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the Translator

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Benefits of pharmacists' management and intervention regarding anticoagulation therapy management.

Pharmacists play an essential role in drug adherence and medication management, and this is especially true when it comes to anticoagulation therapy management. Warfarin is widely used to for anticoagulation therapy, but requires careful monitoring and dose adjustment. Since this topic was first addressed in the Fall 2010 issue of *The Translator*, the scope of practice for pharmacists has expanded, especially regarding therapy management with the advent of portable international normalized ratio (INR) measuring devices and patient self testing.

This issue of *The Translator* highlights four different cases where pharmacists have used their expertise and knowledge to improve management of anticoagulation therapy:

- The cost effectiveness of a pharmacist led patient self testing program for warfarin
- Benefits of a pharmacist managed anticoagulation service
- Effects of a warfarin self management program on quality of life
- Implementing a post discharge home visitation service for new warfarin patients.

The cost effectiveness of a pharmacist led patient self testing program for warfarin.

Gallagher, J., Mc Carthy, S., Woods, N., Ryan, F., O' Shea, S., Byrne, S. Economic evaluation of a randomized controlled trial of pharmacist-supervised patient self-testing of warfarin therapy. *Journal of Clinical Pharmacy and Therapeutics*, 2015. 40: 14–19. doi: 10.1111/jcpt.12215. (Gallagher J, 2015) Corresponding author: James Edward Gallagher, j.e.gallagher@umail.ucc.ie

Issue: Warfarin is a well established medication for anti-coagulation management, but constant management and regular dose adjustment are necessary due to its narrow therapeutic index and serious side effects. Although several new oral anticoagulant agents that do not require constant monitoring have been developed, they are not well established and warfarin therapy, along with anticoagulant management, is still necessary. Continuous therapy monitoring, usually done at a clinic, puts enormous stress on the

The Translator is an initiative by the Canadian Pharmacists Association to support the knowledge translation between pharmacy practice research and health policy. Each issue selects a number of pharmacy practice research articles, briefly summarizes them and discusses the health care policy implications. These articles are submitted by researchers who have a strong desire to support evidence-based health care policy and best practices.

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health care system, and is also inconvenient for the patient. The expenses associated with the monitoring and management stage of warfarin therapy are significant in terms of time invested by health care professionals. In addition, the patient also has to make regular and frequently time-consuming visits to the clinic to get the testing done.

A solution: Patient self-testing (PST) of warfarin therapy is a concept that allows the management of warfarin therapy to move away from overburdened clinics to a primary care level. The PST model involves patients measuring their international normalized ratio (INR) levels using a portable point-of-care device that makes dose adjustment recommendations based on the patients' previous INR values. The reported INR values are also communicated via the Internet to supervising pharmacists who can monitor the recommendations for any discrepancies, override the software and make their own recommendations when necessary. Previous studies have shown that PST is just as effective, if not more effective, as regular therapy management.[1]

To determine the cost effectiveness of PST in comparison with usual care (management in a hospital-based anti-coagulation clinic), 132 long-term anticoagulation patients were recruited for a six-month crossover study between PST and routine care in an anticoagulation clinic. The economic evaluation was done from a health care provider perspective. It was found that on a per patient basis, over a six-month period, PST resulted in an incremental cost of $80 in comparison with routine care. The total estimated cost for a patient on PST over a six-month period was $307.18. In comparison with a six-month treatment cost of drugs that do not require management, such as dabigatran ($619.88) and rivaroxabin ($522.82), warfarin management therapy is cheaper. In addition, patients achieved a significantly higher time in therapeutic range (TTR) during PST (72 ± 19.7%) in comparison with routine care (59 ± 13.5%). Significantly, the TTR levels associated with this study were greater than the 70% range, considered a good level of control. Previous studies have shown that patients with a TTR of greater that 70% had a significantly reduced risk of stroke.[2] The PST model was also found to have significantly improved societal benefits in terms of working or leisure time lost to attending appointments and driving to and from the hospital, compared to the cost of the point-of-care devices and equipment for self-testing.

Pharmacy-supervised PST should be considered as an alternative to other, non-monitored oral anticoagulants.

Implications: PST is marginally more expensive than centralized testing, but it offers additional benefits to the health care payer. It is too early to tell whether this strategy is cost effective, as there is no suggested threshold for TTR, but there is a 15.4% difference between the median values of the two groups. Other studies have shown that incidence of death, major bleeding and stroke may be halved by a 15% improvement in TTR.[3] PST provides a significant increase in anticoagulation control for a modest increase in expenditure, compared to traditional clinic-based management. However, the associated increase in INR control provides evidence that optimally managed warfarin therapy remains a viable strategy for anticoagulation management, and pharmacy-supervised PST should be considered as an alternative to other, non-monitored oral anticoagulants.

Background and methods: Patients were initially assigned to either six months of routine care or six months of PST. At the end of the six-month period, the patient was transferred to the alternative group. The crossover design of the study eliminated the potential for covariate disparities. Overall TTR was calculated using the Rosendaal method. Patients were required to have been on warfarin for at least two months prior to the starts of the study and expected to have a requirement for warfarin for the duration of the 12 months. PST was done using Coaguchek XS (Roche Diagnostics), with reporting and recommendations managed through the CoagCare system (ZyCare Inc.). For the economic analysis, costs of staff were calculated based on expert guidance from staff, internal hospital data and published salary scales. For the pharmacist, a cost of $40.63/hr was applied, and the cost of the system was sourced from Roche Diagnostics.

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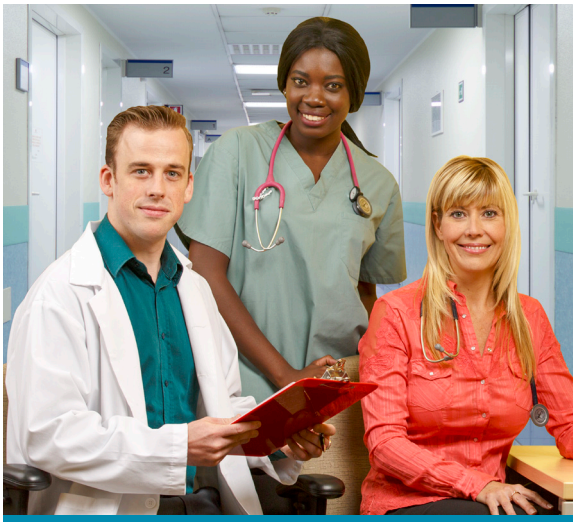
Benefits of a pharmacist managed anticoagulation service.

Rudd KM, Dier JG. Comparison of two different models of anticoagulation management services with usual medical care. *Pharmacotherapy*. 2010 Apr; 30(4):330-8. doi: 10.1592/phco.30.4.330. (Rudd KM, 2010). Corresponding author: Kelly Rudd, Kelly.Rudd@bassett.org'

Issue: Warfarin is an effective therapy for a variety of thromboembolic disorders, but the risk of side effects remains a major concern if therapy is not maintained within the narrow therapeutic index. Anticoagulation management services are well known to improve the quality of care provided to patients, as well as reduce the rates of hospitalizations and emergency department visits due to adverse events.[1] There are currently four primary structures for managing oral anticoagulant therapy in the United States: usual care by the patient's primary care provider, pharmacist-managed anticoagulation management, nurse-managed anticoagulation management and patient self-directed management overseen by a clinician. Although there has been plenty of data indicating that anticoagulation management improves international normalized ration (INR) time in therapeutic range (TTR) and reduces adverse events,[2] there is little data that directly compares the models of management to determine the most effective structure.

A solution: A study was done comparing pharmacist-managed anticoagulation services, nurse-managed anticoagulation services and usual care in a health care network of 25 outreach primary health care centres throughout the rural upstate New York region. Data was collected for one year for all three groups, and INR TTR was compared. Hospitalizations and emergency department visits were recorded for each group and the economic costs for each were calculated. Data was collected for 996 patients who were receiving warfarin therapy for at least six months. No statistically significant difference was found in the results from the nurse-managed service and usual care, so both groups were independently comparedto the pharmacist-managed service.

The pharmacist-managed anticoagulation management services achieved superior anticoagulation control to both the nurse-managed anticoagulation management and usual care. The pharmacist-managed group also had a favourable impact on reducing both hospitalizations and emergency department visits due to anticoagulation-related adverse dug effects. Hospitalizations were reduced by 56% versus the nurse-managed service and 61% versus usual care ($p<0.01$). Emergency department visits were reduced by 78% compared to both the nurse-managed and the usual care models ($p<0.002$). Based on the visit rates, the pharmacist-managed service saved $141,277.34 in hospitalization costs, and $10,183.76 in emergency department visit costs versus the nurse-managed service, and $95 579.08 in hospitalization costs and $5511.21 in emergency department costs compared with the usual care model. The pharmacist-managed service had significantly more point-of-care (POC) assessments of INR than the other groups. This meant that patients received more direct counselling and intervention because of the face-to-face encounters and relatively longer durations. Although this might be a confounding factor, these differences were not unusual and are the core components of many pharmacist-managed anticoagulation services. In addition, a subgroup analysis was done on non-POC pharmacist-managed anticoagulation services, and clinical outcomes were still improved compared to the other two groups.



Pharmacists, nurses and physicians working together to improve patient outcomes

Implications: The data demonstrates that a pharmacist-managed anticoagulation management service, in collaboration with nurses and physicians, may be superior to other accepted anticoagulation management service models. It can lead to improved patient outcomes, as well as reduce the financial strain on the health care system. Unfortunately, the most significant limitation to this study was that the data from the usual care and nurse-managed service were from a different, earlier year than the pharmacist-managed service. The improvement in clinical outcome may be due to improved guidelines, practice changes and care advances. In addition, the potential costs of implementing these programs, including pharmacist personnel costs, must be considered in the overall economic impact.

Background and methods: Patients were included in the study if they were receiving warfarin therapy for at least six months. They were excluded if they did not have at least three recorded INR values, or if the indication for warfarin therapy could not be determined. All three groups used the same central laboratory, and POC testing, where available, was performed using the i-STAT device (Abbot Laboratories). INRs were considered within range if they were within ± 0.2 of the designated therapeutic range. Economic data was taken from the Basset Medical Center billing database.

Patient characteristics were compared using analysis of variance (ANOVA) or Fisher exact tests, with Bonferroni correction, where appropriate. Mean number of drugs was compared using ANOVA as well. Anticoagulation control was calculated as the percentage of INR values in the therapeutic range and as a percent-time in range. Differences in anticoagulation control were assessed using ANOVA tests. Event rates were calculated individually for each study group as the total number of events divided by the total number of treatment days during the study period, and reported as the number of event/100 patient years. Results were analyzed by Poisson regression analysis.

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Effects of a warfarin self management program on quality of life.

Verret L, Couturier J, Rozon A, et al. Impact of a pharmacist-led warfarin self-management program on quality of life and anticoagulation control: A randomized trial. *Pharmacotherapy.* 2012;32(10):871-9. doi: 10.1002/j.1875-9114.2012.01116. (Verret L, 2012). Corresponding author: Lucie Verret, lucie.verret@icm-mhi.org

Issue: Warfarin remains the most commonly used oral anticoagulation in North America.[1] It has been extensively studied and its efficacy for the prevention of thromboembolic events is well documented.[1] However, warfarin has a narrow therapeutic window, meaning doses are carefully individualized and monitored to keep the safety and efficacy of the drug in balance. Patients are required to visit specialized clinics regularly to have their blood drawn and international normalized ratio (INR) measured. While monitoring the INR is important, it places the burden on the patient to attend these clinics and can negatively impact one's adherence to therapy and quality of life. This may have an even greater impact on senior patients, where limited mobility or the lack of transportation further increases the difficulty of visiting the clinics.[2] Although portable devices to measure INR are available, health care professionals in North America have yet to adopt the approach of having patients self-manage their warfarin therapy.

A solution: With the advent of validated, portable INR monitoring devices, patients will be able to measure their INR levels without the inconvenience of visiting a clinic. This has the potential to improve their quality of life and also opens up the opportunity for patients to become more involved in their therapy. As medication experts pharmacists are in a great position to educate patients on anticoagulation, aid in the monitoring process and identify candidates capable of self-managing their warfarin therapy. This study was conducted to determine if a pharmacist-led warfarin self-management program improved the quality of life and anticoagulation in patients. A total of 114 people were included in this study, with 58 randomized to the intervention group (IG) and 56 to the control group (CG). The IG was taught to self-monitor INR and adjust warfarin doses based on a dosing algorithm chart while the patients in the CG continued standard treatment at the anticoagulation clinic.

> A pharmacist-led warfarin self-management program is a promising option for patients.

The primary outcome, quality of life, was measured with a survey that covered five sociopsychological topics: general treatment satisfaction, self-efficacy, daily hassles, psychological distress and strained social network. It was administered at baseline and at the end of the four months of study. At the end of four months, IG patients experienced a significant improvement in all areas of the survey compared to the CG except in self-efficacy. Self-efficacy improved in both groups compared to baseline, but there was no significant difference between the two groups.

Secondary outcomes examined include quality of anticoagulation, time spent monitoring INR, knowledge of anticoagulation and adverse events. The quality of anticoagulation was measured as the time spent in therapeutic range. The time in therapeutic range was 80.0 ± 13.5% in the IG and 75.5 ± 24.7% in the CG. There was no significant difference observed between the two groups (p=0.79). However, patients in the IG saw a significant reduction in the time spent monitoring each INR in comparison to the CG. On average, the patients in the IG spent 5.3 minutes whereas patients in the CG spent 158 minutes due to travel and wait times in clinics. Knowledge of anticoagulation was measured by a test administered to all patients at baseline, after the educational session and after four months. Both groups showed a significant improvement from baseline after the educational session delivered by the pharmacist. Moreover, this knowledge was retained when the test was administered again at the end of the four months. Lastly, the incidence of adverse events was similar between both groups. There were 26 bleeding events in the IG and 23 in the CG (p=0.75). Of these bleeding events, two were classified as major bleeding in the IG whereas one was major in the CG. There was no significant difference in the incidence of major bleeding (p=0.59).

Implications: The results of this study suggest that a pharmacist-led warfarin self-management program is a promising option for patients. The IG experienced a significant improvement in quality of life, which was hypothesized to be the result of a decrease in the time spent monitoring each INR. Furthermore, the self-management approach was shown to be just as safe and effective as the traditional approach. If self-management programs become adopted in Canada, pharmacists will play an important role in identifying patients who are likely to succeed and reap the benefits of the program. The patients enrolled in the study were on warfarin for a mean of seven years prior to the study. These patients were probably more aware of the factors that may influence their INR and are accustomed to the blood tests and dose adjustment routine. In addition, all patients in the IG had to demonstrate they were capable of using the portable INR device and dosing algorithm. Taking these factors into consideration, ideal candidates should have a medication history of warfarin use and are competent at using the INR device and dosing algorithm. Otherwise, the improvement in quality of life is not worth compromising the safety and efficacy of warfarin.

Background and research methods: This study was designed as a prospective, open-labeled, randomized, controlled trial and conducted at the Montreal Heart Institute for four months. The inclusion criteria consisted of patients between 18 and 75 years of age who were followed at the Montreal Heart Institute, were receiving warfarin for at least six months and were expected to continue for a minimum of another four months, whose last two INRs were within a certain range. Some of the exclusion criteria included having a hypercoagulable condition, active or recent major bleeding event, and physical or cognitive impairment affecting comprehension or motor skills. All patients were given an educational session on anticoagulation provided by the pharmacist prior to randomization. The IG was given training on how to use a CoaguChek XS device and a warfarin dosing algorithm to self-manage anticoagulation. The CoaguChek XS is a portable INR testing machine that has been previously studied and validated for accuracy. Patients in the CG were asked to continue standard management at the anticoagulation clinic. The primary outcome was quality of life, which was measured with a survey assessing five sociopsychological areas. The secondary outcomes were knowledge of anticoagulation, time in therapeutic range, time spent on measuring INRs and adverse events.

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Implementing a post discharge home visitation service for new warfarin patients.

Stafford L, Peterson GM, Bereznicki LR, Jackson SL, van Tienen EC, Angley MT, Bajorek BV, McLachlan AJ, Mullan JR, Misan GM, Gaetani L. Clinical outcomes of a collaborative, home-based post discharge warfarin management service. *Ann Pharmacother.* 2011 Mar;45(3):325-34. doi: 10.1345/aph.1P617. Epub 2011 Mar 8. (Stafford L, 2011). Corresponding author: Leanne Chalmers, leannes2@utas.edu.au

Issue: A particularly important transition in patient care happens after their discharge from hospital care. Often, without the direction of health care professionals, patients exhibit decreased medication adherence, resulting in health problems or possible hospital readmissions. Despite almost 60 years of clinical experience with warfarin use, it is still a major cause of adverse drug events and hospital admissions, due to its narrow therapeutic index and variety of side effects if mismanaged.[1] Warfarin-related hemorrhagic events and thromboembolic events resulting from therapeutic failures lead to significant morbidity and mortality in individuals and substantial costs for the health care system.[2] This makes patients who are recently discharged and are on warfarin therapy a particularly high risk group for adverse drug effects. The requirement for close international normalized ratio (INR) monitoring often presents a significant burden for patients with mobility or transportation issues,[3] and patients often leave the hospital with inadequate knowledge about their therapy.

A solution: Post-discharge home visitations are one solution to improving clinical outcomes. The education, as well as the face-to-face interaction with a health care professional, can resolve many drug issues before they become serious problems. In this study, patients over 18 years of age who were recently discharged and newly initiated on warfarin, or continuing preadmission therapy, were selected and separated into the usual care (UC) group, or a post-discharge service (PDS) group. Post-discharge, the UC group were managed according to their community health care providers' usual warfarin management practices. No restrictions were placed on what this involved, except that it could not include a formal post-discharge outreach program. UC typically involved patients undergoing venous blood sampling for INR testing at their physician surgeries or pathology specimen collection centres, with the results being reported to the physicians. Patients in the UC group received a single home visit by a project officer for data collection purposes approximately eight days post-discharge. PDS services were provided by accredited pharmacists and patients either received two or three home visits based on a collaborative risk assessment by the pharmacist and the patients' physician. A home visit would consist of point of care INR testing, dose adjustment if necessary, warfarin education and data collection. The study was set up so that the third visit of the PDS group was comparable to the eight-day post-discharge data collected from the UC group. Data was then collected again at 90 days post-discharge for both groups

Home visitations including face-to-face counselling and education can empower patients to have greater involvement in their own care, and could result in improved persistence with therapy

The primary outcome measure was the incidence of combined major and minor hemorrhagic events to day 90 post-discharge. The PDS group was associated with statistically significantly decreased rates of combined major and minor hemorrhagic events to day 90 (5.3% vs. 14.7%, p=0.03) and day 8 (0.9% vs. 7.2%, p=0.01) compared with the UC group. The rate of combined hemorrhagic and thrombotic events to day 90 also decreased (6.4% vs. 19%, p=0.008) and persistence with warfarin therapy improved (95.4% vs. 83.6%, p=0.004). There were no significant differences in unplanned hospital readmissions, warfarin-related readmission or death rates. None of the deaths recorded were deemed to have been warfarin-related. In addition, no difference was found in the mean time in therapeutic range (TTR) for INR values between the two groups. Overall, the PDS resulted in an additional 5.5% of patients continuing therapy, whereas it may otherwise have been ceased due to adverse events or management issues. Notably, there were fewer warfarin cessations in the PDS group at day 8 compared to the UC group.

Implications: This study implies that appropriately trained pharmacists can reduce adverse events and improve persistence in patients taking warfarin following hospital discharge. Home visitations including face-to-face counselling and education can empower patients to have greater involvement in their own care, and could result in improved persistence with therapy. There was also a potential confounding effect associated with physician contact in the UC group. At the day 8 visit, if the project officers felt that their duty of care to a patient required them to contact the patient's physician to inform him or her of any findings, including out-of-range INR results, they were permitted to do so. This occurred for 39.2% of patients receiving UC, meaning that the benefits of PDS may be much larger than reported.

Background and methods: Patients were selected from eight hospitals across five metropolitan, rural and remote regions of Australia. Patients were excluded if they had lupus anticoagulant or antiphospholipid syndrome, were residents of aged-care facilities, had a documented history of dementia or a mini-mental state examination (MMSE) score less than 24, or were entering other pre-existing post-discharge outreach programs. Major hemorrhage was defined as fatal bleeding, symptomatic bleeding in a critical area or organ, bleeding causing a fall in hemoglobin level of 2 g/dL or more, or requiring transfusion of two or more units of whole blood or red cells. Minor hemorrhage was defined as bleeding requiring health care professional consultation but not hospitalization. TTR was calculated using Rosendaal's linear interpolation method at day 90. Independent samples t-testing was used for continuous variables and chi-squared analyses for discrete variables. To confirm the outcomes of the PDS group, the influence of patient characteristics on adverse even rates was investigated using binary univariate and multivariate logistic regression analyses.

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