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Comparison of a clinical pharmacist–managed anticoagulation service with routine medical care: impact on clinical outcomes and health care costs

Key Messages

1. Patients in the pharmacist-managed group spent a higher percentage of time in target therapeutic international normalised ratio range (64%) than those in the physician-managed group (59%).
2. Patients in the pharmacist-managed group experienced a lower incidence of bleeding (1.6 events per 100 patient-years) than those in the physician-managed group (3.1 events per 100 patient-years).
3. Mean cost per patient per month in the pharmacist-managed group (HK$593) was lower than that in the physician-managed group (HK$764).
4. The pharmacist-managed anticoagulation service was less costly and more effective than the physician-managed service.

Hong Kong Med J 2008;14(Suppl 3):S23-7

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HCPF project number: 218013

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Introduction

Warfarin is commonly prescribed for the treatment and prevention of thromboembolic events. The anticoagulant effect of warfarin, measured as the international normalised ratio (INR), is subject to wide inter- and intra-individual variability and could possibly lead to haemorrhagic or thromboembolic events, despite careful dosage titration.[1]

Overseas, the discipline of clinical pharmacy has been involving in anticoagulation services for over 20 years. Descriptive reports and comparative trials indicate that clinical pharmacist–managed anticoagulation services significantly lowered incidences of haemorrhagic and thromboembolic events, and improved INR control as compared to routine medical care. The cost savings ranged from US$375-1620 per patient-year.

The purposes of the present study were: (1) to compare the impact of a clinical pharmacist–managed and physician-managed anticoagulation services on the clinical outcomes of warfarin therapy in an ambulatory care setting in Hong Kong, and (2) to determine the cost-effectiveness of the clinical pharmacist–managed anticoagulation service from the perspective of a public health organisation.

Methods

Study design

This 2-year randomised clinical trial was conducted at the anticoagulation clinic of the Prince of Wale Hospital (PWH) in Hong Kong from October 2002 to September 2004. The patients were randomised to the physician-managed or pharmacist-managed service. A management protocol was developed by a haematologist, a clinical pharmacologist, and a pharmacotherapy specialist. Patients in the pharmacist-managed group were managed by a clinical pharmacist, strictly as per the management protocol. The physician-managed patients were managed at the discretion of individual physicians in the anticoagulation clinic.

Sample size

One hundred and thirty-seven patients aged 18 years or older, newly starting on warfarin, were enrolled at the anticoagulation clinic from November 2002 to June 2004. Patients started on warfarin with anticipated treatment duration of less than 3 months were excluded.

Outcome assessments

The primary outcome was the control of INR as per the expanded therapeutic INR ranges in the agreed management protocol. Therapeutic INR ranges for low- and high-intensity anticoagulation being 2-3, and 2.5-3.5, respectively, which was in accordance with recommendations of the American College of Chest Physicians Consensus Conference on Antithrombotic Therapy.[1] The expanded therapeutic INR range was defined as the therapeutic range ± 0.2 INR units. 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

Table 1. Patient demographics and indications for warfarin therapy

Demographics/indications	No. (%)	
	Pharmacist-managed group (n=68)	Physician-managed group (n=69)
Male*	24 (35)	38 (55)
Age (mean±SD) [years]	58±14.0	60±14.0
Patient-years	62	64
Intensity of anticoagulation therapy		
Low (therapeutic INR†: 2-3)	63 (93)	62 (90)
High (therapeutic INR: 2.5-3.5)	5 (7)	7 (10)
Indications		
Atrial fibrillation	37 (54)	35 (51)
Heart valve replacement	10 (15)	14 (20)
Deep vein thrombosis	8 (12)	9 (13)
Pulmonary embolism	5 (7)	4 (6)
Cerebrovascular accident	2 (3)	2 (3)
Valvular heart diseases	3 (4)	2 (3)
Cardiomyopathy	1 (1)	1 (1)
Miscellaneous	2 (3)	2 (3)

* P=0.031
† INR denotes international normalised ratio

Table 2. Control of international normalised ratio (INR) and incidence of complications

	% of patient-time	
	Pharmacist-managed group	Physician-managed group
Therapeutic INR range*	64%	59%
Expanded therapeutic range*†	78%	76%
Incidence of Bleeding (No. per 100 patient-years)		
Major	1.6	3.1
Fatal	0	0
Incidence of thromboembolic events (No. per 100 patient-years)		
Major	1.6	1.6
Fatal	0	0

* P<0.001 (Chi squared test)
† Expanded therapeutic range = therapeutic range ± 0.2 INR units

by Rosendaal et al.[2] The incidences of warfarin-related complications per 100 patient-years and direct health care costs, expressed as cost per patient per month (cPPPM) for anticoagulation therapy, were assessed as secondary outcomes. The cost-effectiveness ratio, presented as cost per patient-time spent in the therapeutic INR, was calculated for each group. The cost of the pharmacist-managed service was assumed to be 50% of that in the physician-managed service in the base-case analysis. A sensitivity analysis on the costs of the pharmacist-managed clinic was also performed.

Results

From November 2002 to June 2004, 68 and 69 patients (amounting to 62 and 64 patient-years respectively) were randomised to the pharmacist-managed and physician-managed services, respectively. Patient demographic data are shown in Table 1. There were no significant differences in age, intensity of anticoagulation therapy, and indications between the two groups, but the percentage of males was significantly lower in the pharmacist-managed group (P=0.031).

Patients in the pharmacist-managed and physician-managed groups spent 64% and 59% of patient-time in the therapeutic INR range (P<0.001), and 78% and 76% of patient-time in the expanded therapeutic range (P<0.001), respectively (Table 2). Further comparison of INR control by stratifying patients by gender showed that females in the pharmacist-managed group spent significantly more patient-time in both the therapeutic INR (65% vs 56%, P<0.001) and expanded therapeutic (79% vs 74% P<0.001) ranges than females in the physician-managed group. Male patients in the pharmacist-managed group spent more patient-time in therapeutic INR range than those in the physician-managed group, but this difference did not attain statistical significance. The distributions of patient-years in various INR categories for low-intensity and high-intensity anticoagulation therapy for the two study groups are shown in Figures 1 and 2. Overall, patients spent 61% of the time in the therapeutic INR range and 77% of time in the expanded range.

No patient had fatal events in the present study. One patient in each group experienced a transient ischaemic attack (1.6 events per 100 patient-years; P=1.00). Both patients were hospitalised and their symptoms resolved spontaneously. One patient in the pharmacist-managed group experienced menorrhagia with anaemic symptoms, whilst two in the

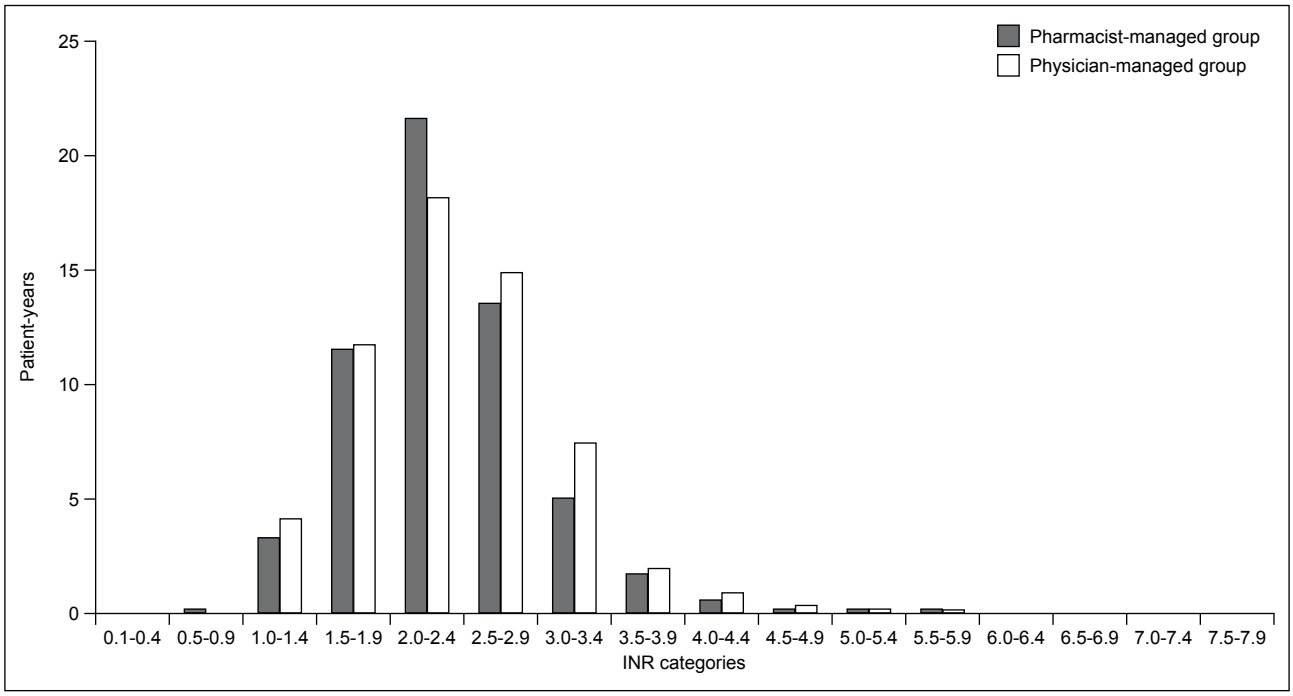

Fig 1. Distribution of patient-years among the international normalised ratio (INR) categories in the low-intensity group (target INR, 2-3)

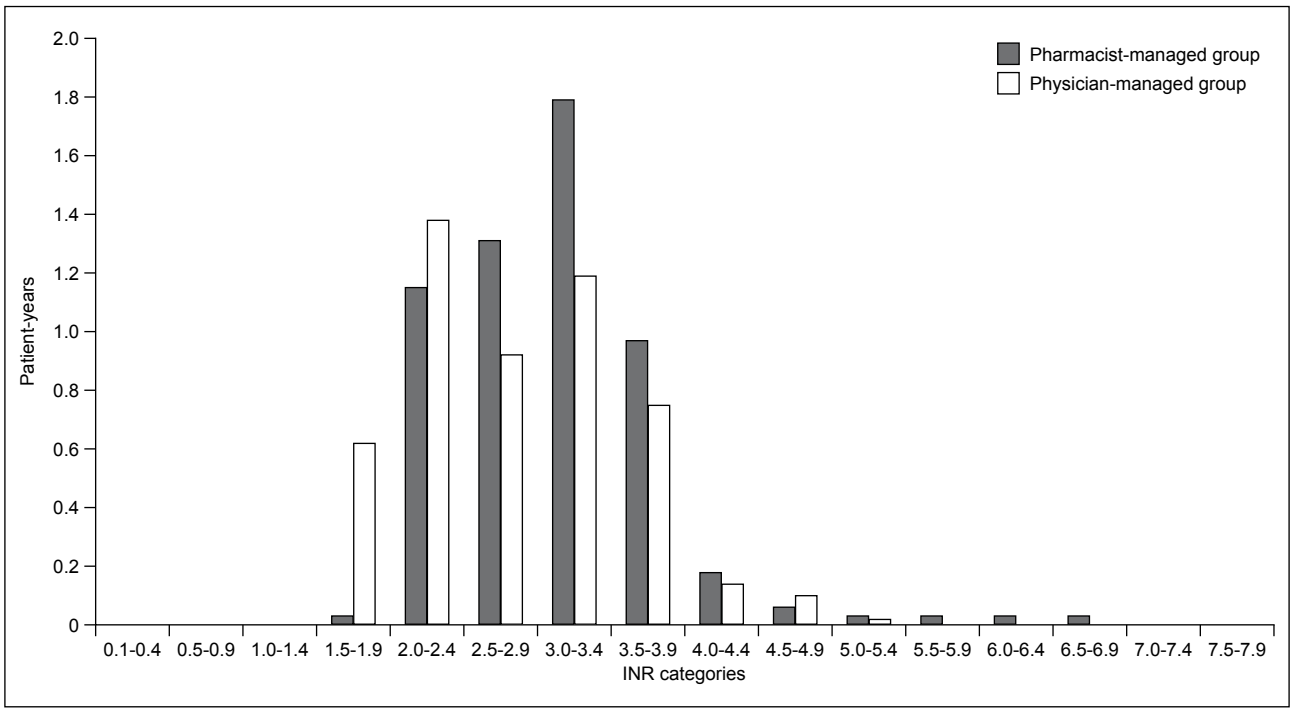

Fig 2. Distribution of patient-years among the international normalised ratio (INR) categories in the high-intensity group (target INR, 2.5-3.5)

physician-managed group experienced bleeding (one had extensive bruising with gross haemoptysis and another a major bleed from a peptic ulcer). Corresponding events per 100 patient-years amounted to 1.6 versus 3.1 (P=1.0). By logistic regression, the odds ratio for the occurrence of complications in the pharmacist-managed group was 0.67 (95% confidence interval [CI], 0.108-4.120; P=0.663).

The costs of major health care resource items and mean cPPPM values and their components are shown in

Table 3. Cost of major health care resource items

Cost item	HK$
Clinic visit	
Specialties clinic	700
Pharmacist-run clinic	350
Accident and Emergency Department visit	570
General ward hospitalisation (per day)	3300

Tables 3 and 4, respectively. The mean total cPPPM of the pharmacist-managed group was significantly lower than that of the physician-managed group ($593±741 vs $764±1232; P<0.01). The cost-effectiveness ratios of the pharmacist- and physician-managed groups were $927 and $1295 per patient month per 100% patient-time spent in the therapeutic INR range, respectively.

The cost of clinic visits was estimated by the number of visits and the cost per visit. The mean number of clinic visits in the pharmacist-managed group was significantly higher than that of the physician-managed group (8.1±3.7 vs 6.3±3.0; P=0.0027). The actual time-spent by each patient during the clinic visit was not recorded. Based on the number of providers per clinic session, duration of clinic sessions, and number of patients attending each session, the time-spent with each patient by each provider was roughly estimated to be 20 minutes and 16 minutes in the pharmacist-managed and physician-managed groups, respectively. The cost of each clinic consultation per patient in the pharmacist-managed group, assuming the salary of a pharmacist was 50% that of a physician, was approximately 60% of the cost of a clinic consultation in the physician-managed group, after adjustment for the difference in time-spent with each patient.

A sensitivity analysis was conducted on the cost of the pharmacist-managed service over a range of 10 to 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 to 60% of the cost of the physician-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 to 90% 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 the physician-managed clinic.

Discussion

The results of the present study showed that patients in the pharmacist-managed group spent a significantly higher percentage of time in the therapeutic and expanded therapeutic INR ranges, as compared to those in the physician-managed group. The mean cPPPM in the pharmacist-managed group was also significantly less by 22% (HK$593 vs HK$764).

Patients achieved 'high-quality' anticoagulation control in both the pharmacist- and physician-managed groups; the overall percentage of patient-time spent in therapeutic and expanded INRs ranges were 61% and 77%, respectively. Achievement of such control could be explained by the fact that the services of both groups were offered in an anticoagulation clinic. Coordinated anticoagulation care has been endorsed by the American College of Chest Physicians Consensus Conference on Antithrombotic Therapy to be the primary approach to improving control, and has also been accepted as the standard of care for warfarin therapy in the Netherlands and the United Kingdom.[3,4] Our results were consistent with other reported findings, namely management in anticoagulation clinics can achieve therapeutic and expanded therapeutic INR ranges in 40 to 64% of patients[5] and for over 75%[6] of the time.

In a study conducted by Fihn et al,[7] the relative risk for a first-time serious bleeding event was 1.9 (95% CI, 1.3-3.0) times greater in women than men, even after adjusting for the intensity of treatment. In our study, although the pharmacist-managed service had significantly more female patients than in the physician-managed service (65% vs 45%; P=0.031), the incidence of major bleeding complications was lower in the former group (1.6% vs 3.1%), though due to the small numbers involved this difference did not achieve statistical significance. The bleeding rates detected in the pharmacist-managed group (1.6%) and physician-managed group (3.1%) were similar to those reported in anticoagulation services as a whole (0-2.4%), but lower than those reported in usual medical care (3.9-17.8%).[5,6] Similarly, the rates of thromboembolic events in both groups were the same (1.6%) and consistent with the reported thromboembolic event rates for anticoagulation services (0-3.5%) but lower than the reported rates in usual medical care (6.2-11.8%).[5,6]

The cost-effectiveness analysis showed that the pharmacist-managed group was superior to the physician-

Table 4. Costs per patient per month (HK$)

	Mean±SD		P value
	Pharmacist-managed group	Physician-managed group	
Clinic visit	356±271	526±399	<0.01
Medication	21±12	20±9	0.269
Emergency room	8±21	8±31	0.195
Hospitalisation	204±707	210±1133	0.102
Total	593±741	764±1232	<0.01

managed group, such that the INR control of patients was significantly improved and the cPPPM was significantly lower. These results were consistent with overseas cost-effectiveness analyses of pharmacist-managed anticoagulation services as compared to those provided by physicians.[8]

One of the limitations of this study was that the number of patients recruited did not achieve the pre-determined proposed sample size. Nevertheless, the present sample size provided adequate power to detect the difference in the percentage of patient-time within the target INR ranges and the cPPPM between the two study groups. The study was also limited by the actual (and proposed) sample size not being powered to detect differences in the incidence of bleeding or thromboembolic events; this would have required a duration of much longer than 2 years. One limitation in our cost analysis was that the study was performed from the perspective of a public health organisation, and only direct medical costs documented in the PWH were considered. Direct medical costs associated with private medical care or non-PWH public health care were not captured.

In conclusion, the pharmacist-managed anticoagulation service was more effective than the physician-managed service in achieving target INR ranges, particularly with respect to female patients, and was also less costly (as long as the pharmacist's hourly consultation rate did not exceed 60% that of the physicians). Further investigation of the impact of a pharmacist-managed anticoagulation services on complication rates is warranted to determine their long-term effectiveness.

Acknowledgements

This study was supported by the Health Care and Promotion Fund (#218013). We thank Dr Raymond SM Wong for supporting the service in physician-managed group, Mr Fredric WH Chan for supporting the service in pharmacist-managed group, and Mr WH Lau for data collection and analysis.

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