Comparison of an Anticoagulation Clinic With Usual Medical Care

Anticoagulation Control, Patient Outcomes, and Health Care Costs

Elaine Chiquette, PharmD; Mary G. Amato, PharmD, MPH; Henry I. Bussey, PharmD

Background: The outcomes of an inception cohort of patients seen at an anticoagulation clinic (AC) were published previously. The temporary closure of this clinic allowed the evaluation of 2 more inception cohorts: usual medical care and an AC.

Objective: To compare newly anticoagulated patients who were treated with usual medical care with those treated at an AC for patient characteristics, anticoagulation control, bleeding and thromboembolic events, and differences in costs for hospitalizations and emergency department visits.

Results: Rates are expressed as percentage per patient-year. Patients treated at an AC who received lower-range anticoagulation had fewer international normalized ratios greater than 5.0 (7.0% vs 14.7%), spent more time in range (40.0% vs 37.0%), and spent less time at an international normalized ratio greater than 5 (3.5% vs 9.8%). Patients treated at an AC who received higher-range anticoagulation had more international normalized ratios within range (50.4% vs 35.0%), had fewer international normalized ratios less than 2.0 (13.0% vs 23.8%), and spent more time within range (64.0% vs 51.0%). The AC group had lower rates (expressed as percentage per patient-year) of significant bleeding (8.1% vs 35.0%), major to fatal bleeding (1.6% vs 3.9%), and thromboembolic events (3.3% vs 11.8%); the AC group also demonstrated a trend toward a lower mortality rate (0% vs 2.9%; $P = .09$). Significantly lower annual rates of warfarin sodium–related hospitalizations (5% vs 19%) and emergency department visits (6% vs 22%) reduced annual health care costs by $132 086 per 100 patients. Additionally, a lower rate of warfarin-unrelated emergency department visits (46.8% vs 168.0%) produced an additional annual savings in health care costs of $29 972 per 100 patients.

Conclusions: A clinical pharmacist–run AC improved anticoagulation control, reduced bleeding and thromboembolic event rates, and saved $162 058 per 100 patients annually in reduced hospitalizations and emergency department visits.

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From the Clinical Pharmacy Programs at The University of Texas at Austin and The University of Texas Health Sciences Center at San Antonio (Drs Chiquette, Amato, and Bussey); Anticoagulation Clinic, University Health Center Downtown, San Antonio (Dr Amato); Pharmacotherapy Consultants Clinic, University Health Center Downtown, and Anticoagulation Clinics of North America, San Antonio (Dr Bussey). Dr Chiquette is now with the San Antonio Cochrane Center, Audie Murphy Memorial Veterans Affairs Hospital, San Antonio. Dr Amato is now with the Frank M. Tejeda Veteran Affairs Outpatient Clinic, San Antonio.

ALMOST A half century ago Askey and Cherry[1] endorsed the essential components of an anticoagulation clinic (AC) by noting that "The successful use of [anticoagulation] . . . depends on an essential triad: a vigilant physician, a cooperative patient, and a readily available, reliable laboratory." In 1996, Rosendaal[2] concluded that anticoagulation "should be monitored by specialized anticoagulation clinics to minimize risks." The American College of Chest Physicians Consensus Conference on Antithrombotic Therapy endorsed ACs[3] and concluded that failure to use them likely increases the risk of legal liability.[4] Finally, in a 1995 news conference that received national television and press coverage, the Agency for Health Care Policy and Research announced the findings of a study that indicated that the underuse of warfarin sodium in patients with atrial fibrillation costs $600 million annually for 40 000 preventable strokes. The deterrent to warfarin use was that physicians "needlessly fear its side effects," and the suggested solution was monitoring by nurse practitioners or physician assistants. Even so, Ansell et al[5,6] questioned the benefits of ACs, and Fihn[7] noted that "There are regrettably few studies addressing such important topics as whether nurses or pharmacists operating an AC perform as well as or better than cardiologists or primary care physicians providing usual care." In fact, descriptive reports of 9 ACs[8-16] and 3 usual medical care (UMC) groups,[17-19] together with 7 comparative trials,[20-26] indicate that ACs can reduce the annual major bleeding rate from 5% to 28% in UMC to 6% or less. Firm conclusions, however, cannot be based on descriptive reports, and the comparative trials had flawed study designs or sample size limitations.

PATIENTS AND METHODS

SETTING AND PATIENTS

After 12 years of operation, a university-affiliated AC was closed to new patients from January 1991 to September 1992. The inpatient and outpatient medical records of patients who began to receive warfarin between January 1991 and May 1994 were examined to assess the impact of the AC on anticoagulation control, patient outcomes, and costs of hospitalization and emergency department (ED) visits. Patients were included if they had received warfarin for at least 3 months and had at least 1 outpatient visit. Because the university health care system exists to serve the indigent population of the area, patients typically were not seen elsewhere during the study periods.

USUAL MEDICAL CARE

The management of the patients who underwent UMC was at the discretion of the attending faculty physicians in the general medicine, family medicine, and subspecialty clinics. This process could involve medical residents, nurses, and nurse practitioners for patient education and communication. No algorithms were used.

ANTICOAGULATION CLINIC

The AC, which operated within the general medicine clinics, was supervised by a clinical pharmacist (M.G.A.) with most patient encounters provided by pharmacy students or residents. Backup support was provided by faculty physicians. At the first visit, a medical history, limited physical examination, and medication review were completed to determine the patient's risks of bleeding and thromboembolic (TE) events. The appropriateness of the antithrombotic regimen was assessed and modified as indicated. Finally, intensive patient education was provided. Follow-up visits included a targeted physical assessment and a detailed interview. Warfarin dosage adjustments were at the discretion of the clinical pharmacist (M.G.A.); an algorithm was not used. Changes in other medications also were made as clinically indicated, with the approval of the attending physician in the general medicine clinic. Patients were usually seen at intervals of 4 weeks or less.

PROTHROMBIN TIME AND INTERNATIONAL NORMALIZED RATIO REPORTING

Laboratory prothrombin time results were reported in seconds and as international normalized ratios (INRs) throughout both study periods. All clinics used the same laboratory.

DATA COLLECTION

All data were collected by a postdoctoral fellow (E.C.), who resolved any questions or uncertainties through consultation with a faculty member (H.I.B.). Neither of these individuals was involved in the AC. The patients were divided into UMC or AC groups; data were collected until the patients changed groups, until they terminated warfarin use, or until September 1994. The data collected included demographics, indications for anticoagulation, risk factors for TE events or hemorrhage, INR values, events related to

The temporary closure of an AC to new patients provided a unique opportunity to assess the impact of such a clinic. The complication rates prior to the closure of the AC were published previously.[13] Although the earlier article provides an interesting historical comparison, this report focuses on the 2 subsequent periods of UMC and AC care.

RESULTS

PATIENTS

The UMC group included 145 newly anticoagulated patients with 104 patient-years of data, and the AC group included 183 newly anticoagulated patients with 131 patient-years of data. The groups were similar except that congestive heart failure was a more frequent anticoagulation indication in the AC group and a history of stroke was a more common risk factor in the UMC group (**Table 1**). The incidence of antiphospholipid antibody syndrome was not significantly different between the 2 groups, but the substantially higher bleeding rate (87% and 100% per patient-year in the AC and UMC groups, respectively) in this subgroup of 10 patients (10 patient-years) identified this condition as an "effect modifier," which justified excluding this subgroup for the overall analysis.[31] The analysis, therefore, included 142 patients in the UMC group (102 patient-years) and 176 patients in the AC group (123 patient-years).

ANTICOAGULATION CONTROL

Among the patients receiving lower-range anticoagulation therapy (INR, 2-3; n = 249), the difference in percentage of INRs in the therapeutic range did not achieve statistical significance, but the proportion of INRs above 5 was significantly less in the AC group (7.0% vs 14.7%, $P<.001$) (**Table 2**). Among patients receiving higher-range anticoagulation therapy (INR, 2.5-4.5; n = 69), the AC group had significantly more INRs within the therapeutic range (50.4% vs 35%; $P<.001$) and significantly fewer INRs below 2 (13% vs 23.8%; $P<.001$). Because INRs may be obtained more frequently when a value is out of the target range, the patient-time spent within the therapeutic range may be a better indicator of anticoagulation control. This was assessed using a modified version of the computer program used by Rosendaal,[27] as described previously.

Although the mean interval between INR measurements was not significantly different (29 vs 34 days in the AC vs UMC groups, respectively), periods exceeding 12 weeks without an INR being measured required the exclusion of 28% of the AC data and 53% of the UMC data. The remaining data indicated that patients receiving both lower- and higher-range anticoagulation therapy were in

warfarin treatment (specifying severity and management), and hospitalizations and ED visits (categorized as related or unrelated to anticoagulation therapy). The target INR range was defined for each patient according to the American College of Chest Physicians Consensus Conference recommendations. Bleeding events were classified according to a modified version of the Warfarin Optimized Outpatient Follow-up Study classification.[15] "Minor" bleeding had little or no clinical significance and did not require referral or additional visits. "Significant" bleeding required evaluation or referral or was associated with a decrease in hematocrit greater than 3% or a decrease in the hemoglobin level of more than 1.2 mg/dL. "Major" bleeding required hospitalization and transfusion of at least 2 U of blood, and "life-threatening" bleeding led to cardiopulmonary arrest, surgical or angiographic intervention, or irreversible sequelae. In "fatal" bleeding, death was directly related to the bleeding. Similarly, TE events were classified by severity. A minor TE event had no significant health care impact, while a significant TE event required evaluation or hospitalization. A life-threatening TE event caused irreversible damage, required an emergency procedure, or necessitated admission to an intensive care unit.

DATA ANALYSIS AND STATISTICS

Patient characteristics were compared using an unpaired *t* test, a χ^2 test, or the Fisher exact test, where appropriate.

Anticoagulation control was calculated as the percentage of INRs and the percentage of patient-time spent within the target range. Calculating patient-time within range required using a modified version of the program developed by Rosendaal et al, as described elsewhere.[27] Because the program rejects any period that exceeds 8 weeks without an INR being measured, it was modified to include intervals of 12 weeks or less between INR measurements. Additionally, the proportion of INRs and patient-time spent below an INR of 2 and above an INR of 5 were calculated. This was done because recent trials in patients following myocardial infarction,[28] with atrial fibrillation,[29] and those with mechanical prosthetic heart valves[30] have reported a dramatic increase in complication rates when the INR exceeds these limits. Differences in anticoagulation control were assessed using a χ^2 test.

Event rates were calculated as the number of events divided by the total number of patient-years of follow-up in each group. Event rates, therefore, are expressed as percentage per patient-year or events per 100 patient-years. Differences in event rates were calculated as relative risks with 95% confidence intervals. The mean INR associated with events and the number of events that occurred above or below a given INR were examined to further assess the impact of INR control on complications. These differences were compared by a χ^2 test.

The costs of hospitalization and ED visits were used to assess the financial impact of the AC. These were subdivided according to whether they were related or unrelated to anticoagulation. The differences in rates were compared by χ^2 analysis. Cost comparisons were made only for those rates that were significantly different between the 2 groups. Diagnosis related group figures were used to calculate hospitalization costs. The costs for ED visits for prescription refills were allocated as the minimal ED cost and physician charge. Other ED visits were assigned different charges reflecting the level of complexity of the visit ($30-$650 per visit).

the therapeutic range significantly more often in the AC groups. Patients in the AC group who received lower-range anticoagulation therapy were in range 40.0% of the time vs 37.0% for those in the UMC group ($P<.001$). Because some clinicians may consider INRs slightly outside of this range acceptable, the percentage of time spent in an expanded range of 1.5 to 3.5 was assessed and found to be 71% vs 65% for the AC vs UMC groups, respectively ($P<.001$). Similarly, patients in the AC group who received higher-range anticoagulation therapy were in range more often (64% vs 51% for patients in the UMC group; $P<.001$), and their INRs were below 2 less often (6.9% vs 15.3% for patients in the UMC group; $P<.001$).

PATIENT OUTCOMES

Bleeding Events

The 35% reduction in the risk of minor bleeding in the AC group (18.0% vs 27.5% per patient-year) did not achieve statistical significance, but the 77% reduction in significant bleeding (8.1% vs 35.3% per patient-year) was highly significant ($P<.001$) (**Table 3**). Similarly, the major to fatal bleeding rate in the AC group was reduced by more than 50% (1.6% vs 3.9% per patient-year; $P<.05$); these events were more severe in the UMC group with 3 life-threatening and 1 fatal bleeding event (Table 3).

The level of anticoagulation at the time of events also indicated a need for better INR control in the UMC group (**Table 4**). For each bleeding event classification, the mean INR in the UMC group was above 5 and was significantly higher in the UMC group ($P<.05$). In the UMC group, the mean INRs for significant and major to fatal bleeding events were unusually high (10.49 and 35.51, respectively). In fact, all major to fatal bleeding in the UMC group occurred at INRs of 16 or greater (Table 4). This suggests that the incidence of serious bleeding might have been reduced if extreme overanticoagulation had been avoided in the patients in the UMC group.

Thromboembolism

Thromboembolism was reduced by almost 80% in the AC group (3.3% vs 11.8% per patient-year; $P<.05$). Also, the most severe TE events occurred in the UMC group. Of the 12 TE events in the UMC group patients, 8 were significant, 1 was life-threatening, and 2 were fatal. In the AC group, all 4 events were significant; none was life-threatening or fatal (Table 3). The mean INRs at the time of TE events tended to be lower in the UMC group, and 2 of the 3 major to fatal TE events occurred at INRs less than 1.8 (Table 4). Again, this suggests that more aggressive anticoagulation control might have prevented some of these events.

Combined Events

The combined rate of major to fatal bleeding and TE events was reduced by two thirds in the AC group (4.9% vs 15.7% per patient-year; $P<.05$). Additionally, there was a trend toward a lower mortality rate in the AC group (0% in 123 patient-years vs 2.9% per patient-year; $P=.09$).

COST ANALYSIS

Related to Anticoagulation

Hospitalizations and ED visits related to anticoagulation were reduced by 73% in the AC group. Hospitalization rates were 5 and 19 per 100 patient-years in the AC and UMC groups, respectively. This difference yielded an annual savings of $128 937 per 100 patients enrolled in the AC. The related ED visits also were reduced in the AC group (6 vs 22 per 100 patient-years). This produced annual savings of $3149 per 100 patients. The AC, therefore, saved $132 086 annually in expenses for

Table 1. Patient Characteristics*

Variable	No. (%) of Patients	
	UMC Group	AC Group
No. of patients	145	183
Male	71 (49)	104 (57)
Female	74 (51)	79 (43)
Age, y		
≤65	130 (90)	162 (89)
66-74	12 (8)	16 (9)
≥75	3 (2)	3 (2)
Indications		
DVT	30 (21)	30 (16)
PE	8 (6)	9 (5)
Atrial fibrillation	22 (15)	25 (14)
Cardiomyopathy	12 (8)	28 (15)
CHF	9 (6)	19 (10)†
Myocardial infarction	8 (6)	17 (9)
CVA	11 (8)	10 (6)
Mechanical heart valve	33 (23)	26 (14)
Miscellaneous	12 (8)	11 (6)
Risk factors		
APLS	3 (2)	7 (4)
Protein C/S deficiency	5 (3)	1 (0.6)
Previous CVA	17 (12)	11 (6)†
CHF	14 (10)	21 (12)
Diabetes	39 (27)	50 (27)
Hypertension	56 (39)	80 (44)
Ulcers	5 (3)	6 (3)

**UMC indicates usual medical care; AC, anticoagulation clinic; DVT, deep vein thrombosis; PE, pulmonary embolus; CHF, congestive heart failure; CVA, cerebrovascular accident; and APLS, antiphospholipid antibody syndrome.*

†P<.05, AC vs UMC data.

Table 2. Anticoagulation Control*

Variable	Target INR Range			
	2-3		2.5-4.5	
	UMC (n = 106)	AC (n = 143)	UMC (n = 36)	AC (n = 33)
INR values (n)	821	1232	374	385
% Values				
Within range	29.6	32.3	35.0	50.4†
<2.0	36.2	39.6	23.8	13.0†
>5.0	14.7	7.0†	19.0	15.0
% Time‡				
Within range	37.0† (65†)§	40.0† (71†)§	51.0	64.0†
<2.0	30.0	33.0	15.3	6.9†
>5.0	9.8	3.5†	13.4	12.2

**INR indicates international normalized ratio; UMC, usual medical care; and AC, anticoagulation clinic.*

†P<.001, AC vs UMC data.

‡Because of infrequent follow-up, only 72% of the AC data and 47% of the UMC data could be included in the analysis of time spent in INR ranges.

§Time in range increased substantially if the INR range was expanded to 1.5 to 3.5.

Table 3. Bleeding and Thromboembolic Event Rates*

Variable	1989 AC (n = 82; 199 Patient-Years)†	UMC (n = 142; 102 Patient-Years)	AC (n = 176; 123 Patient-Years)	Relative Risk (95% CI)
Bleeding				
Minor	. . .	27.5	18.0	0.65 (0.35-1.20)
Significant	15.6	35.3	8.1‡	0.23 (0.11-0.46)
Major	. . .	0.0	1.6	. . .
Life-threatening	. . .	2.9	0.0	. . .
Fatal	. . .	1.0	0.0	. . .
Major to fatal (total)	1.5	3.9	1.6§	0.41 (0.24-0.70)
Thromboembolism				
Minor	. . .	1.0	0.0	. . .
Significant	. . .	7.8	3.3	. . .
Life-threatening	. . .	1.0	0.0	. . .
Fatal	. . .	2.0	0.0	. . .
Total	3.5	11.8	3.3§	0.28 (0.10-0.84)
Related mortality	. . .	2.9	0.0	. . .

**Values are given as percentage per patient-year. AC indicates anticoagulation clinic; UMC, usual medical care; CI, confidence interval; and ellipses, data are not available. The relative risk is calculated for UMC vs the second AC column.*

†Results when similar criteria were applied to data published previously from the same clinic (by Bussey et al[13]), presented for comparison.

‡P<.001, AC vs UMC data.

§P<.05, AC vs UMC data.

Table 4. INR Values at Time of Events*

Events	UMC Group	AC Group
Bleeding		
Minor		
Mean INR	6.19	3.75†
No. with an INR >5	12/28	3/22†
Significant		
Mean INR	10.49	4.35†
No. with an INR >5	20/36	4/10
Major to fatal		
Mean INR	35.51	5.60†
No. with an INR >5	4/4	1/2
Actual INRs	16.00, 25.30, 27.60, 73.20	1.47, 9.80
Thromboembolism		
Minor		
Mean INR	1.64 (n = 1)	NA (n = 0)
Significant		
Mean INR	1.98 (n = 8)	3.75 (n = 4)
Major to fatal		
Mean INR	2.58 (n = 3)	NA (n = 0)
Actual INRs	1.00, 1.79, 4.94	NA

**INR indicates international normalized ratio; UMC, usual medical care; AC, anticoagulation clinic; and NA, data are not applicable.*

†P<.05, AC vs UMC data.

warfarin-related hospitalizations and ED visits for every 100 patients enrolled in the AC (**Table 5**).

Unrelated to Anticoagulation

The hospitalization rates for problems unrelated to anticoagulation were not significantly different. Emergency department visits, however, were different. Emergency department visits for prescription refills were reduced. This accounted for only a small amount of the total health care expense (Table 5). Emergency department visits for other reasons unrelated to anticoagulation also were reduced (46% vs 133% per patient-year for AC and UMC groups, respectively). The total rate for ED visits unrelated to warfarin (for prescription refills and other unrelated reasons) was reduced (46.8% vs 168.0% per patient-year in the AC vs UMC groups). This difference saved $29 972 per year for every 100 patients enrolled in the AC.

Total Cost Savings

The establishment of an AC saved $162 058 per 100 patients per year owing to fewer hospitalizations and ED visits (Table 5).

COMMENT

An AC achieved better anticoagulation control, reduced complication rates by 50% to 80%, and reduced health care costs by more than $1600 per patient per year. Although these results are consistent with previous reports, there are a few potential criticisms and considerations that may limit their application.

Even though this study was not randomized, there are several strengths that compensate for this. Specifically, patient capture during the 2 study periods was essentially complete, and the 2 groups were comparable. Once the earlier AC was closed to new patients, there were no exceptions; all new patients were managed by UMC. When the AC later opened to new patients, patient capture of more than 95% was confirmed by comparing the names of new warfarin prescriptions with new patients enrolled in the AC. Additionally, the new AC did not refuse any referrals, nor did it expel any patients. Consequently, the 2 groups (UMC and AC) were nearly identical for demographics, indications, and risk factors. Another strength is the completeness of the data. Because the university health system is the care system for the indigent population of the area, virtually all medical encounters were documented in the system's medical records.

A weakness in other reports has been that the studies' complication rates were evaluated before and after an AC was established. In such studies, perceived benefits could be time dependent because more complications may occur early in therapy. The use of 2 inception cohorts eliminated this criticism, and the earlier report from the same clinic further supports a lack of a time effect.[13] Applying the same criteria to the data from a similar inception cohort in that report yielded similar AC event rates. After the AC closed, the event rates increased from 15.6 to 35.3 for significant bleeding, from 1.5 to 3.9 for major to fatal bleeding, and from 3.5 to 11.8 for TE events. After the AC reopened, the event rates in the third inception cohort declined to previous values or lower (8.1%, 1.6%, and 3.3% per patient-year for significant bleeding, major to fatal bleeding, and TE rates, respectively) (Table 3). This scenario is analogous to a challenge, dechallenge, and rechallenge with an intervention in 3 inception cohorts.

The major to fatal bleeding event rate of 3.9% per patient-year in the UMC group is unusually low for a UMC group and, in fact, is as low as that reported by several ACs. This unusually low rate may be due to interaction between the UMC group physicians and the AC group clinical pharmacists. For 7 years prior to closure of the AC to new patients and throughout both study periods, the AC group clinical pharmacists worked closely with the general medicine clinic physicians who supervised most of the UMC. Not only may this interaction have influenced the treatment of the patients in the UMC group, but the UMC group physicians also consulted the AC group clinical pharmacists during the UMC period. Such interaction would reduce differences between the 2 groups. Therefore, the benefits of the AC would have been even greater if this complication rate in the UMC group had been similar to those in other UMC reports. It is unclear if interaction with clinical pharmacists influenced the TE event rate. The rate of 11.8% per year seems high, but it is consistent with other reported event rates of 6.6% to 17.7% per year[17,20-22,25] and is lower than the 48.0% per year reported by Wilt et al.[24]

Also, the INR was reported throughout the AC and UMC periods. Otherwise, differences in complication rates could have been due to inappropriate dosage adjustments based on misleading laboratory results. This might

Table 5. Hospitalizations and ED Visits*

Variable	UMC Group (per 100 Patient-Years)	AC Group (per 100 Patient-Years)	Difference (per 100 Patient-Years)
Related to Warfarin Use			
No. of hospitalizations	19	5†	14
Hospital costs, $	154 512	32 525	121 987
Physician charges, $	8784	1834	6950
Subtotal, $	**163 296**	**34 359**	**128 937**
No. of ED visits	22	6†	16
ED costs, $	2581	592	1989
Physician charges, $	1535	375	1160
Subtotal, $	**4116**	**967**	**3149**
"Related" Total, $	**167 412**	**35 326**	**132 086**
Not Related to Warfarin Use			
No. of hospitalizations	52	59	7
ED visits for refills	35	0.8†	34.2
ED costs, $	973	22	951
Physician charges, $	723	15	703
Subtotal, $	**1696**	**37**	**1654**
ED visits for "other" reasons	133	46†	87
ED costs, $	40 000	16 341	23 659
Physician charges, $	7585	2931	4654
Subtotal, $	**47 585**	**19 272**	**28 313**
"Not Related" Total, $	**49 281**	**19 309**	**29 967**
Total Expenses, $	**216 693**	**54 635**	**162 053**

**ED indicates emergency department; UMC, usual medical care; and AC, anticoagulation clinic. The diagnosis-related amounts are as follows: $5897 for deep vein thrombosis, $11 117 for pulmonary embolus, $11 733 for cerebrovascular accident, $2718 or $11 375 (for survivors) for myocardial infarction, $4139 for hemoptysis, and $4193 for gastrointestinal tract bleeding. The average cost for ED visits was $300.*

†$P<.001$.

explain the relatively higher significant bleeding rate of 15.6% per patient-year in the earlier report from this AC before the INR was adopted.

Obviously, it is reasonable to question how these results apply to other sites. Perhaps results would be different if private practitioners were involved or if the patients were more affluent. The report by Cortelazzo et al,[25] which included approximately 600 patient-years of data in each period, found that an AC reduced the incidence of major bleeding and thromboembolism by 80% to 90% compared with management provided by private general practitioners and cardiologists. Major bleeding events declined from 4.9% to 1.0% per patient-year (numbers that are similar to those reported in this article). Similarly, TE declined from 6.6% to 0.6% per patient-year. Additionally, we recently performed a limited analysis of anticoagulation management in the affluent population of a local health maintenance organization.[32] Follow-up was rather poor, INRs not being measured within 8 weeks 43% of the patient-time. Excessive anticoagulation was usually avoided (INRs were above 5 less than 5% of the time), and there were no life-threatening to fatal bleeding (vs none in the AC group and 3.9% per patient-year in the UMC group in our study). International normalized ratios, however, were below the therapeutic range approximately 30% to 64% of the time (depending on patient classification), and this was associated with a 5% per year life-threatening to fatal TE event rate (vs 0% in the AC and 3.0% in the UMC in our study). In this health maintenance organization population, the frequency of inadequate follow-up was intermediate between that found in the AC group and that found in the UMC group and the frequency of overanticoagulation and serious bleeding complications was similar to that seen in the AC group, but the level of underanticoagulation and serious TE events was at least as bad as that seen in the UMC group.

There are several issues related to cost calculations that should be considered. Costs of AC services were not included because they represented a reallocation of resources. The average frequency of INR measurements and follow-up were not different in the UMC and AC groups. Simply stated, the follow-up in the AC was systematic and provided by clinical pharmacy students and residents under a clinical pharmacist's supervision (M.G.A.), while the follow-up in the UMC group was more sporadic and provided by nurses or medical residents under the supervision of an attending physician. Also, almost $30 000 of the $162 000 savings was due to a 70% reduction in ED visits that were unrelated to anticoagulation. Emergency department visits were probably averted because the limited history taking and physical examination at each AC visit allowed evolving problems to be identified and addressed at the AC visit. Possibly, a less rigorous approach might not have achieved these savings. Similarly, the training of the supervising AC clinical pharmacists included entry-level undergraduate pharmacy education, graduate school–based doctor of pharmacy degrees, and postdoctoral residency or fellowship training. Perhaps clinicians with less training or experience would not have generated similar savings.

The reported savings, however, are similar to those found in earlier studies from clinical pharmacist–run ACs: annual savings of $86 088 (based on 1985 dollars

and a daily hospital cost of only $271) and $407 268 per 100 patients were found.[21,24] The estimated annual savings of $162 000 per 100 patients in this report, however, is an underestimate of the true savings for several reasons. First, diagnosis-related figures tend to underestimate the true patient management costs. Second, costs of additional clinic visits and outpatient procedures for further evaluation were not considered; only hospitalizations or ED visits were used. Third, costs of rehabilitation, lost wages, potential litigation, or funeral expenses were not included.

This report demonstrates that a systematic approach to anticoagulation management, as offered by a clinical pharmacist–run AC, can improve the safety and effectiveness of warfarin therapy by reducing related and unrelated complications. These improved patient outcomes were achieved with an average savings in health care costs of more than $1600 per patient per year. Finally, there are approximately 4 million patients in the United States with indications for warfarin therapy. If the data from this report are applied to 4 million patient-years of management, the failure to use an AC would result annually in an additional 92 000 major to fatal bleeding, 340 000 TE events, and health care costs of $6.4 billion.

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Reprints: Henry I. Bussey, PharmD, Division of Pharmacotherapy, The University of Texas Health Sciences Center at San Antonio, 7703 Floyd Curl Dr, San Antonio, TX 78284-6220 (e-mail: bussey@uthscsa.edu).

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