OUTCOMES OF PHARMACIST COUNSELING ON OUTPATIENTS RECEIVING WARFARIN AT SAMUTPRAKARN HOSPITAL

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A Thesis Submitted in Partial Fulfillment of the Requirements
for the Degree of Master of Science Program in Social and Administrative Pharmacy
Department of Social And Administrative Pharmacy
Faculty of Pharmaceutical Sciences
Chulalongkorn University
Academic Year 2010
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ผลลัพธ์ของการให้คำแนะนำของเภสัชกรแก่ผู้ป่วยนอกที่รับประทานยาวาร์ฟาริน
ณ โรงพยาบาลสมุทรปราการ

นางสาว ศิระยา เล็กเจริญ

ศูนย์วิทยทรัพยากร
จุฬาลงกรณ์มหาวิทยาลัย

วิทยานิพนธ์นี้เป็นส่วนหนึ่งของการศึกษาตามหลักสูตรปริญญาวิทยาศาสตรมหาบัณฑิต
สาขาวิชาเภสัชศาสตร์สังคมและบริหาร ภาควิชาเภสัชศาสตร์สังคมและบริหาร
คณะเภสัชศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย
ปีการศึกษา 2553
ลิขสิทธิ์ของจุฬาลงกรณ์มหาวิทยาลัย

Thesis Title	OUTCOMES OF PHARMACIST COUNSELING ON OUTPATIENTS RECEIVING WARFARIN AT SAMUTPRAKARN HOSPITAL
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Field of Study	Social and Administrative Pharmacy
Thesis Advisor	Assistant Professor Puree Anantachoti, Ph.D.

Accepted by the Faculty of Pharmaceutical Sciences, Chulalongkorn University in Partial Fulfillment of the Requirements for the Master's Degree

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ศิระยา เล็กเจริญ: ผลลัพธ์ของการให้คำแนะนำของเภสัชกรแก่ผู้ป่วยนอกที่รับประทานยาวาร์ฟาริน ณ โรงพยาบาลสมุทรปราการ. (OUTCOMES OF PHARMACIST COUNSELING ON OUTPATIENTS RECEIVING WARFARIN AT SAMUTPRAKARN HOSPITAL) อ. ที่ปรึกษาวิทยานิพนธ์หลัก: ผศ. ภญ. ร.ต.ท.(ญ) ดร.ภูรี อนันตโชติ, 81 หน้า.

การศึกษาเปรียบเทียบผลก่อนและหลังการให้คำแนะนำของเภสัชกรแก่ผู้ป่วยนอกที่รับประทานยาวาร์ฟาริน จากระดับความรู้เกี่ยวกับยาวาร์ฟาริน ความร่วมมือในการใช้ยาของผู้ป่วย ค่า INR ภาวะเลือดออก ภาวะลิ่มเลือดอุดตัน ค่าใช้จ่ายของการเข้านอนในโรงพยาบาล และ เข้ารักษาที่ห้องฉุกเฉิน ในช่วงเดือนมกราคม 2551 ถึงเดือนมกราคม 2552 โดยตัวอย่างเป็นผู้ป่วยนอกที่ได้รับการรักษาด้วยยา วาร์ฟารินแบบระยะยาว ในโรงพยาบาลสมุทรปราการ ระหว่างช่วงที่มีการศึกษา และกลับมาตามนัดติดตามไม่น้อยกว่า 3 ครั้ง เก็บข้อมูลจากผู้ป่วยทั้งสิ้น 132 คน ตั้งแต่วันแรกที่ได้รับคำแนะนำจนถึงการนัดติดตามครั้งที่ 3 ผลการศึกษาพบว่าผู้ป่วยที่ได้รับคำแนะนำจะมีระดับความรู้เกี่ยวกับยาวาร์ฟารินเพิ่มขึ้น และคงอยู่จนถึงการนัดติดตามครั้งที่ 3 ความร่วมมือในการใช้ยาของผู้ป่วยเพิ่มขึ้นในนัดถัดไปของการติดตาม ร้อยละของผู้ป่วยที่มีค่า INR อยู่ในช่วงการรักษาที่เหมาะสมเพิ่มขึ้นในช่วงหลังจากที่ได้รับคำแนะนำ (ร้อยละ 22.1 และ ร้อยละ 73.5) ร้อยละของผู้ป่วยที่มีค่า INR ต่ำกว่า และมากกว่าช่วงที่ให้ผลดีต่อการรักษา ลดลงในช่วงหลังจากที่ได้รับคำแนะนำ (ร้อยละ 53.8 และ ร้อยละ 14.1 ร้อยละ 24.1และ ร้อยละ 12.4 ตามลำดับ) ภาวะเลือดออกและอาการที่บ่งชี้ว่ามีภาวะลิ่มเลือดอุดตัน ลดลงหลังได้รับคำแนะนำ (ร้อยละ 3.6 และ ร้อยละ 1.7 ร้อยละ 2.4 และ ร้อยละ 1.6 ตามลำดับ) จำนวนครั้งของการเข้ารับการรักษาในโรงพยาบาลที่มาจากการใช้ยาวาร์ฟารินลดลงหลังจากได้รับคำแนะนำ (10 ครั้ง และ 4 ครั้ง) และช่วยประหยัดค่าใช้จ่ายในการนอนโรงพยาบาลคิดเป็น 242,357.52 บาท

ผลการศึกษาทำให้สรุปได้ว่าการให้คำแนะนำของเภสัชกร ช่วยเพิ่มความรู้เรื่องยาให้แก่ผู้ป่วย เพิ่มความร่วมมือในการใช้ยา ช่วยให้ผู้ป่วยสามารถสังเกตและปฏิบัติตนเพื่อป้องกันภาวะแทรกซ้อนจากการใช้ยา และช่วยประหยัดค่าใช้จ่ายของการเข้ารับการรักษาในโรงพยาบาล

ศูนย์วิทยทรัพยากร
จุฬาลงกรณ์มหาวิทยาลัย

ภาควิชา เภสัชศาสตร์สังคมและบริหาร ลายมือชื่อนิสิต.....

สาขาวิชา เภสัชสังคมศาสตร์และบริหาร ลายมือชื่อ อ.ที่ปรึกษาวิทยานิพนธ์หลัก.....

ปีการศึกษา 2553

5076853033 : MAJOR SOCIAL AND ADMINSTRATIVE PHARMACY

KEYWORDS : WARFARIN / OUTPATIENTS / PHARMACIST COUNSELING

SIRAYA LEKCHAROEN : OUTCOMES OF PHARMACIST COUNSELING ON OUTPATIENTS RECEIVING WARFARIN AT SAMUTPRAKARN HOSPITAL. THESIS ADVISOR : ASST. PROF. PUREE ANANTACHOTI, Ph.D., 81 pp.

This one group pre-test and post-test study was designed to assess the outcome of pharmacist counseling on outpatients receiving warfarin therapy by compare patients' knowledge, compliance, International Normalized Ratio (INR), bleeding and thromboembolic events, and cost for hospitalization and ER visits between pre- and post- pharmacist counseling from January 2008 to January 2009. Samples were outpatients who received long-term warfarin therapy at Samutprakarn Hospital during the study period and have been followed up at warfarin clinic not less than 3 visits. Data were collected on 132 outpatients from an intervention day until three follow-up at warfarin clinic. Patients' knowledge of warfarin therapy increased after receiving pharmacist counseling service and maintained until a third visit. Patients' compliance to warfarin regimens was improved in the second visit. Percentage of patients whose INR within therapeutic range was increase after receiving pharmacist counseling (22.1% VS 73.5%). Percentage of patients whose INR lower and higher than therapeutic range were decreased after receiving pharmacist service (53.8% VS 14.1%, 24.1% VS 12.4%). Bleeding and thromboembolic events at post pharmacist counseling were reported lower than pre-pharmacist counseling (3.6% VS 1.7%, 2.2% VS 1.6%). A lower event of hospitalizations after counseling service (10 events VS 4 events) produced cost saving of 242,357.52 baht.

From this study showed that pharmacist counseling could improved patients' knowledge, compliance, anticoagulation control, reduced bleeding and thromboembolic events and annually saved cost in reduced ER visits and hospitalizations.

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Academic Year :	2010		

ACKNOWLEDGEMENTS

The Author is grateful to Asst. Prof. Puree Ananthachoti, Department of Social and administrative pharmacy, Faculty of Pharmaceutical Sciences, Chulalongkorn University for her support and valuable comment as my major advisor. I also would like to thank Asst. Prof. Sathipong Tanaviriyakul,Ph.D., Asst. Prof. Rungpetch Sakulbumrungsil, Ph.D. and Asst. Prof. Charoen Treesak for their supporting and serving on the members of my committee.

The author also thankful Samutprakarn Hospital for supporting the database for this study. In addition the author would like to pass my gratefulness and sincere appreciation to all pharmacy colleagues at the ambulatory pharmacy unit for help and contribution in data collection.

From my heart, I would like to thankful for my parents and my family for always gave me love, care and special support.

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CHAPTER I

INTRODUCTION

Rational and background

Warfarin is an anticoagulant drug that has been used as an oral anticoagulant therapy for more than 50 years. [1] Warfarin is a vitamin K antagonists. It has been used for treatment and prevention of thromboembolic disorders. [2] It is indicated for various thromboembolism such as deep vein thrombosis (DVT), pulmonary embolism (PE), and thromboembolic complications associated with atrial fibrillation (AF) or mechanical heart valve replacement (MVR) and prevention of stroke, recurrent infarction or death in patients with acute myocardial infarction. [3]

Warfarin is a high alert drug because of its narrow therapeutic range of efficacy and safety. The drug itself can cause serious side effects such as bleeding, thromboembolic complications, and death in some cases. In 2003 and 2004 anticoagulant drug were ranked first among other drugs causing adverse effects in therapeutic use on death certificates. [4] The journal of the American College of Chest Physician 2004 dedicated volume 126 for anticoagulant drug. [5] Many studies presented higher rate of major bleeding and fatal bleeding as a result of warfarin therapy compared to other anticoagulant drugs. A randomized trial in patients with atrial fibrillation reported that the rate of intracranial bleeding was 13% per year with warfarin, compared with 3% per year in placebo, and the rate of fatal bleeding was 3% per year with warfarin, compared with 1% per year in placebo. The results of another randomized trial in patients with ischemic heart disease compared the rate of intracranial bleeding and fatal bleeding between warfarin therapy and aspirin (500 mg three times a day). It was found that intracranial bleeding incidence and fatal bleeding incidence were 21% VS 5% and 8% VS 4% for warfarin and aspirin, respectively. A randomized trial in patients with venous thromboembolism reported that the major bleeding was 12% in warfarin therapy compared with 3% in enoxaparin (4,000 IU subcutaneous one a day) therapy. All 3 randomized control trial in patients with venous thromboembolism reported that the major bleeding was 12% in warfarin

therapy compared with 3% in enoxaparin (4,000 IU subcutaneous one in patients with atrial fibrillation, ischemic heart disease and venous thromboembolism showed that warfarin cause bleeding and fatal bleeding in a higher rate comparing to other anticoagulant drugs such as aspirin and enoxaparin.

Warfarin also has various kinds of drug-drug and drug-food interactions which affect pharmacokinetic and pharmacodynamic variability which result in the response to warfarin. Patients have to pay attention to their lifestyle and diet as it may result in poor anticoagulation control. Because warfarin is a vitamin K antagonist, high vitamin K diets such as broccoli, cauliflower, cabbage, green peas, lettuce, spinach and watercress may result in inhibition of warfarin's effect. [6]

The management of patients on warfarin therapy was developed continually. Originally a model of patient care was usual care (UC) which provided by a primary care physician. As warfarin continued to cause drug related problems, risk management strategies has been developed. A new model proposed that pharmacist and other health care team together help responsible for decrease risk and increase safety among patients receiving warfarin therapy. Over the past 50 years, anticoagulation clinic has been established. The goals are to minimize complications such as thromboembolism and hemorrhage while maintaining an anticoagulation control. [7] Pharmacists in anticoagulation management service (AMS) are responsible for educating the patients, obtaining medication history and providing therapeutic consultation to physicians. Many studies showed that AMS resulted in better clinical outcomes when compared to UC. [4,8,9] These results indicated a reduction in the incidence of major bleeding and thromboembolism.

Samutprakarn Hospital established "Warfarin Clinic" in October, 2007 to help manage risk among patients who receive warfarin therapy. In the past, frequency drug related problems (DRPs) among warfarinized patients who on warfarin were dosage too high, dosage too low, drug-drug interactions, food-drug interaction, non compliance, and life style problems. AMS provided by warfarin clinic should help reduce bleeding and thromboembolic events, and improve anticoagulation control of patients.

Objective

The objective of this study was to evaluate result of warfarin clinic. Program evaluation was divided into two levels. Program level and patient level. First, program level was focus on cost saved from reducing number of emergency department visits and hospitalizations. For patient level evaluation was to compare knowledge score, compliance score, proportion of INR in therapeutic goal, percentage of bleeding events and thromboembolic events before and after pharmacist counseling services.

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CHAPTER II

LITERATURE REVIEW

This chapter is composed of four sections. The first section describes the medical importance of warfarin. The second section describes factors affecting coagulation control. The third section describes the anticoagulation clinic and network of warfarin clinics. And the last section describes program evaluation of warfarin clinic from aboard and Thailand**.**

The medical importance of oral anticoagulant therapy.

Warfarin is the oral anticoagulant drug that has been widely used for various indications. It is well known because of its' adverse drug reaction (ADR) such as major bleeding and embolism. It was also blamed as a leading cause of death among other drugs in death certificate in 2003 and 2004 in the USA. [(1)] American College of Chest Physician in 2004 dedicated 126 th volume of its journal of warfarin presented a high rate of major bleeding and fatal bleeding of warfarin therapy. [(2)] A randomized trial in patients with AF reported intracranial bleeding incidence and fatal bleeding incidence were 21% VS 5% and 8% VS 4% for warfarin and aspirin, respectively. Moreover, results in patients with ischemic heart disease compared the rate of intracranial bleeding and fatal bleeding between warfarin therapy (21% and 8%, respectively) and aspirin (500mg three times a day) (5% and 4%, respectively). And the results in patients with venous thromboembolism reported that the major bleeding was 12% in warfarin therapy compared with 3% in enoxaparin (4,000 IU subcutaneous one a day) therapy.

In 1990 to 2002, The National Patient Safety Agency, United Kingdom reported 480 case of adverse event from the use of anticoagulants. Among these, 120 cases were reported death. Warfarin and heparin were accounted for 72% and 23% of all reported dead cases, respectively. The major reason was from carelessness of health care provider on guidelines following. [(3)]

A meta-analysis of Baglin et al in 2007 found that first time warfarin users had a high risk of major bleeding in the first 3 month to 1 year of warfarin therapy. [4] Moreover in outpatients, it occurred rather frequently in medication error. From its high rate of serious adverse events leaded to increasing cost of emergency department visit and admission.

Frequency monitoring and dose adjustment were improved anticoagulation control and reduced complications of treatment. Many studies demonstrated that pharmacist-managed anticoagulation service could improve efficacy and safety of warfarin therapy more than usual care provided by physicians. They reported clinical outcomes as percentage of INR in therapeutic goal, rate of bleeding, rate of thromboembolism, percentage of hospitalization and patients' compliance. [2, 3]

Duration of time that patients had INR outside therapeutic range could indicate how well one had anticoagulation control. It was found that length of time one had INR outside therapeutic range was significant related to non-compliance. [5,6] Simultaneously, factors that found to be affected compliance were education level, employment status, mental status and cognitive behavior (especially among elderly patient). [5, 6] Although various factors were related to warfarin non-compliance, they founded that low knowledge level about warfarin therapy was a major cause of non-compliance. Patients who understand and responsible for their regimen, weren't often miss of warfarin dosing. [1, 7]

Factors affecting coagulation control

Many factors were found to have effect on anticoagulation control. These factors can be largely identified in 2 groups; drugs related factor and non-drugs factor. Example of drugs related factors are pharmacokinetics, pharmacodynamics, drug-drug interaction and drug-food interaction. For non-drug factor, the examples are patients' knowledge, patients' compliance, health care service factor and patients' genetic.

1. <u>Drug-drug interaction</u>

The drug interaction is classified in 2 types, potentiation (increase effect of warfarin) and inhibition (reduce effect of warfarin). Numerous drugs may interact with warfarin through pharmacokinetic or pharmacodynamic mechanisms by different pathways. The intensity of anticoagulation correlates directly with incidence of

hemorrhage. There are several pharmacokinetic and pharmacodynamic factors that influence effect of warfarin.

1.1 Pharmacokinetic Factors

Drugs influence the pharmacokinetics of warfarin by reducing absorption and interfering metabolic clearance, thus affected the anticoagulant response. Warfarin when taking with phenylbutazone, sulfinpyrazone, metronidazole, trimethoprim-sulfamethoxazole, fluconazole, isoniazid, lovastatin, sertraline and amiodarone will reduce clearance of warfarin which resulted in increase warfarin effect on the prothrombin time. On the other hand, when taking warfarin with barbiturates, rifampicin, and carbamazepine will increase hepatic clearance which reduce warfarin effect. [8, 9, 10]

1.2 Pharmacodynamic Factors

Other drugs influence the pharmacodynamics of warfarin by inhibiting synthesis or increasing clearance of vitamin K-dependent factors. which lead to increasing the anticoagulant effect of warfarin. For example, second- and third-generation cephalosporins which inhibit the cyclic interconversion of vitamin K. Thyroxine increase the metabolism of coagulation factors. [11,8] Sulfonamides increase warfarin effect in patients consuming diets deficient in vitamin K by eliminating bacterial flora and worsen vitamin K deficiency. Erythromycin increase the anticoagulant effect of warfarin by an unknown mechanism. [9,10]

Drugs that potentiate bleeding on their own, when taken with warfarin may increase the risk of bleeding. These drugs which have warfarin-like activity include other anticoagulants (such as heparin), antiplatelet drugs (eg. acetylsalicylic acid, clopidogrel, dipyridamole, sulfinpyrazone and ticlopidine) and all NSAIDs and selective COX-2 NSAIDs. These drugs increase the risk of warfarin-associated bleeding by inhibiting platelet function. Aspirin is the most important because of its widespread use and prolonged effect. Aspirin and NSAIDs can produce gastric erosions that increase the risk of upper gastrointestinal bleeding. The risk of bleeding is heightened when high dose of aspirin are taken during high intensity warfarin therapy (international normalized ratio. INR 3.0 to 4.5). Both celecoxib and rofecoxib are reported to potentiate anticoagulation effect. Acetaminophen which is the

analgesic of choice for patients using warfarin, are moderated potentiation. All of these drugs should be avoided in combination with warfarin unless proven to provide benefit that over the risk of bleeding.

Well et.al. critically analyzed reports of interactions between warfarin and other drugs. [12] Each report received a summary score indicating the level of assurance that a clinically important interaction had occurred (level 1 = highly probable, level 2 = probable, level 3 = possible, and level 4 = doubtful). Many antibiotics are reported to potentiate the effect of warfarin in highly probable level. Several cardiac drugs had highly probable evidence that they potentiated the effect of warfarin such as amiodarone, clofibrate, propafenone, propanolol, and sulfinpyrazone. Quinolone, simvastatin, and acetylsalicylic acid had probable to potentiated warfarin. Highly probable evidence indicated that several drugs did not interact with warfarin, such as atenolol, felodipne, metoprolol, antacids, psyllium, ranitidine, naproxen, fluoxetine, ketoconazole, ibuprofen, diltiazem, tobacco, and vancomycin.

2. Drug-food interaction

Dietary with vitamin K sufficient reduces the anticoagulant response to warfarin. Dietary vitamin K is derived predominantly from phylloquinones in plant material. Phylloquinones neutralize the anticoagulant effect of warfarin because they are reduced to KH_2 (the reduced form of vitamin K) through the warfarin-insensitive pathway. Increased intake of dietary vitamin K sufficient to reduce the anticoagulant response to warfarin occurs in patients consuming green vegetables or vitamin K containing supplements.

Anne et al. concluded drugs and food interactions with warfarin by level of causation and direction of interaction. [9] Foods or vitamin K containing supplements which highly probable to potentiate the warfarin effect such as fish oil and mango, probable potentiations such as grapefruit and herbal products such as danshen, dong quai and Lyceum barbarum L. and cranberry juice was possible. In contrast green vegetable which high vitamin K content food were inhibition of warfarin's effect. These food such as broccoli, cauliflower, cabbage, green peas, lettuce, spinach and watercress. Foods are probable inhibition such as ginseng and soymilk. Herbal products are particularly problem because of the lack of quality control on their

contents and the failure of physicians to ask about their use [9]. Chronic alcohol consumption has a potential to increase the clearance of warfarin but a large amounts of wine has little influence on the prothrombin time. [8] In patients with liver disease, alcohol consumption is highly probable to potentiate the warfarin effect.

3. Various disease states of patients

Study of Rosendaal concluded that hepatic dysfunction potentiates the warfarin effect through impaired synthesis of coagulation factors. [8] Hypermetabolic state produced by fever or hyperthyroidism will increase warfarin effect by increasing the catabolism of vitamin K-dependent coagulation factors. Moreover this study found that disease states also affect warfarin effect. These disease states such as cancer, collagen vascular disease, diarrhea, heart failure, malnutrition and vitamin K deficiency may potentiate warfarin effect, on the contrary hypothyroidism and nephrotic syndrome may reduce warfarin effect.

4. Genetic factors

Warfarin is metabolized by cytochrome oxidase enzymes in the liver (CYP2C9). Mutations of these enzymes lead to changes in the rate of warfarin metabolism. Patients with genetic warfarin resistance require higher dose (5-20 fold) than average to reach an anticoagulant effect. This disorder reduced affinity of warfarin for its hepatic receptor. In some individual, gene mutation may cause change in warfarin response. Those which mutated gene coding for cytochrome oxidase enzymes production are prone to warfarin resistance. In contrast, those with mutations in the gene coding for cytochrome P450 are associated with lower dose requirements and higher risk of bleeding complication. A mutation in the factor IX propeptide were found to increase risk of bleeding without excessive of prothrombin time. [13]

5. Patients' noncompliance

The Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy describes that patient-specific factors such as adherence to a therapeutic plan were important for achieving and maintaining INR in the therapeutic range. [14] Poor compliance with warfarin therapy was major factor leading INR out of the therapeutic range. Study of Platt et al. concluded that patients who were warfarin noncompliance, could not maintain their INR in therapeutic range. [15] Waterman et al. reported 36% of

INR out of therapeutic range were a result of noncompliance, higher proportion than other reasons (dietary, drug interactions and change in clinical states). [16]

6. Patients' knowledge about warfarin therapy

Many studies showed that patients' warfarin knowledge significantly affecting the warfarin compliance. [17, 18, 19, 20, 21] Krittathanmakul et al. discussed in their study that an increasing knowledge of patients could help them to identify complications by themselves, immediately contact their physician in appropriation and associated with a decreased risk of bleeding. [19]

Taking warfarin more than one strength may increase the risk of accidental overdose and need additional patient education, especially in confused person or elderly. [22] Written and verbal information has been shown to improve anticoagulation control. Patients should know the risks of taking other medications and the importance of compliance on their wafarin therapy and anticoagulation clinic visit. Clinical pharmacy at Songklanagarind Hospital concluded that pharmacist counseling through verbal and written reinforcement could improve patients' knowledge about warfarin therapy, and may enable patients to identify complications related to the therapy, particularly minor bleeding. [17] Therefore patient education is significant to the success of warfarin therapy.

7. Miscommunication between the patient and physician or pharmacist

Effective communication between physicians and patients about warfarin therapy, can improve anticoagulation control and reduced complications [10]. Patient and physician communication is a critical part of clinical practice. Research findings reported in the issue of the Joint Commission Journal on Quality and Patient Safety found that nearly one half of patients on anticoagulants were not taking their medication accurately because they did not realize it. Misunderstanding patients in warfarin therapy were more likely to have INR outside the therapeutic range and were at risk for stroke, as well as life-threatening bleeding. Physicians and pharmacists gave a communication tools such as educational leaflet for patients, could be facilitate effective communication. An effective communication skills have correlated to outcomes such as adherence to therapy, understanding of treatment risk, lower health-related costs, reduce emergency department visits and increase patient satisfaction.

The objective of warfarin therapy is to decrease the clotting ability of the blood, so that thrombosis is prevented, while avoiding spontaneous bleeding. Effective therapeutic levels with minimal complications are in part dependent upon cooperative and well-instructed patients who communicate effectively with pharmacists.

The Accreditation Council for Graduate Medical Education recommends that physicians and health care personals become skilled in 5 key communication skills: (1) listening effectively, (2) making information using effective questioning skills, (3) providing information using effective explanatory skills, (4) counseling and educating patients, and (5) making informed decisions based on patient information.[12] The research in the Joint Commission Journal on Quality and Patient Safety 2007 developed a 3 steps communication (1) having the patient describe how much medication taking and how often (to identify misunderstanding), (2) giving the patient a communication tools, and (3) asking the patient what has just learned to ensure common understanding.[10] Therefore, it is essential for the physician or pharmacist to improve communication with patients.

8. Organization factors

One of the barrier to appropriately anticoagulation control have associated to patients, physician, and healthcare system factors. Physician surveys indicated that healthcare system barriers to optimal anticoagulation include delays in laboratory reports for INR and the lack of consultant services in anticoagulation management. [23]

9. Health care provider factors

Failure to achieve professional guidelines and inadequate skills of healthcare professionals prescribing, counseling, and monitoring anticoagualnts are important causes. Improvement can be achieved by desirable physicians and patient's knowledge perform through guidelines or protocols by health care policy. At primary care in UK, anticoagulants are one of the classes of medicines most commonly associated with fatal medication errors. In secondary care warfarin is one of the ten drugs most frequently associated with prescribing or dispensing error. [22]

Anticoagulation clinic and network of warfarin clinics

As many studies showed that anticoagulation management service (AMS) was better than usual care (UC). This section was intended to provide info about AMS history, AMS models, key elements of AMS from aboard and in Thailand.

Warfarin's qualification such as narrow therapeutic range, various medication and dietary interactions, leads to the development of specialized health care services to maximized effectiveness and safety of oral anticoagulation. The first anticoagulation clinic was based at Netherlands in 1949. In the 1950s the University of Michigan developed the first US anticoagulation clinic. [24] A anticoagulation clinics were then expanded in many European countries.

At present, many evidences and studies showed that the systematic care provided by an anticoagulation clinic resulted in improved safety and efficacy of the therapy leading to improve patient outcomes compared to the usual care. Reduction in adverse events such as thrombosis and bleeding, were led to lower hospitalization costs, thus establishing an anticoagulation clinics were more cost effective alternative comparing to conventional care.

Health care professional from various background such as physicians, pharmacists, nurses, and other health care providers gathered together as a group to have 4 major activities; (1) providing education and networking opportunities for health care professionals, (2) promoting the clinical applications of evidence-based practices, (3) facilitating research aimed at improving health outcomes, and (4) informing health care policy and regulatory agencies about best practice. The example of established group of anticoagulation network are The Anticoagulation Forum (ACF) based in the United States has a membership more than 1,500 anticoagulation clinics throughout the world. [14]

Patients on warfarin therapy were managed by different models of care. Patient care management was developed continuously. The initial model of patient care was managed by physicians or known as usual medical care (UC). Next various model was created such as anticoagulation management service (AMS) and Point-of-care (POC) testing.

Routine medical care or usual medical care (UC) is the management of patients who attend in UC, are consideration of physician in the general medicine and subspecialty clinics. [19, 25] In this model, patients are responsible for having laboratory testing, prothrombin time and INR performed as directed by their physician. Patient testing is performed by a conventional laboratory and results are interpreted and managed entirely by the physician who adjust or continued warfarin dosing and follow up testing. The process from initial venous blood draw to completed filed chart can take days, is labor intensive and has the potential for multiple communication errors.

Anticoagulation management service (AMS) is developed to provide more effective anticoagulation management. This clinic focuses on maintaining patient's therapeutic goals and minimizing adverse events. [19, 25] In this model, the clinicians attempt to provide an organized and complete approach in managing warfarin therapy. The most significant component of the patient's visit to the anticoagulation clinic is patient education. AMS has a various model of management service. It was classified by health care providers who managed anticoagulation service. Firstly, pharmacist-managed anticoagulation service is managed by a clinical pharmacist. Support is provided by a physician. Pharmacists review a medical history, physical examination and medication to determine the risk of bleeding and thromboembolism. Pharmacist will assess the appropriateness of warfarin dose, provide patient education and adjust warfarin dosage. Changes in other medications are approval of the physician.

Next nurse-managed anticoagulation service is organized by registered nurses, are indicated as the clinicians and assigned the responsibility, authority and deliver care to monitor patients on warfarin. [15, 26] The Nurses in the warfarin clinic are required to complete a certificate anticoagulation therapy training program. New patients receive counseling from nurse, warfarin dose adjusting and appointment. If patients have any complications, nurse has to inform a physician.

Multidisciplinary team-managed anticoagulation service is managed by a multidisciplinary team such as physicians, pharmacists, nurses, and other health care providers. A multidisciplinary team organized programs of education, coordination, monitoring and communication between patients and health care personals. At each visit, patients are assessed the response to warfarin therapy and received

anticoagulation education. Patient safety, satisfaction, education, and communication are the most important factors for a successful anticoagulation clinic. Much of the available information in the medical literature describes anticoagulation management service (AMS) models in which practitioners conduct face-to-face interviews at each patient visit. [27] Healthcare professionals who manage anticoagulation clinic should be licensed in a patient-oriented field such as medicine, nursing and pharmacy.

The lastest management model is systematic anticoagulation management or point-of-care (POC) INR testing device. It was firstly applied in 1980 for measuring INR and providing an alternative approach for the management of anticoagulation therapy. [16, 19] Point-of-care device was applied by healthcare providers in a clinic or patients. The patient and the result are in the same place at the same time. Thus patients are actively participated in their own care, which may lead to better understanding of how lifestyle can affect INR stability, bring about to improve efficiency and communication. The barriers to self-testing were high price of devices and reagent cartridges that prohibited patient self-testing.

Currently, the anticoagulation clinics in US are provided by a pharmacist-managed anticoagulation service. [27] The pharmacy anticoagulation service is a centralized team of clinical pharmacy (eg. those with a BS or PharmD degree), with specialized knowledge and skill in the coordination and management of anticoagulation therapy, including patient education, the ordering of relevant laboratory tests including INRs, the adjustment of anticoagulation medication doses and the management of adverse events. And changes in other medications are made with the approval of the physician in the general medicine clinic. The primary outcomes are a diagnosis of a major bleeding, thromboembolic complication or fatal event that is directly related to bleeding or thromboembolism. Bleeding resulted in hospitalization and ER visits. The secondary outcome is time spent in the target INR range.

The school of medicine, Boston University, USA provided an anticoagulation guideline for management outpatient on warfarin therapy [16, 21]. The multidisciplinary team delivered anticoagulation service by these procedures.

1. Evaluating specific risks of patients and their benefits to determine the appropriateness of treatment.
2. Facilitating the management of anticoagulation dosages. This is the responsibility of physician, nurse practitioner, physician assistant, or pharmacist.
3. Providing education of the patient and other caregivers about warfarin and the importance of self-care behavior leading to optimal outcomes.
4. Documentation of all dose decisions such as current dose, INR, new dose, next appointment and any anticoagulation-related problems
5. Providing continuous systematic monitoring of patients, INR results, diet, concomitant drug therapy, and disease states. These activity are run according to policies or guidelines of team such as anticoagulant indications, target INR and range, initiation and maintenance dosing policy, frequency of monitoring, management of non-therapeutic INRs, management of bleeding, use of vitamin K, management of anticoagulant during invasive procedures, duration of anticoagulation, and INR management responsibility when physician not available.
6. Communicating with other healthcare practitioners involved in the care of the patient.

To manage and monitor patients on the efficacy and toxicity of the anticoagulant therapy, determine whether INR (international normalized ratio) have been achieved a therapeutic goal (2.0 – 3.0) and identify patient-related factors that affect therapy. A careful assessment of the various factors that influence warfarin dosing (eg diet, disease, other medications, alcohol use, adherence) should be completed at all follow-up visits. Because a risk of thrombosis and bleeding can change over time, the intensity and length of anticoagulation therapy should be reevaluated periodically

Ability to provide patient education that promote safety, enhance adherence and achieved therapeutic goals. Patient safety is enhanced when patients are actively involved in, understand and take responsibility for their care. Knowledge of anticoagulation therapy can be effectively through face-to-face interactions and the use of materials to review and reinforce the educational process. [1, 27, 28]A knowledge

assessment tool may help the clinician to assess an individual patient's educational needs. Important aspects of patient education related to anticoagulation therapy are summarized in Appendix A. In addition, assessing patients' compliance could indicate that patients behave follow their therapeutic plan.

There are several strategies of educational programs that are used to managed the anticoagulation clinic. [28] Some issues such as signs of bleeding and INR monitoring were a component of most educational programs, while other issues such as vitamin K and activities were present only in some program. The personnel involved are varied such as physician, specially trained nurse, clinical pharmacist and multidisciplinary team. The duration of the educational intervention ranged from one to ten sessions. The testing of patient knowledge about warfarin used a variety of instruments such as true-false questions, multiple choice question, specific answers, dichotomous and open-ended questions. And they concluded that the best strategy for measuring patient knowledge would depend on the content of the educational program, but standardization of the testing should be a practical goal. Educational programs should focus on topics essential for patient safety , measured effectiveness and improvement in patient knowledge, adherence and clinical outcomes.

Establishment of warfarin clinic and network in Thailand

Initially, a pharmaceutical care in patients who received warfarin therapy in Thailand, are in form of patient education. Currently, pharmacist managed-anticoagulation clinics have been developed to multidisciplinary approach (Patient Care Team; PCT) in order to solve significant problems such as laboratory errors and transcribing errors in anticoagulation therapy. Pharmaceutical care in warfarin clinic are designed to monitor, and adjust warfarin dose to reach a therapeutic goal.

In 2007, 23.38% of Thai people died from heart attack and 24.41% died from stroke. [29] Cerebrovascular diseases are still a major cause of death in Thai population. American College of Chest Physician 2001 (ACCP) recommended that INR monitoring should be started after the initial 2 or 3 doses of anticoagulation therapy. For patients who received a stable dose of warfarin, their INR should be monitored at an interval of no longer than every 4 weeks. Problems such as a large amount of patients in tertiary care hospitals thus pharmacy responsibilities are increasing,

resulting in a pharmacist-managed anticoagulation clinic could not achieved the standard procedure of the ACCP 2001. From these problems were brought to establishing of the network of warfarin clinics in a primary care hospital in Thailand.

Siriraj Hospital, Maharaj Nakorn Rachasima Hospital and Maharaj Nakorn Chiangmai Hospital are expert and experienced pharmacist-managed anticoagulation clinics in Thailand. These hospitals were collaborated with The Association of Hospital Pharmacy (Thailand) for establishing a project of warfarin clinic training to other hospital. Currently, the network of pharmacist-managed warfarin clinics in Thailand, are compose of 10 hospitals such as Siriraj Hospital, Maharaj Nakorn Rachasima Hospital, Maharaj Nakorn Chiangmai Hospital, Songklanakarind Hospital, Prapokklao Chanthaburi Hospital, Udonthani Hospital, Sappasitthiprasong Ubonratchathani Hospital, Srinakarin Hospital (Khonkaen), Queen Sirikit Heart Center (Khonkaen) and Buddhachinaraj Hospital. Pharmacists are trained at 3 model hospitals which are Siriraj Hospital, Maharaj Nakorn Rachasima Hospital and Maharaj Nakorn Chiangmai Hospital. The model of warfarin clinic is a multidisciplinary team which conduct patient education in order to improve patient knowledge about warfarin's adverse effect and adherence.

The procedure to set up a warfarin clinic is composed of preparation, schedule and scheme for management service. [30] Firstly, pharmacists reviewed self-knowledge about pharmacotherapy, counseling technique and communication skill. And search for alignment to establish a multidisciplinary team. A multidisciplinary team may consist of physicians, pharmacists, nurses and other involved personnels. Preparation of counseling instruments such as a warfarin booklet, a warfarin card, flip chart, warfarin dosing card, patient database form, patient's education and evaluation form. And find a location that middle private for patient counseling. Next, Schedule of specification a strategy and guidelines to facilitate a patient care such as duration and frequency of counseling which appropriate with the total of warfarinized patients, target INR, initiation and maintenance dosing, and management of complications. [16, 30, 31] The next step is outline for warfarin clinic establishment. A multidisciplinary team will formulate a stated goal, a standard operation procedure, the target INR in each indication, warfarin dosing procedure, procedure for improving warfarin clinic in the future and indicators for warfarin clinic management. And the final stage is patient

data collection. Integrating patient database into hospital database or other software for collecting patients' data. Patient database is composed of a demographic information, an indication of warfarin, past and current illness and operative status, a family, social , economic history, drug allergy history, social drug use (alcohol, tobacco), the use of herbal and health food product, the target INR, baseline PT and INR, a routine exercise, baseline warfarin compliance, baseline physical assessment and laboratory data

Role and responsibility of each health care personal were professional difference but they coordinate and work as team working. A pharmacist's role in anticoagulation clinic composed of review patients' history and medication profiles, review and evaluate the relation between patient's INR and warfarin dosage, evaluate factors which effect to INR , for example, evaluate adverse events, interventions physician related dose adjustment and patient counseling to provide education that is promote safety and increase adherence. A physician managed warfarin dosing, follow-up visit and provide support as a consultant of warfarin clinic. Nurses deliver care to patients on interviewing a patient history, primary physical examination and reporting a patient's symptoms to a physician.

The activities of warfarin clinic managed by pharmacists is composed of 3 elements; patient assessment, INR monitoring and patient education. Pharmacists assess patients and prescription before dispense warfarin to patients. This is to double check for possible prescribing errors and dispensing errors. Patients assessment included patient history and medical history, assessment a knowledge of anticoagulation therapy assessment, patients' compliance with recommended dose, the relation between warfarin dosing and INR response, risk factors that influence on the INRs such as drug-drug interaction, diet, disease state and error from laboratory tests, risk of bleeding, signs and symptoms of bleeding and the cause assessment of adverse effects of warfarin. [31, 32, 33]

INR is a significant indicator for monitoring efficacy and safety of warfarin therapy. Various factors such as drugs, diet and clinical status of patients affect the warfarin response. [11, 13] Thus INR should be monitored at least 4 week interval. And if other drugs or herbal products were added or withdrawn from patients' regimen thus

INR should be monitored more frequently than the usual 4 week duration. [8, 13, 24] Due to the reason that sometimes INR testing was ignore because of patient loss to follow-up in their visit. According warfarin clinic take action role in monitoring patients' INR and consult medical physician if INR is outside the therapeutic range or found evidence of bleeding or embolism even though INR is in therapeutic range.

The Association of Hospital Pharmacy (Thailand) specified the patient educational guideline for warfarin clinic which was widely used in Thailand. In case of new patients who began to receive warfarin therapy, pharmacist will educate and provide a warfarin booklet to patients. Issues of anticoagulation therapy patient education such as the need of warfarin identification, the reason for initiating warfarin therapy, the need for blood testing and adherence with visits of warfarin clinic, signs and symptoms of bleeding and what to do if they occur, signs and symptoms of clotting complications and what to do if they occur, inform information if a dose is missed to physician, influence of dietary vitamin K use and potential drug interactions on the effect of warfarin and the importance of notify all health care providers (eg. other physicians, dentists) of the use of warfarin therapy. [31, 32, 33]

Many tools for pharmaceutical care were used in warfarin clinic management. Example for these tools were standard operative procedure, alerting tools; IT and sticker and educational material.

Program evaluation of warfarin clinic: experience from aboard and Thailand

Pharmacist-managed anticoagulation clinic are widely used for anticoagulation management in many countries. Goal of anticoagulation management are effective anticoagulation control and minimized complications. A primary key for achievement of its effectiveness and safety are achieving and maintaining the INR in the therapeutic range [14]. Many studies reported outcomes of anticoagulation therapy which managed by pharmacists compared with usual care (patients are managed by physicians). They assessed outcomes such as time in therapeutic range (TTR), percentage of INR within the therapeutic range which express as the number of INR values in the range divided by the number of INR test , rate of bleeding events and rate of thromboembolic events. And, in addition, they assessed cost-effectiveness of anticoagulation therapy

by anticoagulation clinic, as demonstrated by a cost avoidance per patient year of therapy.

Many studies reported improved outcomes when anticoagulation therapy was managed by a pharmacist compared with patients managed by usual care. Garabedian-Ruffalo et al. evaluated a pharmacist-managed warfarin clinic by compared outcomes with before pharmacists provide patient education and monitoring for complications. [35] The results indicated a percentage of INR outside the therapeutic range (35.5% VS 14.4%) were significantly higher at before pharmacist-managed service. Donovan et.al. reviewed many published studies and concluded that a pharmacist-managed anticoagulation clinic can improved INR in therapeutic goal and decreased length of hospitalizations. [36]

Tammy et.al. assessed a pharmacist- managed anticoagulation clinic compared with a period before a pharmacist management. [37] The study concluded that a pharmacist service could significantly improved INR control (66.5% VS 44.8%), reduced rate of thromboembolic events per 100 patient years (3.6 VS 49.2), reduced rate of bleeding events per 100 patient years (25.1 VS 15.3), saved 53 hours of ER visits and saved 11,415.46 Canadian dollar of hospitalization cost.

Daniel et al. compared a pharmacist-managed anticoagulation service by telephone and mail, with usual care. [27] The results showed that an alternative service could reduce thromboembolic events (41 VS 17), increased ratio of days that INR within therapeutic range (55.2% VS 63.5%) and decreased ratio of days that INR outside therapeutic range (44.8% VS 36.5%). Marvin et al. compared patients' outcomes from a pharmacist-managed anticoagulation clinic and a usual care. [38] The results indicated that patients who received anticoagulation clinic care were fewer INRs outside the therapeutic range compared with usual care (47.3% VS 40.4%) and less hospitalization rates (19.7 VS 4.7 admissions per 100 patient year).

Many studies in Thailand supported the benefit of pharmacist-managed anticoagulation clinic in improved anticoagulation control and minimized complications. Maharaj Nakorn Rachasima hospital established a pharmacist-managed anticoagulation clinic in 2004 and work together with a cardiology physician and

thoracic surgery physician. [39] Pharmacists provided services such as patient education, INR monitoring, warfarin dose adjustment with a physician and improve patient compliance. It was found that pharmacist-managed anticoagulation clinic increased percentage of INR in target range by 33 %, increased percentage of patient with low variability INR by 73% and reduced rate of major bleeding (4.6% VS 4.5%, respectively) and reduced rate of thromboembolic events (2.63% VS 0%, p=0.051, respectively).

Krittathanmakul studied at Songklanagarin Hospital concluded that pharmacist counseling could improved patients' knowledge of warfarin therapy, patients enable to identify complications related to the therapy by themselves result in INR within therapeutic range, and achieved patient compliance. [17] At each visit, the number of patients with INRs remaining in therapeutic range for each indication was 32.0%, 33.0% and 35.1% at the first, second and third visits, respectively. But, from this study, providing knowledge to patients may not be the only factor that effects the INR.

Nisaidee and Chuelueam assessed effects of educating warfarinized outpatients by pharmacists at Nakornpathom Hospital. They showed the results after counseling as increased patients' knowledge (p<0.001), reduced patients' noncompliance (19.62% VS 5.61%), reduced the use of OTC medication (7.48% VS 19.62%), reduced the use of herbal products (13.08% VS 1.87%) and reduced alcohol consumption (6.54% VS 3.74%). [40] Phannakham evaluated outcomes of warfarin clinic service at Sawangdandin Crown Prince Hospital, by compare pre- and post-service on anticoagulation control and complication. At post-service, they found an increased percentage of INR within therapeutic range (24.3 VS 48.3, p=0.008) and lower percentage of INR outside therapeutic range (72.9 VS 46.1, p<0.001). [41] But rate of bleeding events was not different in two phase of the study.

Reviewing the related paper and document, it can be concluded that pharmacist-managed anticoagulation clinic could increase patients' knowledge amd patients' compliance which resulted in improved INR within therapeutic range, lead to decrease bleeding and thromboembolism, and lead to decrease ER visit and hospitalization.

The study will be guided be the following conceptual framework

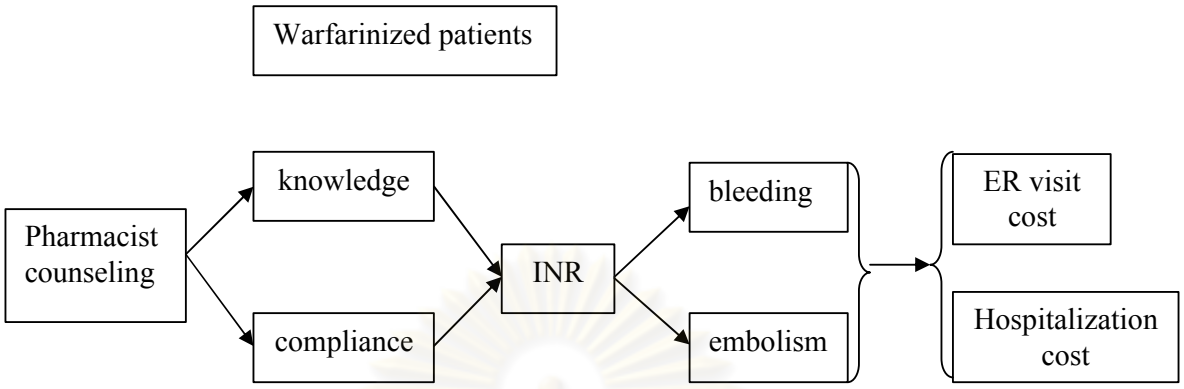

Figure 1: The conceptual framework of the study

In order to answer the research question, the following methodology is planned.

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CHAPTER III

METHODOLOGY

The goal of warfarin clinic establishment was to empower warfarinized patients to have adequate knowledge to care for themselves.The ambulatory care unit of Samutprakarn Hospital has provided routine warfarin since October, 2007. The multidisciplinary team consisted of 3 expert groups. The management team composes of 1 nurse and 2 physicians specialized in medicine, 1 nurse and 1 physician specialized in surgery, and 2 clinical pharmacists were responsible for the clinic. Since the inception of warfarin clinic, none of the evaluation has been done. This particular study is conducted to evaluate warfarin clinic on knowledge score, compliance score, percentage of INR within therapeutic range, bleeding events and embolic events. Moreover the study also planned to assess cost saving as a result of ER and hospitalization reduction.

Study design

The design of this study was a one group pre-test and post-test comparing pre-pharmacist counseling (usual medical care) at 1 year before and after anticoagulation management service (AMS). Patient's knowledge, compliance, anticoagulation control, complications (bleeding and thromboembolic events), number of ER visit and hospitalization were outcome of interest.

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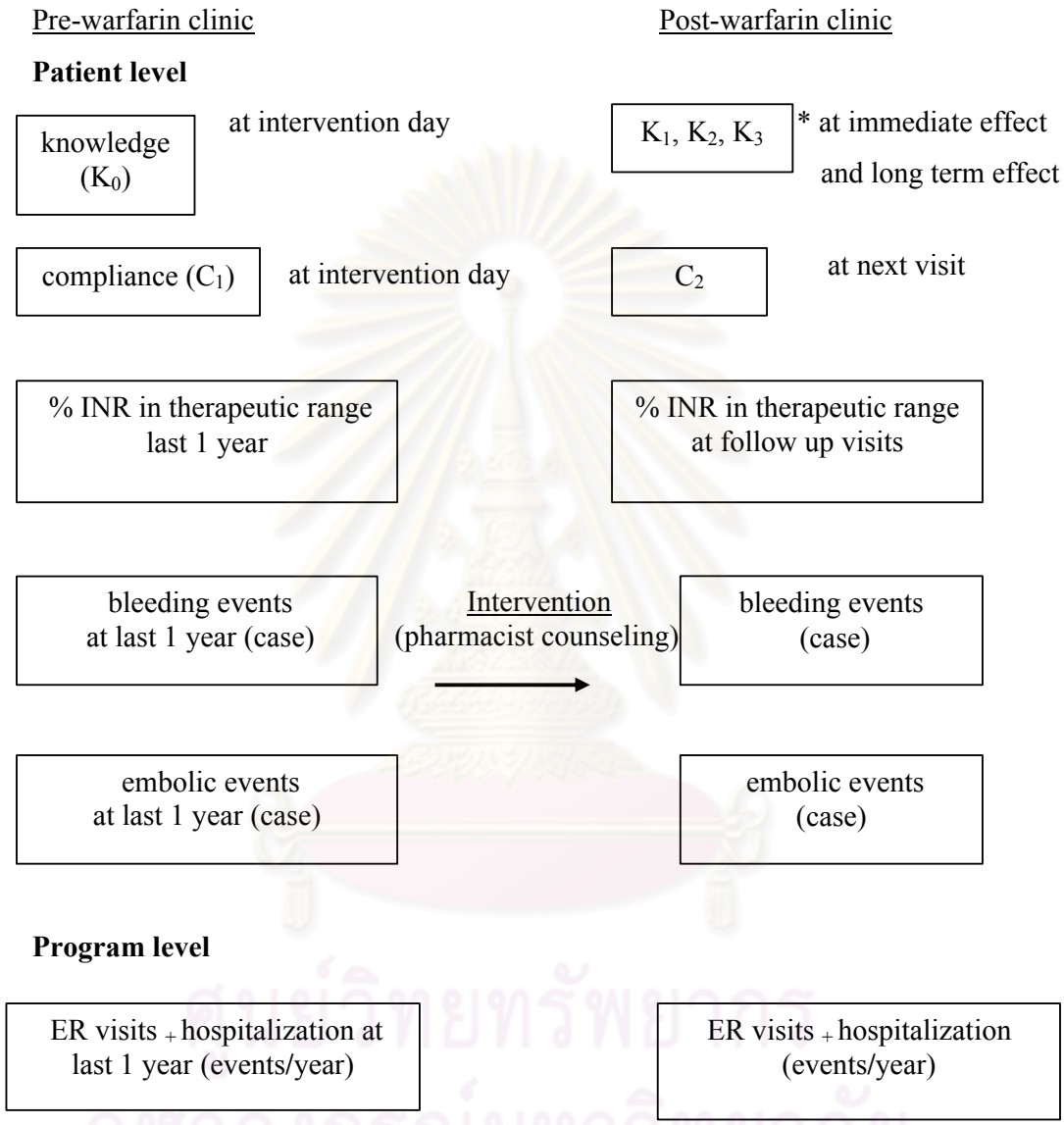
The study design was guided by the evaluation model show in figure 2.

Figure 2: The evaluation model



* mean K_1 is measured immediately at post-pharmacist counseling

K_2 is measured at next session visit (2-6 month)

K_3 is measured at third visit (7-12 month)

Hypotheses

The research questions and alternative hypotheses of this study are as follows:

1. Patients' knowledge (score) of post-pharmacist counseling had more than pre-pharmacist counseling.

H_A : $K_2 \neq K_1$

H_0 : $K_2 = K_1$

2. Patients' compliance (score) of post-pharmacist counseling had more than pre-pharmacist counseling.

H_A : $C_2 \neq C_1$

H_0 : $C_2 = C_1$

3. Percentage of INR within therapeutic range of post-pharmacist counseling had more than pre-pharmacist counseling.

H_A : %INR within therapeutic range $_{after} \neq$ %INR within therapeutic range $_{before}$

H_0 : %INR within therapeutic range $_{after}$ = %INR within therapeutic range $_{before}$

4. An incidence of bleeding events of post-pharmacist counseling had less than pre-pharmacist counseling.

H_A : percentage of bleeding case $_{after} \neq$ percentage of bleeding case $_{before}$

H_0 : percentage of bleeding case $_{after}$ = percentage of bleeding case $_{before}$

5. An incidence of thromboembolic events of post-pharmacist counseling had less than pre-pharmacist counseling.

H_A : percentage of embolic case ≠ percentage of embolic case $_{before}$

H_0 : percentage of embolic case = percentage of embolic case $_{before}$

6. Cost saving of the reduction of ER visit and hospitalization.

Population and Sample

The population for this study consisted of all outpatients who received warfarin therapy at Samutprakarn Hospital during the period of January 2008 to January 2009. Those who passed the Inclusion and exclusion criteria were included in the study.

Inclusion criteria

1.1 Outpatients who received long-term warfarin therapy at Samutprakarn Hospital during the study period of January 2008 to January 2009 were included.

1.2 Outpatients who have been followed up at warfarin clinic not less than 3 visits in 1 year-period of January 2008 to January 2009.

Exclusion criteria

2.1 Outpatients with symptomatic calf vein thrombosis which warfarin therapy is indicated for 6 to 12 weeks. Treatment is short duration.

2.2 Warfarinized outpatients who have a disease states that influenced warfarin effect such as fever, hyperthyroidism, hypothyroidism, nephrotic syndrome, cancer, heart failure, malnutrition and vitamin K deficiency.

2.3 Warfarinized outpatients who have an stable INR in therapeutic range (2-3) for at least 3 visits in last 1 year.

2.4 Warfarinized outpatients who have received warfarin therapy less than 3 months at pre-warfarin clinic.

2.5 Warfarinized outpatients who lost to follow up because of referral to other medical services or failure to contact, were excluded.

2.6 Warfarinized outpatients who were educated about warfarin therapy by other hospital or health care center.

Sample size estimation

This study compared within person change in knowledge. Data are analyzed by Paired *t*-test and the sample size is calculated by the following formula. In case of assessing % INR within therapeutic range, percentage of bleeding event, percentage of embolic event and percentage of hospitalization and ER visit, using Pearson's chi-square test

Snedecor et.al in 1989 suggested equation to estimate sample size for paired study. [51]

$N = 2 + C(S/d)^2$

N = sample size

C = constant value (C=7.85 at α level 0.05)

S = standard deviation of the variable

d = difference between two groups

From a pilot study composed of 30 patients for assess patient's knowledge about warfarin therapy, standard deviation of the variable(S) = 2.345 and difference between two groups (d) = 5.867. C is a constant that depends on the values chosen for α and β. The following list provides values of C for two levels of α and β.

	α	0.05	0.01
power (1-β)	0.8	7.85	11.68
	0.9	10.51	14.88

When power is 0.80, α of 0.05 so C= 7.85. Then $N = 2+7.85(2.345/5.867)^2 = 3.21$ pairs The number of sample required for this study is 6 persons.

Measurements

Data collecting form composed of 5 parts; a demographic data, clinical outcomes, patients' knowledge, other factors that affected warfarin response and hospitalization cost and ER visits cost.

A demographic data such as age, sex, primary and concomitant disease, dose and duration of warfarin therapy. Other factors that affected warfarin response were also collected. These data such as taking other medications, herbal product, supplement, vitamin K dietary, alcohol, smoking and contraceptive. These data were collected from medical record.

Clinical outcomes such as INR (an International Normalization Ratio) and complications associated with warfarin therapy (both bleeding events and thromboembolic events). These outcomes were measured at pre-counseling and the follow up visit and were collected from medical record or from electronic data (from

Hosxp program is a software of Samutprakarn Hospital) and face to face interview by a pharmacist.

Patients' knowledge about warfarin therapy and patients. These data were collected by using the questionnaire. The questionnaires were composed of the 10 opened-end questions for assess patient's knowledge in warfarin therapy. Pharmacist interviewed patients. answer and scores for patients.

One score was given for each question. Full score are 10. These 10 questions were asked in sequential order as showed here.

1) Do you know the name and appearance of your anticoagulant drug?
   (ท่านทราบหรือไม่ว่ายาเม็ดของท่านมีสีอะไร และเป็นยาใด)
2) What is the reason that you need to use this medication?
   (ท่านทราบหรือไม่ว่าทำไมต้องใช้ยานี้)
3) Can you give me the reason why you had your blood testing?
   (ท่านทราบหรือไม่ว่าทำไมต้องเจาะเลือด)
4) Could you tell me about the medicine side effect?
   (ท่านทราบหรือไม่ว่ายานี้มีอาการข้างเคียงอย่างไร)
5) Could you tell me about the symptoms of thromboembolic event?
   (ท่านทราบหรือไม่ว่าอาการลิ่มเลือดอุดตันมีอาการอย่างไร)
6) What will you do if you missed dose?
   (ท่านทราบหรือไม่ว่าหากลืมรับประทานยาจะทำอย่างไร)
7) If you need to visit other healthcare providers, what details you should tell them?
   (หากท่านไปพบทันตแพทย์หรือแพทย์ด้วยปัญหาอื่นควรบอกอะไรแก่แพทย์บ้าง)
8) What will you do if you had a traumatic injury?
   (หากท่านมีบาดแผลหรือเกิดอุบัติเหตุควรปฏิบัติอย่างไร)

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9) If you plan to take other medications such as over-the-counter medications, botanical (herbal) products and dietary supplements, what should you do?
(ท่านทราบหรือไม่ว่าในกรณีที่จะซื้อยารับประทานเองหรือต้องการใช้สมุนไพรหรืออาหารเสริมจะต้องทำอย่างไร)

10) Life style may affect warfarin treatment. Do you know what are they?
(ท่านทราบหรือไม่ว่า การดำเนินชีวิตประจำวันบางอย่างอาจส่งผลต่อประสิทธิภาพหรืออาการข้างเคียงของยาได้)

Patients' compliance with medication taking. In this study the Thai 8-Item Morisky Medication Adherence Scale (MMAS) for compliance measures was used. [52] This scale showed a good convergence validity as it had a high correlation with the 3-item Morisky scale ($r = 0.77$; $p < 0.01$) and a medium correlation with the medication adherence visual analog scale (MA-VAS) ($r = 0.57$; $p < 0.01$). It also exhibited moderate reliability with Cronbach's $\alpha = 0.61$, but excellent test-retest reliability , intraclass correlation coefficient = 0.83; $p < 0.001$. The question items were show below.

1) Do you sometimes forget to take your pills?
(มีบางครั้งที่คุณลืมรับประทานยาใช่หรือไม่)

2) People sometimes miss taking their medications for reasons other than forgetting
(บางคนไม่ได้รับประทานยาด้วยเหตุผลต่างๆนอกเหนือจากลืม คุณคิดทบทวนว่าในช่วง 2สัปดาห์ที่ผ่านมา มีบางวันที่คุณไม่ได้รับประทานยา)

3) Have you ever cut back or stopped taking your medication without telling your doctor, because you felt worse when you took it?
(คุณเคยลดขนาดยาหรือหยุดยา เนื่องจากรู้สึกแย่เวลารับประทานยา โดยที่ไม่ได้บอกแพทย์)

4) When you travel or leave home, do you sometimes forget to bring along your medication?
(เมื่อคุณออกจากบ้านหรือเดินทางไกล มีบางครั้งที่คุณลืมพกยาติดตัวไปด้วย)

5) Did you take your medicine yesterday?
(เมื่อวานนี้ คุณรับประทานยาครบ ใช่หรือไม่)

6) When you feel like your symptom is under control, do you sometimes stop taking tour medicine?

(เมื่อคุณรู้สึกว่าอาการของโรคที่คุณเป็นควบคุมได้แล้ว บางครั้งคุณหยุดรับประทานยา)

7) Taking medication everyday is a real inconvenience for some people. Do you feel hassled about sticking to your treatment plan?

(การรับประทานยาทุกวันอาจไม่สะดวกสำหรับบางคน คุณเคยรู้สึกอัดอัดที่ต้องรับประทานยาอย่างเคร่งครัดหรือเข้มงวด ใช่หรือไม่)

8) How often do you have difficulty remembering to take all your medications?

(คุณรู้สึกว่ามีความยุ่งยากบ่อยเพียงใด ในการจดคำยาทั้งหมดที่ต้องรับประทาน)

8.1) Never/Rarely

(ไม่รู้สึกหรือแทบจะไม่รู้สึกว่ามีความยุ่งยาก)

8.2) Once in a while

(รู้สึกว่ายุ่งยากบ้างเล็กน้อย)

8.3) Sometimes

(รู้สึกว่ายุ่งยากปานกลาง)

8.4) Usually

(รู้สึกว่ายุ่งยากเป็นประจำ)

8.5) All the time

(รู้สึกว่ายุ่งยากทุกครั้งหรือตลอดเวลา)

Response categories are yes/no for each item with a dichotomous response and a 5-point Likert response for the last item.

Each “Yes” scored 0 and “No” scored 1 for item1, 2, 3, 4, 6 and 7. Except scoring of the item 5 is reversed(“Yes” scored 1 and “No” scored 1)

For item 8, choosing “8.1” scored 1, “8.2” scored 0.75, “8.3” scored 0.5, “8.4” scored 0.25 and “8.5” scored 0. The total score provides a measure of compliance. Therefore a higher score indicating higher compliance. The maximum score is 8 and the minimum score is 0.

Other factors that affected warfarin response were also collected. These data such as taking other medications, herbal product, supplement, vitamin K dietary, alcohol, smoking and contraceptive.

Hospitalization cost and ER visits cost. These data were collected from electronic data (from Hosxp program is a software of Samutprakarn Hospital). Cost of hospitalization is calculated from a total of a medical care cost, a nurse care cost, a hospital admission cost, a pharmaceutical cost and the costs of perform procedures and laboratory tests. Cost of emergency department (ER) visits is calculated from a total of a medical care cost, a nurse care cost, an ambulatory one day treatment cost, a pharmaceutical cost and the costs of perform procedures and laboratory tests.

Data analysis

The data of the study is analyzed for 2 part of testing

Patient level testing

This study applied Paired t-test to compare the means of knowledge score and compliance score before and after pharmacist counseling services. Test statistic for compare % INR within therapeutic range, percentage of bleeding event, percentage of embolic event, percentage of hospitalization and ER visit between pre- and post-pharmacist counseling service was using Pearson's chi-square test. The unit of analysis for Chi-square test was number of visit. All analyses were performed by using the SPSS program with default setting $p < 0.05$ as the level of statistical significance.

Cost analysis

Cost analysis is calculated to explore the cost saving as a result of pharmacist managed-warfarin clinic on ER visits and hospitalization. Report result as ratio in cost per case reduction from pharmacist counseling. If patient also had ER visit and hospitalization at the same time. Calculation of cost saving from reduction of ER visit and hospitalization were illustrated below.

ER visit case

1. No. of ER visits of pre-pharmacist counseling = A cases
2. No. of ER visits of post-pharmacist counseling = B cases
3. Sum of ER visits at pre- and post- pharmacist counseling = A + B cases

4. % ER visits at pre-pharmacist counseling
   = (no. of ER visits × 100) / sum of visit = C %
5. % ER visits at post-pharmacist counseling
   = (no. of ER visits × 100) / sum of visit = D %
6. Reduction of % ER visits per year = C% – D% = E%
7. Estimate the sum ER visits cost before and after entry pharmacist-managed warfarin clinic = X
8. Average cost per ER visits = X / (A + B) = $\overline{X}$ (baht per cases)
9. Cost saving from ER visits (per year) = (reduction of % ER visits) × (sum of visit) × (average cost per 1 ER visits) = E × (A+B) × $\overline{X}$ baht saved

Hospitalization case

1. No. of hospitalization of pre-pharmacist counseling = A cases
2. No. of hospitalization of post-pharmacist counseling = B cases
3. Sum of hospitalization at pre- and post- pharmacist counseling = A + B cases
4. % hospitalization at pre-pharmacist counseling
   = (no. of hospitalization × 100) / sum of visit = C %
5. % hospitalization at post-pharmacist counseling
   = (no. of hospitalization × 100) / sum of visit = D %
6. Reduction of % hospitalization per year = C% – D% = E%
7. Estimate the sum hospitalization cost before and after entry pharmacist-managed warfarin clinic = Y
8. Average cost per hospitalization = Y / (A + B) = $\overline{Y}$ (baht per cases)
9. Cost saving from hospitalization (per year) = (reduction of % hospitalization) × (sum of visit) × (average cost per 1 hospitalization) = E × (A+B) × $\overline{Y}$ baht saved

Process of pharmacist counseling

The objectives of a warfarin clinic are to help maintain patients' INR in therapeutic range and preventing a bleeding side effect and throboembolism. The warfarin clinic is operated within the outpatient care unit and managed by pharmacists. There are 10 pharmacists take turn to provide consultation to patients.

At the initial visitation, physicians, nurses and pharmacists will screen all the patients receive warfarin therapy to participate with warfarin clinic. If the patient has ever participated warfarin clinic elsewhere, they may choose to not join this program. The pharmacist will assess the patients' baseline knowledge about disease and drug therapy, through verbal query. Issues of counseling include the name, dosage form and appearance of warfarin, indications and action of warfarin, the prescribed dose, missed dose, a blood testing (an International Normalization Ratio: INR and prothrombin time: PT), diet and vitamin K intake, use of other medication and supplements or herbal medicines, self-monitoring for signs and symptoms of bleeding and thrombosis, traumatic injury, activity or sport and sharing information with other physicians. Patients will also be advised to strictly adherence to prescribed dosage schedule.

The pharmacist monitors the physical examination and INR results. The INR will be monitored as an indicator of optimal therapy. The acceptable INR range for all indications is 2.0-3.0, except 2.5-3.5 for mitral valve replacement. At each follow up visit, the pharmacist will discuss changes in therapy, if any, assess the patients for possible bleeding symptoms, and other signs which could indicate a thromboembolic event. At every three visits, patient's compliance in warfarin therapy will be assessed with a patients'compliance questionnaire. Pharmacist will assess a patients' knowledge result in knowledge score at pre-patient education and post-patient education. After the pharmacist counseling, they were recorded all data on warfarin therapy record form (Appendix B) which be detailed about demographic data, dosage of warfarin, concomitant diseases and drugs, laboratory results, diet, complications associated with warafrin therapy and drug-related problems. All of warfarin therapy record form of each patient is collected in the warfarinized outpatient profile. Pharmacists also record data concerning counseling and monitoring on the warfarin monitoring sheet (Appendix C). The warafrin monitoring sheet will be inserted in OPD card of patient. Warfarinized outpatients will receive a booklet (Appendix E) which contains knowledge about warfarin therapy and an appointment card from a pharmacist. The information in the warfarin booklet consists of topics in line with issues of pharmacist counseling.

CHAPTER IV

RESULTS

This chapter presents the results of study which begins with sample characteristics, and other regarding effect of pharmacist counseling on patients' knowledge, compliance, INR, complications, cost of hospitalization and ER visits.

Study subjects and their characteristics

Study sample was selected from the database of Samutprakarn hospital. Patients were screened by inclusion criteria which was patients who received warfarin therapy during the period of January 2008 to January 2009 and were outpatients. It was found that 198 patients met the inclusion criteria. If these patients were met the exclusion criteria, they will not be included in the study sample. The exclusion criteria were patients who have the symptomatic calf vein thrombosis who use warfarin for a short duration, those who lost to follow up, those who were refer to other hospitals, those who received warfarin therapy less than 3 months before the study started, those who visit hospital less than 3 times per year, and those who have prior experience with warfarin clinic elsewhere. Please see Figure 2 for sample selection procedure.

It was found that the majority of the sample (62.1%) were female. Mean age of patients was 57.23±12.89 years (range 27-90). Mean number of visit per year to warfarin clinic was 4.67±1.36 visits (range2-9). The most common indications for warfarin therapy was atrial fibrillation (50.0%). The second most common indication was valvular heart disease (36.6%) which included mitral valve prolapse (MVP), mitral stenosis (MS), mitral regurgitation (MR) and aortic stenosis (AS). At baseline, most patients (45.9%) had INRs higher than therapeutic range (24.1% were INRs 3.01-4.0 and 21.8% were INRs more than 4).And 32.6% of patients had INRs in the therapeutic range (INR range 2-3). A few of patients (21.0%) had INRs lower than therapeutic range (15.0% of patients were INRs 1.50-1.99 and 6% were INRs less than 1.50). Patients' demographic detail was showed in Table 1.

Process of screening population and sample can be summarized as figure 3

Figure 3: Summary of the screening population for sample procedures.

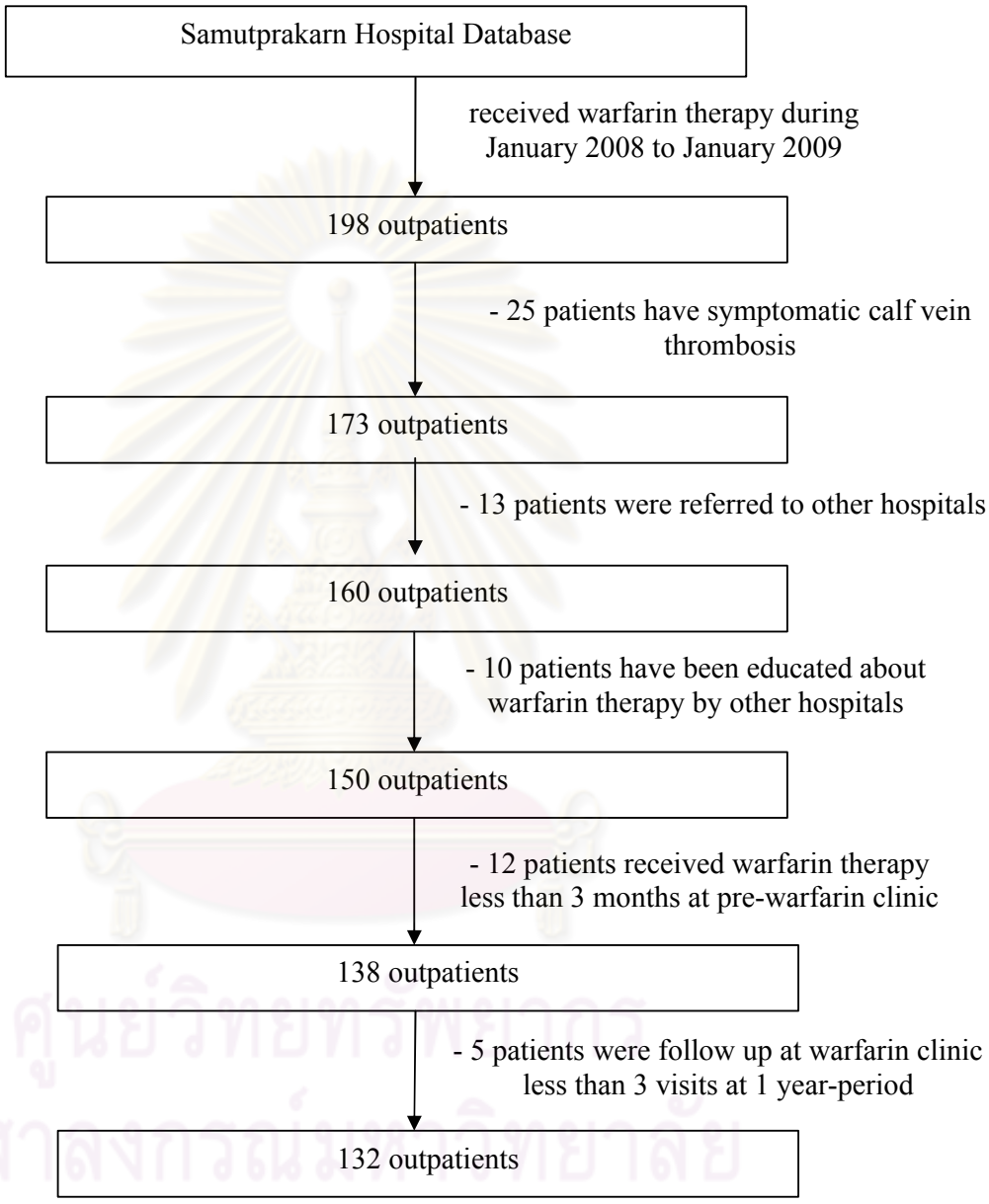

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Table 1: Patients' Characteristics at the intervention day

Demographic data	No. of patients (%)	Mean±SD	Min	Max
Sex				
male	50 (37.9)			
female	82 (62.1)			
Indication for warfarin				
Atrial fibrillation (AF)	67 (50.8)			
Valvular heart disease	48 (36.4)			
Acute myocardial infarction	8 (6.1)			
Cerebral infarction	4 (3.0)			
Congestive heart failure	2 (1.5)			
Cardiomyopathy	2 (1.5)			
Pulmonary embolism	1 (0.8)			
Age		57.23±12.89	27	90
25-34 years	6 (4.5)			
35-44 years	19 (14.4)			
45-54 years	26 (19.7)			
55-64 years	43 (32.6)			
> 65 years	38 (28.8)			
Visit per year		4.67±1.36	3	9
3 visit**s**	25 (18.9)			
4 visit**s**	45 (34.1)			
5 visits	32 (24.2)			
6 visit**s**	16 (12.1)			
7 visit**s**	9 (6.8)			
8 visits	3 (2.3)			
9 visits	2 (1.5)			
INR value*				
>4.00	29 (22.0)	2.31±1.05	0.81	7.72
3.01-4.00	32 (24.2)			
2.00-3.00	43 (32.6)			
1.50-1.99	20 (15.2)			
<1.50	8 (6.1)			

* INR values were tested at the same day

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Patients' knowledge evaluation

This study evaluated the effect of pharmacist counseling on patients' knowledge score regarding warfarin therapy. Pharmacist assessed patients' knowledge at least 4 times at baseline or before providing counseling service, immediate right after the counseling session end, at second visit (around 2 to 6 months), and third visit (around 7 to 12 months).

The questionnaire for assess patients' knowledge about warfarin therapy was develop by the Association of Hospital Pharmacy (Thailand). The result of psychometric test was in subject 4.2.1. Evaluation of pharmacist counseling by compare patients' knowledge score before and after education, and variation at the third visit.

1. Reliability of the measure

The 10 questions for assess patient's knowledge about warfarin therapy were adopt from a warfarin clinic training project which was conducted by the Association of Hospital Pharmacy (Thailand). The content of the measurment was validated by 3 expert groups. Group I consisted of one nurse and two physicians specialized in medicine. Group Π consisted of one nurse and one physician specialized in surgery and two clinical pharmacists.

The reliability was tested using the α-coefficient of Cronbach. The measurement was pilot test in a small sample of 30 patients. The result showed that the Cronbach's alpha = 0.8500 which is considered good. After collecting baseline data from 132 patients, the reliability were re-check and it was found that the Cronbach's alpha = 0.8808. Reliability of this study got better than a pilot test. Therefore, it can be concluded that the measurement of knowledge used in this study was reliable.

Table 2: Patients' knowledge about warfarin therapy at each visit

knowledge	No. of patients responded correctly (%)			
	Pre-counseling at intervention day (N=132)	Post-counseling at intervention day (N=132)	at 2-6 month later (N=113)	at 7-12 month later (N=17)
1.name and appearance of warfarin	79 (59.8)	128 (97.0)	110 (95.5)	17 (100.0)
2.indication	65 (49.2)	124 (93.9)	106 (93.8)	16 (94.1)
3.blood testing	21 (15.9)	106 (80.3)	92 (81.4)	14 (82.4)
4.side effect (bleeding)	22 (16.7)	113 (85.6)	95 (84.1)	13 (76.5)
5.symptoms of thromboembolism	8 (6.1)	98 (74.2)	80 (70.8)	8 (47.1)
6.missed dose	6 (4.5)	113 (85.6)	91 (80.5)	15 (88.2)
7.share information with other physician	42 (31.8)	125 (94.7)	101 (89.4)	17 (100.0)
8.procedure for traumatic injury	40 (30.3)	126 (95.5)	102 (90.3)	15 (88.2)
9.drug interaction ;diet, alcohol, other medications	33 (25.0)	120 (90.9)	104 (92.0)	13 (76.5)
10.activities and sports	20 (15.2)	113 (85.6)	95 (84.1)	15 (88.2)
total score of 10	2.52±2.33	8.84±1.39	8.42±1.59	8.41±1.62
minimum	0	4	3	4
maximum	3	10	10	10

2. Baseline knowledge

At pre-counseling, a mean of knowledge score was 2.50±2.33 (see in table 2) from a full score of 10. None of the patient answered all 10 knowledge questions correctly. Twenty seven percent of patients answered all 10 questions wrong and got a zero mark, 22.0% got a total of 2 mark and 12.1% got a total of 1 marks.

At baseline, there were 2 questions that less than 10% of the samples answered them correctly. First was question 6 “How do you do if you missed dose?” (only 6 patients or 4.5% knew the correct answer) and second was question 5 “Could you tell me about the symptoms of thromboembolic event?”(only 8 patients or 6.1% knew the correct answer) This information might reflect that when patients forgot to take medicine, they didn’t know what appropriate action they should take. Also, if they experienced thromboembolism, they might not know how threaten the symptoms were, and they might not take appropriate action in time.

Besides question 5 and 6, there were question that less than 30% of patients answered correctly question 3 “Can you give me the reason you did blood testing?”, question 4 “Could you tell me about the side effect of drug?”, question 9 “How do you do if you need to take other medications such as over-the-counter medications, botanical (herbal) products and supplements?”, and question 10 “Do you know about life style may affect therapy with warfarin?” Moreover , there were question that less than 50% of patients answered correctly question 2 “What is the reason that you need to use this drug?”, question 7 “If you need to visit other healthcare providers, what details you should report them?”, and question 8 “How do you do if you had a traumatic injury?”.These were area of knowledge that needs to be improved.

3. Effect of the intervention on knowledge

3.1 Immediate effect of pharmacist counseling on knowledge

Right after the pharmacist counseling, patients were asked to do the post test using the same knowledge questionnaire. It was found that 45.5% of patients answer all 10 questions correctly, and a 22.0% of them answer 9 out of 10 questions correctly.

Question that most patients answered correctly was question 1 “Do you know the name and appearance of anticoagulant drug?” (answered correctly by 97.0% of

patients) while question that least patients answered correctly was question 5 “Could you tell me about the symptoms of thromboembolic event?” (answer correctly by74.2%). Knowledge question there was found to be the most improved score was question 6 “How do you do if you missed dose?” which 85.6% more patients answered correctly.

In order to evaluate the effect of pharmacist counseling on patients’ knowledge score between baseline and post-pharmacist counseling at intervention day of the same patients were compared using paired t-test. It was found that mean of knowledge score at baseline was 2.50±2.33, while mean knowledge score at post-pharmacist counseling at intervention day was 8.84±1.39. Knowledge score of 113 patients was significantly increased 6.35±2.22 with *p*-value < 0.0001. (Table 3)

3.2 Long term effect of pharmacist counseling on knowledge

Patient education could improve patients’ knowledge for a while, and knowledge may decrease as time passed. It is interest in alteration of knowledge score at next session visit (2-6month), and third visit (7-12month). This study compared the difference of patients’ knowledge score by using paired t-test.

At 2-6 month later, a most knowledge score was 10 (32.7%) and a secondary score was 9 (27.4%) The most patients were correct answer at item 1 (95.5%). Item 5 was the least correct answer (70.8%).

Comparing patients’ knowledge score of post-pharmacist counseling at intervention day and 2-6 month later, using paired t-test. The mean of patients’ knowledge score measured at 2-6 month later was significantly decrease from the intervention day (Table 3). Paired t-test showed that patients’ knowledge score of the follow up visit (at 2-6 month later) was significantly difference lower than the score of post-pharmacist counseling at intervention day (*p-value* < 0.0001). Mean difference of knowledge score was 0.70±1.99.

At 7-12 month later, a most knowledge score was 10 and 8 (29.4%) and a secondary score was 4 (23.5%) The most patients were correct answer at item 1 and 7 (100.0%). Item 5 was the least correct answer (47.1%).

Comparing patients' knowledge score of post-pharmacist counseling at intervention day and 7-12 month later, using paired t-test. The mean of patients' knowledge score measured at 7-12 month later was significantly decrease from the intervention day (Table 3). Paired t-test showed that patients' knowledge score of the follow up visit (at 7-12 month later) was significantly difference lower than the score of post-pharmacist counseling at intervention day (*p-value* = 0.0300). Mean difference of knowledge score was 1.00±1.73.

Comparing patients' knowledge score of post-pharmacist counseling at 2-6 month later and 7-12 month later, using paired t-test. The mean of patients' knowledge score measured at 7-12 month later was not significantly decrease from 2-6 month after pharmacist counseling (Table 3). Paired t-test showed that patients' knowledge score of the follow up visit (at 7-12 month later) was not significantly difference lower than the score of post-pharmacist counseling at 2-6 month later (*p-value* = 0.9000). Mean difference of knowledge score was 0.07±2.09.

At each visit after pharmacist counseling, the most patients were missed at item 5.At the following visit, the most improvement was item 3. And the most patients were correct answer at item 1.

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Table 3: Patients' knowledge (score) about warfarin therapy at intervention day and the follow up visit (at 2-6 month later and 7-12 month later)

knowledge score	n	M ± SD	*t*	*p-value*	df
Pre at intervention day	132	2.5227±1.3860	32.9280	<0.0001	131
Post at intervention day	132	8.8409±2.3309			
Mean difference		6.3182±2.2045			
Pre (Post at intervention day)	113	8.8319±1.4262	3.7420	<0.0001	112
Post at 2-6 month later	113	8.1327±1.7954			
Mean difference		0.6991±1.9860			
Pre (Post at intervention day)	17	9.2941±0.9852	2.3800	0.0300	16
Post at 7-12 month later	17	8.2941±1.6494			
Mean difference		1.0000±1.7321			
Pre (Post at 2-6 month later)	14	8.3571±1.5984	0.128	0.9000	13
Post at 7-12 month later	14	8.2857±1.8157			
Mean difference		0.0714±2.0926			

Test statistic was paired t-test

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Patients' compliance evaluation

Patients' compliance to warfarin regimens that had a significant effect on anticoagulation control. Compliance evaluation was added toward the end of the study. For this reason, this study had a small number of samples for compliance evaluation.

1. Reliability of the measure

Testing reliability by using a pilot project with 16 samples and evaluating them by using the α-coefficient of Cronbach. Result from a pilot study showed that Cronbach's alpha = 0.5559. Cronbach's alpha was re-evaluated using information from 31 samples at baseline data. The result showed that Cronbach's alpha = 0.5564. It can be concluded that the measurement of compliance used in this study is quite poor internal consistency of the items.

2. Effect of the intervention on compliance

This study compared patients' compliance between pre-pharmacist counseling and post-pharmacist counseling, using paired t-test. Mean of the session was 9.0968 weeks. The mean of patients' compliance score measured at pre- and post-pharmacist counseling was 6.82±1.10 and 7.88±0.54, respectively. Mean difference of compliance score was 1.0565±1.1249.Paired t-test revealed that patients' compliance score of post-pharmacist counseling was significantly higher than pre-pharmacist counseling ($p < 0.0001$).

Table 4: Group differences for patients' compliance (score) between pre-pharmacist counseling and post-pharmacist counseling.

Status	**n**	**M± SD**	***t***	***p-value***	**df**
Pre-counseling	31	6.8226±1.1015	5.229	< 0.0001	30
Post at 2-6 month later	31	7.8790±0.5395			
Mean difference		1.0565±1.1249			

Test statistic was paired t-test

Effect of pharmacist counseling on International Normalized Ratio

Optimized warfarin therapy should incorporate regular laboratory monitoring of anticoagulant effect. Vitamin K antagonists should be monitored with use of the prothrombin time test which reported as an International Normalized Ratio (INR). The INR is related to efficacy of treatment and safety. The American Heart Association (AHA)/American College of Cardiology (ACC) provide a guidance to monitor anticoagulation intensity and recommended the optimum therapeutic range of INR that should be between 2.0 – 3.0. INR lower than 2.0, considered low efficacy and results in an increasing risk of thromboembolism. INR lower than 1.5 is considered no efficacy. However, if INR is higher than 3.0, the risk of bleeding is increasing.

The safety and effectiveness of warfarin therapy depends critically on maintaining the INR within the therapeutic range. The INR is monitored within 2-7 days after start warfarin until a stable dose and response relationship is obtained. If the INR become stable, the frequency of INR testing can be reduced to intervals as long as 4 weeks.

Many studies showed that patients' warfarin knowledge significantly affecting the patients' compliance which related to warfarin dose titration to INR within therapeutic range and realize the importance of regular INRs monitoring.

This study compared a percentage of INR within the therapeutic range between pre-pharmacist counseling and post-pharmacist counseling using Pearson's chi-square test.The proportion of 3 INR status; too low, therapeutic range, too high at pre-pharmacist counseling (a period of 3 months to 1 year before intervention) and post-pharmacist counseling (a period of 1 year after intervention) was significantly difference (Table 5). To test this hypothesis, unit of analysis is number of visit. It was found that percentage of INR within the therapeutic range was increase from 22.1% at pre-pharmacist counseling to 73.5% at post-pharmacist counseling. The percentage of INR lower than therapeutic range was decrease from 53.8% at pre-pharmacist counseling to 14.1% at post-pharmacist counseling. The percentage of INR higher than therapeutic range was decrease from 24.1% at pre-pharmacist counseling to12.4%

at post-pharmacist counseling. Results from relationship testing between INR and pharmacist counseling by Pearson's chi-square test, χ^2 = 322. 37, df = 2 and *p*-value < 0.0001.

Table 5: Status of pharmacist counseling and INR of therapeutic range crosstabulation.

	INR status	N (%)			Total
		INR lower than therapeutic range	INR within therapeutic range	INR higher than therapeutic range	
Pre -counseling		261 (53.8)	107 (22.1)	117 (24.1)	485 (100.0)
Post-counseling		103 (14.1)	537 (73.5)	91 (12.4)	731 (100.0)
Total		364 (29.9)	644 (53.0)	208 (17.1)	1216 (100.0)

Test statistic was Pearson's chi-square

χ^2 = 322.37, df = 2, *p-value* < 0.0001

Effect of pharmacist counseling on adverse events

1. Effect of pharmacist counseling on bleeding events

This study compared incidence of bleeding events between pre-pharmacist counseling and post-pharmacist counseling by using Pearson's chi-square test. The incidence and percentage of bleeding events of the post-pharmacist counseling (13 events, 1.7%) was less than the pre-pharmacist counseling (18 events, 3.6%) (Table 6). The unit of analysis is number of visit. Results from relationship testing between pharmacist counseling and bleeding events by Pearson's chi-square test was χ^2 = 4.6670, df = 1 with *p-value*. = 0.0310. It can be concluded that pharmacist counseling and bleeding is significantly related.

Table 6: Status of pharmacist counseling and bleeding events crosstabulation.

	Bleeding events	N (%)		Total
		No bleeding	bleeding	
Pre-counseling		481(96.4)	18(3.6)	499(100.0)
Post-counseling		751(98.3)	13(1.7)	764(100.0)
Total		1232(97.5)	31(2.5)	1263(100.0)

Test statistic was Pearson's chi-square

$\chi^2 = 4.5780$, df = 1, *p-value* = 0.0270

2. Effect of pharmacist counseling on thromboembolic events

To compare an incidence of thromboembolic events between pre-pharmacist counseling and post-pharmacist counseling. The incidence of thromboembolic events of the pre-pharmacist counseling (11 events, 2.2%) and the post-pharmacist counseling (11 events, 1.6%). The incidence at 2 points were difference but the percentage of thromboembolic events was decrease at post-pharmacist counseling (Table 7). Results from relationship testing between pharmacist counseling and thromboembolic events by using Chi-Square Test was $\chi^2 = 0.6780$, df = 1 with *p-value* = 0.2690. Data from this study can be concluded that pharmacist counseling is not significantly related to embolism.

Table 7: Status of pharmacist counseling and thromboembolic events crosstabulation.

embolic events	N (%)		Total
	no embolism	embolism	
Pre-counseling	488 (97.8)	11 (2.2)	499 (100.0)
Post-counseling	752 (98.4)	11 (1.6)	764 (100.0)
Total	1240 (98.2)	23 (1.8)	1263(100.0)

Test statistic was Pearson's chi-square

$\chi^2 = 0.6780$, df = 1, *p-value* = 0.2690

Effect of pharmacist counseling on ER visits and hospitalizations

To compare event of ER visits and hospitalizations between pre-pharmacist counseling and post-pharmacist counseling. The unit of analysis was number of visit. After pharmacist counseling, an incidence rate of ER visits and hospitalizations were decreased from 1.8% (9 from 490 events) to 0.5% (4 from 760 events) at post-pharmacist counseling (Table 8). Hospitalization was decreased from 9 events to 4 events at pre-pharmacist counseling and post- pharmacist counseling, respectively. Results from relationship testing between ER visits and hospitalizations and pharmacist counseling by using Pearson's chi-square test was $\chi^2 = 4.8550$, df = 1 with *p*-value = 0.0290

Table 8: Difference in ER visits and hospitalizations of pre- and post- pharmacist counseling by crosstabulation.

ER visit and hospitalization	N (%)		Total
	None of ER visit and hospitalization	Sum of ER visit and Hospitalization	
Pre-counseling	489 (98.0)	10 (2.0)	499 (100.0)
Post-counseling	760 (99.5)	4 (0.5)	764 (100.0)
Total	1250 (99.0)	13 (1.0)	1263(100.0)

Test statistic was Pearson's chi-square

$\chi^2 = 4.8550$, df = 1, *p-value* = 0.0290

The relationship between knowledge and other variables

1. Relationship between knowledge and INR

Many studies suggested that patient education about warfarin may be associated with better clinical outcomes. This study was to find out that prior knowledge about warfarin could improve control of INR in therapeutic range. To examine the relationship between knowledge and INR, data collecting after the last visit will be concluded.

To compare the mean scores of patients' knowledge of INR range 2 levels at the last visit after a pharmacist counseling (Table 9), One Way Analysis of Variance (ANOVA) was conducted. The result revealed that knowledge score at each INR level were not significantly difference (*F* = 2. 6340, df = 1 with *p*-value = 0.1070). Data

from Table 9 showed that the maximum knowledge score was form patients who have INR value within therapeutic range (INR 2-3) while patients with INR lower or higher than therapeutic range had knowledge score lower.

Table 9: Means difference of patients' knowledge score in INR range 2 levels

Status	N (no. of patient)	knowledge score Mean ± SD
INR out of therapeutic range (INR ≤ 1.99 or INR ≥ 3.01)	28	7.71±1.98
INR within therapeutic range (INR 2-3)	104	8.33±1.72
Total	132	8.20±1.78

Test statistic was One Way ANOVA

$F = 2.6340$, df = 1 with p-value = 0.1070

2. Relationship between knowledge and complications(bleeding or embolism)

Increasing a patient knowledge about warfarin has been associated with a decreased risk of bleeding and embolism. To examine the relationship between knowledge and complications, data collecting at the last visit will be analyzed. To compare mean scores of patients' knowledge in complications at the last visit after pharmacist counseling (Table 10) by using One Way Analysis of Variance (ANOVA) was conducted. Patients who were bleeding or embolism, had lower knowledge score, compared with patients who were not bleeding or embolism ($F = 1.7030$, df = 1, p-value = 0.1940).

Table 10: Means difference of patients' knowledge score in complications

	N (no.of patient)	knowledge score Mean±SD
No bleeding or embolism	129	8.30±1.71
Bleeding or embolism	3	7.00±1.73
Total	132	8.27±1.71

Test statistic was One Way ANOVA

$F = 1.7030$, df = 1, p-value = 0.1940

3. Relationship between knowledge and hospitalization

The mean scores of patients' knowledge for effect of hospitalization after pharmacist counseling was less than non-hospitalization group(Table 11) (t=1. 421, df=130, *p*-value = 0.1580). Hospitalization patients had lower knowledge score when compared with patients who were not hospitalization.

The demographics for those hospitalization patients included the following, mostly the age of 42-54 years and 1 patient was 75 years, a warfarin indication for atrial fibrillation, rheumatic aortic valve disease and pulmonary embolism, with a hospitalization diagnosis of atrial fibrillation, pulmonary embolism, intracranial hemorrhage, myocardial infarction and bleeding.

It should be noted that hospitalization patients were more likely to have more co-morbidity, more complication, and took more medications compare with those non hospitalization patients.

Table 11: Means difference of patients' knowledge score in hospitalization

	N	**knowledge score**
	(no.of patient)	**Mean±SD**
Non-hospitalization	128	8.31±1.72
hospitalization	4	7.20±1.48

Test statistic was t-test, t=1.421, df=130, *p*-value =0.1580

Cost saving of pharmacist counseling

Samutprakarn Hospital wanted to estimate cost saving as a result of warfarin clinic. This estimation was done from hospital perspective. It was found that there were 0 ER visit and 10 hospitalization before warfarin clinic was established, and there were 0 ER visit and 4 hospitalization after warfarin clinic was established

Before warfarin clinic established, cost data were not available in hospital database. Foe 10 hospitalization events, cost for each admission were bundled. In 2008 HosXP has been implemented. Cost of 4 admissions after warfarin clinic were drawn and showed in table 12. Detail of hospitalization of 4 patients were shown in Appendice F

The hospitalization costs of 4 patients at post-pharmacist counseling were detailed as following table.

Table 12: Hospitalizations cost of 4 patients at post-pharmacist counseling.

item	Cost per patient (baht)			
	Patient 1	**Patient 2**	**Patient 3**	**Patient 4**
total admitted day	7	2	2	1
hospital cost (room + food)	2,100	600	600	300
medications	3,670	126	1,013	67
INR and laboratory test	240	730	970	160
radiology diagnosis	0	170	3,570	0
nursing cost	2,100	600	1,100	300
physician charges	0	0	0	0
equipment and supplies	0	200	1850	0
total of expenditure	8,081	2,142	11,726	827

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The cost saving from warfarin clinic as a result of decreasing hospitalization rate was calculate here

Hospitalization case

1. No. of hospitalization of pre-pharmacist counseling = 10 cases
2. No. of hospitalization of post-pharmacist counseling = 4 cases
3. Sum of hospitalization at pre- and post- pharmacist counseling =10+4= 6 cases
4. % hospitalization at pre-pharmacist counseling
   = (no. of hospitalization × 100) / sum of visit = 2.0 %
5. % hospitalization at post-pharmacist counseling
   = (no. of hospitalization × 100) / sum of visit = 0.5 %
6. Reduction of % hospitalization per year = 2.0% - 0.5% = 1.5%
7. Estimate the sum hospitalization cost before and after entry pharmacist-managed warfarin clinic = 177,273 baht
8. Average cost per hospitalization = 177,273 /14 = 12,662.3571 (baht per cases)
   Data from January 2008 to January 2009, total visit of patients = 1276 visits
9. Cost saving from hospitalization (per year) = (reduction of % hospitalization) × (sum of visit) × (average cost per 1 hospitalization)
   = 1.5% x 1276 x 12,662.3571 baht saved
   = **242,357.5157 baht saved**

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CHAPTER V

DISCUSSION AND CONCLUSIONS

This chapter is composed of two sections. The first section presented a discussion on research finding, which included a discussion of the results of the pharmacist counseling on knowledge, compliance, INR, bleeding events, thromboembolic events, cost of hospitalizations and ER visit of patient receiving warfarin. The second section presented the conclusions of the research and the recommendations derived from the findings.

Discussion

This study focused on the pharmacist counseling service that influenced knowledge, compliance, INR, bleeding, thromboembolism, hospitalization and ER visit of the outpatients receiving warfarin at Samutprakarn Hospital. Comparing a pre-pharmacist counseling (usual medical care) from October 2006 to October 2007(a period of 1 year before the warfarin clinic was established) and a post-pharmacist counseling from January 2008 to January 2009.The sample included 132 outpatients who were purposively screened into the study.

The establishment process of warfarin clinic composed of 3 steps, as follows

1. Formation a multidisciplinary team which consisted of physicians, pharmacist and nurses
2. Formulation a strategy, stated goal, a standard operation procedure, indicators for warfarin clinic management and procedure for improving warfarin clinic in the future
3. Patients' data collecting

The pharmacist counseling service in the warfarin clinic consisted of: 1) assessing patients' baseline knowledge and compliance, 2) patient education through verbal query, 3) sending a warfarin booklet to patient, 4) monitoring the physical examination and INR results. These processes was conducted for three visits which each personal were vary such as 2 weeks, 1 month, 2 month and 3 month. The follow-up in the warfarin clinic was systematic and provided by a physician.

Descriptive statistics were used to analyze demographic characteristics, t-test and analysis of variance were conducted to test the research hypotheses. The summary of findings is as follow:

1. Demographic Characteristics of the patients

The results revealed that the mean of age was 57.23±12.89 years old. Female was the majority of samples. Most of indications for warfarin therapy were atrial fibrillation. Mean of visit per year was 4.67±1.36 visits. Samples were mostly INR range 2.00-3.00 which in the therapeutic range.

2. Effects of pharmacist counseling on knowledge

The pharmacist counseling procedure was based on the model of the Association of Hospital Pharmacy (Thailand), which established a project of warfarin clinic training to other hospital. Mean of baseline knowledge of patients was 2.52±2.33 from a full score of 10. This result might indicate that patients who were not educated, their knowledge were poor. It was found that patients' knowledge score was increased apparently after receiving pharmacist counseling at the intervention day.

At follow-up visit, pharmacist assessed knowledge and educated in part that patients were lacking. Patients' knowledge score measured at 2-6 month later was significantly decreased from the intervention day. And also patients' knowledge score measured at 7-12 month later. Most of patients were elderly at aged around 60 years up and low-level of education (mostly elementary education). These results indicated that some local factors might influence patients' knowledge, for examples cognitive factors and genetic factors.

At the follow-up visit from 2-12 month, patients were mostly loss of knowledge about symptoms of side effect and thromboembolism. It may result from these two topics were more apply cognition and understanding than others. However, a pharmacist counseling could improve patients' knowledge and have maintained for 6 months to 1 year. Thus, pharmacist counseling using face-to-face communication and verbal information could find out patients' problem in cognition and enhanced knowledge of warfarin therapy. Because of practical procedure in workplace, pharmacist would add knowledge at any follow-up visit. Therefore there were not find out alteration of patients' knowledge.

These were accord with Krittathanmakul S and colleagues (2006), who studied effects of pharmacist counseling on outpatients receiving warfarin at Songklanagarind

Hospital. The 97 patients received pharmacist counseling through verbal and written reinforcement. The results showed that patients' knowledge of warfarin therapy had increased after receiving the counseling service ($p<0.05$). But the results at the follow up visit were opposed with this literature, which patients' knowledge increased after each visit.

3. Effects of pharmacist counseling on compliance

The evaluation of patients' compliance was added toward the end of this study, thus it had a small number of samples. Patients' compliance was increase after receive counseling service. Patients may satisfy carefulness of pharmacy service due to personal communication and patient's health perception. This result was in accordance with the study that compliance associated with patients' behavior [43]. This information might aid in the development of intervention to enhance warfarin adherence. And pharmacist should examine specific patient attitude that might explain warfarin non-compliance of outpatients.

4. Effects of pharmacist counseling on International Normalize Ratio (INR)

After receiving counseling service, the number of visits with INR remaining in the therapeutic range was increased. And the number of visits with INR lower than therapeutic range, considered low efficacy and increasing risk of embolism was decreased at post counseling service. Similarly, the number of visits with INR higher than therapeutic range was decreased after pharmacist counseling. It can be concluded that prior knowledge about warfarin could improve patients' compliance as a result, good control of INR in therapeutic range.

5. Effects of pharmacist counseling on complications

Patients' knowledge could assist patients to detect sign or symptoms of bleeding or embolism, and know how to take action when suspected complication was occur. The incidence rate of bleeding event was decrease after counseling service. Bleeding event was decreased 5 events but it was significantly relation, because of the large sample size (at power 77%).

Embolism event at pre- and post-counseling service were unchanged. The incidence rate of embolism event was decreased 1.6% but the relation was not significant. Because of small sample size at power 26.6%. Patients who have sign or

symptoms of embolism at post-counseling status, had a high mean knowledge score. It indicated that other factor may affect embolic occurrence such as age and disease status of patients.

6. Effects of pharmacist counseling on ER visit and hospitalization

ER visit and hospitalization related to warfarin were reduced by 1.5% after receiving pharmacist counseling. And the total event was decreased from 10 events to 4 events after counseling service.

7. Effects of pharmacist counseling on cost saving

The estimated cost saving was 242,357.5157 baht saved in this study. However, is an underestimate of the true saving for several reasons. First, cost for admission had invisible costs such as cost for nurse assistant and patient escort officer. Second, There were several issues related to cost calculations that should be considered. Cost of physician and pharmacist were not included because the public hospital pay their salaries. Third, an underestimated hospital cost.

8. The relation between knowledge and other variables

8.1 The relation between knowledge and INR

Patients' knowledge score at each INR level were not significantly difference, but it had a tendency that patients who have high knowledge score, they often INR value within therapeutic range. It can be concluded that prior knowledge about warfarin could improve control of INR in therapeutic range.

8.2 The relation between knowledge and complications

Patients' knowledge score was not significantly related to complications because of a small sample size, but it trended to reduce complications in patient with improved knowledge.

9. The relation between knowledge and hospitalization

Patients' knowledge score was not significantly related to hospitalizations. But the results showed that patients who had higher knowledge score, had more

reduction in the risk of bleeding or embolism, resulted in decreasing of hospitalization.

Conclusion

Warfarin is an anticoagulant drug that has been used extensively in Thailand for a variety of disease. Because of its narrow therapeutic range of effectiveness and safety, drug itself can cause serious side effects such as bleeding and its thromboembolic complications that may lead to death in patients. Factors that can influence the anticoagulation control such as vitamin K dietary, others medication, concurrent illness, alcohol consumption, patients' compliance, and physical activity. Written and verbal information by health care provider, has been shown to improve control of the level of anticoagulation.Many studies showed that patients' warfarin knowledge significantly could improved anticoagulation control, patients' compliance and patients may be able to identify the complications by themselves.

The Pharmacy unit of Samutprakarn Hospital established a pharmacist-managed warfarin clinic on October 2007, to solve the anticoagulant related problems. Pharmacist processed the warfarin clinic on outpatients who receive warfarin therapy , both the initial visit and the follow up. An effectiveness of establishment of warfarin clinic in aspect of clinical outcomes and health care costs which the administrator need to know, have never assessed. This study is proposed to evaluate the effect of pharmacist counseling on knowledge, compliance, INRs, complications, hospitalization and ER visit, and cost saving. Results of this study showed that a pharmacist counseling service improved patients' knowledge, compliance, anticoagulation control, reduced bleeding and thromboembolic events rates, and saved **242,357.52** baht of total patients during the study period in reduced hospitalization.

Limitations of the Study

1. The study was operated on condition of routine work therefore sample size was the total patients during the study period, and it is possible that the sample size was rather smaller effect size to assess the relation between knowledge and other factors. And more influence or others factor would be detected if increase sample size.

2. Initially this study intensely focused on the influencing factor from knowledge to anticoagulation control, but the evaluation of patients' compliance was

added toward the end of this study. Thus it had a small number of samples and a short session to assess the relation and the alteration of patients' compliance.

3. The questionnaire for assess patient's compliance about warfarin therapy was using The 8-Item Morisky Medication Adherence Scale (MMAS). Each item measured a specific medication-taking behavior and not a determinant of other influencing factors.Patients' compliance might have other influencing factor from the Health Belief Model and Theory of Planned Behavior (TPB). The more useful of investigation should concern other aspects of behavior.

Recommendation and Suggestions

1. For more complete and in-dept data should improve a questionnaire to analyze the compliance behavior problem of patients receiving warfarin therapy.
2. This study focused on the patients' knowledge so for the further study should be expand to the knowledge of patient career.
3. For more complete on patients' compliance evaluation, the further study should be more longer duration in order to see the alteration of compliance score.

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APPENDICES

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APPENDICE A

ศูนย์วิทยทรัพยากร
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แบบประเมินความรู้ความเข้าใจเกี่ยวกับการใช้ยา Warfarin โรงพยาบาลสมุทรปราการ

ชื่อ-สกุลผู้ป่วย.....

หัวข้อประเมิน	**ก่อน**	**ติดตาม**		
		ครั้งที่1	**ครั้งที่2**	**ครั้งที่3**
1.ท่านทราบหรือไม่ว่ายาเม็ดของท่านมีสีอะไร และเป็นยาใด?				
2.ท่านทราบหรือไม่ว่าทำไมต้องใช้ยานี้?				
3.ท่านทราบหรือไม่ว่าทำไมต้องเจาะเลือด?				
4.ท่านทราบหรือไม่ว่ายานี้มีอาการข้างเคียงอย่างไร?				
5.ท่านทราบหรือไม่ว่าอาการลิ่มเลือดอุดตันมีอาการอย่างไร?				
6.ท่านทราบหรือไม่ว่าหากลืมรับประทานยาจะทำอย่างไร?				
7.ท่านทราบหรือไม่ว่าหากไปพบทันตแพทย์หรือแพทย์ด้วยปัญหาอื่นควรบอกอะไรแก่แพทย์บ้าง?				
8.ท่านทราบหรือไม่ว่าหากมีบาดแผลหรือเกิดอุบัติเหตุควรปฏิบัติอย่างไร?				
9.ท่านทราบหรือไม่ว่าในกรณีที่จะซื้อยารับประทานเองหรือต้องการใช้สมุนไพรหรืออาหารเสริมจะต้องทำอย่างไร?				
10.ท่านทราบหรือไม่ว่า การดำเนินชีวิตประจำวันบางอย่างอาจส่งผลต่อประสิทธิภาพหรืออาการข้างเคียงของยาได้?				

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รวมคะแนน				
<u>หมายเหตุ</u> การให้คะแนน รู้ =1 ไม่รู้/เข้าใจผิด = 0				
NOTE ครั้งที่ 1				
ครั้งที่ 2				
ครั้งที่ 3				

เกณฑ์การให้คะแนน

1. คำถามข้อ1 10 สำหรับข้อที่ตอบถูก ให้คะแนน = 1 และหากตอบผิด หรือตอบไม่ได้ ให้คะแนน = 0
2. รวมคะแนนความความรู้ในการใช้ยาวาร์ฟารินคะแนนต่ำสุดคือ 0 และสูงสุด คือ 10
3. คะแนนสูง บ่งชี้ว่าผู้ป่วยมีความรู้ในการใช้ยาวาร์ฟารินดีกว่าผู้ป่วยที่ได้คะแนนต่ำ

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APPENDICE B

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NO. ……

WARFARIN THERAPY RECORD FORM

1. DEMOGRAPHIC DATA

HN…… NAME……

SEX …….. AGE…..... Indication for warfarin ……

Other disease states ( ) HTN ( ) DM ( ) DLP ( ) Others ……

Drug allergy……

( ) Alcohol ( ) Smoking

2. WARFARIN MONITORING DATA

( ) New case ( ) Old case

dd/mm/yy	INR	knowledge score	compliance score	Complication	ER/ Admit-Cost
		K_1 =…… K_2 =……	C_1 =…… C_2 =…… C_3 =……...		

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3. DATA OF PRE-WARFARIN CLINIC

dd/mm/yy	INR	Complication	ER/ Admit-Cost

4. FACTORS AFFECTING ANTICOAGULATION CONTROL

Drug interaction		Vitamin K dietary		Other factors	
Pre-WC	Post-WC	Pre-WC	Post-WC	Pre-WC	Post-WC

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APPENDICE C

ศูนย์วิทยทรัพยากร
จุฬาลงกรณ์มหาวิทยาลัย

แบบบันทึกการให้คำแนะนำและติดตามการใช้ยา Warfarin **Code…….**

กลุ่มงานเภสัชกรรม โรงพยาบาลสมุทรปราการ **HN…….**

---

1. ข้อมูลพื้นฐาน

ชื่อ-สกุล (นาย/นาง/นางสาว).....อายุ.....ปี

ที่อยู่.....โทรศัพท์.....

ชื่อ-สกุล ผู้ที่ติดต่อ (นาย/นาง/นางสาว).....โทรศัพท์.....

อาชีพ.....ระดับการศึกษา.....

ประวัติทางสังคม [ ] ดื่มสุรา [ ] สูบบุหรี่

ความต้องการมีบุตร [ ] ต้องการ [ ] ไม่ต้องการ

2. โรคและภาวะการเจ็บป่วย

โรคและภาวการณ์เจ็บป่วยที่ทำให้ใช้ยา Warfarin.....

โรคประจำตัวอื่นๆ [ ] HTN [ ] DM [ ] Dyslipidemia [ ] Other……

3. ประวัติการใช้ยาและผลิตภัณฑ์สมุนไพร

ประวัติการแพ้ยา/อาหาร.....

ประวัติการใช้ยาสมุนไพร/อาหารเสริม.....

ประวัติการใช้ยาอื่นๆที่ใช้ประจำ.....

4. ตารางบันทึกการเข้ารับบริการ

ครั้งที่	วัน/เดือน/ปี	ประเภทของการเข้ารับบริการ
		( ) คัดกรอง ( )ติดตาม ( )ขอรับบริการเอง ( )แพทย์/พยาบาลส่งมา
		( ) คัดกรอง ( )ติดตาม ( )ขอรับบริการเอง ( )แพทย์/พยาบาลส่งมา
		( ) คัดกรอง ( )ติดตาม ( )ขอรับบริการเอง ( )แพทย์/พยาบาลส่งมา
		( ) คัดกรอง ( )ติดตาม ( )ขอรับบริการเอง ( )แพทย์/พยาบาลส่งมา

ตารางบันทึกประวัติการใช้ยา ครั้งที่..... ชื่อ-สกุล..... Code……..				
วัน/เดือน/ปี	**ขนาดยาที่ได้รับเดิม**	**INR**	**ขนาดยาที่ปรับเปลี่ยน**	**รายการยาอื่นที่ใช้ร่วม**

บันทึกการให้คำแนะนำและติดตามการใช้ยา Warfarin ครั้งที่..... วันที่.....	
คำแนะนำที่ให้กับผู้ป่วย	**ปัญหาที่พบของผู้ป่วย**
[ ]โรคและอาการแทรกซ้อน.....	……
[ ]ผล Lab.....	……
[ ]สรรพคุณ/การบริหารยา/หากลืมกินยา	……
[ ]อาการข้างเคียงจากการใช้ยา.....	……
การปฏิบัติตน	……
[ ]กรณีพบบุคลากรทางการแพทย์อื่น.....	……
[ ]กรณีเกิดอุบัติเหตุ.....	……
[ ]การใช้อาหารเสริม/สมุนไพร.....	**สรุป** [ ]พบ DRP [ ]ไม่พบ DRP
[ ]อาหาร/บุหรี่/ออกกำลังกาย.....	**เภสัชกรผู้ให้คำแนะนำ**……
[ ]**ติดตามเรื่อง**.....	
[ ]**วันที่นัด**.....	

ปัญหาการบำบัดยา

1. Unnecessary drug therapy 2. Needs additional drug therapy 3. Ineffective drug 4. Dosage too low
5. ADR 6. Dosage too high 7. Non-adherance 8. Life-style

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APPENDICE D

ศูนย์วิทยทรัพยากร
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แบบประเมินความร่วมมือในการใช้ยา: Morisky Medication Adherence Scale (MMAS)

คำชี้แจง : กรุณากาเครื่องหมาย ✓ลงในกล่อง ❒ ในคำถามต่อไปนี้ให้ตรงกับความเป็นจริง

1. มีบางครั้งที่คุณลืมรับประทานยาใช่หรือไม่	❒ ใช่	❒ ไม่ใช่
2. บางคนไม่ได้รับประทานยาด้วยเหตุผลต่างๆนอกเหนือจากลืม คุณคิดทบทวนว่าในช่วง 2 สัปดาห์ที่ผ่านมา มีบางวันที่คุณไม่ได้รับประทานยา	❒ ใช่	❒ ไม่ใช่
3. คุณเคยลดขนาดยาหรือหยุดยา เนื่องจากรู้สึกแย่เวลารับประทานยา โดยที่ไม่ได้บอกแพทย์	❒ ใช่	❒ ไม่ใช่
4. เมื่อคุณออกจากบ้านหรือเดินทางไกล มีบางครั้งที่คุณลืมพกยาติดตัวไปด้วย	❒ ใช่	❒ ไม่ใช่
5. เมื่อวานนี้ คุณรับประทานยาครบ ใช่หรือไม่	❒ ใช่	❒ ไม่ใช่
6. เมื่อคุณรู้สึกว่าอาการของโรคที่คุณเป็นควบคุมได้แล้ว บางครั้งคุณหยุดรับประทานยา	❒ ใช่	❒ ไม่ใช่
7. การรับประทานยาทุกวันอาจไม่สะดวกสำหรับบางคน คุณเคยรู้สึกอึดอัดที่ต้องรับประทานยาอย่างเคร่งครัดหรือเข้มงวด ใช่หรือไม่	❒ ใช่	❒ ไม่ใช่
8. คุณรู้สึกว่ามีความยุ่งยากบ่อยเพียงใด ในการจดจำยาทั้งหมดที่ต้องรับประทาน (กาเครื่องหมาย ✓ลงในกล่อง ❒ **โดยเลือกเพียง 1 ข้อเท่านั้น**)		
❒8.1) ไม่รู้สึกหรือแทบจะไม่รู้สึกว่ามีความยุ่งยากในการจดจำยาที่ใช้ (หรือมี 0 ถึง 1 ครั้งต่อสัปดาห์ที่จำไม่ได้ว่ายาตัวไหนทานอย่างไร)		
❒ 8.2) รู้สึกว่ายุ่งยากบ้างเล็กน้อย ในการจดจำวิธีทานยาแต่ละอย่างให้ถูกต้อง		

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(หรือมี 1 ถึง 2 ครั้งต่อสัปดาห์ที่จำไม่ได้ว่ายาตัวไหนทานอย่างไร)
❒ 8.3) รู้สึกว่ายุ่งยากปานกลาง ในการจดจำวิธีทานยาแต่ละอย่างให้ถูกต้อง (หรือมี 3 ถึง 4 ครั้งต่อสัปดาห์ที่จำไม่ได้ว่ายาตัวไหนทานอย่างไร)
❒ 8.4) รู้สึกว่ายุ่งยากเป็นประจำ ในการจดจำวิธีทานยาแต่ละอย่างให้ถูกต้อง (หรือมี 5 ถึง 6 ครั้งต่อสัปดาห์ที่จำไม่ได้ว่ายาตัวไหนทานอย่างไร)
❒ 8.5) รู้สึกว่ายุ่งยากทุกครั้งหรือตลอดเวลา ในการจดจำวิธีทานยาแต่ละอย่างให้ถูกต้อง (มีความยุ่งยากทุกวัน จำไม่ได้ว่ายาตัวไหนทานอย่างไร)

เกณฑ์การให้คะแนน

1. คำถาม MMAS ในข้อ 1, 2, 3, 4, 6 และ 7 (ยกเว้นข้อ 5) หากผู้ป่วยเลือกคำตอบว่า “ใช่ ” ให้คะแนน = 0 และหากตอบว่า “ ไม่ใช่ ” ให้คะแนน = 1 กรณีการให้คะแนนในข้อ 5 ให้กลับคะแนนตรงข้าม
2. ในข้อ 8 ให้คะแนนดังนี้ ข้อ 8.1 ให้คะแนน = 1, ข้อ 8.2 ให้คะแนน = 0.75, ข้อ 8.3 ให้คะแนน = 0.5, ข้อ 8.4 ให้คะแนน = 0.25 และ ข้อ 8.5 ให้คะแนน = 0
3. รวมคะแนนความร่วมมือในการใช้ยา คะแนนต่ำสุดคือ 1 และสูงสุด คือ 8 คะแนนสูง บ่งชี้ว่าผู้ป่วยมีความร่วมมือในการใช้ยาดีกว่าคะแนนต่ำ

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APPENDICE E

ศูนย์วิทยทรัพยากร
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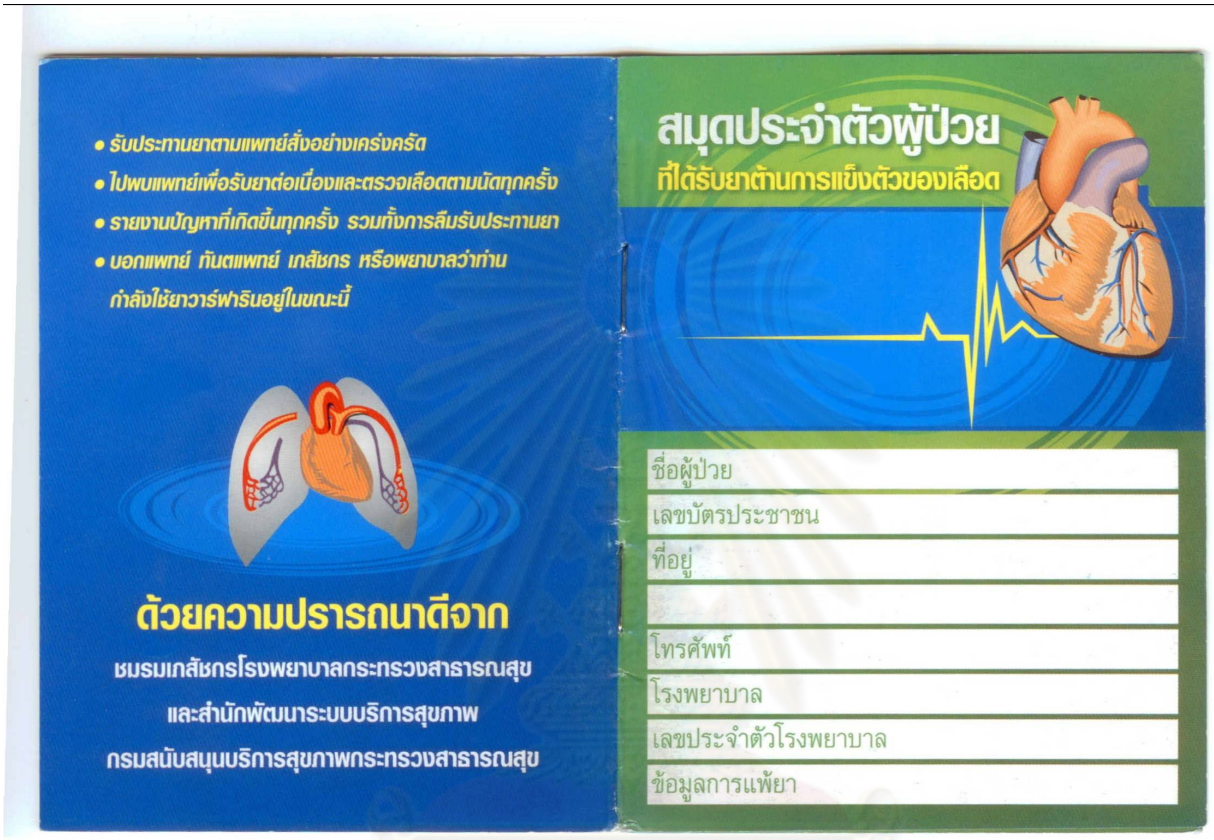

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APPENDICE F

ศูนย์วิทยทรัพยากร
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patient	warfarin indication	hospitalized diagnosis	INR at admitted day	medications	laboratory test
1	atrial fibrillation	gum bleeding	3.27	-warfarin 2mg -enoxaparin sodium injection 0.6ml -doxazosin 2mg -losartan 50mg -simvastatin 10mg -allopurinol 100mg -colchicine 0.6mg -gabapentin 600mg -betahistine 6mg -amitryptyline 10mg -lorazepam 0.5mg -omeprazole 20mg	-INR -hematology -clinical chemistry

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patient	warfarin indication	hospitalized diagnosis	INR at admitted day	medications	laboratory test
2	atrial fibrillation , pulmonary embolism	embolism	1.30	- warfarin 2mg, 3mg -furosemide 40mg - furosemide 20mg injection -enalapril 5mg - simvastatin 40mg	- INR
3	rheumatic aortic valve disease	intracranial hemorrhage	3.65	-warfarin 3mg -digoxin 0.25mg -paracetamol -omeprazole 40mg injection -dopamine HCl 250mg injection -vitamin K_1 10mg/ml injection -CPM 10mg/ml injection	-BUN -creatinine -CBC -chest PA upright -electrolyte -ABO blood group tube method -CT brain (non contrast

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patient	warfarin indication	hospitalized diagnosis	INR at admitted day	medications	laboratory test
				-dexamethasone 4mg/ml injection	-clinical chemistry
4	atrial fibrillation	atrial fibrillation and flutter	1.62	-warfarin 3mg -digoxin 0.25mg -paracetamol -lorazepam	-INR

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BIOGRAPHY

Siraya Lekcharoen was born in Chonburi, Thailand, on August 9, 1979. She graduated from St. Joseph Bangna School in 1998 and received her Bachelor of Science degree in Pharmacy from Silapakorn University in March 2005. Siraya worked in Siridhorn College of Public Health, Chonburi from 2005 to 2006 , the Ambulatory Care Unit, Samutprakarn Hospital. from 2006 to 2010 in the position of pharmacist. She entered the Degree of Master of Science in Social and Administrative Pharmacy Program, Faculty of Pharmaceutical Science at Chulalongkorn University in 2007.

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