Management of Chinese patients on warfarin therapy in two models of anticoagulation service – a prospective randomized trial

Fredric W. H. Chan, Raymond S. M. Wong,¹ Wing-Hung Lau, Thomas Y. K. Chan,² Gregory Cheng¹ & Joyce H. S. You

School of Pharmacy, Faculty of Medicine, ¹Division of Haematology, Department of Medicine & Therapeutics, Faculty of Medicine, The Prince of Wales Hospital and ²Division of Clinical Pharmacology, Department of Medicine & Therapeutics, The Chinese University of Hong Kong, Hong Kong

Correspondence

Joyce H. S. You PharmD, BCPS,
Associate Professor, School of
Pharmacy, Faculty of Medicine, The
Chinese University of Hong Kong,
Shatin, N.T., Hong Kong.
Tel: + 852 2609 6830
Fax: + 852 2603 5295
E-mail: joyceyou@cuhk.edu.hk

Keywords

Chinese, cost analysis, INR control,
patient satisfaction, warfarin

Received

25 November 2005

Accepted

23 March 2006

Published OnlineEarly

26 May 2006

Aim

To compare the treatment outcomes of a clinical pharmacist-managed anticoagulation service with physician-managed service in Chinese patients.

Methods

A prospective, randomized clinical trial was conducted at the anticoagulation clinic of a teaching hospital in Hong Kong. Patients aged ≥ 18 years who would require warfarin therapy for at least 3 months were recruited. Patients were randomized to the pharmacist-managed or physician-managed group. Primary clinical outcome was assessed by the percentage of patient time spent within the target international normalized ratio (INR) range. The incidence of major thromboembolic events (TEs) and major bleeding was assessed as secondary clinical outcomes. The cost per patient per month (cPPPM) was calculated and patient satisfaction was assessed by patient satisfaction questionnaire (PSQ)-18.

Results

One hundred and forty-one patients were recruited at the anticoagulation clinic and 137 patients completed the study. Patients in the pharmacist-managed group ($n = 68$) were in the target INR 64% of patient time vs. 59% in the physician-managed group ($n = 69$) ($P < 0.001$). There was no significant difference in incidence of major TEs or bleeding. The cPPPM in the pharmacist-managed group ($\text{US\$}76 \pm 95$) ($\text{£}43 \pm 53$) was lower than in the physician-managed group ($\text{US\$}98 \pm 158$) ($\text{£}55 \pm 89$) ($P < 0.001$). The PSQ-18 score of the pharmacist-managed group (3.8 ± 0.2) was higher than that of the physician-managed group (3.6 ± 0.3) ($P < 0.001$).

Conclusion

The pharmacist-managed anticoagulation service was more effective and less costly than the physician-managed service in achieving target anticoagulation control for Chinese patients on warfarin therapy.

Introduction

Warfarin is the most commonly prescribed oral anticoagulant worldwide for the treatment and prevention of various thromboembolic events (TEs). The anticoagula-

tion effect of warfarin, measured by the international normalized ratio (INR), is subject to wide inter- and intraindividual variability. In addition, warfarin has such a narrow therapeutic window that it could lead to haem-

orrhagic or thromboembolic events even with careful dosage titration [1, 2].

Management of warfarin therapy in Chinese patients has been challenging because Chinese patients are reported to be more sensitive to the anticoagulation effect of warfarin and require a 40–50% lower maintenance dose of the drug when compared with Europeans [3–5]. The incidence of major bleeding increased sharply as INR rose from 2.4 to 2.9 in a cohort of Chinese patients receiving warfarin therapy with a target INR of 2–3 [6]. Beside the influence of environmental factors such as diet and drug–drug interactions, genetic factors apparently play an important role in affecting the dose requirement of warfarin therapy in the Chinese population [7–9]. The gene for K epoxide reductase complex 1 (VKORC1), which encodes the warfarin target protein, was recently identified. It was reported that over 70% of Hong Kong Chinese patients were homozygous for the VKORC1 H1/H1 genotype and this was associated with a lower warfarin maintenance dose in this cohort of patients [8].

In Hong Kong, all anticoagulation clinics are managed by physicians. Studies conducted in Western populations had indicated that clinical pharmacist-managed anticoagulation services decreased warfarin-related hospitalization, lowered the incidence of haemorrhagic and thromboembolic events and improved INR control when compared with routine medical care [10–14]. We therefore hypothesized that a new management model (with a pharmacist as the primary care provider) is more effective than the usual practice model (managed solely by physicians) in achieving target INR control in Chinese patients receiving warfarin therapy in Hong Kong. A pharmacist-managed anticoagulation clinic was recently implemented in a teaching hospital in Hong Kong to test this hypothesis and the objective of the present study was to compare the effects of a clinical pharmacist-managed anticoagulation service with those of the physician-managed service on treatment outcomes of warfarin therapy among Chinese patients in Hong Kong.

Methods

Setting and subjects

This was a 2-year randomized clinical trial conducted at the anticoagulation clinic of the Prince of Wales Hospital in Hong Kong. The anticoagulation clinic was established in 1998 and it was managed solely by physicians. A clinical pharmacist-managed anticoagulation service was added to the clinic in 2002. Patients on warfarin therapy are referred to the anticoagulation clinic for follow-up by their primary care physicians. The present study was approved by the Joint Chinese University of

Hong Kong-New Territories East Cluster Clinical Research Ethics Committee. From November 2002 to June 2004, all patients newly enrolled at the anticoagulation clinic were screened for eligibility for the study at their first clinic visit. Chinese patients who were ≥ 18 years old with anticipated treatment duration of ≥ 3 months were invited to participate. Those who agreed to provide written consent were randomized to the physician-managed group (usual practice model) or the pharmacist-managed group (newly proposed model) according to a computer-generated table with random assignment in blocks of four. The patients were followed prospectively until September 2004 or until the patients were off warfarin, whichever occurred first.

Interventions

Newly proposed model Patients in the pharmacist-managed group were managed by one clinical pharmacist (F.W.H.C.). The clinical pharmacist received training on warfarin management from two haematologists (G.C., R.S.M.W.) at the physician-managed warfarin clinic for 1 month before the start of the pharmacist-managed clinic. A management protocol was developed by a haematologist (G.C.), a clinical pharmacologist (T.Y.K.C.) and a pharmacotherapy specialist (J.H.S.Y.) to guide the clinical pharmacist to manage patients on warfarin therapy. The management protocol included recommended target INR ranges for various indications of warfarin, conditions requiring physician consultation, recommendations on follow-up interval and on dosage adjustment based upon INR, risk factors for bleeding, potential drug–disease, drug–drug, drug–food and drug–herb interactions and patient education information.

Patients were attended by a haematologist during the first clinic visit to decide the duration of therapy and target INR range. In every follow-up visit, the INR measurement was obtained using a point-of-care testing monitor (CoaguChek Pro DM; Roche, Mannheim, Germany). The accuracy of CoaguChek Pro DM was validated with hospital laboratory testing on 86 INR measurements as described by Havrda *et al.* [15]. The clinical pharmacist screened for the criteria that required physician consultation, including INR > 4.5 or failure to reach therapeutic range after three visits, signs and symptoms of thromboembolism or major bleeding, patients who intended to undergo dental or other operations, and upon completion of intended treatment course to determine whether treatment should be continued. Those patients who received physician consultation continued follow-up in the pharmacist-managed clinic. The clinical pharmacist adjusted the warfarin

dosage and scheduled the follow-up visit according to the INR control. The patient was followed every 2–6 weeks if a dosage adjustment was made and every 8–10 weeks if the same warfarin regimen continued. The clinical pharmacist also followed a predetermined management checklist to provide intense education to patients and caregivers on warfarin therapy, monitor patient adherence and identify potential warfarin–drug, warfarin–herb and warfarin–food interactions. Intense patient education counselling included the indications and benefits of warfarin therapy, symptoms of bleeding and TEs, drugs, food supplements and herbs to avoid and missing dose management. Written patient information was also provided. Between clinic visits, the clinical pharmacist conducted telephone follow-up for those patients with questionable adherence (as assessed by patient interview and pill-counts) or difficult INR control. Pharmacist consultation for the warfarin therapy was available to patients through a telephone hotline.

Usual practice model The physician-run clinic was managed by the two haematologists (G.C., R.S.M.W.). No support personnel such as nurses or physician trainees were used. INR measurements were performed by hospital laboratory testing. Patients therefore needed to have venous blood drawn 2–3 h prior to their clinic appointment. During each consultation, the haematologists adjusted the warfarin dosage using the same dosage adjustment protocol as the pharmacist-managed group. The haematologists also monitored the signs and symptoms of thromboembolism and bleeding, drug interactions and patient adherence, as their usual practice, and no predetermined checklist was used.

Outcome measures

The primary clinical outcome was the control of INR per therapeutic range and per expanded therapeutic range. Therapeutic INR ranges for low-intensity (INR = 2–3) and high-intensity (INR = 2.5–3.5) indications were adopted from the American College of Chest Physicians (ACCP) Consensus Conference on Antithrombotic Therapy [1]. The expanded therapeutic INR range, defined as the therapeutic range $\text{INR} \pm 0.2$, was considered clinically acceptable and would not require dosage adjustment. The INR value at each clinic visit was recorded for each study patient. The percentage of patient time spent in the therapeutic (and expanded therapeutic) INR range was estimated using linear interpolation between measured INR values as described by Rosendaal *et al.* [16]. The control of INR was expressed as the distribution of patient-years spent among various INR ranges.

The incidence of warfarin-related major complications per 100 patient-years, as the secondary clinical outcome measurement, was also calculated for both study groups. Patients were interviewed at each follow-up visit to capture the incidences of warfarin-related major events requiring medical attendance or treatment, such as unscheduled outpatient clinic visits, emergency room visits and hospitalization. Major bleeding events included haemorrhagic stroke, gastrointestinal bleed, genitourinary bleed and haemoptysis. Major TEs included transient ischaemic attack, stroke, recurrent venous thrombosis and pulmonary embolism. Each event was confirmed by reviewing the patient's medical record.

Direct healthcare costs for anticoagulation therapy including the cost for treatment of adverse drug events and major complications were assessed as the economic outcome measurement. The utilization of the following healthcare resources related to warfarin therapy was documented or retrieved from medical records to assess the total direct cost per patient: medication, laboratory and diagnostic tests, clinic visits, emergency room visits and hospitalization. The total direct medical cost was presented as cost per patient per month (cPPPM).

The unit cost of each target healthcare resource was estimated from the perspective of a public health organization in Hong Kong. The Hospital Authority is non-profit-making and the largest public health organization in Hong Kong. It charges patients who are nonresidents of Hong Kong based upon the latest charges of healthcare services of public hospitals and clinics posted in the *Hong Kong Gazette*. Assuming the charges listed in the *Gazette* represent only the cost components (including costs of labour and supplies) with no addition of profits, the costs associated with the target healthcare resources were therefore approximated using charges listed in the *Hong Kong Gazette*. Drug cost was based on Hospital Authority-specific acquisition cost. The pharmacist-managed service in the present study was operated as an experimental service so that no standard cost for clinic visit managed by pharmacists is available for reference. Since the salary of the clinical pharmacist was approximately 50% of the average salary of the two haematologists and the salary of the healthcare professionals was the major component of the clinic cost, the cost of clinic visit in the pharmacist-managed group was therefore adjusted to be 50% of the cost of a physician-managed specialist clinic visit. The cost of clinic visit included the labour cost of the clinical pharmacist for both the clinic management and phone call follow-ups and cost of physician time for occasional consultations. A sensitivity analysis was conducted to examine the

effect of variation of the cost of clinic visit provided by the pharmacist-managed group on the results of cost analysis.

Patient satisfaction was determined using the patient satisfaction questionnaire (PSQ)-18 (RAND Corporation, Santa Monica, CA, USA), which was completed after a patient had been recruited and followed for at least 3 months. Each patient was interviewed using the PSQ once during the following period. The questionnaire was administered by a research assistant who was not blinded to patient allocation. Seven scales were assessed by PSQ-18: general satisfaction, technical quality, interpersonal manner, communication, financial aspects, time spent with clinician and accessibility and convenience.

Sample size estimation

It was estimated that the physician-managed anticoagulation service would achieve target the INR about 50% of the time, similar to routine medical care by physicians [16]. Assuming that the pharmacist-managed anticoagulation service would increase the time of target INR control to 60% of the time and the standard deviations of the means in the two groups were 0.25, a sample size of about 60 patients per group would have a statistical power of 80% with an α error of 5% to detect the difference.

Statistical analysis

Statistical analysis was performed using Microsoft Excel 2000 (Microsoft Corp., Redmond, WA, USA) and SPSS for Windows 11.5 (SPSS Inc., Chicago, IL, USA). Data were presented in mean $\pm$ standard deviation (SD). Patient demographics, percentage of patients within the therapeutic range of INR and incidence of bleeding and TEs between the two groups were compared by unpaired Student's *t*-test, χ^2 test or Fisher's exact test, as appropriate. A *P*-value <0.05 was considered to be statistically significant. The cPPPM of total direct medical resources consumed in either group was significantly skewed ($P < 0.001$) and it failed to be normalized by square root, logarithm or arcsin transformation. It was therefore compared by Mann-Whitney test. The mean scores of the PSQ-18 subscales between the two groups were compared by unpaired Student's *t*-test.

Results

From November 2002 to June 2004, 141 patients enrolled at the anticoagulation clinic were evaluated for eligibility for the study (Figure 1). Two patients had postpartum deep vein thrombosis and were started on warfarin for 6 weeks and one patient refused to partici-

pate. A total of 138 patients provided written consent and were randomized to the pharmacist-managed group ($n = 69$) and the physician-managed group ($n = 69$). One patient in the pharmacist-managed group did not return for follow-up after the first visit. The outcome analysis was conducted on the 68 patients in the pharmacist-managed group and the 69 patients in the physician-managed group.

The patients' demographic data are shown in Table 1. Patients' characteristics in the two groups were similar, with no significant differences in age, intensity of anticoagulation therapy or type of indication, but the percentage of male patients was significantly lower in the pharmacist-managed group (35% vs. 55%; $P = 0.031$). One hundred and twenty-five patients (91%) were on warfarin therapy for a target INR 2–3. The most common indications for warfarin therapy were atrial fibrillation ($n = 72$; 53%), heart valve replacement ($n = 24$; 18%), deep vein thrombosis ($n = 17$; 12%) and pulmonary embolism ($n = 9$; 7%).

The distribution of patient-years of the two study groups among various INR categories for low-intensity and high-intensity anticoagulation therapy is shown in Figures 2 and 3, respectively. Table 2 shows that the patients in the pharmacist-managed group spent more patient time (64%) in therapeutic INR range than those in the physician-managed group (59%) ($P < 0.001$). Similarly, for both low-intensity and high-intensity anticoagulation therapy, patients in the pharmacist-managed group consistently spent more patient time in the therapeutic range than those in the physician-managed group ($P < 0.001$). When the INR results from both groups were pooled, the 137 patients spent 61% of time in the therapeutic INR range and 77% of time in the expanded range.

No patient had a fatal event in the present study. One patient from each group experienced a transient ischaemic attack (1.6 events per 100 patient-years; $P = 1.00$). Both patients were hospitalized and the symptoms resolved spontaneously. The INR at the time of the event was not documented in either case. One patient in the pharmacist-managed group experienced menorrhagia with anaemic symptoms at an INR of 2.39 during admission (1.6 events per 100 patient-years) and two patients in the physician-managed group experience bleeding (one had extensive bruising with gross haemoptysis with an INR of >5 and one had a peptic ulcer with iron deficiency anaemia; 3.1 events per 100 patient-years) ($P = 1.00$).

The mean cPPPM and its components are shown in Table 3. There were no significant differences in the mean cPPPM regarding medication use, emergency

Figure 1

Flow of patients through the trial

Figure 2

Distribution of patient-years among the international normalized ratio (INR) categories in the low-intensity group (target INR = 2–3, extended target INR = 1.8–3.2). Pharmacist group (■), Physician group (▨)

room utilization and hospitalization. The mean cPPPM for the pharmacist-managed clinic (US\$46 ± 35) (£26 ± 20) was significantly lower than that for the physician-managed clinic (US\$67 ± 51) (£38 ± 29) ($P < 0.01$). The mean total cPPPM of the pharmacist-

managed group (US\$76 ± 95) (£43 ± 53) was also significantly lower than that of the physician-managed group (US\$98 ± 158) (£55 ± 89) ($P < 0.01$). The cost of the pharmacist-managed service was assumed to be 50% of the physician-managed service in the base-case anal-

Table 1

Patient demographics and indications for warfarin therapy

	Number (%) Pharmacist-managed group	Physician-managed group	P-value
No. of patients	68	69	–
Male	24 (35)	38 (55)	0.031
Age (mean $\pm$ SD)	58 $\pm$ 14.0	60 $\pm$ 14.0	0.484
Patient-years	62	64	–
Intensity of anticoagulation therapy			
Low (therapeutic INR: 2–3)	63 (93)	62 (90)	0.783
High (therapeutic INR: 2.5–3.5)	5 (7)	7 (10)	
Indications			
Atrial fibrillation	37 (54)	35 (51)	0.794
Heart valve replacement			
Mitral valve replacement only	6 (9)	4 (6)	0.725
Aortic valve replacement only	3 (4)	6 (8)	0.505
Both mitral and aortic valve replacement	1 (2)	4 (6)	0.371
Deep vein thrombosis	8 (12)	9 (13)	1.00
Pulmonary embolism	5 (7)	4 (6)	0.745
Cerebrovascular accident	2 (3)	2 (3)	1.00
Valvular heart diseases	3 (4)	2 (3)	0.681
Cardiomyopathy	1 (2)	1 (1)	1.00
Miscellaneous	2 (3)*	2 (3)†	–

*Arterial embolism (n = 1) and ischaemic heart disease (n = 1). †Ischaemic heart disease (n = 1) and arterial thrombosis (n = 1). INR, International normalized ratio.

Figure 3

Distribution of patient-years among the international normalized ratio (INR) categories in the high-intensity group (target INR = 2.5–3.5, extended target INR = 2.3–3.7). Pharmacist group (■), Physician group (□)

ysis. A sensitivity analysis was therefore conducted of the cost of the pharmacist-managed service over a range of 10–100% of the cost of the physician-managed service. It showed that the total cPPPM of the pharmacist-managed group was significantly lower than that of the physician-managed group when the cost per pharmacist-managed clinic was 10–60% of the cost of the physi-

cian-managed clinic. There was no significant difference in the total cPPPM between the two groups when the cost of the pharmacist-managed clinic was 70–90% of that of the physician-managed clinic. The pharmacist-managed group became significantly more costly when the cost of the pharmacist-managed clinic was the same as that of the physician-managed clinic.

Table 2

Control of INR and incidence of complications

	Pharmacist-managed group	Physician-managed group	P-value
Patient time (%) in therapeutic INR range	64	59	< 0.001
Patient time (%) in therapeutic range for the group with target INR of 2–3	64	60	< 0.001
Patient time (%) in therapeutic range for the group with target INR of 2.5–3.5	66	44	< 0.001
Patient time (%) in expanded therapeutic range*	78	76	< 0.001
Numbers with bleeding (number per 100 patient-years)			
Major	1 (1.6)	2 (3.1)	1.00
Fatal	0	0	
Number of thromboembolic events (number per 100 patient-years)			
Major	1 (1.6)	1 (1.6)	1.00
Fatal	0	0	

*Expended therapeutic range = therapeutic range ± 0.2 international normalized ratio (INR) units.**Table 3**

Mean cost per patient per month

	Pharmacist-managed group, US\$ (£)	Physician-managed group, US\$ (£)	P-value
Clinic visit	45.7 $\pm$ 34.7 (25.6 $\pm$ 19.4)	67.4 $\pm$ 51.1 (37.7 $\pm$ 28.6)	< 0.01
Medication	2.7 $\pm$ 1.6 (1.5 $\pm$ 0.8)	2.6 $\pm$ 1.1 (1.4 $\pm$ 0.6)	0.269
Emergency room	1.0 $\pm$ 2.7 (0.5 $\pm$ 1.5)	1.0 $\pm$ 4.0 (0.5 $\pm$ 2.2)	0.195
Hospitalization	26.1 $\pm$ 90.7 (14.6 $\pm$ 50.8)	26.9 $\pm$ 145.3 (15.0 $\pm$ 81.4)	0.102
Total	76 $\pm$ 95 (43 $\pm$ 53)	98 $\pm$ 158 (55 $\pm$ 88)	< 0.01

Table 4

Results of PSQ-18 assessment

	Mean score (SD) Pharmacist-managed group	Physician-managed group	P-value
General satisfaction	4.0 (0.5)	3.8 (0.5)	0.134
Technical quality	4.0 (0.3)	3.8 (0.4)	0.014
Interpersonal manner	4.0 (0.4)	3.7 (0.6)	0.003
Communication	4.0 (0.4)	3.7 (0.6)	0.003
Financial aspect	3.6 (0.6)	3.6 (0.8)	0.901
Time spent	3.9 (0.4)	3.3 (0.6)	< 0.001
Accessibility	3.6 (0.4)	3.3 (0.4)	< 0.001

The results of PSQ-18 survey are shown in Table 4. The scores for technical quality, interpersonal manner, communication, time spent with clinician and accessibility were significantly higher in the pharmacist-managed group. There was no significant dif-

ference in the scores for general satisfaction and financial aspect. The overall mean score of the pharmacist-managed group (3.8 ± 0.2) were significantly higher than that of the physician-managed group (3.6 ± 0.3) ($P < 0.001$).

Discussion

In the present study, the Chinese patients in the pharmacist-managed group spent more time in the therapeutic and the expanded therapeutic INR ranges when compared with those in the physician-managed group and the difference achieved statistical significance. The mean cPPPM was significantly reduced by 22% [US\$98 (£55) in the physician-managed group vs. US\$76 (£43) in the pharmacist-manage group].

Coordinated anticoagulation care has been endorsed by the ACCP to be the primary approach in the management of warfarin therapy and it has also been accepted as the model of care in the UK and in the Netherlands [2]. Physicians, pharmacists and nurses, if properly trained, can all be providers of an anticoagulation service. In our study, both the pharmacist-managed and the physician-managed clinic were operated as a coordinated anticoagulation service and the 137 patients managed by the two groups achieved high-quality anticoagulation control of 61% and 77% of patient time spent in the therapeutic and the expanded therapeutic INR ranges, respectively. These results are consistent with the findings in European ancestries that the therapeutic and the expanded therapeutic INR ranges were achieved 40–64% [17] and >75% [18] of the time, correspondingly, in patients managed by an anticoagulation clinic. Nonetheless, the patients in the pharmacist-managed group had a slightly but significantly better INR control when compared with those in the physician-managed group. The clinical pharmacist in the pharmacist-managed group provided intense education to the patients and their caregivers, checked patients' adherence more thoroughly and, as a drug expert, provided extra attention to the potential warfarin–drug and warfarin–herb interactions at each clinic visit. Moreover, the pharmacist conducted telephone follow-up of those with poor adherence or difficult INR control and a hotline telephone was available to the patients to inquire about warfarin-related issues. All these may contribute to the improved INR control in the patients managed by the clinical pharmacist.

In a study conducted by Fihn *et al.* [19], the relative risk for a first serious bleeding event was 1.9 (95% confidence interval 1.3, 3.0) times greater in women than in men even after adjustment for intensity of treatment. In our study, though the pharmacist-managed group had significantly more female patients than the physician-managed group (65% vs. 45%, $P = 0.031$), there was no significance difference in the incidence of major bleeding complications between the study and control groups. Nevertheless, the planned sample size of our study was not powered to assess the difference in incidence of

complications between the two groups. The bleeding rates detected in our study (1.6–3.1%) were similar to those reported in the anticoagulation service (0–2.4%) but lower than that reported in usual medical care (3.9–17.8%) [13, 17, 18, 20, 21]. Similarly, the rates of TE in both groups were the same (1.6%) and they were also consistent with the reported TE rates for anticoagulation service (0–3.5%) but lower than that reported in usual medical care (6.2–11.8%) [13, 17, 18, 20, 22].

The mean total cPPPM was significantly reduced when patients were managed in the pharmacist-managed clinic. The result was similar to overseas cost-effectiveness analyses of pharmacist-managed anticoagulation service – it was less costly and more effective than the usual medical service provided by physicians [13, 17, 21]. The cost saving was due mainly to the decreased running cost of the clinic visits in the pharmacist-managed group. Sensitivity analysis showed that the pharmacist-managed service became more costly if the cost of the clinic visit was the same as that of the physician-managed clinic.

The patients in the pharmacist-managed group showed a significantly higher overall patient satisfaction score compared with that of the physician-managed group, attributed to the improved satisfaction scores in technical quality, interpersonal manner, communication, time spent and accessibility. In addition, the pharmacist conducted telephone follow-up for selected patients with difficult INR control or adherence issues between their clinic visits and a phone line was available for accessing pharmacist consultation. Our finding of higher patient satisfaction in the pharmacist-managed anticoagulation clinic was consistent with the results of patient satisfaction of a trial conducted by Wilson *et al.* [14].

One limitation of the study is that the present sample size did not provide enough power to detect the difference in incidence of complications between the study and control groups. Nevertheless, the sample size provided adequate power to detect the difference in the percentage of patient time in target INR ranges, total direct medical cost as well as patient satisfaction. Another limitation was that the administrator of PSQ-18 was not blinded to the patient allocation despite the survey administrator not being an investigator of the present study. The actual 'time spent' by the pharmacist or physician for clinic visits in the two groups was not captured in our study. A sensitivity analysis was therefore included to examine the variation of cost of clinic visit that might arise due to different 'time spent' in the two groups. Other potential limitations applicable to both groups included self-reporting of complications,

change in brand/generic of warfarin and adherence to treatment recommendations by the patients.

In conclusion, a management model for anticoagulation therapy including a pharmacist as the primary care provider with physician consultation for predetermined conditions was more effective and less costly than a model of care managed solely by physicians in achieving target INR control for Chinese patients on warfarin therapy. Currently, this is the only pharmacist-managed anticoagulation clinic in Hong Kong. The results of the present study support the implementation of this model of care for anticoagulation management in other hospital settings in Hong Kong. Future research should also investigate the cost-effectiveness of a pharmacist service to manage anticoagulation therapy in other settings such as nursing home patients and patients engaged in self-monitoring of anticoagulation therapy.

We thank Ms Caroline Cheng for administration of the PSQ-18 survey. The present study was supported by the Health Care and Promotion Fund (reference no. 218013), Hong Kong.

References

- Hirsch H, Dalen JE, Anderson DR, Poller L, Bussey H, Ansell J, Deykin D. Oral anticoagulants: mechanism of action, clinical effectiveness, and optimal therapeutic range. *Chest* 2001; 119: 85–21S.
- Ansell J, Hirsh J, Dalen J, Bussey H, Anderson D, Poller L, Jacobson A, Deykin D, Matchar D. Managing oral anticoagulant therapy. *Chest* 2001; 119: 22S–38S.
- Weibert RT, Palinkas LA. Differences in warfarin dose requirements between Asian and Caucasian patients. *Clin Pharmacol* 1991; 49: 151.
- Yu HCM, Chan TYK, Critchely JAJH, Woo KS. Factors determining the maintenance dose of warfarin in Chinese patients. *QJM* 1996; 89: 127–35.
- Chenhsu RY, Chiang SC, Chou MH, Lin MF. Long-term treatment with warfarin in Chinese population. *Ann Pharmacotherapy* 2000; 34: 1395–401.
- You JHS, Chan FWH, Wong RSM, Cheng G. Is INR between 2.0 and 3.0 the optimal level for Chinese patients on warfarin therapy for moderate-intensity anticoagulation? *Br J Clin Pharmacol* 2005; 59: 582–7.
- Rieder MJ, Reiner AP, Gage BF, Nickerson DA, Eby CS, McLeod HL, Blough DK, Thummel KE, Veenstra DL, Rettie AE. Effect of VKORC1 haplotypes on transcriptional regulation and warfarin dose. *N Engl J Med* 2005; 352: 2285–93.
- Veenstra DL, You JHS, Rieder MJ, Farin FM, Wilkerson H, Blough DK, Cheng G, Rettie AE. Association of vitamin K epoxide reductase complex 1 (VKORC1) variants with warfarin dose in a Hong Kong Chinese patient population. *Pharmacogenetics Genomics* 2005; 15: 687–91.
- Yuan HY, Chen JJ, Lee MTM, Wung JC, Chen YF, Charng MJ, Lu MJ, Hung CR, Wei CY, Chen CH, Wu JY, Chen YT. A novel functional VKORC1 promoter polymorphism is associated with inter-individual and inter-ethnic differences in warfarin sensitivity. *Human Mol Genet* 2005; 14: 1745–51.
- Ellis RF, Stephens MA, Sharp GB. Evaluation of a pharmacy-managed warfarin-monitoring service to coordinate inpatient and outpatient therapy. *Am J Hosp Pharm* 1992; 49: 387–94.
- Ansell JE, Hughes R. Evolving models of warfarin management: anticoagulation clinics, patients self-monitoring, and patient self-management. *Am Heart J* 1996; 132: 1095–100.
- Foss MT, Schoch PH, Sintek CD. Efficient operation of a high-volume anticoagulation clinic. *Am J Health-Syst Pharm* 1999; 56: 443–9.
- Wilt VM, Gums JG, Ahmed OI, Moore LM. Outcome analysis of a pharmacist-managed anticoagulation service. *Pharmacotherapy* 1995; 15: 732–9.
- Wilson SJ, Wells PS, Kovacs MJ, Lewis GM, Martin J, Burton E, Anderson DR. Comparing the quality of oral anticoagulation management by anticoagulation clinics and by family physicians: a randomized controlled trial. *CMAJ* 2003; 169: 293–8.
- Havrdá DE, Hawk TL, Marvin CM. Accuracy and precision of the CoaguChek S versus laboratory INRs in a clinic. *Ann Pharmacother* 2002; 36: 769–75.
- Rosendaal FR, Cannegieter SC, van der Meer FJ, Briet E. A method to determine the optimal intensity of oral anticoagulant therapy. *Thromb Haemost* 1993; 69: 236–9.
- Chiquette E, Amato MG, Bussey HI. Comparison of an anticoagulation clinic with usual medical care: anticoagulation control, patient outcomes, and health care costs. *Arch Intern Med* 1998; 158: 1641–7.
- Garabedian-Ruffalo SM, Gray DR, Sax MJ, Ruffalo RL. Retrospective evaluation of a pharmacist-managed warfarin anticoagulation clinic. *Am J Hosp Pharm* 1985; 42: 304–8.
- Fihn SD, McDonnell M, Martin D. Risk factors for complications of chronic anticoagulation: a multicenter study. *Ann Intern Med* 1993; 118: 511–20.
- Conte RR, Kehoe WA, Nielson N, Lodhia H. Nine-year experience with a pharmacist-managed anticoagulation clinic. *Am J Hosp Pharm* 1986; 43: 2460–4.
- Lafata JE, Martin SA, Kaatz S, Ward RE. The cost-effectiveness of different management strategies for patients on chronic warfarin therapy. *J Gen Intern Med* 2000; 15: 31–7.
- Cortelazzo S, Finazzi G, Viero P, Galli M, Remuzzi A, Parenzan L, Barbui T. Thrombotic and hemorrhagic complications in patients with mechanical heart valve prosthesis attending an anticoagulation clinic. *Thromb Haemost* 1993; 69: 316–20.