Prevention of venous thromboembolism in hospitalised patients: Analysis of reduced cost and improved clinical outcomes.

ABSTRACT

The impact of implementing a guideline on venous thromboembolism (VTE) prophylaxis was evaluated in a metropolitan private hospital with a before and after intervention study. This subsequent study aimed to identify if improved prophylaxis rates translated into cost savings and improved clinical outcomes. A conceptual decision tree analytical model incorporating local treatment algorithms and clinical trial data was used to compare prophylaxis costs and clinical outcomes before and after the guideline implementation. The study analysed data from 21,942 medical and surgical patients admitted to a 250 bed acute care private hospital in Sydney, Australia. The modelled simulation estimated the incidence of symptomatic deep vein thrombosis (DVT) and pulmonary embolism (PE) as well as adverse events such as heparin-induced thrombocytopenia (HIT), post-thrombotic syndrome (PTS), major bleeding, and mortality. The costs of prophylaxis therapy and treating adverse events were also calculated. The improvement in prophylaxis rates following the implementation of the guideline was estimated to result in 13 fewer deaths, 84 fewer symptomatic DVTs, 19 fewer symptomatic PEs, and 512 fewer hospital bed days. Improved adherence to evidence-based prophylaxis regimens was associated with overall cost savings of $245,439 over 12 months. We conclude that improved adherence to evidence-based guidelines for VTE prophylaxis is achievable and is likely to result in fewer deaths, less VTE events, and a significant overall cost saving.

BACKGROUND

Venous thromboembolism (VTE) is the collective term used to describe deep vein thrombosis (DVT) and pulmonary embolism (PE). It is a complex vascular condition which poses a considerable challenge to the healthcare system, resulting in significant mortality, morbidity, and healthcare resource expenditure. Although the exact incidence of VTE is unknown, it is believed there are approximately 1 million cases of VTE in the United States each year resulting in 300,000 deaths annually.[1] VTE is also linked to the development of a number of debilitating chronic cardiopulmonary and vascular health conditions such as pulmonary hypertension and post thrombotic syndrome (PTS).[2] The economic burden of the disease is also considerable, costing the health care system in the United States an estimated $1.5 billion/year.[3]

VTE is primarily a problem for hospitalised or recently hospitalised patients. The reported incidence of VTE in the hospital population is 100 times greater than the general community.[4] In fact, studies reveal that without any form of VTE prophylaxis the rate of objectively confirmed, hospital-acquired VTE is approximately 10% to 40% in medical and general surgery patients and 40% to 60% in major orthopaedic surgery patients.[5] This results in 10% of all in-hospital deaths which makes VTE the single most preventable cause of hospital-related mortality.[6] VTE is now internationally recognised as the number one priority patient safety issue.[7]

VTE in hospitalised patients is almost entirely preventable when the appropriate prophylaxis is provided to those at-risk.[5, 7-9] There are a number of national and international guidelines [5, 7-9] which provide evidence-based recommendations for the use of chemoprophylaxis such as low molecular weight heparin (LMWH), or low-dose

unfractionated heparin (LDUH), however, these guidelines are often not adhered to in clinical practice. An international audit of 70,000 patients identified that only 50% of at-risk patients were receiving the appropriate prophylaxis.[10]

A significant evidence practice gap was identified in our own private hospital in Sydney Australia. We found that only 62% of surgical patients and 19% of medical patients were receiving the recommended VTE prophylaxis. In an effort to improve prophylaxis rates our organisation undertook a hospital guideline implementation project.[11] Following that study, we used a conceptual decision tree analytical model to determine whether the changes brought about by the guideline implementation project translated into cost savings and improved clinical outcomes. Decision tree analytical models offer a systematic quantitative approach for assessing the relative value of one or more health care interventions and are commonly used to help determine health care policies that provide the best outcomes and the most value in certain clinical settings.[12]

Overview of the evidence implementation project

The implementation was conducted in a 250 bed acute care private hospital in Sydney Australia. The hospital has approximately 20,000 admissions annually with a case mix of 70% surgical and 30% medical patients. Forty five percent of the patient population is over 65 years of age. The hospital does not offer maternity, paediatric, or trauma services but all other major medical and surgical specialties are provided.

The aim of the project was to implement an evidence-based VTE prevention guideline and improve VTE prophylaxis rates for all medical and surgical inpatients. An iterative practice improvement method based on the model described by Grol et al[13] was

employed (see Figure 1). This method uses qualitative and quantitative approaches to identify, diagnose, and overcome local barriers to evidence-based care.

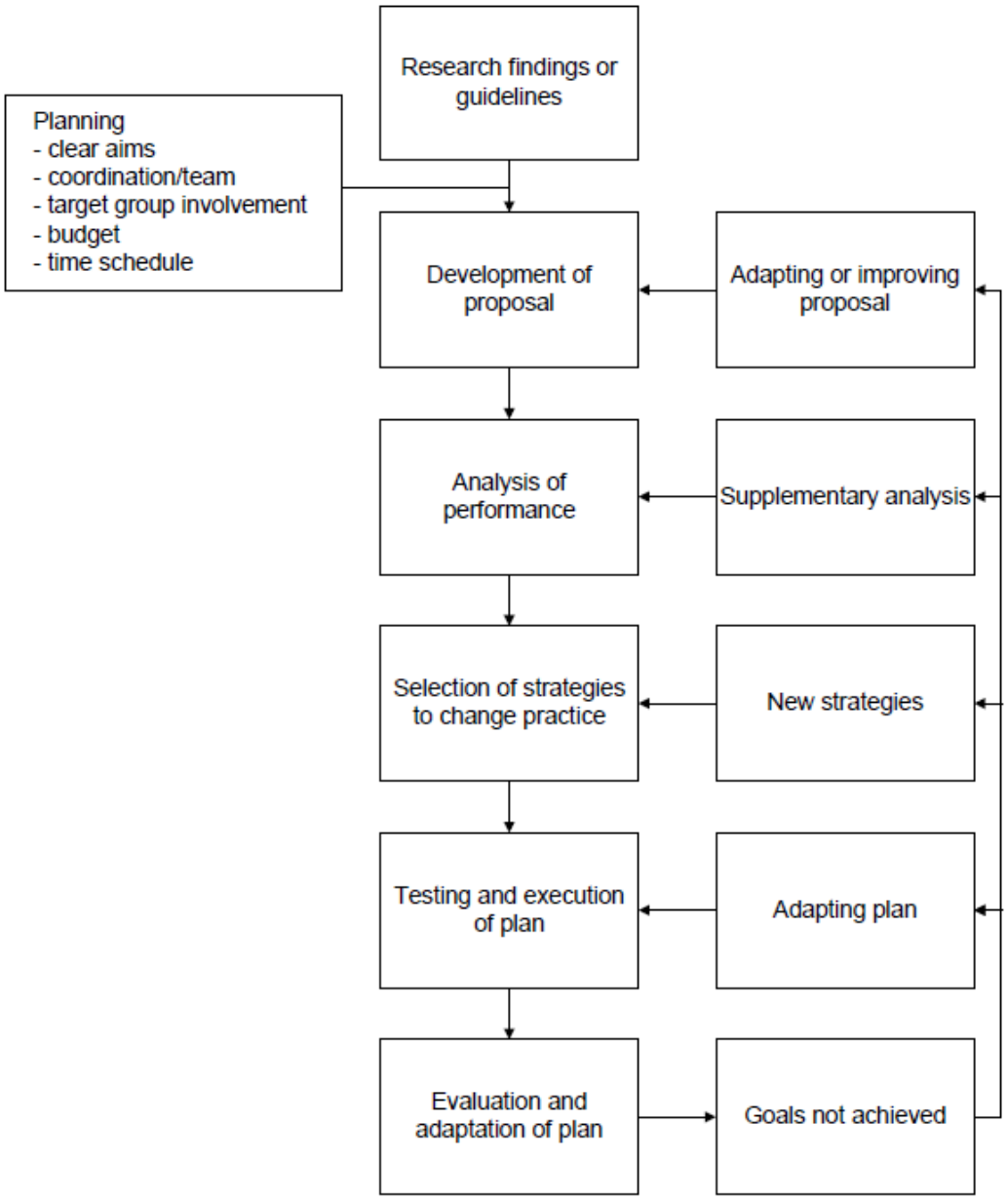

Figure 1: The iterative practice improvement method based on the model described by Grol et al.

Structured brain storming sessions were conducted with a multidisciplinary group of clinicians (medical, nursing, pharmacy, allied health) and managers to identify local barriers to the implementation of the guideline and to identify possible change strategies to overcoming these barriers. Four barriers were identified during the session and included a lack of motivation to change; a lack of systems support; a knowledge and awareness deficit; and disputed evidence. Evidence-based change strategies were selected from the literature on effective guideline implementation [14, 15] and incorporated into a multifaceted intervention. The strategies were:

- Audit and feedback: The results of the baseline audit and of a midpoint 'snapshot' audit were fed back to the clinicians in short presentations.
- Documentation and decision support aids: A tool for assessing VTE risk and choosing appropriate prophylaxis (based on the national VTE prevention guideline[9]) was developed and printed in the medication chart. A reminder system incorporating VTE risk alert stickers was also implemented.
- Provider education: A series of education sessions was delivered to all departments to raise VTE awareness and train staff in the use of the risk assessment and decision support tool. This was complemented by an in-house multidisciplinary VTE prevention conference with expert speakers invited from across the country.
- Local policy and procedure: A hospital-wide policy on VTE prevention which clearly outlined roles and responsibilities was developed and promulgated.

The proportion of orthopaedic, general surgical and medical patients receiving appropriate prophylaxis prior to the guideline implementation and 12 months following implementation was assessed in clinical audits by an experienced registered nurse. The

primary project measure was the percentage of patients receiving appropriate VTE prophylaxis. The audit results were entered into Statistical Package for the Social Sciences (IBM SPSS Statistic version 18) and compared using Chi square or Fisher's exact test.

The project resulted in significant changes from baseline to follow-up. The proportion of all patients who received appropriate VTE prophylaxis increased by 19%, from 49% at baseline to 68% at follow-up (p=0.02). The improvement was similar for both surgical and medical patients with a 21% increase for surgical patients and a 26% increase for medical patients (p=0.02 and p=0.05, respectively). The proportion of all patients receiving appropriate pharmacological prophylaxis increased by 20%, from 61% at baseline to 81% at follow-up (p=0.01). Of this, surgical patients' prophylaxis rates increased by 26%, while medical patients' rates increased by only 13% (p=0.01 and p=0.26, respectively).

The results of this study were then evaluated using a decision tree analytic economic model which incorporated local audit data, national VTE associated Diagnostic Related Group costing data and freely available clinical trial data to determine how the improvement in prophylaxis rates translated into cost savings and improved clinical outcomes.

METHOD

Clinical and economic modelling

A conceptual decision tree analytical model was used to evaluate the impact on cost and clinical outcomes of changes in VTE prophylaxis regimens (LMWH, LDUH, or no

prophylaxis) resulting from the implementation of a VTE prophylaxis guideline. The model was validated by thirty clinicians across Australia to ensure that the structure, inputs and outputs of the model were relevant to the Australian clinical setting.

Data on the prophylaxis regime of medical, general surgical and orthopaedic patients admitted to our hospital between January 2010 and January 2011 was entered into the model (n=21,942). The efficacy and safety of the prophylaxis regimens included in the model were assessed via a mixed treatment comparison of publicly available clinical trial data.[16-21] This method enabled the comparison of prophylaxis regimes that have not been directly compared in head-to-head studies.[22] This data was also used to estimate the incidence of VTE (symptomatic DVT and PE) and costs of prophylaxis as well as adverse events such as HIT, PTS, prophylaxis and treatment related major bleeding, and mortality. Treatment costs in relation to DVT, PE, major bleeds, HIT, and PTS were based on the Australian register of Diagnosis Related Groups for Private Hospitals that are associated with treatment for VTE related events as well as hospital specific costs for the included prophylaxis regimens.[23]

Structure of the decision tree

Our decision tree consisted of three pathways, one for each prophylaxis option (LMWH, LDUH, and no prophylaxis). The decision tree begins at the far left with the initial decision node (represented by the circle). Decision nodes represent the points at which alternative actions can be selected, with each alternative action represented by a separate branch of the decision tree. Possible outcomes resulting from a particular intervention are defined at chance nodes (represented by a rectangle). Each event emanating from a given chance node is assigned a value which represents the

probability of that event occurring. The sum of the probabilities for all possible events from the same chance node must equal one, as ~~the~~ all events must be mutually exclusive and exhaustive. For example, in Figure 2, patients will either die (probability 0.3) or survive (probability 0.7) their asymptomatic PE. The end of a branch of the decision tree is represented by a terminal node (represented by a side-house). Pay-offs (costs) were assigned to each branch of the decision tree based on data from the Australian register Diagnosis Related Groups for Private Hospitals.

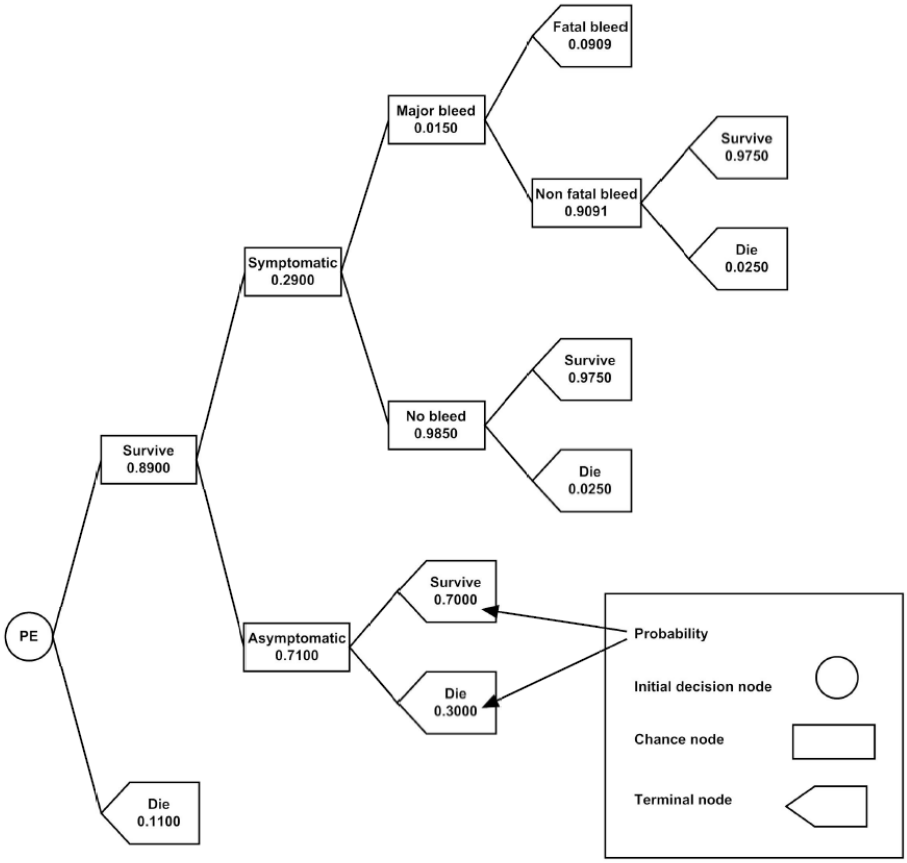

Figure 2: Structure of the decision tree analytic model for VTE prevention in surgical and high-risk medical patients when patients experience a PE (PE= pulmonary embolism).

Analysis of the decision tree

The cost-effectiveness of VTE prophylaxis following the implementation of the guidelines was analysed via a 'folding back and averaging' process. The weighted average net value for each decision node of the three pathways was calculated starting from the terminal node of each branch working backwards to the initial node. The weighted average net value is the sum of the pay-offs (costs) weighted by the probability of their occurrence. This process was repeated working backwards to the initial node for each branch of the decision tree and then comparing the expected results from each of the three pathways (LMWH, LDUH, and no prophylaxis). This process of folding back and averaging is standard for decision-tree analysis.[12]

RESULTS

Actual project outcomes

The proportion of orthopaedic, general surgical and medical patients receiving a particular prophylaxis regimen (either LMWH, LDUH, or no prophylaxis) prior to the guideline implementation and ~~at~~ 12 months following implementation are shown in Table 1. There was an increase in the percentage of orthopaedic patients who received no prophylaxis at follow-up (21% at baseline, 25% at follow-up). This was related to a decrease in patients receiving LDUH (5% at baseline, 0% at follow-up) which was not countered by an equivalent increase in patients receiving LMWH (74% at baseline, 75% and follow-up). There was a decrease in the percentage of general surgical patients who received no prophylaxis (68% at baseline, 52% at follow-up) which was attributable to an increase in the use of both LDUH (20% at baseline, 31% at follow-up) and LMWH (12% at baseline, 17% at follow-up). Medical patients provided no prophylaxis also decreased from 95% at baseline to 80% at follow-up. This was related

to an increase in both LDUH (0% at baseline, 5% at follow-up) and LMWH (5% at baseline, 15% at follow-up) prophylaxis regimes.

Table 1: The proportion of orthopaedic, general surgical and medical patients receiving a particular prophylaxis regimen prior to the guideline implementation and 12 months following implementation (PTS= post thrombotic syndrome, HIT= heparin-induced thrombocytopenia, PE= pulmonary embolism, DVT= deep vein thrombosis, LMWH= low molecular weight heparin, LDUH= low-dose unfractionated heparin).

Specialty	Prophylaxis regimen	Baseline (%)	Follow-up (%)
Orthopaedics	LMWH	74	75
	LDUH	5	0
	No prophylaxis	21	25
General surgery	LMWH	12	17
	LDUH	20	31
	No prophylaxis	68	52
Medical	LMWH	5	15
	LDUH	0	5
	No prophylaxis	95	80

Projected clinical outcomes

Table 2 shows the projected change in clinical outcomes following the introduction of the VTE prevention guideline. The economic modelling estimated that there were 13 fewer deaths (183 at baseline, 170 at follow-up), 84 fewer symptomatic DVTs (865 at baseline, 781 at follow-up), 19 fewer symptomatic PEs (177 at baseline, 158 at follow-up), 48 fewer PTS events (455 at baseline, 407 at the follow-up) and 512 fewer hospital

bed days (11,119 at baseline, 10,607 at follow-up) over baseline, across medical and surgical patients. The model also estimated 34 more major bleeding events (392 at baseline, 426 at follow-up) and 22 more episodes of HIT (44 at baseline, 66 at follow-up).

Table 2: Estimated health outcomes for surgical and high-risk medical patients-prior to the guideline implementation and 12 months following implementation (PTS= post thrombotic syndrome, HIT= heparin-induced thrombocytopenia, PE= pulmonary embolism, DVT= deep vein thrombosis).

Clinical outcomes	Baseline (A)	Follow-up (B)	Incremental (=A–B)
Symptomatic DVT	865	781	-84
Symptomatic PE	177	158	-19
Deaths	183	170	-13
Major bleeding events	392	426	34
HIT	44	66	22
PTS	455	407	-48
Hospital days	11,119	10,607	-512

Projected economic outcomes

Table 3 shows the projected change in economic outcomes following the guideline's introduction. According to the modelled analysis, improved adherence to evidence based prophylaxis regimens was associated with overall cost savings of $245,439 over 12 months ($5,078,522 at baseline, $4,833,083 at follow-up). In-patient prophylaxis costs were estimated to increase by $38,553 from $107,311 at baseline to $142,864 at follow-up. The costs for LMWH were estimated to increase by $20,982 (from $71,313 to $92,295) whilst costs for heparin were estimated to rise by $17,571 (from $32,998 to $50,569). The model estimated that costs associated with the treatment of DVT

would be reduced by $231,765 (from $2,375,532 at baseline to $2,143,767 at follow-up), that costs associated with the treatment of PE reduced by $50,104 (from $470,284 at baseline to $420,180 at follow-up), and that costs associated with the treatment of PTS reduced by $130,735 (from $1,247,732 at baseline to $1,116,997 at follow-up). The model also estimated that the cost of treating major bleeds increased by $66,920 (from $762,057 at baseline to $828,977 at follow-up) and that the costs of treating HIT increased by $61,693 (from $118,605 at baseline to $180,298 at follow-up).

Table 3: Estimated costs for surgical and high-risk medical patients prior to the guideline implementation and 12 months following implementation (PTS= post thrombotic syndrome, HIT= heparin-induced thrombocytopenia, PE= pulmonary embolism, DVT= deep vein thrombosis, LMWH= low molecular weight heparin, LDUH= low-dose unfractionated heparin). All values are in Australian dollars.

Clinical costs	Baseline (A)	Follow-up (B)	Incremental (=A–B)
Total costs	$5,078,522	$4,833,083	-$245,439
Prophylaxis (inpatient)	$104,311	$142,864	$38,553
LMWH	$71,313	$92,295	$20,982
LDUH	$32,998	$50,569	$17,571
DVT treatment	$2,375,532	$2,143,767	-$231,765
PE treatment	$470,284	$420,180	-$50,104
Major bleeds	$762,057	$828,977	$66,920
HIT	$118,605	$180,298	$61,693
PTS	$1,247,732	$1,116,997	-$130,735

DISCUSSION

Our modelling demonstrated that the positive improvements in VTE prevention practices following the introduction of the evidence-based guideline was estimated to result in 13 fewer deaths, 84 fewer symptomatic DVTs,19 fewer symptomatic PEs, 512 fewer hospital bed days, and a saving of $245,439 over 12 months. These findings are comparable to similar studies conducted in European[24] and North America.[25]

There are a number of important characteristics about this disease process which help explain why relatively small changes in clinical practice result in such dramatic improvements in clinical and economic outcomes. The combination of a high incidence rate, significant mortality and morbidity, and costly treatment are all characteristics of the disease that contribute to its significant burden. The most insidious characteristic, however, is the extended natural history of the VTE disease process.[26] Heit et al found the incidence of recurrent VTE was 10% at six months, 13% after one year, and 30% after 10 years.[27]

Decision tree analytic modelling is the perfect tool for demonstrating the compounding costs associated with each VTE event. As illustrated in Figure 2, all patients who survive VTE are at a significant ongoing risk of a recurrent event which in turn places them at risk of experiencing a serious adverse clinical outcome (death, major bleed, PTS, or HIT).[28] The sequelae of serious adverse events following VTE helps to explain why relatively small changes in practice result in such dramatic improvements in clinical and economic outcomes.

Strengths and limitations

Decision tree analytic economic modelling helps healthcare providers and funders to make informed decisions regarding the cost-effectiveness of alternative treatment options. Decision trees are the simplest form of analytical economic modelling, providing a relatively simple and transparent economic evaluation of the options available for a healthcare problem.[22] A tailored economic model, such as the one used here, ensures that the treatment pathways and costs reflect the environment to which the model is applied which adds to the validity of the economic evaluation.

The decision tree model used in this analysis was designed exclusively for the assessment of pharmacological VTE prophylaxis. As such it is limited to drawing conclusions surrounding the pharmacologic aspects of the guideline implementation. The underlying data in the model, while being sourced from a robust and extensive mixed treatment comparison of published VTE prophylaxis data, only reflects the outcomes likely to be achieved by adherence to best practice and are not necessarily representative of the local hospital context. The analysis of cost-effectiveness could be further tailored by including more local hospital data such as VTE, major bleeding and HIT event rates.

CONCLUSION

Improved adherence to evidence-based guidelines for VTE prophylaxis in the Australian clinical setting is achievable and can result in significant improvements in clinical and economic outcomes. Practice improvement initiatives such as these are likely to result in fewer deaths, VTE events and significant overall healthcare cost savings.

REFERENCES

1. Heit JA, O'Fallon WM, Petterson TM, et al. Relative impact of risk factors for deep vein thrombosis and pulmonary embolism: a population-based study. *Archives Of Internal Medicine.* 2002;162(11):1245.

2. Mason C. Venous thromboembolism: A chronic illness. *Journal of Cardiovascular Nursing.* 2009;24(6 SUPPL.):s4-s7.

3. Dobesh PP. Economic burden of venous thromboembolism in hospitalized patients. *Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy.* 2009;29(8):943-953.

4. Heit J, Melton L, Lohse C, et al. Incidence of venous thromboembolism in hospitalized patients vs community residents2001.

5. Geerts WH, Bergqvist D, Pineo GF, et al. Antithrombotic and thrombolytic therapy:Prevention of venous thromboembolism. American College of Chest Physicians evidence-based clinical practice guidelines (8th Edition). *Chest.* Jun 2008;133(6 Suppl):110S-112S.

6. MacDougall DA, Feliu AL, Boccuzzi SJ, et al. Economic burden of deep-vein thrombosis, pulmonary embolism, and post-thrombotic syndrome. *American Journal of Health-System Pharmacy.* Oct 15 2006;63(20 Suppl 6):S5-15.

7. National Health and Medical Research Council. Clinical practice guideline for the prevention of venous thromboembolism (deep vein thrombosis and pulmonary embolism) in patients admitted to Australian hospitals. Melbourne: National Health and Medical Research Council; 2009.

8. National Institute of Health and Clinical Excellence. *Reducing the risk of venous thromboembolism in patients admitted to hospital.* London2010.

9. The Australian and New Zealand Working Party on the Management and Prevention of Venous Thromboembolism. Prevention of Venous Thromboembolism: Best Practice Guidelines for Australia and New Zealand (4th ed). Sydney: Health Education and Management Innovations; 2007.

10. Cohen AT, Tapson VF, Bergmann J-F, et al. Venous thromboembolism risk and prophylaxis in the acute hospital care setting (ENDORSE study): a multinational cross-sectional study. *Lancet.* 2008;371(9610):387-394.

11. Duff J, Walker K, Omari A. Translating venous thromboembolism (VTE) prevention evidence into practice: a multidisciplinary evidence implementation project. *Worldviews Evid Based Nurs.* Mar 2011;8(1):30-39.

12. Pettiti D. Overview of the Methods. In: Pettiti D, ed. *Meta-Analysis, Decision-Analysis and Cost-Effectiveness Analysis – Methods for Quantitative Synthesis in Medicine*. 2nd ed. New York: Oxford University Press; 2000:17-28.

13. Grol R, Eccles M, Wensing M. *Improving patient care : the implementation of change in clinical practice* Edinburgh. : Elsevier 2005.

14. Grimshaw J, Thomas RE, MacLennan G, et al. Effectiveness and efficiency of guideline dissemination and implementation strategies. *Health Technology Assessment.* Feb 2004;8(6):iii-iv, 1-72.

15. Tooher R, Middleton P, Pham C, et al. A systematic review of strategies to improve prophylaxis for venous thromboembolism in hospitals. *Ann Surg.* Mar 2005;241(3):397-415.

16. Dalen JE, Alpert JS. Natural history of pulmonary embolism. *Prog. Cardiovasc. Dis.* Jan-Feb 1975;17(4):259-270.

17. Gould MK, Dembitzer AD, Doyle RL, et al. Low-molecular-weight heparins compared with unfractionated heparin for treatment of acute deep venous thrombosis. A meta-analysis of randomized, controlled trials. *Ann Intern Med.* May 18 1999;130(10):800-809.

18. Greinacher A, Janssens U, Berg G, et al. Lepirudin (recombinant hirudin) for parenteral anticoagulation in patients with heparin-induced thrombocytopenia. Heparin-Associated Thrombocytopenia Study (HAT) investigators. *Circulation.* Aug 10 1999;100(6):587-593.

19. Prandoni P, Lensing AW, Cogo A, et al. The long-term clinical course of acute deep venous thrombosis. *Ann Intern Med.* Jul 1 1996;125(1):1-7.

20. Bell WR, Simon TL. Current status of pulmonary thromboembolic disease: pathophysiology, diagnosis, prevention, and treatment. *Am. Heart J.* Feb 1982;103(2):239-262.

21. Gordois A, Posnett J, Borris L, et al. The cost-effectiveness of fondaparinux compared with enoxaparin as prophylaxis against thromboembolism following major orthopedic surgery. *J Thromb Haemost.* Oct 2003;1(10):2167-2174.

22. Petrou S, Gray A. Economic evaluation using decision analytical modelling: design, conduct, analysis, and reporting. *BMJ.* 2011;342.

23. National Hospital Cost Data Collection. *Estimated Round 11 (2006–2007) AR-DRG 5.1 cost report.* Canberra: Commonwealth of Australia;2008.

24. Ferrando A, Pagano E, Scaglione L, et al. A decision-tree model to estimate the impact on cost-effectiveness of a venous thromboembolism prophylaxis guideline. *Quality and Safety in Health Care.* August 1, 2009 2009;18(4):309-313.

25. Amin AN, Lin J, Johnson BH, et al. Clinical and economic outcomes with appropriate or partial prophylaxis. *Thrombosis research.* 2010;125(6):513-517.

26. Hansson PO, Sörbo J, Eriksson H. The recurrence rate of venous thromboembolism after a first or second episode of deep venous thrombosis was high. *Evidence Based Medicine.* 2000;5(6):188-188.

27. Heit J. The epidemiology of venous thromboembolism in the community. *Arterioscler. Thromb. Vasc. Biol.* 2008;28(3):370.

28. Iorio A, Kearon C, Filippucci E, et al. Risk of Recurrence After a First Episode of Symptomatic Venous Thromboembolism Provoked by a Transient Risk Factor: A Systematic Review. *Archives Of Internal Medicine.* 2010;170(19):1710.