



Pharmacy Practice

ISSN: 1885-642X

ISSN: 1886-3655

Centro de Investigaciones y Publicaciones Farmaceuticas

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Pharmacy Practice, vol. 6, no. 1, 2008, January-March, pp. 43-50  
Centro de Investigaciones y Publicaciones Farmaceuticas

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## Original Research

# Improving outpatient warfarin use for hospitalized patients with atrial fibrillation

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Received (first version): 19-Jul-2007

Accepted: 22-Nov-2007

### ABSTRACT\*

Atrial fibrillation affects an estimated 5 million Americans and accounts for approximately 15% of all strokes. Few studies have successfully addressed patient screening, assessment, and introduction of appropriate antithrombotic therapy in patients with atrial fibrillation.

**Objective:** To assess whether an intervention improved planned antithrombotic prescribing at the time of discharge in hospitalized patients.

**Methods:** The study was a prospectively designed, retrospectively evaluated, non-blinded, historical control study of a pharmacist-initiated intervention.

The intervention, consisting of pharmacist review and assessment of antithrombotic prescribing in patients with non-valvular atrial fibrillation, was conducted in an urban teaching hospital.

**Results:** Although antithrombotic prescribing was not significantly higher at discharge in the 252 enrolled subjects (control 67.3% vs. intervention 70.8%;  $p = 0.58$ ), a significantly greater number of patients had a written discharge plan for antithrombotic therapy (control 73.5% vs. intervention 88.3%;  $p < 0.01$ ). The adjusted odds ratio that the study group was associated with an improvement in planned or actual warfarin use was 2.46 (95% CI 1.63-3.74). In addition, clinicians adhered to guidelines for antithrombotic therapy in patients with atrial fibrillation more frequently in the intervention group (control 70.4% vs. intervention 88.2%;  $p < 0.01$ ).

**Conclusion:** A program designed to identify hospitalized patients with non-valvular atrial fibrillation, assess their need for stroke prophylaxis, and initiate appropriate antithrombotic therapy led to an increase in planned antithrombotic, and most importantly, warfarin use upon discharge from the

hospital. Confirmation that an increase in planned antithrombotic use upon discharge results in an actual increase in use after discharge is needed to determine the true effectiveness of this intervention.

**Keywords:** Pharmacists. Anticoagulants. Atrial Fibrillation. United States.

### MEJORA DEL USO AMBULATORIO DE WARFARINA EN PACIENTES HOSPITALIZADOS CON FIBRILACIÓN AURICULAR

#### RESUMEN

La fibrilación auricular afecta aproximadamente a 5 millones de norteamericanos y aparece en el aproximadamente el 15% de todos los infartos.

Pocos estudios han afrontado con éxito el cribado de pacientes, la evaluación y la introducción de tratamiento antitrombótico apropiado en pacientes con fibrilación auricular.

**Objetivo:** Evaluar si una intervención mejoraba la prescripción antitrombótica planeada en el alta en pacientes hospitalizados.

**Métodos:** El estudio fue diseñado prospectivamente y evaluado retrospectivamente, no ciego, con control histórico de una intervención iniciada por el farmacéutico. La intervención, que consistía en la revisión y evaluación por un farmacéutico de la prescripción antitrombótica de pacientes con fibrilación auricular no valvular, se llevó a cabo en un hospital universitario urbano.

**Resultados:** Aunque la prescripción antitrombótica no fue significativamente mayor en el alta en los 252 individuos (control 67.3% vs. intervención 70.8%;  $p = 0.58$ ), un número significativamente mayor de pacientes tuvo un plan escrito al alta para el tratamiento antitrombótico (control 73.5% vs. intervención 88.3%;  $p < 0.01$ ). El odds ratio ajustado de que el grupo de estudio estaba asociado a un mejor uso de la warfarina planificada o real fue 2.46 (CI95% 1.63-3.74). Además, los clínicos se adhirieron a las guías de tratamiento antitrombótico en pacientes con fibrilación auricular más frecuentemente en el grupo intervención (control 70.4% vs. intervención 88.2%;  $p < 0.01$ ).

**Conclusión:** Un programa diseñado para identificar pacientes hospitalizados con fibrilación auricular, evaluar su necesidad de prevención de infarto e iniciar tratamiento antitrombótico llevó a un aumento de antitrombóticos planificados, y más importante, al uso de warfarina al alta del hospital. Se necesita la confirmación de que un aumento en

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los antitrombóticos planificados lleve a un aumento en el uso real para determinar la verdadera efectividad de esta intervención.

**Palabras clave:** Farmacéuticos. Anticoagulantes. Fibrilación auricular. Estados Unidos.

## INTRODUCTION

Atrial fibrillation affects over 5 million Americans.<sup>1</sup> It has been estimated that the lifetime risk for the development of atrial fibrillation is approximately 1 in 4.2. The major complication of atrial fibrillation is stroke, with an estimated annual risk of 1.8% in untreated men and 3.5% in untreated women with atrial fibrillation in one study and may be as high as 8.5% in certain patient populations.<sup>3,4</sup> Individuals with multiple risk factors or prior strokes are at greatest risk for stroke with rates exceeding 20% in some studies.<sup>5-8</sup> Conversely, approximately 15% of all strokes are attributable to patients with atrial fibrillation.<sup>8</sup>

Effective medications for patients with non-valvular atrial fibrillation are available. Warfarin has been shown to reduce the risk of stroke in patients with non-valvular atrial fibrillation by 62%.<sup>9</sup> Aspirin confers a reduced protection, reducing stroke risk by 36%.<sup>10</sup> Also, patients with atrial fibrillation receiving warfarin live longer than those who do not.<sup>11,12</sup> These agents are recommended for use in all eligible patients by the American Heart Association.<sup>7,13</sup>

Despite the demonstrated efficacy and effectiveness of warfarin and aspirin for stroke prophylaxis, a number of studies have demonstrated poor utilization rates in a variety of settings.<sup>14-19</sup> Difficulties with antithrombotic prescribing have often been cited as reasons for the low utilization rates.<sup>20-22</sup> Examples of patient-related barriers include advanced age, perceived low embolic risk, and perceived high risk for hemorrhage. Noncompliance and belief that a patient would refuse therapy have also been cited as reasons for not prescribing warfarin.<sup>23-25</sup> Patient characteristics, clinical uncertainty, previous experiences with warfarin therapy, and the need for continued intense monitoring likely are major contributing factors to a physician's decision to use warfarin in a patient. Unfortunately, many of the cited barriers stem from a lack of clinical familiarity with the evidence supporting antithrombotic use and involve patients who would benefit most from stroke prophylaxis.

There are a number of studies addressing the monitoring and management of antithrombotic agents through anticoagulation clinics.<sup>26-35</sup> In general, these studies have demonstrated an overall improvement in time within therapeutic range. Some studies have also demonstrated improved outcomes.<sup>28,34,35</sup> Access to such clinics may improve antithrombotic use by removing some of the system barriers, but utilization still remains

suboptimal.<sup>36,37</sup> Unfortunately, there are very few studies that successfully address the screening, assessment, and introduction of patients to appropriate antithrombotic therapy.<sup>38-44</sup> These studies were either conducted in a setting outside of the United States,<sup>38-42,44</sup> failed to optimize warfarin use,<sup>39-41</sup> or were screening-only interventions.<sup>44</sup>

The study described in this paper addresses these major gaps in the literature. It describes a program designed to identify hospitalized patients with non-valvular atrial fibrillation, assess the need for stroke prophylaxis, and initiate appropriate antithrombotic therapy prior to discharge. The objective of the study was to determine if this intervention was effective at improving the prescribing of, or having a discharge plan for, appropriate antithrombotic utilization at the time of patient discharge from hospital.

## METHODS

This study was a single-site, inpatient, prospective, effectiveness analysis of a newly created pharmacy service at a suburban teaching hospital. It was non-blinded and utilized a prospectively identified historical control group. Study outcomes and other data were collected retrospectively, by chart review, to minimize the potential for interference by the study on the practice patterns being evaluated. Chart review was conducted by 2 non-investigator study nurses who were blinded to study group. This study was approved by the Oregon State University and Southwest Washington Medical Center IRB's and was conducted in accord with the ethical standards of the Helsinki Declaration of 1975.

Patients were identified for this study through EKG readings. At the end of each day, printouts for all patients with EKG readings consistent with atrial fibrillation were forwarded by the Cardiology Department to the Pharmacy. To be enrolled, patients had to be 18 years of age or over and have an attending physician from medicine, surgery, cardiology, or short term rehabilitation (<30 days) services. Patients serviced by neurosurgery, trauma, short stay (emergency or observation units), psychiatric, cardiac surgery, gynecology, and oncology services were excluded. These exclusions were chosen as a quick way of separating patients with stays that were too short to identify and intervene on or instances where warfarin therapy may not be recommended, as in the case of surgical patients. Finally, when patients were admitted to the hospital more than once during the study period, only the first hospitalization was used in the analyses.

The control group was identified in the 3 month period prior to initiating the intervention throughout the hospital. Patients in the control group were identified as having an EKG consistent with atrial fibrillation. The list was generated by the Cardiology Department and forwarded to the Pharmacy Director and co-investigator (JE) who maintained the list of potential control patients. The study's inclusion and exclusion criteria were applied to the control group at the time of data collection. Clinical

pharmacists were not assigned to these patients and there was no intervention other than routine medical care.

Prior to enrolling the intervention group, clinical pharmacists were recruited from the hospital staff to provide the intervention (in addition to their other regular clinical duties). Pharmacists were given a one-hour educational session by one of the study investigators (MM) focusing on appropriate identification of non-valvular atrial fibrillation and orientation to consensus guidelines on managing antithrombotic therapies in patients with non-valvular atrial fibrillation.<sup>7</sup> They were then provided several scenarios to assess their ability to apply the guidelines appropriately. Finally, instruction was provided on how to document their interventions in the patient chart.

As in the control group, patients in the intervention group were identified by an EKG consistent with atrial fibrillation. However, this list was then sent to the pharmacist assigned to follow the atrial fibrillation patients. This pharmacist determined if the patient was on warfarin from the medication administration record. If so, no further intervention was made. For patients not currently receiving warfarin, the patient chart was reviewed for confirmed or suspected non-valvular atrial fibrillation. Confirmation of non-valvular atrial fibrillation was obtained from the patient's physician, if necessary. A medication history was obtained in patients with confirmed or suspected non-valvular atrial fibrillation, focusing on current and prior antithrombotic use, risk factors for bleeding, and medications that interact with antithrombotic therapies through chart review and direct patient interview. A summary of the patient's therapy and a recommended plan was developed and communicated to the patient's physician. If a change in antithrombotic therapy was recommended, the pharmacist documented the recommendation in the Progress Notes section of the patient's chart. If a no response was received from the physician within 24 hours, the pharmacist contacted the physician to ensure that the recommendation was received and considered by the patient's physician. If a change in drug therapy was not necessary, but additional documentation was required, either the physician or pharmacist documented the additional information in the chart.

The purpose of this study was to determine the impact of the pharmacist intervention on the proportion of atrial fibrillation patients receiving antithrombotic therapies according to consensus guidelines.<sup>7</sup> Our hypothesis was that the pharmacist intervention would increase appropriate antithrombotic therapy and the documentation of indications and bleeding risk factors, resulting in improved adherence to the guidelines. Patient demographics and other data including age, gender, type of atrial fibrillation, number and type of stroke risk factors, and number and type of bleeding risk factors to antithrombotic therapy were collected. Outcomes evaluated included warfarin utilization in hospital, aspirin utilization in hospital, and

recommendations for warfarin and aspirin use in discharge plans.

The sample size was determined based on the expected difference between the intervention and the control group. Based on recently conducted cross-sectional analyses, we expect a warfarin utilization of approximately 50% in patients with non-valvular atrial fibrillation and without contraindications to its use.<sup>14-19</sup> To detect a change in planned or actual warfarin utilization from 50% to 60% (10% absolute or 20% relative increase) with a power of 0.8 and alpha of 0.05 using the Chi-square statistic would require 408 patients in each study arm. A change in planned or actual warfarin utilization from 50% to 70% (20% absolute or 40% relative increase) would require 103 patients in each arm.

Data were analyzed using appropriate parametric and non-parametric tests for two independent samples to determine if there were significant differences between the two samples. Warfarin, aspirin, and overall antithrombotic actual or planned usage at discharge were compared between the two groups using chi-square tests. Adherence to consensus guidelines for antithrombotic therapy in atrial fibrillation was compared using chi-square tests.

A multivariate logistic regression model was developed to identify and control for confounding factors influencing the use or planned use of antithrombotic therapies. Independent variables considered for inclusion in the model were the intervention, patient age at admission, patient gender, number of stroke risk factors, and the number of bleeding risk factors. Candidate independent variables were required to have a p-value of less than 0.25 for inclusion in the multivariate model. All independent variables were entered into the multivariate model and all possible models were evaluated using the Score Statistic, except for intervention which was forced into the model.<sup>45</sup> The final model selected was chosen based on the simplest model that offers a considerable improvement over the next best model. Results were considered statistically significant if the p-value was <0.05. Statistical analysis was performed with SPSS Version 13.0 for Windows.

## RESULTS

A total of 252 eligible patients were enrolled between May 1, 2001 and Feb 28, 2002. Ninety-eight patients were enrolled in the control group between May 1, 2001 and Jul 25, 2001, while 154 patients were enrolled in the intervention group between Sep 20, 2001 and Feb 28, 2002. There were no significant differences in demographics between the two groups at entry. Patients were closely matched in their type of atrial fibrillation. (Tables 1 and 2)

There were no significant differences between the control and intervention groups in the in-hospital use of warfarin at discharge (41.8% vs. 45.5% respectively;  $p=0.60$ ) or in the in-hospital use of

aspirin at discharge (33.7% vs. 35.1% respectively;  $p=0.89$ ). The proportion of patients receiving any antithrombotic therapy at discharge was also not

significantly affected by the intervention (control 67.3% vs. intervention 70.8%;  $p=0.58$ ).

Table 1 Comparison of demographic and baseline information on the treatment and control groups			
	Control n = 98	Intervention n = 154	P value
Female	57 (58.2%)	76 (49.4%)	0.20
Age at admission (SD)	77.8 (10.1)	79.7 (10.2)	0.17
Type of AF			
New Onset	10 (10.2%)	15 (9.7%)	0.71
Chronic	49 (50.0%)	85 (55.2%)	
Unspecified	39 (39.8%)	54 (35.1%)	
Median (interquartile range) Number of Stroke Risk Factors	3 (2-4)	3 (2-4)	0.42
Median (interquartile range) Number of Contraindications	0 (0-1)	0 (0-1)	0.57

Table 2 Observed risk factors for stroke and contraindications to antithrombotic therapy.		
Stroke Risk Factor and Level of Risk	Control	Intervention
Previous TIA, stroke, or embolus (high)	34 (34.7%)	50 (32.4%)
Poor left ventricular function (high)	49 (50.0%)	89 (57.8%)
Diabetes mellitus (moderate <sup>a</sup> )	30 (30.6%)	52 (33.8%)
Age over 75 years (high)	68 (69.4%)	117 (76.0%)
Hypertension (high)	56 (57.1%)	94 (61.0%)
Coronary artery disease (moderate <sup>b</sup> )	43 (43.9%)	69 (44.8%)
Age 65 to 75 (moderate)	18 (18.4%)	20 (13.0%)
Factors Increasing Bleeding Risk	Control	Intervention
Active bleed (bleeding within last 24 hours or gross bleeding during current admission)	9 (9.2%)	13 (8.4%)
Surgery within past 7 days	11 (11.2%)	22 (14.3%)
Intracranial hemorrhage (hx or current)	1 (1.0%)	4 (2.6%)
Uncontrolled seizures (hx or current)	1 (1.0%)	2 (1.3%)
Current severe uncontrolled hypertension	0 (0.0%)	2 (1.3%)
Documented poor compliance	1 (1.0%)	4 (2.6%)
Recent bleed (active or gross bleeding $\leq$ 2 months, incl. Heme + stools)	5 (5.1%)	7 (4.5%)
Syncope ( $\geq$ 2 falls within the past year, including syncope, seizures, blackouts etc)	3 (3.1%)	7 (4.5%)
Dementia (includes senility, memory loss, forgetfulness, or memory deficit)	14 (14.3%)	24 (15.6%)
Schizophrenia (hx) or active psychosis (includes hallucinations, delusions, schizophrenia)	0 (0.0%)	1 (0.6%)
Diagnosis of current malignancy	3 (3.1%)	6 (3.9%)
Thrombocytopenia (current)	2 (2.0%)	1 (0.6%)
Alcohol / illicit drug abuse (current documentation of alcoholism, evidence of ongoing abuse or binge drinking)	1 (1.0%)	4 (2.6%)
Other Factors Reducing Warfarin Use	Control	Intervention
Terminal illness (patients undergoing supportive care only, end-stage illness)	7 (7.1%)	4 (2.6%)
Patient refusal for therapy	2 (2.0%)	6 (3.9%)
<sup>a</sup> Considered high risk in Chest 2004 guidelines <sup>13</sup>		
<sup>b</sup> Not considered an independent risk factor in Chest 2004 guidelines <sup>13</sup>		

There were significant differences between the control and intervention groups in discharge plans including warfarin (56.1% vs. 77.9% respectively;  $p<0.01$ ), but not aspirin (33.7% vs. 38.3% respectively;  $p=0.50$ ). There was a significant difference in the proportion of patients with a discharge plan for anticoagulation upon discharge (control 73.5% vs. intervention 88.3%;  $p<0.01$ ). Similar results were obtained when comparing the proportion of patients either on an antithrombotic agent in-hospital or with a discharge plan for one. (Table 3) A multivariate logistic regression analysis was conducted to adjust for potential confounding factors. Independent variables assessed in the model were study group (control vs. intervention), age at admission, sex, number of stroke risk factors, and number of bleeding risk

factors. The final model included study group, age at admission, sex, and the number of stroke risk factors. All of these variables were statistically significantly associated ( $p<0.05$ ) with a plan for warfarin at discharge except for sex ( $p=0.059$ ), which was forced into the model. The odds ratio that the study group was associated with an improvement in planned or actual warfarin use was 2.46 (95%CI 1.63-3.74).

Documented treatment matched the documented patient risk factors significantly more often in the intervention group than in the control group. Table 4 shows the proportion of patients on or with a discharge plan for antithrombotic therapy by their level of stroke risk and number of bleeding risk factors. Clinicians adhered to the Chest guidelines

for antithrombotic therapy in patients with atrial fibrillation more frequently in the intervention group

(control 70.4% vs. intervention 88.2%;  $p < 0.01$ ).

	Control n = 98	Intervention n = 154	P value
Receiving warfarin	41 (41.8%)	70 (45.5%)	0.60
Receiving aspirin	33 (33.7%)	54 (35.1%)	0.89
Receiving warfarin or aspirin (or both)	66 (67.3%)	109 (70.8%)	0.58
Plan for warfarin	55 (56.1%)	120 (77.9%)	<0.01
Plan for aspirin	33 (33.7%)	59 (38.3%)	0.50
Plan for warfarin or aspirin (or both)	72 (73.5%)	136 (88.3%)	<0.01
Receiving or plan for warfarin	56 (57.1%)	121 (78.6%)	<0.01
Receiving or plan for aspirin	42 (42.9%)	66 (42.9%)	1.00
Receiving or plan for warfarin or aspirin (or both)	80 (81.6%)	141 (91.6%)	0.03

Table 4 Proportion of patients either receiving antithrombotic therapy in-hospital or with a discharge plan for antithrombotic therapy and their documented level of stroke risk and presence of bleeding risk factors.

Level of stroke and bleeding risk	No Antithrombotic Therapy		Aspirin		Warfarin	
	Control / Intervention		Control / Intervention		Control / Intervention	
Low stroke risk, no bleeding risk factors	0.0%	0.0%	1.0%	0.0%	1.0%	0.6%
Medium risk, no bleeding risk factors	1.0%	0.6%	0.0%	0.0%	0.0%	1.3%
High risk, no bleeding risk factors	9.2%	2.6%	10.2%	3.2%	30.6%	42.2%
Low risk, at least 1 bleeding risk factor	0.0%	0.6%	1.0%	0.0%	0.0%	0.0%
Medium risk, at least 1 bleeding risk factor	0.0%	0.0%	0.0%	0.0%	1.0%	0.0%
High risk, at least 1 bleeding risk factor	8.2%	4.5%	12.2%	9.7%	24.4%	34.4%

## DISCUSSION

This study demonstrated that an intervention in the inpatient setting could significantly improve the prescribing and/or documentation of a plan for antithrombotic therapy at the time of discharge in patients with atrial fibrillation. This was especially true for warfarin, with 21.5% more patients receiving or having a discharge plan for this agent. According to an economic model by Caro, increasing the appropriate use of warfarin by 50% (approximately our observed increase if all of the patients with discharge plans receive warfarin in the outpatient setting) would result in significant reductions in morbidity, mortality, and medical cost savings.<sup>46</sup> Under the best-case scenario of assuming all patients with a discharge plan received warfarin in the outpatient setting (ie. there is a good system for transitioning from the inpatient to the outpatient setting), the Caro model predicts this intervention would prevent 1.6 strokes and cause 0.08 more bleeding events annually in a population of 350 patients (the estimated number of atrial fibrillation patients seen annually in this institution). The average annual medical cost savings of the program, not including the hospital program costs, extra drug, and monitoring costs, would be approximately USD 94,620.

To date, there have been few studies that have focused on programs to screen for patients with atrial fibrillation and fewer that affect antithrombotic prescribing. A nurse-led invitational screening program in the UK was effective at identifying some patients with atrial fibrillation, but the proportion of patients accepting the invitation varied by site (from 8% to 52%).<sup>44</sup> There was no systematic attempt described in this study to treat patients once they were identified as having atrial fibrillation and antithrombotic utilization was not assessed. Similar

screening initiatives have demonstrated that programs directed at higher risk patients are both effective and cost-effective for identifying patients with atrial fibrillation.<sup>41,43,47</sup>

Physician education and feedback programs have also been suggested as a method of identifying and treating patients with atrial fibrillation. Community programs taking this approach have demonstrated limited impact on outcomes. One such study of educational outreach visits provided information on stroke risk reduction practices to residential care staff and physicians in twenty facilities.<sup>39</sup> At follow-up, there was no statistically significant difference in aspirin use for patients at risk of stroke. Another study provided general practitioners in one region with locally produced guidelines on stroke risk stratification and antithrombotic prescribing, followed by academic detailing visits.<sup>42</sup> Compared with a similar region which did not receive the mailings and academic detailing, warfarin use was higher among hospitalized patients and in the general community. However, warfarin use remained low, with only 46% of hospitalized patients at a high-risk of stroke actually receiving warfarin.

An audit and provider feedback program for medical, pharmacy, and nursing staff resulted in improved antithrombotic therapy rates in the hospital setting.<sup>40</sup> The appropriateness of the decision to use an antithrombotic agent increased from 72% immediately before to 92% four to eight weeks after the program. The effect was sustained, but attenuated, six months after the program. Warfarin utilization remained low, with only 40% of patients for whom warfarin was indicated actually receiving it after the intervention.

One study, employing similar methods and intervention to our study, was identified from the

literature.<sup>38</sup> This study, performed in an elderly population, employed a pharmacist-coordinated multidisciplinary review process to assess patient risk and make recommendations on therapy. The intervention resulted in a significant increase in the proportion of patients receiving antithrombotic drugs by 21.5% (from 59.6% to 81.1%). However, this increased antithrombotic usage was due to aspirin, with fewer patients receiving warfarin after the intervention than upon admission (20.7% vs. 17.4% respectively).

Although both Bajorek et al and our study were successful in increasing appropriate antithrombotic prescribing, our results differ from theirs in some critical ways.<sup>38</sup> It is unclear from their study why so few patients ended up receiving warfarin at the time of discharge, especially after consultation by the multidisciplinary team. One possible explanation is that their patient population was considerably older than our population (by 6 years on average). Cognitive impairment was cited as a contraindication to warfarin in roughly half of the patients. Another possible explanation was that the assessment perceived benefit to risk ratio for therapy with warfarin was more conservative in their study (or more aggressive in ours), with bleeding risk given more weight than in our setting. This may be due to regional beliefs as warfarin utilization appears to be much lower in all of the studies conducted in Australia.<sup>38-40,42</sup> This is further evidenced by an increased warfarin utilization in our population, despite the presence of risk factors for bleeding. The time-dependent manner of many bleeding risk factors (e.g. bleeding with last 24 hours, surgery within past 7 days, etc.) may also explain why a large proportion of patients only had a discharge plan for warfarin. From the Australian studies and our model, it appears that an in-hospital model may be an effective method of increasing antithrombotic use, especially in the most vulnerable populations. The transition from a hospital discharge plan to actual warfarin use in the community (with appropriate follow up by an anticoagulation clinic) is crucial to the success of such programs. Furthermore, these programs need not be confined to patients with non-valvular atrial fibrillation. Patients with valvular heart disease may derive even greater benefit from appropriate warfarin use.

There are several important considerations regarding our intervention and the ability to test the effectiveness of the intervention. We were unable to follow patients after discharge. It was therefore not clear what proportion of patients with a written discharge order for an antithrombotic agent actually received that medication in the outpatient setting or how patients on warfarin were followed up and monitored. Potential barriers to patients receiving warfarin after a discharge note has been written include a lack of communication between the inpatient and outpatient primary care clinicians. Even if sufficient communication exists and the inpatient prescriber's intent is relayed to the outpatient primary care clinician, additional barriers may be present that prevent the patient from ever receiving appropriate antithrombotic therapy and

monitoring. Outpatient practitioner biases, such as patient age, lower perceived embolic risk, higher perceived risk of hemorrhage, and previous experiences with warfarin can influence the decision to recommend warfarin after patient discharge.<sup>22</sup> Lack of familiarity with current guidelines has also been cited as an important barrier. Since our inpatient intervention did not attempt to follow up with practitioners in the outpatient setting, there is the potential for decreased uptake once the patient is discharged from the hospital. Anticoagulation clinics may improve the uptake and monitoring of patients on warfarin in the community setting.<sup>48</sup> Southwest Washington Medical Center does have an anticoagulation clinic to which many of the study patients may have been referred for ongoing monitoring and warfarin dose adjustment.<sup>26</sup> The coordination of care between the hospital and ambulatory settings is an incredibly important aspect of patient care and safety.<sup>49</sup>

Another important consideration regarding whether or not to adopt this intervention strategy is the institution's ability to implement it. This study was originally designed to be conducted in four different health systems. Unfortunately we were able to implement the study in only one of the systems for various reasons. One of the health systems was not able to report patients identified with atrial fibrillation to the pharmacy department due to a software issue in the EKG equipment. One health system had a clinical pharmacist shortage and could not commit the necessary resources to staff the intervention. The final health system had a change in their pharmacy director at the time the study was to be implemented and was not in a position to support the study. These last two sites were prepared to conduct the intervention within a year of the study's implementation, but due to the delay, the study was already closed to enrollment.

There are several important methodologic limitations to this study that must be addressed. This study, although it does not meet all of the criteria for a pragmatic clinical trial, was designed to be a prospective, practice-based study involving clinically relevant alternatives and a diverse patient population.<sup>50,51</sup> The lack of randomization and concurrent control group can be seen as either a limitation or strength of this study. These study design limitations allow for the possibility that unseen confounders may impact the outcomes. However, we chose this design specifically, as it reduced the risk of the crossover bias that might occur with two concurrent research groups in a single institution. We believed that crossover bias would pose a more serious threat to this study's validity and therefore chose the current study design while attempting to control for observed differences between groups. Given the dramatic and sudden increase in warfarin use and planned use, it is unlikely that unseen confounders were responsible for the observed change in practice. However, it is possible that unseen confounding could bias the point estimates resulting in either an over- or under-estimation of the program's effectiveness.

## CONCLUSIONS

A program designed to identify hospitalized patients with non-valvular atrial fibrillation, assess their need for stroke prophylaxis, and initiate appropriate antithrombotic therapy led to an increase in planned antithrombotic use upon discharge from the hospital. Confirmation of this study's findings with a similar program using a prospective, randomized design is needed. Also, confirmation that an

increase in planned antithrombotic use upon discharge results in an actual increase in use after discharge is needed to determine the true effectiveness of this intervention.

## CONFLICT OF INTEREST

None declared. This study was supported by an unrestricted educational grant from DuPont Pharma.

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