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# Recent National Patterns of Warfarin Use in Atrial Fibrillation

Randall S. Stafford, MD, PhD; Daniel E. Singer, MD

**Background**—Studies of selected populations suggest that anticoagulation in atrial fibrillation is underused and that nonclinical factors influence the use of this stroke-preventing therapy. We wished to examine recent national trends and predictors of warfarin sodium use in atrial fibrillation.

**Methods and Results**—A nationally representative sample of office visits from the 1989 to 1996 National Ambulatory Medical Care Surveys was used. We selected 1125 visits by patients with atrial fibrillation, including 877 visits to cardiologists and primary care physicians in which apparent contraindications for anticoagulation were absent. The principal outcome measure was the proportion of visits with warfarin reported. We analyzed trends in warfarin use and statistically evaluated the predictors of warfarin use. Warfarin use increased from 13% of atrial fibrillation visits in 1989 to 40% in 1993 ( $P$  for trend  $<.001$ ) in patients without contraindications. Between 1993 and 1996, however, there was no change in warfarin use. Independent of other factors, warfarin was significantly more likely to be reported in patients with a history of stroke and in patients residing outside of the South.

**Conclusions**—Warfarin use in atrial fibrillation has not increased recently, indicating inadequate implementation of this highly effective therapy. Barriers to anticoagulation in real-world clinical practice need to be identified and addressed. (*Circulation*. 1998;97:1231-1233.)

**Key Words:** atrial fibrillation ■ anticoagulants ■ physician practice patterns

Anticoagulation with warfarin sodium reduces the risk of ischemic stroke in patients with atrial fibrillation by two thirds.<sup>1</sup> Despite consensus that warfarin is strongly indicated in most patients with atrial fibrillation, past studies demonstrate that anticoagulation in atrial fibrillation is inadequately used. Most studies have investigated selected, local populations with atrial fibrillation. Studies of nursing home populations indicate that 20%<sup>2</sup> to 32%<sup>3</sup> of eligible nursing home patients are taking warfarin. Even in populations of hospitalized patients, three studies found that only 38%<sup>4</sup> to 44%<sup>5,6</sup> of patients without contraindications were taking warfarin at hospital discharge. Although less information is available on community settings, warfarin use in these settings may be lower than in institutional settings, with rates between 11% and 32% noted.<sup>4,7,8</sup> Investigation of recent time trends in warfarin use in atrial fibrillation, particularly at a national level, is limited. To extend past findings and elucidate possible barriers to dissemination of this stroke-preventing practice, we analyzed data from a nationally representative sample of physician office visits from 1989 through 1996. We hypothesized that despite continued suboptimal use in atrial fibrillation, warfarin use would be increasing.

## Methods

We used data from the 1989 to 1996 National Ambulatory Medical Care Surveys (NAMCS) conducted by the National Center for

Health Statistics.<sup>9</sup> To provide a representative sample of visits to US office-based physicians each year, NAMCS randomly samples physicians by specialty and geographic area. For each participating physician (mean participation rate for 1989 to 1996 was 72%), patient visits during a randomly selected week were sampled systematically. The survey includes between 33 795 (1991) and 43 469 (1990) annual outpatient visits to between 1345 (1991) and 1883 (1995) physicians. For each selected patient visit, physicians completed encounter forms detailing clinical services, patient demographics, clinical diagnoses, and continuing and newly ordered medications. Available visit weights were used to extrapolate to national practice patterns<sup>9</sup> and were modified to derive effective sample sizes for statistical testing.<sup>10</sup>

A total of 1125 visits by patients with atrial fibrillation were identified by an ICD-9-CM diagnostic code of 427.31<sup>11</sup> among any of the three diagnoses coded for each visit: 94 in 1989, 146 in 1990, 120 in 1991, 141 in 1992, 131 in 1993, 164 in 1994, 177 in 1995, and 152 in 1996. We focused on a subset of 877 visits to assess patterns of warfarin use more reliably. We excluded 58 visits by patients with potential contraindications for anticoagulation, including peptic ulcer disease, gastritis and duodenitis, other gastrointestinal bleeding, alcoholism, gait abnormality, ataxia, Alzheimer's or other dementia, cerebral hemorrhage, seizure disorder, benign or malignant central nervous system tumors, gastrointestinal and genitourinary tract malignancies, thrombocytopenia, hematuria, esophageal varices, and renal insufficiency. We also excluded 90 visits by patients  $<65$  years old lacking other risk factors for stroke (congestive heart failure, ischemic heart disease, diabetes mellitus, hypertension, valvular disease, or previous stroke) because warfarin may not be indicated in these patients.<sup>12</sup> Finally, to focus on the physicians most likely to

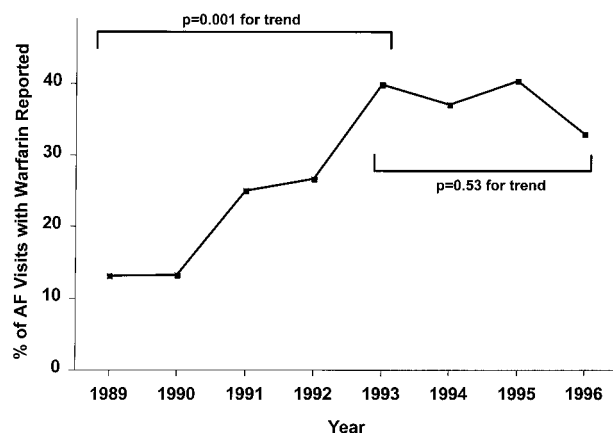
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Time trends in percentage of visits by US patients with atrial fibrillation (AF) reported to be receiving warfarin. These trends exclude patients with concomitant contraindications for warfarin therapy, patients at apparent low risk for stroke, and visits to physicians other than cardiologists and primary care physicians (see text).

prescribe warfarin, we excluded an additional 100 visits made to physicians other than cardiologists, general internists, family physicians, and general practitioners. Within this restricted sample, we also defined subsets of patient visits in which other risk factors for stroke were present ( $n=683$ ) and in which atrial fibrillation was the primary reason for the visits ( $n=430$ ).

Patients receiving warfarin therapy were identified by the coding of generic or proprietary names for warfarin, dicumarol, or anisindione among the five (1989 through 1994) or six (1995–1996) possible medication codes associated with each visit. Aspirin use was assessed similarly. Annual information on atrial fibrillation visits was evaluated for trends in warfarin use with the  $\chi^2$  test for trend.<sup>13</sup> The independent impact of physician and patient characteristics on warfarin use was assessed for our sample of 877 visits by multiple logistic regression.<sup>14</sup> US Census Bureau definitions were used for four geographic regions in the US. Statistical analyses were performed with SAS.<sup>13</sup>

## Results

Our sample of 1125 visits over 8 years is representative of an estimated 2.8 million (95% CI, 2.5 million to 3.1 million) annual national visits by patients with atrial fibrillation. Reported warfarin use in these patient visits increased steadily from 12% in 1989 to 38% in 1993 ( $P$  for trend  $<.001$ ) but failed to increase between 1993 and 1996 (32%,  $P=.54$ ). A similar pattern was noted when we excluded visits by patients with reported contraindications for warfarin, patients  $<65$  years old without other risk factors for stroke, and visits to specialists other than cardiologists and primary care physicians: warfarin use increased from 13% in 1989 to 40% in 1993 ( $P<.001$ ) but failed to increase between 1993 and 1996 (33%,  $P=.53$ ) (Fig). Warfarin use in the excluded population of visits was not substantially different from that in the full sample. Aspirin use among visits by patients not taking warfarin increased steadily from 6% in 1989 to 20% in 1996 ( $P=.05$ ).

When we further restricted our analysis to patients with other risk factors for stroke, warfarin use varied from 12% in 1989, 44% in 1993–94, and 35% in 1995–96. Similarly, when atrial fibrillation was the reason for the visit, warfarin use varied from 12% in 1989 to 41% in 1993–94 to 43% in 1995–96.

Using our restricted sample for 1989 through 1996 ( $n=877$ , see “Methods”), we developed a multiple logistic regression model to describe the independent predictors of warfarin use. Patients with a history of stroke (odds ratio [OR], 5.1; 95% CI, 2.0 to 13.5) were much more likely to receive warfarin than were other patients. Patients residing in the South (OR, 0.57; CI, 0.35 to 0.93) were much less likely to receive warfarin than were those from all other geographic regions. Warfarin use tended to be more likely in patients seen by cardiologists or internists (OR, 1.57; CI, 0.98 to 2.54) than in those seen by family and general practitioners and less likely in those  $>80$  years old (OR, 0.60; CI, 0.37 to 0.98) than in younger patients. There were no significant associations between warfarin use and sex, race, payment source, or the presence of hypertension, congestive heart failure, atherosclerosis, valvular disease, or diabetes.

## Discussion

We have examined a nationally representative sample of visits by patients with atrial fibrillation, focusing on visits to cardiologists and primary care physicians by patients in whom warfarin was likely to be indicated and not contraindicated. Warfarin use increased dramatically between 1989 and 1993 but failed to increase between 1993 and 1996. Increases between 1989 and 1993 were associated temporally with the publication of the results of six clinical trials demonstrating the benefits of warfarin in preventing strokes in atrial fibrillation.<sup>15–20</sup> Rising use of aspirin in patients not treated with warfarin is of concern, given that aspirin is less effective in reducing the risk of ischemic strokes.<sup>21</sup>

It is difficult to precisely define an optimal rate of warfarin use even in patients without reported contraindications. Among other reasons, differences in patient preferences may lead to different decisions about anticoagulation. Nonetheless, the 33% rate of warfarin use noted in 1996 certainly appears to be suboptimal, considering the substantial benefits of anticoagulation in atrial fibrillation seen in randomized clinical trials. This finding suggests that a large number of patients with atrial fibrillation remain at higher than necessary risk for ischemic strokes. The feasibility and safety of warfarin in a high proportion of eligible patients with atrial fibrillation have been observed in a modest-sized study from an urban health maintenance organization.<sup>22</sup>

As with other studies,<sup>3–8</sup> we found that warfarin was used less frequently in patients  $>80$  years old. Although warfarin therapy in the most elderly can be a complicated task, this population has the greatest absolute reduction in stroke rates with warfarin therapy.<sup>1</sup> In addition, we found less warfarin use in patients residing in the South and a tendency for less use by family and general practitioners. These factors may indicate specific barriers to further adoption of warfarin therapy.

Several limitations of our analysis must be acknowledged. Because our analysis used patient visits as the unit of analysis, we could not identify longitudinal trends in warfarin use for a cohort of patients with atrial fibrillation. In addition, our estimates may differ from a community-based assessment because patients visiting physicians more frequently will be overrepresented in our sample. Although we defined a sub-

population in whom warfarin is likely to be indicated, even this sample may include patients with unreported contraindications for warfarin, such as poor adherence.

Our evidence that warfarin use in atrial fibrillation has stabilized at a suboptimal level suggests a need for broader health system strategies to provide anticoagulation. In particular, specialized anticoagulation clinics may make it easier for physicians to initiate and maintain safe warfarin therapy. The personal, societal, and financial burden of preventable strokes in patients with atrial fibrillation argues that substantial investment in new strategies is warranted.

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### References

1. Atrial Fibrillation Investigators. Atrial fibrillation: risk factors for embolization and efficacy of antithrombotic therapy. *Arch Intern Med.* 1994; 154:1449–1457.
2. Lackner TE, Battis GN. Use of warfarin for nonvalvular atrial fibrillation in nursing home patients. *Arch Fam Med.* 1995;4:1017–1026.
3. Gurwitz JH, Monette J, Rochon PA, Eckler MA, Avron J. Atrial fibrillation and stroke prevention with warfarin in the long-term care setting. *Arch Intern Med.* 1997;157:978–984.
4. Antani MR, Beyth RJ, Covinsky KE, Anderson PA, Miller DG, Cebul RD, Quinn LM, Landefeld CS. Failure to prescribe warfarin to patients with nonrheumatic atrial fibrillation. *J Gen Intern Med.* 1996;11: 713–720.
5. Whittle J, Wickenheiser L, Vendittii LN. Is warfarin underused in the treatment of elderly persons with atrial fibrillation? *Arch Intern Med.* 1997;157:441–445.
6. Albers GW, Yim JM, Belew KM, Bittar N, Hattemer CR, Phillips BG, Kemp S, Hall EA, Morton DJ, Vlasses PH. Status of antithrombotic therapy for patients with atrial fibrillation in university hospitals. *Arch Intern Med.* 1996;156:2311–2316.
7. Stafford RS, Singer DE. Warfarin use in atrial fibrillation by U. S. physicians. *Arch Intern Med.* 1996;156:2537–2541.
8. Sudlow M, Rodgers H, Kenny RA, Thomson R. Population based study of use of anticoagulants among patients with atrial fibrillation in the community. *BMJ.* 1997;314:1529–1530.
9. National Center for Health Statistics. *Public Use Data Tape Documentation: 1989–1996 National Ambulatory Medical Care Survey.* Hyattsville, MD: National Center for Health Statistics, US Public Health Service. 1991–1998.
10. Potthoff RF, Woodbury MA, Manton KG. ‘Equivalent sample size’ and ‘equivalent degrees of freedom’ refinements for inference using survey weights under superpopulation models. *J Am Stat Assoc.* 1992;87: 383–396.
11. National Center for Health Statistics. *International Classification of Diseases, 9th Revision, Clinical Modification.* 3rd ed, vol 1. Washington, DC: US Public Health Service; 1989. DHHS publication (PHS) 89–1260.
12. Laupacis A, Albers G, Dalen J, Dunn M, Feinberg W, Jacobson A. Antithrombotic therapy in atrial fibrillation. *Chest.* 1995;108(suppl): 352S–359S.
13. Statistical Analysis System. *SAS/STAT User’s Guide, Version 6.* 4th ed, vol 1 and 2. Cary, NC: Statistical Analysis System; 1990:851, 1072.
14. Hosmer DW, Lemeshow S. *Applied Logistic Regression.* New York, NY: Wiley; 1989.
15. The Boston Area Anticoagulation Trial for Atrial Fibrillation Investigators. The effect of low-dose warfarin on the risk of stroke in patients with nonrheumatic atrial fibrillation. *N Engl J Med.* 1990;323:1505–1511.
16. Petersen P, Godtfredsen J, Boysen G, Andersen ED, Andersen B. Placebo-controlled, randomized trial of warfarin and aspirin for prevention of thromboembolic complications in chronic atrial fibrillation: the Copenhagen AFASAK Study. *Lancet.* 1989;1:175–179.
17. Stroke Prevention in Atrial Fibrillation Investigators. Stroke prevention in atrial fibrillation study: final results. *Circulation.* 1991;84:527–539.
18. Connolly SJ, Laupacis A, Gent M, Roberts RS, Carins JA, Joyner C. Canadian Atrial Fibrillation Anticoagulation (CAFA) Study. *J Am Coll Cardiol.* 1991;18:349–355.
19. Ezekowitz MD, Bridgers SL, James KE, Carliner NH, Colling CL, Gornick CC, Krause-Steinrauf H, Kurtake JF, Nazarian SM, Radford MJ, Rickles FR, Shabetai R, Deykin D. Warfarin in the prevention of stroke associated with nonrheumatic atrial fibrillation. *N Engl J Med.* 1992;327: 1406–1412.
20. EAFT (European Atrial Fibrillation Trial) Study Group. Secondary prevention in nonrheumatic atrial fibrillation after transient ischaemic attack or minor stroke. *Lancet.* 1993;342:1256–1262.
21. Atrial Fibrillation Investigators. The efficacy of aspirin in patients with atrial fibrillation: analysis of pooled data from 3 randomized trials. *Arch Intern Med.* 1997;157:1237–1240.
22. Gottlieb LK, Salem-Schatz S. Anticoagulation in atrial fibrillation: does efficacy in clinical trials translate into effectiveness in practice? *Arch Intern Med.* 1994;154:1945–1953.