per day	Rivaroxaban list price
Enoxaparin	40 mg per day	8.20 per day	ODB formulary
Enoxaparin administration	Daily homecare visits in outpatients (19% of patients)	58.27 per visit	Harrison <i>et al.</i> 1998; OACCAC
Bleeding	Non-fatal	6,396.59	OCCI
	Fatal	35,814.24	OCCI
DVT diagnosis	1 Doppler ultrasound	303.00 per test	Expert opinion; OCCI; OSB
PE diagnosis	1 lung scan (50% of patients)	810.55 per test	Skedgel <i>et al.</i> 2007; OCCI; OSB
	1 spiral CT scan (50% of patients)	513.90 per test	
Inpatient VTE	Extra hospital days: DVT	2,929 per stay	OCCI
	Extra hospital days: PE	7,105 per stay	OCCI
	Hospitalization due to DVT	8,472.14 per stay	OCCI
	Hospitalization due to PE	7,151.89 per stay	OCCI
	First hematologist visit	132.50	OSB
	Follow-up hematologist visit	82.90	OSB
	Outpatient visit	132.50	Skedgel <i>et al.</i> 2007; OSB
	Warfarin	0.30 per day	Skedgel <i>et al.</i> 2007; ODB formulary
	INR every 5 days (16.5 tests)	10.68 per test	Skedgel <i>et al.</i> 2007; BCMSCPS
	3 months' INR monitoring (1 test per month)	10.92 per test	Skedgel <i>et al.</i> 2007; BCMSCPS
Outpatient VTE	1 general practitioner visit	56.10 per visit	Skedgel <i>et al.</i> 2007; OSB
	1 specialist consultation	132.50 per visit	Skedgel <i>et al.</i> 2007; OSB
	2 specialist follow-ups	82.90 per visit	Skedgel <i>et al.</i> 2007; OSB
	2 complete blood counts	10.47 per test	Skedgel <i>et al.</i> 2007; BCMSCPS
	5 days' LMWH	14.37 per day	Skedgel <i>et al.</i> 2007; ODB formulary
	5 homecare visits (19% of patients)	58.27 per visit	Skedgel <i>et al.</i> 2007; OACCAC
	90 days' warfarin	0.30 per day	Skedgel <i>et al.</i> 2007; ODB formulary
	3 months' INR monitoring	10.92 per month	Skedgel <i>et al.</i> 2007; BCMSCPS
	17 INR tests	10.68 per test	Skedgel <i>et al.</i> 2007; BCMSCPS
Recurrent VTE	Same as post-discharge DVT		
PTS	Diagnosis	1,037.39	Caprini <i>et al.</i> 2003
	Treatment	773.83	Caprini <i>et al.</i> 2003

BCMSPS, British Columbia Medical Services Commission Payment Schedule; DVT, deep vein thrombosis; INR, international normalized ratio; LMWH, low molecular weight heparin; OACCAC, Ontario Association of Community Care Access Centres; OCCI, Ontario Case Costing Initiative; ODB, Ontario Drug Benefits; OSB, Ontario Schedule of Benefits; PE, pulmonary embolism; PTS, post-thrombotic syndrome; VTE, venous thromboembolism.

Table 2. Cost-effectiveness of rivaroxaban versus enoxaparin after total hip replacement in Canada

	Rivaroxaban	Enoxaparin	Incremental
35 days' rivaroxaban versus 35 days' enoxaparin (RECORD1)			
Medication costs	C\$356.85	C\$313.60	C\$43.26
Direct medical costs	C\$95.99	C\$404.18	-C\$308.19
Total costs	C\$452.85	C\$717.78	-C\$264.93
QALYs	4.18577	4.18520	0.0006
Symptomatic VTE events	0.0060	0.0130	-0.0070
Incremental cost per QALY gained			Rivaroxaban dominates
Incremental cost per symptomatic VTE averted			Rivaroxaban dominates
35 days' rivaroxaban versus 14 days' enoxaparin (RECORD2)			
Medication costs	C\$356.85	C\$110.11	C\$246.75
Direct medical costs	C\$78.21	C\$233.40	-C\$155.19
Total costs	C\$435.35	C\$345.01	C\$90.34
QALYs	4.1857	4.1830	0.0027
Symptomatic VTE events	0.0080	0.0385	-0.0306
Incremental cost per QALY gained			C\$33,323
Incremental cost per symptomatic VTE averted			C\$2,956

QALY, quality-adjusted life year; VTE, venous thromboembolism.

Results

- ◆ When comparing 35 days' rivaroxaban with 35 days' enoxaparin, based on RECORD1, rivaroxaban was associated with an incremental gain of 0.0006 quality-adjusted life years (QALYs) and a saving of C\$264.93 per patient
- ◆ Savings were driven by improved efficacy, reduced long-term complication costs, and reduced outpatient administration costs (Table 2)
 - Probabilistic sensitivity analyses showed dominance in 98% of cases versus 35 days' enoxaparin (Figure 3)
 - When compared with 14 days' enoxaparin followed by placebo, based on RECORD2, 35 days' rivaroxaban produced an incremental cost of C\$90.34 and a QALY gain of 0.0027 per patient. The increased drug costs associated with 35 days' rivaroxaban were partially offset by reduced costs of VTE events and long-term complications (Table 2). The resulting incremental cost per QALY gained is C\$33,323
 - In addition, rivaroxaban is cost-effective at a threshold of C\$50,000 per QALY in more than 70% of cases versus 14 days' enoxaparin (Figure 4)
 - These results demonstrate that baseline results are reliable and withstand changes to the value of key variables

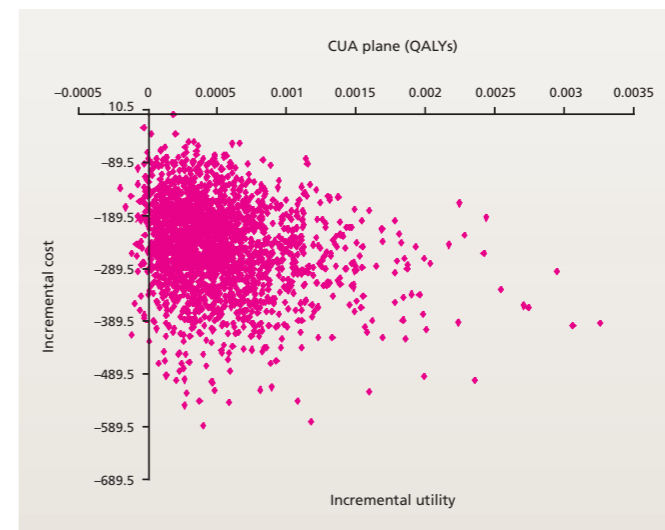


Figure 3. Cost-effectiveness scatter plot: 35 days' rivaroxaban versus 35 days' enoxaparin (RECORD1). CUA, cost-utility analysis; QALY, quality-adjusted life year.

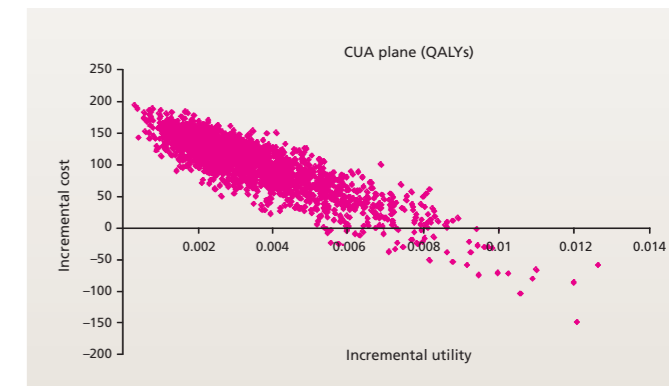


Figure 4. Cost-effectiveness scatter plot: 35 days' rivaroxaban versus 14 days' enoxaparin (RECORD2). CUA, cost-utility analysis; QALY, quality-adjusted life year.

Conclusions

- ◆ Rivaroxaban improves QALYs against both enoxaparin regimens
- ◆ Rivaroxaban is cost-saving against the 35-day regimen of enoxaparin and has a small incremental cost against the 14-day regimen of enoxaparin after THR
- ◆ Disaggregated results show that savings from long-term complications may be key drivers of cost offsets in Canada
- ◆ Probabilistic sensitivity analyses show that these results are robust

References and Disclosures

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