Cost-Effectiveness of Dabigatran Compared With Warfarin for Stroke Prevention in Patients With Atrial Fibrillation — A Real Patient Data Analysis in a Hong Kong Teaching Hospital

Address for correspondence:
Vivian W. Y. Lee, PharmD, BCPS (AQ Cardiology)
School of Pharmacy, Faculty of Medicine
The Chinese University of Hong Kong
Shatin, N.T., Hong Kong
vivianlee@cuhk.edu.hk

Andy M. Chang, B.Pharm; Jason C. S. Ho, B.Pharm; Bryan P. Yan, MBBS; Cheuk Man Yu, MB ChB, MD; Yat Yin Lam, MBBS, MD; Vivian W. Y. Lee, PharmD, BCPS (AQ Cardiology)

School of Pharmacy (Chang, Ho, Lee), Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong; Division of Cardiology, Department of Medicine and Therapeutics (Yan, Yu, Lam), Prince of Wales Hospital, Li Ka Shing Institute of Health and Sciences, Institute of Vascular Medicine, The Chinese University of Hong Kong, Hong Kong

ABSTRACT

Background: To compare the management cost and cost-effectiveness of dabigatran with warfarin in patients with nonvalvular atrial fibrillation (AF) from the hospital's and patients' perspectives.

Hypothesis: Dabigatran is more cost-effective than warfarin for stroke prevention of AF in Hong Kong.

Methods: The analysis was performed in conjunction with a drug utilization evaluation of dabigatran study in a teaching hospital in Hong Kong. The study recruited 244 patients who received either dabigatran or warfarin for stroke prevention of AF. A cost-effectiveness analysis was performed and was expressed as an incremental cost-effectiveness ratio (ICER) in averting a cardiac event or a bleeding event. A sensitivity analysis was used on all relevant variables to test the robustness.

Results: From the hospital's perspective, the dabigatran group had a lower total cost of management than that of the warfarin group (median: US$421 vs US$1306, $P < 0.001$) (US$1 = HK$7.75) and was dominant over warfarin. From the patients' perspective, the total cost of management in the dabigatran group was higher than that in warfarin group (median: US$1751 vs US$70, $P < 0.001$), and the ICER in preventing a cardiac or bleeding event of dabigatran vs warfarin was estimated at US$68 333 and US$20 500, respectively. If dabigatran was subsidized by the hospital, a higher cost would be incurred by the hospital (median: US$1679 vs US$1306, ICER (cardiac and bleeding events): US$15 163 and US$4549, respectively).

Conclusions: The study favored dabigatran for stroke prophylaxis in patients with nonvalvular AF in Hong Kong under the current hospital's perspective and provided a reference for further comparisons under patient and subsidization perspectives.

Introduction

Atrial fibrillation (AF) is a known risk factor of stroke and affects 1% to 2% of the general population worldwide.[1] Anticoagulant therapy is recommended for stroke prevention in nonvalvular AF patients who have a $CHADS_2$ score ≥ 1.[2] Warfarin has been used as the first-line oral anticoagulant,[3] but its use is limited by various drawbacks, including a narrow therapeutic window, extensive drug interactions, and frequent monitoring with an international normalized ratio (INR) test.[4]

Dabigatran is a potential alternative to warfarin, as shown in the large phase III Randomized Evaluation of Long-Term Anticoagulant Therapy (RE-LY) study. It has multiple advantages over warfarin, including that it has a more predictable pharmacokinetic profile, does not require regular INR monitoring, and has fewer drug and food interactions.[5] In February 2012, an update on the antithrombotic therapy guideline by American College of Chest Physicians recommended dabigatran over adjusted-dose warfarin in most AF patients.[2] Currently in Hong Kong, dabigatran is a self-financed item (SFI) under the local public health organization,[6] meaning that patients have to pay out-of-pocket in community pharmacies. In contrast to warfarin, which is a general drug, patients pay only US$1.3 (US$1 = HK$7.75) for a supply of up to

This study was supported by the School of Pharmacy, The Chinese University of Hong Kong.
The authors have no funding, financial relationships, or conflicts of interest to disclose.

Clin. Cardiol. 36, 5, 280–285 (2013)
Published online in Wiley Online Library (wileyonlinelibrary.com)
DOI:10.1002/clc.22112

Received: October 18, 2012
Accepted: February 6, 2013

16 weeks. Patients would pay much more for dabigatran compared to warfarin. However, using dabigatran should theoretically reduce the frequency of blood monitoring and thereby reduce the number of clinic visits. In Hong Kong, 110 mg dabigatran twice-daily dosing is commonly used. Although this dosing failed to show superiority in stroke prophylaxis over adjusted-dose warfarin in the RE-LY study,[7] it was associated with a lower rate of major bleeding when compared to adjusted-dose warfarin. The cost for the management of emergency and inpatient admissions due to undesirable bleeding may be lower in dabigatran than warfarin patients.

There have been at least 6 studies comparing the cost-effectiveness of dabigatran and warfarin for stroke prophylaxis in AF patients in different countries,[8–13] but all of them were based on hypothetical model simulations using RE-LY data. We therefore conducted a cost-effectiveness analysis (CEA) based on real-world data to provide information on whether dabigatran is more cost-effective than warfarin from the hospital's and patients' perspectives.

Methods

This CEA was performed in conjunction with a drug utilization evaluation of a dabigatran study in a teaching hospital in Hong Kong.[14] In this study, subjects were recruited from the teaching hospital in Hong Kong. Dabigatran patients (n = 122) and warfarin patients (n = 122) were randomly recruited through a computer system, and both groups were matched with age, sex, and anticoagulation treatment duration. All patients were followed up from the starting date of anticoagulation until March 31, 2012, so as to allow sufficient anticoagulant treatment and follow-up.

The probabilities of cardiac events occurred during anticoagulation treatment duration from both groups were recorded. Cardiac events were defined as a composite of any cardiac deaths, stroke, transient ischemic attack, systemic embolism, pulmonary embolism, myocardial infarction, and unstable angina. Bleeding events were defined as a composite of bleedings of any degree. The costs of management included clinic visit, investigation, and treatment. For hospital admissions, only those related to an anticoagulation issue were counted. The charges were based on the teaching hospital drug formulary, Hong Kong Government Gazette (an official source for procedural charges in a local public hospital), and the Hospital Authority (HA) Annual Report 2010/2011 (Table 1).[15–17] All monetary values were expressed in United States dollars (US$) (US$1 = HK$7.75).

A CEA of dabigatran was carried out from the hospital's and patients' perspectives. The effectiveness was expressed in rates of cardiac events, and the result was expressed as incremental cost-effectiveness ratio (ICER). The ICER of dabigatran over warfarin to prevent 1 cardiac event or bleeding event was calculated by: ICER = Δcost/Δevent rate.

Due to the SFI nature of dabigatran, the hospital did not need to pay for the cost of the drug, and thus the hospital was expected to pay less and the patients were expected to pay more. The drug cost was the main cost-driven parameter according to previous published literature.[9,10] Therefore, a hypothetical situation assuming the hospital bore the drug cost was set, and a CEA was done subsequently.

Table 1. Unit Costs of the Hospital Authority Services and Medications[15–17]

Services	Cost to patients (US$)	Cost to Healthcare Provider (US$)
A&E attendance	12.9	103
SOPC	12.9 for the first attendance, 7.7 per subsequent attendance	117
GOPC	5.8	37.4
Family medicine clinic	7.7	111
Inpatient (per day)	6.5 admission fee, plus 12.9 per day	465
Blood coagulation test	0	55.5
Medications		
Pradaxa (dabigatran etexilate)	2.3 for 75 mg, 2.4 for 110 mg, 2.5 for 150 mg	1.7 for all doses
Warfarin	1.3 per visit	0.03 for 1 mg, 0.03 for 3 mg, 0.04 for 5 mg
Famotidine	1.3 per visit	0.008 for 20 mg, 0.02 for 40 mg
Pantoprazole	1.3 per visit	0.13 for 20 mg, 0.11 for 40 mg
Esomeprazole	1.3 per visit	0.5 for 20 mg, 0.9 for 40 mg
Prochlorperazine 5 mg	1.3 per visit	0.014
Magnesium trisilicate mixture 500 mL	1.3 per visit	1.94
Hypromellose eye drops 10 mL	1.3 per visit	0.26
Zolpidem 10 mg	1.3 per visit	0.11
Paracetamol 500 mg	1.3 per visit	0.004
Tramadol 50 mg	1.3 per visit	0.04
Heparin injection	0	1.37
Fresh frozen plasma	0	N/A
Red blood cells	0	N/A
Procedures		
Colonoscopy	0 (local citizen)	1316

Abbreviations: A&E, accident and emergency; GOPC, general outpatient clinic; SOPC, specialist outpatient clinic.

The costs were expressed as costs per person per year from the hospital and patients' perspectives separately. Cost data that showed a skewed distribution were expressed as median (25th percentile, 75th percentile).[18,19] They were then compared using the Mann-Whitney U test. A P value <0.05 was defined as statistically significant. The study

Published online in Wiley Online Library (wileyonlinelibrary.com)
DOI:10.1002/clc.22112

Table 2. Baseline Characteristics of the Study Participants

Characteristics	Dabigatran (n = 122)	Warfarin (n = 122)
Age, y	70.0 ± 11.4	70.1 ± 10.3
Male sex, no. (%)	68 (55.7)	64 (52.5)
Smoking, no. (%)		
Yes	9 (7.4)	9 (7.4)
No	59 (48.4)	67 (54.9)
Ex-smoker	30 (24.6)	23 (18.9)
Unknown	24 (19.7)	23 (18.9)
$CHADS_2$ score[a]	2.48 ± 1.34	2.32 ± 1.47
0, no. (%)	7 (5.7)	11 (9.0)
1, no. (%)	23 (18.9)	34 (27.9)
≥2, no. (%)	92 (75.4)	77 (63.1)
Medical history, no. (%)		
Hypertension	85 (69.7)	77 (63.1)
Diabetes mellitus	35 (28.7)	42 (34.4)
Heart failure	31 (25.4)	38 (31.1)
Hyperlipidemia	40 (32.8)	36 (29.5)
Ischemic heart disease	30 (24.6)	25 (20.5)
Prior myocardial infarction	9 (7.4)	12 (9.8)
Previous stroke or transient ischemic attack	53 (43.4)	39 (32.0)
Chronic kidney disease	9 (7.4)	13 (10.7)

[a] $CHADS_2$ was calculated by 1 point each for C (congestive heart failure), H (hypertension), A (age ≥75 years), D (diabetes mellitus), and 2 points for S (prior stroke or transient ischemic attack).

protocol was approved by the ethics committee of the HA in Hong Kong.

Results

A total of 244 patients were recruited (122 in the warfarin group and 122 in the dabigatran group). The 2 groups were similar with respect to demographic characteristics and medical history (Table 2). The mean age of all patients was 70.1 years, and 54.1% were male. The median treatment duration was 310 days. The rate of cardiac events and bleeding events were 4.10% and 22.95% in dabigatran group and 6.56% and 31.15% in warfarin group, respectively (Table 3).

From the hospital's perspective, it would bear a significantly lower cost of management for dabigatran patients than for warfarin patients ($P < 0.001$) (Table 4). The average costs for clinic visit, investigation, and treatment were also significantly lower in the dabigatran group ($P < 0.001$ for all). ICER was negative, indicating dabigatran dominance (ie, it was less costly and at the same time more effective and safer than warfarin). From the patients' perspective (Table 5), they would instead bear a significantly higher cost in the dabigatran group as compared to the warfarin group ($P < 0.001$). The ICER for averting a cardiac event and bleeding event with dabigatran were US$68 333 and US$20 500, respectively.

To investigate whether the HA would bear significantly more cost if dabigatran was financed by the HA, a hypothetical cost analysis was carried out. Currently, the HA buys any dosage of dabigatran at US$1.68 per capsule. In this situation, the cost of management of dabigatran would be significantly higher than warfarin ($P < 0.001$) (Lower part of Table 5). The ICER for averting a cardiac event and bleeding event with dabigatran was US$15 163 and US$4549, respectively.

A post hoc analysis was carried out to determine the price of dabigatran at which the HA would pay significantly less (ie, significant cost savings) if it was covered by the HA. The result was US$0.82 per capsule, with the median cost of management per year per person by dabigatran at US$1061 vs warfarin US$1306 ($P = 0.049$). Cost savings per patient per year was estimated at US$245 at a cost-saving rate of 23%. We also determined the price of dabigatran at which the median cost of management for dabigatran would be the same for warfarin (ie, cost neutral). Such a situation was found at US$1.07 per capsule.

Discussion

It has been estimated that there are over 70 000 patients (~1% of the population) with AF in Hong Kong,[21] and the prevalence will increase as a result of population aging. Anticoagulation therapy is an important intervention to reduce thromboembolic events in high-risk patients. With warfarin as the standard of care for many years, patients generally had no other options before dabigatran was introduced. In the RE-LY trial, efficacy and safety of dabigatran had been established, and it showed superiority over warfarin from various perspectives. However, the economic outcomes of such alternative treatment have not been studied in clinical trials.

In this analysis, it showed that from the hospital's perspective, the total cost of management using dabigatran was significantly lower than using warfarin. This is not surprising, because the cost of dabigatran was paid for by the patients instead of the hospital. Another driving factor was that there were more follow-up clinic visits and laboratory tests in warfarin patients. This difference was due to the necessity of INR monitoring in patients taking warfarin. Moreover, the warfarin group had higher hospitalization fees, mainly due to a higher cardiac event rate and the need for inpatient warfarin titration. On the other hand, dabigatran patients would instead bear a significantly higher cost compared to warfarin patients. Although the clinic visit and hospitalization costs were significantly lower in the dabigatran group, this difference could not offset the higher treatment cost of dabigatran, because warfarin, as a general drug in the drug formulary, was supplied to patients at a very low cost (US$1.3 per visit).

The hypothetical cost analysis, in which the HA pays the dabigatran drug cost, showed that the median cost of management was found to be significantly higher in the

Published online in Wiley Online Library (wileyonlinelibrary.com)
DOI:10.1002/clc.22112

Table 3. Efficacy and Safety Outcomes

Event	Dabigatran, n = 122, No. (%)	Warfarin, n = 122, No. (%)	Dabigatran vs Warfarin, Adjusted HR (95% CI)	*P* Value
Efficacy outcomes				
Stroke	2 (1.64)	4 (3.28)	0.53 (0.10-2.96)	0.469
Hemorrhagic	2 (1.64)	1 (0.82)	1.50 (0.01-227.74)	0.875
Ischemic	0 (0.00)	3 (2.46)	—	—
Transient ischemic attack	2 (1.64)	2 (1.64)	1.06 (0.15-7.60)	0.958
Myocardial infarction	0 (0.00)	1 (0.82)	—	—
Unstable angina	1 (0.82)	2 (1.64)	0.50 (0.04-5.71)	0.579
Death from stroke	1 (0.82)	2 (1.64)	0.65 (0.06-7.55)	0.734
Death from any cause	3 (2.46)	4 (3.28)	0.99 (0.22-4.48)	0.986
Cardiac events	5 (4.10)	8 (6.56)	0.69 (0.22-2.12)	0.516
Safety outcomes				
Intracranial bleeding	2 (1.64)	2 (1.64)	1.94 (0.01-402.82)	0.808
Gastrointestinal bleeding	8 (6.56)	15 (12.3)	0.57 (0.24-1.35)	0.199
Subconjunctival hemorrhage	4 (3.28)	5 (4.10)	0.81 (0.22-3.03)	0.754
Gum	2 (1.64)	3 (2.46)	0.62 (0.11-4.02)	0.654
Hemoptysis	1 (0.82)	3 (2.46)	0.32 (0.03-3.15)	0.330
Hematuria	4 (3.28)	5 (4.10)	0.97 (0.26-3.65)	0.968
Nose	1 (0.82)	4 (3.28)	0.25 (0.03-2.22)	0.212
Bruising	7 (5.74)	9 (7.38)	0.66 (0.23-1.65)	0.428
Hematoma	2 (1.64)	0 (0.00)	—	—
Others	1 (0.82)	1 (0.82)	—	—
Major bleeding[a]	2 (1.64)	3 (2.46)	0.72 (0.19-4.37)	0.719
Minor bleeding	26 (21.31)	37 (30.33)	0.71 (0.43-1.18)	0.188
All bleeding[b]	28 (22.95)	38 (31.15)	0.76 (0.45-1.25)	0.281

Abbreviations: CI, confidence interval; HR, hazard ratio.
[a]Major bleeding was defined according to the guideline by International Society on Thrombosis and Haemostasis.[20] [b]For those who encountered both major and minor bleeding, each of them were only counted once in all bleeding events. Thus, the sum of major bleeding and minor bleeding events did not necessarily equal that of all bleeding.

dabigatran group, indicating that the drug cost actually played a major role in the cost of management. That finding was consistent with 2 previously published studies.[9,10]

Under the current situation, both ICERs for dabigatran from the HA's perspective were dominant over warfarin, and dabigatran is thus considered as both a cost-effective and cost-saving intervention. However, although the ICERs from the current patients' perspective and hypothetical HA situation were determined, it is difficult to determine whether this intervention is cost-effective, because in Hong Kong there is no standard for cost-effectiveness in terms of cost per event prevented. Therefore, this study serves as a basis for future comparison with other novel oral anticoagulants, such as rivaroxaban and apixaban, in terms of cost-effectiveness.

Based on the post hoc cost calculation, our finding might provide insight for hospitals to consider subsidizing dabigatran to patients. If dabigatran was to be fully subsidized by the HA, dabigatran at current price would incur a higher cost for the HA. A post hoc analysis showed that at the price of US$1.07 per capsule, the hospital would be paying the same cost of management for both groups of patients. At an even lower price of US$0.83 per capsule, which is about half the current price, the hospital would benefit from it not only being cost-effective, but also from it being a significant cost savings of 23%.

Published online in Wiley Online Library (wileyonlinelibrary.com)
DOI:10.1002/clc.22112

Table 4. Cost of Management per Year per Person and Cost-Effectiveness Analysis (Healthcare Provider's Perspective)

Cost	Dabigatran (n = 122)	Warfarin (n = 122)	*P* Value
Median total cost (25th, 75th percentile), US$	461 (341, 886)	1306 (914, 2584)	<0.001[a]
Median clinic visit cost (25th, 75th percentile), US$	430 (321, 748)	932 (602, 1727)	<0.001[a]
GOPC[b]	0–212	0–85	0.191
FM[b]	0–622	0–802	0.576
SOPC	388 (292, 591)	713 (491, 983)	<0.001[a]
A&E[b]	0–210	0–673	0.012[c]
Inpatient[b]	0–14 323	0–40 617	<0.001[a]
Median investigation cost (25th, 75th percentile), US$	16 (0, 57)	325 (195, 526)	<0.001[a]
Laboratory test	16 (0, 57)	325 (195, 524)	<0.001[a]
Procedures[b]	0–1575	0–1579	0.995
Treatment cost, US$[b]	0–232	6–40	<0.001[a]
Drug cost[b]	0	6–40	<0.001[a]
Side effects[b]	0–232	0–21	0.071
Cost-effective analysis			
ICER, US$ per cardiac event prevented	−34 350 (dabigatran dominant)		
ICER, US$ per bleeding event prevented	−10 305 (dabigatran dominant)		

Abbreviations: A&E, accident and emergency; FM, family medicine; GOPC, general outpatient clinic; ICER, incremental cost-effectiveness ratio; SOPC, specialist outpatient clinic.
[a]$P \leq 0.01$. [b]If the median, 25th percentile, and 75th percentile are all zero, the range is shown. [c]$P < 0.05$.

Table 5. Cost of Management per Year per Person and Cost-Effectiveness Analysis

Cost	Dabigatran (n = 122)	Warfarin (n = 122)	*P* Value
Patients' perspective			
Median total cost (25th, 75th percentile), US$	1751 (1741, 1781)	70 (49, 114)	<0.001[a]
Clinic visit cost (25th, 75th percentile), US$	28 (21, 52)	59 (41, 99)	<0.001[a]
GOPC[b]	0–31	0–12	0.191
FM[b]	0–42	0–55	0.576
SOPC	25 (19, 38)	46 (32, 63)	<0.001[a]
A&E[b]	0–26	0–84	0.012[c]
Inpatient[b]	0–434	0–890	<0.001[a]
Treatment cost (25th, 75th percentile), US$[d]	1724 (1724, 1724)	10 (8, 14)	<0.001[a]
CEA			
ICER, US$ per cardiac event prevented	68 333		
ICER, US$ per bleeding event prevented	20 500		
Hypothetical Hospital Authority's perspective, if dabigatran cost is to be borne by the Hospital Authority			
Median total cost (25th, 75th percentile), US$	1679 (1550, 2108)	1306 (914, 2584)	<0.001[a]
Treatment cost, US$	1225 (1225, 1225)	17 (15, 21)	<0.001[a]
CEA			
ICER, US$ per cardiac event	15 163		
ICER, US$ per bleeding event	4549		

Abbreviations: A&E, accident and emergency; CEA, cost-effectiveness analysis; FM, family medicine; ICER, incremental cost-effectiveness ratio; GOPC, general outpatient clinic; SOPC, specialist outpatient clinic.
[a]$P \leq 0.01$. [b]If the median, 25th percentile, and 75th percentile are all zero, the range is shown. [c]$P \leq 0.05$. [d]Equivalent to drug cost.

In Hong Kong, 110 mg dabigatran twice daily was the most commonly used dosage. However, according to foreign CEA studies using models, 110 mg twice daily dosing of dabigatran did not show cost-effectiveness over warfarin due to a higher event occurrence rate.[8,11] Contrary to the results from foreign studies, this economic analysis of real patient data supports the use of such dosing in Hong Kong.

There are several limitations in the study. First, the retrospective nature of the study might lead to missing some cardiac and especially bleeding events, because the data were collected from the electronic patient records, which might not be fully complete. The hospitalizations other than anticoagulation were also omitted during the data collection process. The sample size was small when compared with other similar foreign studies, although they ran a hypothetical cohort. Moreover, the subjects were recruited from only 1 public hospital, which may not be representative of the actual situation in Hong Kong.

Conclusion

To our knowledge, the present study was the first CEA using real patient data in comparing dabigatran vs warfarin in prevention of AF-related stroke. Although dabigatran contributes a considerable proportion in the total cost of management because of the drug's high cost, it is considered a highly cost-effective measure as compared to warfarin under the current situation in Hong Kong. Drug cost is an important factor in determining whether the hospital should subsidize a new drug. This local study thus supported the use of dabigatran for stroke prevention in AF patients in

Published online in Wiley Online Library (wileyonlinelibrary.com)
DOI:10.1002/clc.22112

Hong Kong from the current economic perspective and its subsidization from the hospital if the drug cost is lowered.

References

1. Wolf PA, Abbott RD, Kannel WB. Atrial fibrillation as an independent risk factor for stroke: the Framingham Study. *Stroke.* 1991;22:983–988.
2. Guyatt GH, Akl EA, Crowther M, et al. Executive summary: antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians evidence-based clinical practice guidelines. *Chest.* 2012;141:7S–47S.
3. Singer DE, Albers GW, Dalen JE, et al. Antithrombotic therapy in atrial fibrillation: American College of Chest Physicians evidence-based clinical practice guidelines (8th edition). *Chest.* 2008;133:546S–592S.
4. Ma TK, Yan BP, Lam YY. Dabigatran etexilate versus warfarin as the oral anticoagulant of choice? A review of clinical data. *Pharmacol Ther.* 2011;129:185–194.
5. Stangier J. Clinical pharmacokinetics and pharmacodynamics of the oral direct thrombin inhibitor dabigatran etexilate. *Clin Pharmacokinet.* 2008;47:285–295.
6. Hong Kong Hospital Authority. Hospital authority drug formulary 2005 [updated January 14, 2012]. http://www.ha.org.hk/hadf/. Accessed April 16 2012.
7. Connolly SJ, Ezekowitz MD, Yusuf S, et al. Dabigatran versus warfarin in patients with atrial fibrillation. *N Engl J Med.* 2009;361:1139–1151.
8. Shah SV, Gage BF. Cost-effectiveness of dabigatran for stroke prophylaxis in atrial fibrillation. *Circulation.* 2011;123:2562–2570.
9. Langkilde LK. Cost-effectiveness of dabigatran etexilate for stroke prevention in non-valvular atrial fibrillation. Applying RE-LY to clinical practice in Denmark. *J Med Econ.* 2012;15:1–9.
10. Sorensen SV, Kansal AR, Connolly S, et al. Cost-effectiveness of dabigatran etexilate for the prevention of stroke and systemic embolism in atrial fibrillation: a Canadian payer perspective. *Thromb Haemost.* 2011;105:908–919.
11. Freeman JV, Zhu RP, Owens DK, et al. Cost-effectiveness of dabigatran compared with warfarin for stroke prevention in atrial fibrillation. *Ann Intern Med.* 2011;154:1–11.
12. Kansal AR, Sorensen SV, Gani R, et al. Cost-effectiveness of dabigatran etexilate for the prevention of stroke and systemic embolism in UK patients with atrial fibrillation. *Heart.* 2012;98:573–578.
13. Pink J, Lane S, Pirmohamed M, et al. Dabigatran etexilate versus warfarin in management of non-valvular atrial fibrillation in UK context: quantitative benefit-harm and economic analyses. *BMJ.* 2011;343:d6333.
14. Ho JC, Chang AM, Yan BP, et al. Dabigatran compared with warfarin for stroke prevention with atrial fibrillation: experience in Hong Kong. *Clin Cardiol.* 2012;35:E40–E45.
15. Hong Kong SAR. Hong Kong Government Gazette No. 13/2003 S.S. No. 4. Hong Kong: Hong Kong SAR Government; 2003.
16. Prince of Wales Hospital. Drug formulary. Hong Kong: Hospital Authority; 2011.
17. Hong Kong Hospital Authority. Hospital Authority annual report 2010/11. Hong Kong: Hospital Authority; 2011.
18. Brumley R, Enguidanos S, Jamison P, et al. Increased satisfaction with care and lower costs: results of a randomized trial of in-home palliative care. *J Am Geriatr Soc.* 2007;55:993–1000.
19. Liu L, Cowen ME, Strawderman RL, et al. A flexible two-part random effects model for correlated medical costs. *J Health Econ.* 2010;29:110–123.
20. Schulman S, Kearon C; Subcommittee on Control of Anticoagulation of the Scientific and Standardization Committee of the International Society on Thrombosis and Haemostasis. Definition of major bleeding in clinical investigations of antihemostatic medicinal products in non-surgical patients. *J Thrombost Haemost.* 2005;3:692–694.
21. Fung JWH. An update in AF management. *Hong Kong Med Bull.* 2011;16:4–6.

Published online in Wiley Online Library (wileyonlinelibrary.com)
DOI:10.1002/clc.22112