Taylor & Francis
Taylor & Francis Group

Journal of Medical Economics

ISSN: 1369-6998 (Print) 1941-837X (Online) Journal homepage: informahealthcare.com/journals/ijme20

A cost-analysis model for anticoagulant treatment in the hospital setting

Samir H. Mody, Lynn Huynh, Daisy Y. Zhuo, Kevin N. Tran, Patrick Lefebvre & Brahim Bookhart

To cite this article: Samir H. Mody, Lynn Huynh, Daisy Y. Zhuo, Kevin N. Tran, Patrick Lefebvre & Brahim Bookhart (2014) A cost-analysis model for anticoagulant treatment in the hospital setting, Journal of Medical Economics, 17:7, 492-498, DOI: 10.3111/13696998.2014.914032

To link to this article: https://doi.org/10.3111/13696998.2014.914032

Journal of Medical Economics Vol. 17, No. 7, 2014, 492–498

1369-6998
doi:10.3111/13696998.2014.914032

Article 0015.R1/914032

Original article

A cost-analysis model for anticoagulant treatment in the hospital setting

Samir H. Mody
Janssen Scientific Affairs, LLC, Raritan, NJ, USA

Lynn Huynh
Daisy Y. Zhuo
Kevin N. Tran
Analysis Group, Inc., Boston, MA, USA

Patrick Lefebvre
Groupe d'analyse, Ltée, Montréal, Québec, Canada

Brahim Bookhart
Janssen Scientific Affairs, LLC, Raritan, NJ, USA

Address for correspondence:
Lynn Huynh, Associate, Analysis Group, Inc., 111 Huntington Ave. Tenth Floor, Boston, MA 02199, USA. Tel.: 617-425-8189; Fax: 617-425-8001; lhuynh@analysisgroup.com

Keywords:
Cost-analysis – Anticoagulant – Economic model – Rivaroxaban

Accepted: 4 April 2014; published online: 30 April 2014
Citation: J Med Econ 2014; 17:492–8

Abstract

Background:
Rivaroxaban is the first oral factor Xa inhibitor approved in the US to reduce the risk of stroke and blood clots among people with non-valvular atrial fibrillation, treat deep vein thrombosis (DVT), treat pulmonary embolism (PE), reduce the risk of recurrence of DVT and PE, and prevent DVT and PE after knee or hip replacement surgery. The objective of this study was to evaluate the costs from a hospital perspective of treating patients with rivaroxaban vs other anticoagulant agents across these five populations.

Methods:
An economic model was developed using treatment regimens from the ROCKET-AF, EINSTEIN-DVT and PE, and RECORD1-3 randomized clinical trials. The distribution of hospital admissions used in the model across the different populations was derived from the 2010 Healthcare Cost and Utilization Project database. The model compared total costs of anticoagulant treatment, monitoring, inpatient stay, and administration for patients receiving rivaroxaban vs other anticoagulant agents. The length of inpatient stay (LOS) was determined from the literature.

Results:
Across all populations, rivaroxaban was associated with an overall mean cost savings of $1520 per patient. The largest cost savings associated with rivaroxaban was observed in patients with DVT or PE ($6205 and $2742 per patient, respectively). The main driver of the cost savings resulted from the reduction in LOS associated with rivaroxaban, contributing to ~90% of the total savings. Furthermore, the overall mean anticoagulant treatment cost was lower for rivaroxaban vs the reference groups.

Limitations:
The distribution of patients across indications used in the model may not be generalizable to all hospitals, where practice patterns may vary, and average LOS cost may not reflect the actual reimbursements that hospitals received.

Conclusion:
From a hospital perspective, the use of rivaroxaban may be associated with cost savings when compared to other anticoagulant treatments due to lower drug cost and shorter LOS associated with rivaroxaban.

Introduction

Rivaroxaban was approved by the US Food and Drug Administration in 2011 and is the first oral factor Xa inhibitor used to reduce the risk of stroke and blood clots among people with non-valvular atrial fibrillation (NVAF), treat deep vein thrombosis (DVT), treat pulmonary embolism (PE), reduce the risk of recurrence of DVT and PE, serve as a prophylaxis of DVT, which may lead to PE, after knee replacement surgery, and serve as a prophylaxis of DVT after hip replacement surgery[1]. Clinical studies have shown the efficacy of rivaroxaban compared

with other anticoagulant treatments for patients with NVAF, DVT, PE, knee, and hip replacement surgery, separately[2–7].

Each of these indications is associated with significant costs to the healthcare system; and cost analyses have been reported for each population independently[8–10]. For AF, over 460,000 hospitalizations were admitted each year with an estimated direct cost of $20,670 per AF patient[10]. In a retrospective claims study, the cost of hospitalization for primary DVT was $9805 per patient as compared to PE with an estimate of $14,146 per patient[8]. The American College of Chest Physicians (ACCP) recommended pharmacological prophylaxis for a minimum of 10 days up to 35 days after total knee or hip surgery[11]. The total hospital cost of knee or hip surgeries was $16,267 per patient and $17,588 per patient, respectively[9].

Despite the extensive literature describing the safety and efficacy profiles of rivaroxaban across these indications, there is a paucity of research assessing the utilization and cost of rivaroxaban across all five patient populations, specifically, in the inpatient setting. Given the substantial inpatient cost burden associated with each of these disease areas and the multiple indications that rivaroxaban may be used, an economic model that evaluates the cost of rivaroxaban across the five populations (NVAF, DVT, PE, knee, and hip surgeries) vs traditionally used anticoagulant agents (e.g., enoxaparin and warfarin) would be informative in the selection of inpatient anticoagulant treatment therapies. To fulfil this gap in the literature, we developed an economic model to evaluate the costs from a hospital perspective of treating patients with rivaroxaban vs other anticoagulant agents across these five populations.

Methods

An economic model from a hospital perspective was developed using treatment regimens from the ROCKET-AF, EINSTEIN-DVT and PE, and RECORD1-3 randomized clinical trials that compared rivaroxaban with vitamin K antagonist (e.g., warfarin), enoxaparin plus warfarin, and enoxaparin alone, respectively, among patients with NVAF, DVT, PE, knee, and hip surgeries (Table 1).

Study populations

The distribution of hospital admissions across the different study populations used in the model was derived from the 2010 Healthcare Cost and Utilization Project (HCUP) database, as described in Table 2. The HCUP distribution (24.6% for NVAF, 9.3% for DVT, 10.4% for PE, 38.2% for knee replacement surgery, and 17.5% for hip replacement surgery) was applied to a hypothetical cohort of 1636 inpatients, a sample approximating the total number of admissions per hospital in 2010 for these five conditions. We determined this number by dividing the average number of admissions for the five populations by the number of hospitals in the 2010 HCUP database.

Resource utilization and costs

Resource utilization and cost were evaluated from the hospital perspective to the extent that treatment and care occurred in the hospital setting. We classified cost into four categories: anticoagulant treatment, monitoring, inpatient stay, and administration and patient education.

Dosage and treatment schedules were obtained from the ROCKET-AF, EINSTEIN-DVT and PE, and

Table 1. Summary of pivotal trials of rivaroxaban by population.

Population	Trial	Treatment comparator	*n**	Age, years†	Male, *n* (%)
NVAF	ROCKET AF	Rivaroxaban	7131	73 (65–78)	4300 (60)
		Warfarin	7133	73 (65–78)	4301 (60)
DVT	EINSTEIN DVT	Rivaroxaban	1731	56 (16)	993 (57)
		Enoxaparin + Warfarin	1718	56 (16)	967 (56)
PE	EINSTEIN PE	Rivaroxaban	2419	58 (7)	1309 (54)
		Enoxaparin + Warfarin	2413	58 (7)	1247 (52)
Knee	RECORD3	Rivaroxaban	1220	68 (28–91)	363 (30)
		Enoxaparin	1239	68 (30–90)	418 (34)
Hip	RECORD1	Rivaroxaban	2209	63 (18–91)	989 (45)
		Enoxaparin	2224	63 (18–93)	982 (44)
	RECORD2	Rivaroxaban	1228	61 (18–93)	561 (46)
		Enoxaparin	1229	62 (19–93)	578 (47)

*The sample counts for the ROCKET AF, EINSTEIN DVT, and PE trials were based on the intention-to-treat population, while the RECORD1-3 trials were based on the safety population.
†The ROCKET AF trial reported the median age with interquartile range, EINSTEIN DVT, and PE reported mean age with SD, and the RECORD1-3 reported mean age with range.

Table 2. Population distribution.

	Population				
	NVAF	DVT	PE	Knee	Hip
ICD-9 code	427.31	451.11–451.19, 451.2, 453.40–453.42, 453.8–453.89, 453.9	415.11–415.19	81.54	81.51
Inputs from HCUP[21]					
Number of admissions	422,933	160,363	179,160	656,635	301,798
% as overall number of admissions	24.6%	9.3%	10.4%	38.2%	17.5%
Mean cost per inpatient stay (2010 USD)	$8474	$8304	$11,083	$15,924	$16,596
Mean length of stay (days)	3.5	4.8	5.4	3.3	3.4
Economic model inputs					
Number of admissions in the assumed cohort	403	152	170	625	286
Mean cost per day (2010 USD)	$2421	$1730	$2052	$4825	$4881

Table 3. Model inputs.

	Population					
	NVAF	DVT	PE	Knee	Hip	Source
Resource utilization						
Length of stay						
Rivaroxaban	3.0	5.0	6.0	3.0	3.0	Laliberte *et al.*[15]; Van Bellen *et al.*[16]; HCUPnet[21]
Warfarin	4.0	–	–	–	–	Laliberte *et al.*[15]
Enoxaparin	–	–	–	3.0	3.0	HCUPnet[21]
Enoxaparin/warfarin	–	8.0	7.0	–	–	EINSTEIN DVT/PE[2,3]
Frequency of PT/INR tests performed per day	1.0	1.0	1.0	–	–	Assumption
Unit costs						
Anticoagulant treatment cost						
Rivaroxaban (20/15/10 mg QD)	$8.84	–	–	$8.84	$8.84	AnalySource[13]
Rivaroxaban (2.5/5/15 mg BID)	–	$17.68	$17.68	–	–	AnalySource[13]
Generic enoxaparin (1 mg/kg BID)	–	$88.00	$88.00	–	–	RED BOOK[12]; assume 80 kg weight
Generic enoxaparin (40 mg DQ)	–	–	–	$22.00	$22.00	RED BOOK[12]
Generic warfarin (per day)	$0.12	$0.12	$0.12	–	–	RED BOOK[12]
Monitoring cost						
PT/INR monitoring	$5.56	$5.56	$5.56	–	–	Center for Medicare and Medicaid Services[14]
Inpatient stay cost						
Cost per day (2012 USD)	$2586	$1848	$2192	$5155	$5214	HCUPnet[21]

RECORD1-3 trials. Anticoagulant costs for rivaroxaban, enoxaparin, and warfarin were based on the Wholesale Acquisition Costs (WAC) and were obtained from RED BOOK[12] and AnalySource[13] (Table 3). Generic brands were selected for enoxaparin and warfarin. An average weight of 80 kg was assumed for the weight-based dosing of enoxaparin for patients treated for DVT and PE.

Associated costs of treatment regimens such as warfarin that required monitoring were included. The frequency of monitoring was once-per-day at an average cost of $5.56 per test[14]. Costs of anticoagulant and monitoring were restricted to the inpatient stay only. Outpatient costs were not included in the model. No adverse events and associated costs were considered in the model, as the respective clinical trials showed that the adverse event profile of rivaroxaban was similar to or better than its comparators, specifically, among DVT and PE patients[2–7].

Information on the difference in length of stay (LOS) for NVAF, DVT and PE patients receiving rivaroxaban and comparators was obtained from the published literature. Among adult patients with NVAF, a recent study using data from the Premier Perspective Comparative Hospital Database reported that rivaroxaban was associated with shortened inpatient stay by a median of 1 day compared with warfarin[15]. In this retrospective study, patients receiving rivaroxaban during initial hospitalization for NVAF were matched to patients receiving warfarin[15]. Rivaroxaban treated NVAF patients had a mean (median) hospital LOS of 4.46 (3) days compared with warfarin-treated NVAF patients who had a mean (median) hospital LOS of 5.27 (4) days[15]. In the

Table 4. Economic model of inpatient hospital cost (2012 USD) per patient.

Cost savings analysis ($)	Population					
	NVAF	DVT	PE	Knee	Hip	Overall*
Total costs under other agents	10,368	15,533	16,003	15,530	15,708	14,340
Total costs under rivaroxaban	7785	9328	13,260	15,490	15,669	12,821
Potential savings	2582	6205	2742	39	39	1520
Savings as a percentage of total costs under other agents	24.9%	39.9%	17.1%	0.3%	0.3%	10.6%

*The overall potential cost savings per patient is a weighted average of the five populations based on the HCUP hospital admission distribution from Table 2.

EINSTEIN DVT and PE trials, shortened LOS by 3 days ($p<0.0001$) and 1 day ($p<0.0001$), respectively, were observed for the initial hospitalization of patients treated with rivaroxaban compared with enoxaparin plus warfarin[16]. Differences in LOS for NVAF, DVT, and PE reported in these studies were included in this economic model. For knee or hip replacement surgery patients, differences in LOS were not available and an assumption of no difference in LOS among patients taking rivaroxaban and enoxaparin was made. Mean LOS for knee and hip replacement surgery patients were obtained from the HCUP database.

In the HCUP database, International Statistical Classification of Diseases, 9th Revision (ICD-9), was used to identify inpatient stay related to NVAF, DVT, PE, knee, and hip replacement surgeries. For each population, the mean inpatient cost per day was calculated by dividing the mean cost per inpatient stay by the mean LOS obtained from the HCUP database (Table 2). We computed cost of hospitalization in the model by taking the mean inpatient cost per day multiplied by LOS for each population. All costs were inflated to 2012 US dollars based on the medical care component of the Consumer Price Index.

Cost analysis

The economic model estimated the cost differences between rivaroxaban and other anticoagulants for the five populations. We assumed all patients were exclusively taking rivaroxaban or other anticoagulant treatments during hospitalizations. For each patient population, the proportion of the cost differences from each inpatient cost component (anticoagulant treatment, monitoring, and inpatient stay costs) was compared between treatment groups.

One-way sensitivity analyses were conducted by varying the difference in hospital LOS, the inpatient cost per day, and the proportion of patients receiving rivaroxaban in the model. For the hospital LOS, the upper bound of the sensitivity analysis was based on the difference in the 75th percentile LOS between rivaroxaban and comparators from the literature. For the lower bound, no difference in LOS between rivaroxaban and comparators was assumed for each population. For inpatient cost, mean cost per day was varied by ±50% from the base case values for the sensitivity analysis. Finally, we assumed that the lower bound was 50% for the proportion of patients receiving rivaroxaban.

Table 5. Simulated potential cost savings (2012 USD) per patient.

	Population					
	NVAF	DVT	PE	Knee	Hip	Overall*
Total	2582	6205	2742	39	39	1520
Anticoagulant treatment	−26†	617	511	39	39	126
Monitoring	22	44	39	0	0	14
Inpatient stay	2586	5544	2192	0	0	1380
Administration/ education/other	0	0	0	0	0	0

*The overall potential cost savings per patient is a weighted average of the five populations based on the HCUP hospital admission distribution from Table 2.
†A negative value indicates higher costs per patient for rivaroxaban.

Results

Across all populations, rivaroxaban was associated with an overall mean cost savings of $1520 per patient, or ~$2.4 million for the cohort. The estimated cost savings associated with rivaroxaban for the NVAF, DVT, PE, knee surgery, and hip surgery populations were $2582, $6205, $2742, $39, and $39 per patient, respectively (Table 4). The main driver of the cost savings resulted from the reduction in LOS associated with rivaroxaban, contributing to ~90% of the total savings (Table 5). Anticoagulant treatment contributed 8% of potential cost savings. The cost saving as a percentage of total cost was most impactful for NVAF, DVT, and PE (~25%, 40%, and 17%, respectively) due to both a reduction in the LOS and a decrease in the cost of anticoagulant for DVT and PE patients. The modest cost savings observed for knee and hip replacement surgeries were driven by differences in anticoagulant treatment costs (i.e., rivaroxaban vs generic enoxaparin).

Table 6. One-way sensitivity analyses—simulated potential cost savings per patient by varying input parameters.

Parameters	Parameter value		Cost savings under rivaroxaban ($)	
	Lower bound	Upper bound	Lower bound	Upper bound
LOS difference (days)*	0	NVAF: 1, DVT: 3, PE: 4	102	2233
Inpatient stay cost ($)				
All populations	–	–	830	2209
NVAF	1293	3879	1201	1838
DVT	924	2772	1262	1777
PE	1096	3289	1406	1634
Rivaroxaban usage rate	50%	100%	760	1520

*For the lower bound cost savings, no difference in LOS between rivaroxaban and comparators for each population was assumed. For the upper bound cost savings, the difference in the 75th percentile LOS between rivaroxaban and comparators for NVAF, DVT, and PE was applied.

Sensitivity analyses

The extent of cost savings based on the lower and upper bound for the LOS difference, inpatient cost per day, and percentage of rivaroxaban usage is illustrated in Table 6. Cost savings could be as high as $2233 per patient based on the sensitivity analyses examining the difference in LOS of 1, 3, and 4 days for NVAF, DVT, and PE, respectively. Even when no difference in LOS was assumed for NVAF, DVT, and PE patients, cost savings of $102 per patient were observed due to overall differences in medication costs, specifically, for patients with DVT, PE, hip, and knee surgeries. When the inpatient cost per day was varied by ±50% for NVAF, DVT, and PE patients, the total cost savings per patient ranged from $830–$2209. At rivaroxaban usage rate of 50%, the potential cost savings were $760 per patient.

Discussion

From a hospital perspective, rivaroxaban is associated with important cost savings based on the results of the current cost-analysis model across all five populations. Apart from the potential cost-savings that rivaroxaban offers, many key characteristics about the agent differentiate it from existing anticoagulants previously administered (i.e., enoxaparin, warfarin) for NVAF, DVT, PE patients, and prophylaxis for patients who had knee or hip replacement surgeries. Rivaroxaban is a novel orally-administered anticoagulant, has a rapid onset of action with maximum plasma concentrations achieved 1–4 h after oral administration, fixed dosing schedule, no known food interaction, minimum interactions with other pharmacologic agents, and does not require daily laboratory monitoring[17]. As a result of no daily monitoring of International Normalized Ratio (INR), hospital discharges may occur quicker for rivaroxaban-treated patients than other anticoagulant treatment because clinicians are not required to wait for patients to achieve a therapeutic INR[18].

In the economic model from the hospital perspective, patients receiving rivaroxaban resulted in less resource utilization for the hospital which translated to potential cost savings. The economic model showed that the majority of the cost savings resulted from the reduction in LOS observed in the NVAF, DVT, and PE patient populations. Anticoagulant treatment and monitoring costs also contributed to a small percentage of the overall cost savings. The cost of anticoagulant treatment was lower than the generic enoxaparin for DVT, PE, knee, and hip replacement surgery patients, while it was higher for NVAF patients (i.e., when compared to generic warfarin).

Consistent with the literature, Bullano *et al.*[19] found that over 50% of the cost of the VTE follow-up management was driven by LOS and shortening LOS would reduce the overall cost to treat VTE patients. The sensitivity analyses examining the LOS difference across NVAF, DVT, and PE showed that the potential cost-savings at the upper bound of LOS difference could be as high as $2233 per patient or ~$3.5 million for the cohort. When no difference in LOS across the five populations was assumed, the economic cost of treating patients with rivaroxaban was still cost-saving when patients received rivaroxaban (cost-saving of $102 per patient or $167,434 for the cohort). This finding suggests that, even with no difference in LOS, a small cost saving may be incurred due to lower anticoagulant treatment costs among patients receiving rivaroxaban compared with other anticoagulant treatments.

For patients who had knee or hip replacement surgeries, no difference in LOS was conservatively assumed; thus, cost savings resulted from the difference in cost between rivaroxaban and generic enoxaparin treatment. Beyer-Westendorf *et al.*[20] compared LOS as an end-point among knee and hip replacement patients taking rivaroxaban and a low-molecular-weight heparin (LMWH). The study utilized the ORTHO-TEP registry from 2006–2011 and found that patients on rivaroxaban had shorter LOS compared to LMWH patients (8.3 days vs 11.08 days, $p < 0.001$). Because clinical practice patterns may not be

representative of that in the US, we did not apply the LOS data to the knee and hip replacement patient population. We took a conservative approach and assumed no difference in the LOS between rivaroxaban and the comparator agent for patients receiving knee or hip replacement surgeries. Furthermore, costs for administration were assumed to be the same across the five populations in the model. Additional potential cost savings may be observed and not accounted for in the model from the reduction in patients' burden and clinicians' workload because injection or INR monitoring is not required for patients receiving rivaroxaban.

The model assumed that all patients received rivaroxaban. The assumption of 100% rivaroxaban usage rate may not be observed in the 'real-world' setting because of physicians' treatment patterns and patients' conditions. For example, Weitz and Gross[17] provided a table to assist physicians in selecting anticoagulants based on patient characteristics. If patients were stable on anticoagulant treatment such as warfarin and INR values were mostly in the therapeutic range, then there is less need to choose rivaroxaban unless the patient preferred the convenience of an oral anticoagulant that does not require monitoring. To address the variability in the percentage of patients receiving rivaroxaban, sensitivity analyses were performed and showed that cost savings remained even when a rivaroxaban usage rate was lower.

Several strengths are worth highlighting in this study. The economic model, specifically, focused on inpatient costs that occurred during hospitalization. We estimated potential cost savings across five populations in one model. The assumptions in the model could be adjusted to apply to a hospital setting with different patient distribution. In addition, the robustness of the cost savings observed was tested across several parameters in the sensitivity analyses.

This study has a few notable limitations. Firstly, the economic model is a representation of costs incurred in the hospital for patients receiving rivaroxaban or other anticoagulant treatments. Of note, the average LOS cost utilized may not represent the cost of the last days of a patients' hospitalization, as the reduction in LOS does not save an 'average day'. Hence, sensitivity analyses were conducted varying the cost per day across patient population. The mean cost per inpatient day was assumed to be constant over the course of the inpatient stay. In a real-world setting, it is possible to observe high cost in hospital treatment and care during the earlier part of hospital stay than on the day of hospital discharge. Our assumption did not account for differences in resource utilization between the time of hospital admission and the time of hospital discharge. Secondly, as clinical trials that compared rivaroxaban to other anticoagulant treatment showed that the adverse event profile for patients treated with rivaroxaban was similar to its comparators[2–7], only initial hospitalization treatments in the inpatient setting were captured and accounted for in the cost model. Thirdly, the model assumed a distribution of anticoagulant indications using US average hospital admissions, which may not be generalizable to all hospitals, where practice patterns may vary. Table 4 provides a breakdown of costs for each population and the potential cost savings that a hospital may expect for the patient population. Finally, the model assumed that the diagnosis was mutually exclusive. In a real-world setting, patients may have more than one of these conditions.

Conclusion

The economic model showed that administering rivaroxaban in the inpatient setting offered cost savings for the hospital. From a hospital perspective, the use of rivaroxaban may be associated with lower cost when compared to other anticoagulant treatments due to lower drug cost and shortened hospital LOS associated with rivaroxaban.

Transparency

Declaration of funding

Financial support for this study was provided by Janssen Scientific Affairs, LLC.

Declaration of financial/other relationships

Patrick Lefebvre, Kevin N. Tran, Daisy Y. Zhuo, and Lynn Huynh are employees of Analysis Group, Inc., a consulting company that has received research grants from Janssen Scientific Affairs, LLC. Brahim K. Bookhart and Samir H. Mody are employees of Janssen Scientific Affairs, LLC.

Acknowledgments

No assistance in the preparation of this article is to be declared.

References

1. Janssen Pharmaceuticals, Inc. Xarelto Prescribing Information [online]. 2012. Available at http://www.xareltohcp.com/sites/default/files/pdf/xarelto_0.pdf. [Last accessed 13 March 2013]
2. Bauersachs R, Berkowitz SD, Brenner B, et al. Oral rivaroxaban for symptomatic venous thromboembolism. N Engl J Med 2010;363:2499-510
3. Buller HR, Prins MH, Lensin AW, et al. Oral rivaroxaban for the treatment of symptomatic pulmonary embolism. N Engl J Med 2012;366:1287-97
4. Eriksson BI, Borris LC, Friedman RJ, et al. Rivaroxaban versus enoxaparin for thromboprophylaxis after hip arthroplasty. N Engl J Med 2008;358:2765-75
5. Kakkar AK, Brenner B, Dahl OE, et al. Extended duration rivaroxaban versus short-term enoxaparin for the prevention of venous thromboembolism after total hip arthroplasty: a double-blind, randomised controlled trial. Lancet 2008;372:31-9
6. Lassen MR, Ageno W, Borris LC, et al. Rivaroxaban versus enoxaparin for thromboprophylaxis after total knee arthroplasty. N Engl J Med 2008;358:2776-86
7. Patel MR, Mahaffey KW, Garg J, et al. Rivaroxaban versus warfarin in nonvalvular atrial fibrillation. N Engl J Med Sep 2011;365:883-91

8. Spyropoulos AC, Lin J. Direct medical costs of venous thromboembolism and subsequent hospital readmission rates: an administrative claims analysis from 30 managed care organizations. JMCP 2007;13:475-86
9. Kozma CM, Slaton T, Paris A, et al. Cost and utilization of healthcare services for hip and knee replacement. J Med Econ 2013;16:888-96
10. Kim MH, Johnston SS, Chu BC, et al. Estimation of total incremental health care costs in patients with atrial fibrillation in the United States. Circulation. Cardiovasc Qual Outcome 2011;4:313-20
11. Falck-Ytter Y, Francis CW, Johanson NA, et al. Prevention of VTE in orthopedic surgery patients: Antithrombotic Therapy and Prevention of Thrombosis, 9th edn: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest 2012;141(2 Suppl):e278S-325S
12. RedBook. Truven Health Analytics: Average Wholesale Price (AWP). [online]. Available at http://sites.truvenhealth.com/redbook/index.html. [Last accessed 18 October 2012]
13. AnalySource. AnalySource online: the online resource for drug pricing and deal information. [online]. Available at http://www.analysource.com. [Last accessed 3 January 2013]
14. Clinical Diagnostic Laboratory Fee Schedule. Baltimore, MD: Center for Medicare and Medicaid Services, 2012. http://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/ClinicalLabFeeSched/clinlab.html. Accessed September 4, 2012
15. Laliberte F, Pilon D, Raut MK, et al. Hospital length of stay: is rivaroxaban associated with shorter inpatient stay compared to warfarin among patients with non-valvular atrial fibrillation? Curr Med Res Opin 2014;30:645–53
16. van Bellen B, Bamber L, Correa de Carvalho F, et al. Reduction in the length of stay with rivaroxaban as a single-drug regimen for the treatment of deep vein thrombosis and pulmonary embolism. Curr Med Res Opin 2014;30:829–37
17. Weitz JI, Gross PL. New oral anticoagulants: which one should my patient use? Hematology/the Education Program of the American Society of Hematology. American Society of Hematology. Education Program 2012;2012:536-40
18. Aujesky D, Roy PM, Verschuren F, et al. Outpatient versus inpatient treatment for patients with acute pulmonary embolism: an international, open-label, randomised, non-inferiority trial. Lancet 2011;378:41-8
19. Bullano MF, Willey V, Hauch O, et al. Longitudinal evaluation of health plan cost per venous thromboembolism or bleed event in patients with a prior venous thromboembolism event during hospitalization. J Manag Care Pharm 2005;11:663-73
20. Beyer-Westendorf J, Lutzner J, Donath L, et al. Efficacy and safety of thromboprophylaxis with low-molecular-weight heparin or rivaroxaban in hip and knee replacement surgery: findings from the ORTHO-TEP registry. Thromb Haemost 2013;109:154-63
21. National statistics - principal diagnosis only. Outcomes by ICD-9-CM diagnosis codes. Rockville, MD: Agency for Healthcare Research and Quality, 2012. http://hcupnet.ahrq.gov/HCUPnet.jsp. Accessed August 31, 2012

