ORIGINAL RESEARCH

Provider Specialty, Anticoagulation Prescription Patterns, and Stroke Risk in Atrial Fibrillation

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Background—Differences in anticoagulation rates and direct oral anticoagulant use by provider specialty may identify an area of practice improvement to reduce future stroke events in patients with atrial fibrillation (AF).

Methods and Results—We examined anticoagulant prescription fills in 388 045 (mean age, 68±15 years; 59% male) patients with incident AF from the MarketScan databases between 2009 and 2014. Provider specialty and filled anticoagulant prescriptions around the time of AF diagnosis (3 months before through 6 months after) were obtained from outpatient services and pharmacy claims. We estimated the association of provider specialty (cardiology versus primary care) with filling oral anticoagulant prescriptions, adjusting for patient characteristics. The risk of stroke and bleeding events also was explored. A total of 235 739 patients (61%) had a cardiology provider claim, whereas 152 306 (39%) were exclusively managed by primary care. Patients seen by cardiology providers were more likely to fill anticoagulant prescriptions than those seen by primary care (39% versus 27%; relative risk, 1.39; 95% confidence interval [CI], 1.37–1.40). Differences were observed for direct oral anticoagulants (relative risk, 1.74; 95% CI, 1.71–1.78) and warfarin (relative risk, 1.24; 95% CI, 1.22–1.26). A reduced risk of stroke events was observed among those seen by cardiology providers (hazard ratio, 0.90; 95% CI, 0.86–0.94) compared with primary care, without an increased bleeding risk (hazard ratio, 1.03; 95% CI, 0.98–1.07).

Conclusions—Patients seen by an outpatient cardiology provider shortly after AF diagnosis were more likely to initiate oral anticoagulation and were at lower risk of future stroke events without a higher rate of bleeding. Early referral to cardiology specialists may increase initiation of anticoagulant therapies and improve outcomes in AF. (*J Am Heart Assoc*. 2018;7:e007943. DOI: 10.1161/JAHA.117.007943.)

Key Words: anticoagulation • atrial fibrillation • outcomes

The mainstay of stroke prevention in atrial fibrillation (AF) is the initiation and maintenance of anticoagulant therapies. The oral anticoagulants currently recommended include warfarin and the direct oral anticoagulants (DOACs). All 3 DOACs (dabigatran, rivaroxaban, and apixaban) have more predictable pharmacological profiles, fewer drug interactions, the absence of major dietary effects, and a reduced risk of intracranial bleeding compared with warfarin.[1] Accordingly, these agents currently account for ≈50% of anticoagulants

prescribed for patients with AF, and their use is associated with more patients with AF receiving anticoagulant therapies.[2,3]

Recent reports have suggested that cardiology providers are more likely to prescribe oral anticoagulants compared with primary care providers,[4–6] and this possibly results in a lower risk of stroke among patients who are managed by cardiology specialists.[5] However, these data have come from a population of veterans from a single-payer system[4,5] and from a registry in which anticoagulant prescriptions were

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Clinical Perspective

What Is New?

- This study examined if early cardiology involvement influenced oral anticoagulant prescription fills and outcomes in patients with atrial fibrillation from a large commercial claims database.
- Patients with atrial fibrillation who saw an outpatient cardiology provider shortly after their diagnosis were more likely to fill an oral anticoagulant prescription, and these patients had a lower risk of stroke without increased risk of bleeding.

What Are the Clinical Implications?

- Early referral to cardiology specialists may increase the initiation of oral anticoagulant therapies and improve atrial fibrillation–related outcomes in patients who have this common arrhythmia.

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tabulated by providers.[6] These reports also were limited to warfarin[4,5] and dabigatran.[6] Therefore, it is unclear if the appropriate delivery of anticoagulant therapies and specific oral anticoagulant therapies (DOAC versus warfarin) used in patients with AF varies by provider specialty and if cardiology specialty care improves AF-related outcomes in a cohort representative of real-world AF care. A careful examination of anticoagulant use by provider specialty is needed, because differences in the rate of anticoagulation and/or DOAC use may identify an area of practice improvement for providers to reduce the burden of stroke in this high-risk group.

Methods

Study Design and Cohort

The data, analytic methods, and study materials will not be made available to other researchers for purposes of reproducing the results or replicating the procedures. This study used data from the Truven Health MarketScan Commercial Claims and Encounter Database and the Medicare Supplemental and Coordination of Benefits Database (Truven Health Analytics, Ann Arbor, MI) between January 1, 2009, and December 31, 2014. The MarketScan Commercial Claims and Encounter Database consists of health insurance claims from all levels of care from several large employers and health plans across the United States. The database is composed of private healthcare coverage for employees, their spouses, and other dependents. The MarketScan Medicare Supplemental Database includes claims from individuals and their dependents with employer-sponsored Medicare Supplemental plans. Both databases link medical and outpatient prescription drug claims and encounter data with

patient enrollment data to provide individual-specific clinical use, expenditure, and outcomes information across inpatient and outpatient services and outpatient pharmacy services.

This analysis included health plan enrollees with ≥6 months of enrollment before the first nonvalvular AF diagnosis. A minimum of 6 months between enrollment and first AF diagnosis was selected to identify incident cases of AF. AF was defined by the presence of *International Classification of Diseases, Ninth Revision, Clinical Modification* (*ICD-9-CM*) codes 427.31 or 427.32 in any position on an inpatient claim or on 2 outpatient claims at least 7 days but less than 1 year apart, and without any inpatient diagnosis of mitral stenosis (*ICD-9-CM* code 394.0) or mitral valve disorder (*ICD-9-CM* code 424.0). Cases of atrial flutter were included in this definition, because >80% of patients who undergo radiofrequency catheter ablation of typical atrial flutter will have AF within the following 5 years.[7] The AF diagnosis date was defined as the earlier of the following: (1) the discharge date for the qualifying inpatient claim or (2) the service date of the second qualifying outpatient claim.[8] The analytic sample was further restricted to patients who had at least 1 outpatient claim with a medical provider in a window of 3 months before AF diagnosis to 6 months after AF diagnosis. We considered the period before AF diagnosis to account for imprecisions in the actual date of diagnosis for patients with outpatient AF, which required 2 outpatient claims for AF. Participants with oral anticoagulant prescriptions >3 months before AF diagnosis were presumed to use these agents for other conditions (eg, venous thromboembolism). This analysis was approved by the Institutional Review Board at Emory University (Atlanta, GA), and a waiver of informed consent was obtained.

Provider Type

Cardiology and primary care outpatient claims were used to identify outpatient visits. Providers seen by patients in the hospital were not included, because the main purpose of the analysis was to determine the influence of outpatient specialty referral on oral anticoagulant use. Patients who saw a cardiology provider within the predetermined period (3 months before AF diagnosis to 6 months after AF diagnosis) were classified as the cardiology group, whereas patients seen exclusively by internal medicine, family practice, medical physician, or unspecified multispecialty group were classified as primary care. Patients seen by a cardiologist were included in the cardiology provider group, regardless of a primary care visit.

Oral Anticoagulant Use

Filled outpatient pharmaceutical claims are included in the MarketScan databases. Each claim includes the National Drug Code, prescription fill date, and the number of days supplied.

All claims for oral anticoagulants in use during the study period (warfarin, dabigatran, rivaroxaban, and apixaban) were identified. Oral anticoagulant prescriptions were limited to outpatient claims between 3 months before to 6 months after AF diagnosis. Although there is no information on the validity of DOAC claims, warfarin prescription in claims databases has had a positive predictive value of >99%.[9] DOAC prescriptions were included independently of the dosage prescribed. We considered filled prescription claims as a proxy for actual anticoagulant prescription.

Covariates

We used the MarketScan databases to evaluate the presence of the following comorbid conditions: heart failure, hypertension, diabetes mellitus, stroke, myocardial infarction, peripheral artery disease, kidney disease, liver disease, alcohol use, and bleeding history. At least 1 *ICD-9-CM* diagnosis code, in any position, was considered evidence of the condition. Conditions were considered present if the claims were present before AF diagnosis. In addition, the CHA$_2$DS$_2$-VASc (congestive heart failure, hypertension, aged ≥75 years, diabetes mellitus, stroke/transient ischemic attack, vascular disease, aged 65 to 75 years, and sex category) and HAS-BLED (hypertension, abnormal renal/liver function, stroke, bleeding history or predisposition, labile international normalized ratio, elderly [aged >65 years], drugs/alcohol concomitantly) scores were computed for each patient at the time of AF diagnosis.[10,11] *ICD-9-CM* codes to define each condition are shown in Table S1. Filled outpatient pharmaceutical claims also were assessed to ascertain the use of the following medications: angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, β blockers, calcium channel blockers, diuretics, amiodarone, and digoxin. These medications were ascertained if filled before or at the time of AF diagnosis.

Outcomes

The main outcome variable was hospitalization for an ischemic stroke event that occurred after AF diagnosis. *ICD-9-CM* codes in the primary position of an inpatient claim were used to identify events. The codes used to detect ischemic stroke events are shown in Table S1. We also obtained major bleeding events (intracranial, gastrointestinal, or other) using *ICD-9-CM* codes in the primary position, as previously described.[12] The *ICD-9-CM* codes used to identify intracranial, gastrointestinal, and other bleeding events are shown in Table S1.

Statistical Analysis

We examined the anticoagulant prescription fill patterns between patients with AF who were managed by cardiology versus those managed exclusively by primary care providers. Baseline characteristics were compared by provider specialty. Categorical data were compared using the χ^2 test, and continuous data were compared using the Student *t* test. The proportion of patients with AF who filled oral anticoagulant prescriptions was evaluated by provider type (eg, cardiology versus primary care providers). Comparisons also were made for DOAC use and warfarin use, separately. Poisson regression models with robust variance estimates were used to compute relative risk (RR) and 95% confidence intervals (CIs) of anticoagulant prescription fills for patients managed by cardiology versus primary care providers.[13] Models were adjusted for age, sex, heart failure, hypertension, diabetes mellitus, stroke, myocardial infarction, kidney disease, liver disease, bleeding history, alcohol use, antiplatelet agents, angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, calcium channel blockers, diuretics, amiodarone, digoxin, CHA$_2$DS$_2$-VASc, and HAS-BLED. We also performed a greedy propensity score–matched analysis using multivariable logistic regression to predict the probability of being seen by cardiology versus primary care using the same covariates in the primary analysis, and a 1:1 matching was performed in which the absolute difference between propensity scores was ±0.01. The primary analysis was then repeated in the propensity score–matched cohort.

Several secondary analyses were performed. Due to the fact that the first DOAC received Food and Drug Administration approval in October 2010, separate analyses were performed that limited AF diagnoses to the period between 2011 and 2014. An additional analysis limited to patients with AF who would quality for oral anticoagulants (CHA$_2$DS$_2$-VASc scores ≥2) was performed. We also compared the anticoagulant use across each year of the study period. To determine if the rate of DOAC use was increasing over time, we computed the proportion of filled anticoagulant prescriptions that were DOACs between 2011 and 2014 by provider type. A Cochran-Armitage test for trend was used to test for the presence of significant trends. We also compared if individual DOAC prescription fills varied between patients managed by cardiology versus primary care providers. In addition, we examined the percentage of individual DOAC prescription fills across each year of the study period. We also examined if the number of outpatient visits influenced the relationship between cardiology and anticoagulant prescription fills.

A Cox regression model was used to estimate hazard ratios and 95% CIs of the future risk of ischemic stroke and major bleeding events associated with cardiology compared with primary care providers. The model was adjusted for the same covariates as the oral anticoagulant analysis. We also examined the risk of each outcome in the propensity score–

matched cohort previously described, with adjustment for the same covariates. To determine if cardiology specialists provided additional benefit in stroke reduction beyond oral anticoagulants, a secondary analysis was performed that was limited to those who filled an oral anticoagulant prescription (N=132 188). Statistical significance was defined as $P<0.05$. SAS Version 9.4 (SAS Institute Inc, Cary, NC) was used for all analyses.

Results

A total of 388 045 (mean age, 68±15 years; 59% male) patients met the inclusion criteria. Of these patients, 235 739 (61%) had a cardiology provider claim, whereas 152 306 (39%) were exclusively managed by primary care during the window of 3 months before to 6 months after AF diagnosis. A total of 204 932 patients (87%) who saw a cardiology provider also saw a primary care physician. Patients who were seen at least once in the 9-month window by a cardiology provider were more likely to be younger and male, were less likely to have hypertension, diabetes mellitus, stroke, and peripheral artery disease, and had lower CHA_2DS_2-VASc scores than patients who were seen exclusively by primary care providers. In addition, patients seen by cardiology providers were less likely to have kidney disease, liver disease, alcohol use, or prior bleeding. Patients who saw a cardiology provider were more likely to fill prescriptions for angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, β blockers, and amiodarone compared with patients who did not see a cardiology provider. Baseline characteristics by provider specialty are shown for the entire cohort in Table 1, and the characteristics for the propensity score–matched cohort are shown in Table S2.

The proportion of patients who filled an oral anticoagulant prescription by provider specialty is shown in Table 2. A total of 132 188 patients (34%) filled oral anticoagulant prescriptions. Patients seen by a cardiology provider were more likely to fill prescriptions for any oral anticoagulant (RR, 1.39; 95% CI, 1.37–1.40), DOACs (RR, 1.74; 95% CI, 1.71–1.78), and warfarin (RR, 1.24; 95% CI, 1.22–1.26) than those managed by primary care, with similar results obtained among patients with CHA_2DS_2-VASc scores ≥2. Similarly, when the analysis was limited to 2011 to 2014, prescriptions for oral anticoagulants, DOACs, and warfarin were more likely to be filled by patients who were seen by a cardiology provider. In the propensity score–matched cohort (N=292 386), results were similar to the full cohort (Table 2). Further adjustment for the number of outpatient visits did not materially alter the relationship between cardiology involvement and anticoagulant prescription fills (anticoagulants: RR, 1.39 [95% CI, 1.37–1.41]; DOACs: RR, 1.74 [95% CI, 1.71–1.78]; warfarin: RR, 1.24 [95% CI, 1.22–1.26]).

Table 1. Patient Characteristics at the Time of Nonvalvular AF Diagnosis, MarketScan, 2009 to 2014 (N=388 045)

Characteristic	Cardiology 235 739 (61%)	Primary Care 152 306 (39%)	P Value*
Age, mean±SD, y	67±14	70±15	<0.001
Female sex, %	39	45	<0.001
Heart failure, %	25	25	0.59
Hypertension, %	72	73	<0.001
Diabetes mellitus, %	27	29	<0.001
Stroke, %	20	23	<0.001
Myocardial infarction, %	11	10	<0.001
Peripheral artery disease, %	2.2	2.6	<0.001
CHA_2DS_2-VASc score, mean±SD	3.0±2.0	3.4±2.0	<0.001
Kidney disease, %	10	14	<0.001
Liver disease, %	5.5	6.8	<0.001
Alcohol use, %	2.0	3.1	<0.001
Bleeding history, %	17	21	<0.001
Antiplatelet agents, %	2.2	2.1	0.048
HAS-BLED score, mean±SD	1.8±1.2	2.0±1.3	<0.001
ACE inhibitors, %	32	31	<0.001
ARBs, %	20	18	<0.001
β Blockers, %	61	52	<0.001
Calcium channel blockers, %	31	31	0.32
Diuretics, %	33	35	<0.001
Amiodarone, %	8.6	5.7	<0.001
Digoxin, %	9.3	9.2	0.20

ACE indicates angiotensin-converting enzyme; AF, atrial fibrillation; ARB, angiotensin II receptor blocker; CHA_2DS_2-VASc, congestive heart failure, hypertension, aged ≥75 years, diabetes mellitus, stroke/transient ischemic attack, vascular disease, aged 65 to 75 years, and sex category; and HAS-BLED, hypertension, abnormal renal/liver function, stroke, bleeding history or predisposition, labile international normalized ratio, elderly (aged >65 years), drugs/alcohol concomitantly.
*Statistical significance for continuous data was tested using the Student's t test; and for categorical data, the χ^2 test.

When we examined the proportion of patients with AF who filled an oral anticoagulant prescription by each year in the study period, similar findings were observed over time (Table 3). Although the proportion of patients receiving DOACs increased, the proportion of patients who received oral anticoagulants remained constant between 2009 and 2014 for cardiologists and primary care providers (Table 3).

A total of 45 437 patients (12%) filled DOAC prescriptions. Of these prescriptions, dabigatran (n=20 922 [46%]) was the most common. There were 17 945 patients (40%) who filled a prescription for rivaroxaban and 6570 patients (14%) who

Table 2. Anticoagulation Patterns of Patients With Nonvalvular AF: MarketScan, 2009 to 2014

Variable	Total, n (%)	Cardiology, n (%)	Primary Care, n (%)	RR (95% CI)*†	RR (95% CI)*‡
2009–2014					
All	N=388 045	n=235 739	n=152 306		
Anticoagulation	132 188 (34)	91 226 (39)	40 962 (27)	1.39 (1.37–1.40)	1.37 (1.36–1.39)
DOAC	45 437 (12)	33 687 (15)	11 750 (8)	1.74 (1.71–1.78)	1.73 (1.69–1.77)
Warfarin	86 751 (22)	57 539 (24)	29 212 (19)	1.24 (1.22–1.26)	1.23 (1.21–1.24)
CHA$_2$DS$_2$-VASc ≥2	N=292 840	n=172 928	n=119 912		
Anticoagulation	105 750 (36)	71 633 (41)	34 117 (28)	1.38 (1.37–1.40)	1.36 (1.35–1.38)
DOAC	34 889 (12)	25 177 (15)	9712 (8)	1.68 (1.64–1.72)	1.66 (1.62–1.70)
Warfarin	70 861 (24)	46 456 (26)	24 405 (20)	1.26 (1.25–1.28)	1.25 (1.23–1.26)
2011–2014					
All	N=240 596	n=145 868	n=94 728		
Anticoagulation	82 115 (34)	56 758 (39)	25 357 (27)	1.40 (1.39–1.42)	1.39 (1.37–1.41)
DOAC	43 730 (18)	32 386 (22)	11 344 (12)	1.73 (1.70–1.77)	1.72 (1.69–1.76)
Warfarin	38 385 (16)	24 372 (17)	14 013 (15)	1.13 (1.11–1.15)	1.12 (1.09–1.14)
CHA$_2$DS$_2$-VASc ≥2	N=182 730	n=107 457	n=75 273		
Anticoagulation	66 237 (36)	44 866 (42)	21 371 (28)	1.40 (1.38–1.42)	1.38 (1.36–1.40)
DOAC	33 566 (18)	24 193 (23)	9373 (12)	1.68 (1.64–1.72)	1.66 (1.62–1.70)
Warfarin	32 671 (18)	20 673 (19)	11 998 (16)	1.18 (1.15–1.20)	1.16 (1.13–1.19)

AF indicates atrial fibrillation; CHA$_2$DS$_2$-VASc, congestive heart failure, hypertension, aged ≥75 years, diabetes mellitus, stroke/transient ischemic attack, vascular disease, aged 65 to 75 years, and sex category; CI, confidence interval; DOAC, direct oral anticoagulant; HAS-BLED, hypertension, abnormal renal/liver function, stroke, bleeding history or predisposition, labile international normalized ratio, elderly (aged >65 years), drugs/alcohol concomitantly; and RR, relative risk.

*Comparison between cardiology and primary care.

†Relative risk of anticoagulant, DOAC, or warfarin prescription fills for patients seen by cardiology vs primary care providers. Adjusted for age, sex, heart failure, hypertension, diabetes mellitus, stroke, myocardial infarction, kidney disease, liver disease, bleeding history, alcohol use, antiplatelet agents, angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, calcium channel blockers, diuretics, amiodarone, digoxin, CHA$_2$DS$_2$-VASc, and HAS-BLED.

‡Results of 1:1 propensity-matched analysis. Propensity score was computed using multivariable logistic regression with the following variables: age, sex, heart failure, hypertension, diabetes mellitus, stroke, myocardial infarction, kidney disease, liver disease, bleeding history, alcohol use, antiplatelet agents, angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, calcium channel blockers, diuretics, amiodarone, digoxin, CHA$_2$DS$_2$-VASc, and HAS-BLED (N=292 386).

received apixaban. Apixaban was more likely to be filled by patients with AF seen by cardiology providers (cardiology, 14.9%; primary care, 13.3%), whereas rivaroxaban was more likely to be filled by patients who exclusively saw a primary care provider (cardiology, 38.9%; primary care, 41.0%). No differences were observed in filling of dabigatran between cardiology and primary care providers (cardiology, 46.2%; primary care, 45.7%).

DOACs accounted for 41% of oral anticoagulant prescription fills in 2011, and this increased to 72% by 2014. Patients seen by cardiology providers were more likely to fill prescriptions for DOACs in each year between 2011 and 2014 than those seen exclusively by primary care providers (Figure 1). Increases in the percentage of filled DOAC prescriptions over time were observed for both cardiology and primary care providers (Figure 1). For the period from 2011 to 2014, filled prescriptions for dabigatran decreased (from 98.0% to 7.3%), whereas those for rivaroxaban (from 2.0% to 56.8%) and

apixaban (from 0% to 35.9%) increased. Similar trends were observed for cardiology and primary care providers (Figure 2).

A reduced risk of stroke was observed among those seen by cardiology providers (hazard ratio, 0.90; 95% CI, 0.86–0.94) compared with primary care, and similar results were observed in the propensity score–matched cohort (Table 4). The risk of major bleeding events was similar between cardiology and primary care providers in the main analysis and in a 1:1 matched cohort (hazard ratio, 1.03; 95% CI, 0.98–1.07). The risk of ischemic stroke remained significant when the analysis was limited to those who filled an oral anticoagulant prescription (hazard ratio, 0.83; 95% CI, 0.78–0.89 for cardiology versus primary care).

Discussion

In this analysis from a large commercial claims database, patients with AF seen by an outpatient cardiology provider

Table 3. Anticoagulation Patterns by Year of Patients With Nonvalvular AF: MarketScan, 2009 to 2014

Variable	2009 Cardiology	2009 Primary Care	2010 Cardiology	2010 Primary Care	2011 Cardiology	2011 Primary Care	2012 Cardiology	2012 Primary Care	2013 Cardiology	2013 Primary Care	2014 Cardiology	2014 Primary Care
All	n=43 581	n=26 343	n=46 290	n=31 235	n=51 133	n=33 627	n=30 142	n=23 429	n=32 344	n=19 433	n=32 249	n=18 239
Anticoagulation	16 503 (38)	6987 (27)*	17 965 (39)	8618 (28)*	20 727 (40)	9420 (28)*	11 499 (38)	6104 (26)*	12 493 (39)	5204 (27)*	12 039 (37)*	4629 (25)*
DOAC	···	···	1301 (3)	···	9338 (18)	406 (1)*	5944 (20)	2394 (10)*	8103 (25)	2778 (14)*	9001 (28)	3021 (17)*
Warfarin	16 503 (38)	6987 (27)*	16 664 (36)	8212 (26)*	11 389 (22)	6269 (19)*	5555 (18)	3710 (16)*	4390 (14)	2426 (12)*	3038 (9.4)	1608 (8.8)*
CHA$_2$DS$_2$-VASc ≥2	n=31 154	n=19 618	n=34 317	n=25 021	n=39 154	n=27 123	n=21 594	n=18 638	n=23 465	n=15 471	n=23 244	n=14 041
Anticoagulation	12 577 (40)	5530 (28)*	14 190 (41)	7216 (29)*	16 825 (43)	7895 (29)*	8782 (41)	5115 (27)*	9754 (42)	4431 (29)*	9505 (41)	3930 (28)*
DOAC	···	···	984 (3)	···	7151 (18)	339 (1)*	4150 (19)	1936 (10)*	6006 (26)	2327 (15)*	6886 (30)	2539 (18)*
Warfarin	12 577 (40)	5530 (28)*	13 206 (38)	6877 (27)*	9674 (25)	5324 (20)*	4632 (22)	3179 (17)*	3748 (16)	2104 (14)*	2619 (11)	1391 (10)*

Data are given as number (percentage) unless otherwise indicated. Comparison is given between cardiology and primary care providers. AF indicates atrial fibrillation; CHA$_2$DS$_2$-VASc, congestive heart failure, hypertension, aged ≥75 years, diabetes mellitus, stroke/transient ischemic attack, vascular disease, aged 65 to 75 years, and sex category; and DOAC, direct oral anticoagulant.
*P<0.05.

were more likely to fill prescriptions for oral anticoagulants, and their care was associated with a lower risk of future stroke events without an increased bleeding risk. In addition, we have shown that DOAC use is increasing, with these therapies being selected as the initial oral anticoagulant for 72% of patients with AF. We also observed significant variation in the use of specific DOAC agents, with rivaroxaban and apixaban accounting for most filled DOAC prescriptions among patients with AF in recent years. Overall, our data suggest that early outpatient cardiology involvement is associated with greater use of oral anticoagulants in patients who have AF, and their involvement has a positive impact on AF-related outcomes.

Recent reports from specific patient populations have examined the influence of provider specialty on anticoagulation practices in patients with AF. Data from TREAT-AF (The Retrospective Evaluation and Assessment of Therapies in AF) study demonstrated that veterans who were evaluated by a cardiology provider within 90 days of their AF diagnosis were more likely to have a dispensed prescription for warfarin than those who saw a primary care provider.[4,5] Data from the ORBIT-AF (Outcomes Registry for Better Quality Care in the Treatment of AF) also demonstrated that oral anticoagulant use (eg, warfarin or dabigatran) was higher for patients seen by cardiology providers than those treated in primary care.[6] Although the aforementioned reports have demonstrated a positive association between cardiology providers and initiation of oral anticoagulation, these studies were limited to warfarin and/or dabigatran because other DOACs were not yet approved. In addition, TREAT-AF consisted of data from the Veterans Administration, which are largely representative of AF care in men from a single payer system. Furthermore, ORBIT-AF was limited to determine if provider specialty influenced anticoagulant prescription fills shortly after diagnosis, because incident and prevalent cases of AF were included.

The findings of the current analysis are concordant with those from prior studies that have shown that significant differences exist in the initiation of oral anticoagulant therapy between patients seen by cardiology and primary care providers. Although primary care providers have provided excellent rates of antithrombotic care in AF,[14,15] reports have suggested that certain patients with AF do not receive oral anticoagulants when indicated.[16] In addition, we must acknowledge that the data in this report may simply reflect a referral bias in which patients with more comorbid conditions were deemed less likely to benefit from specialist care and, subsequently, were less likely to be referred to see a cardiology provider. This is supported by the higher prevalence of comorbid conditions in patients who only saw a primary care provider shortly after AF diagnosis. Nonetheless, anticoagulation represents an important aspect of AF care to
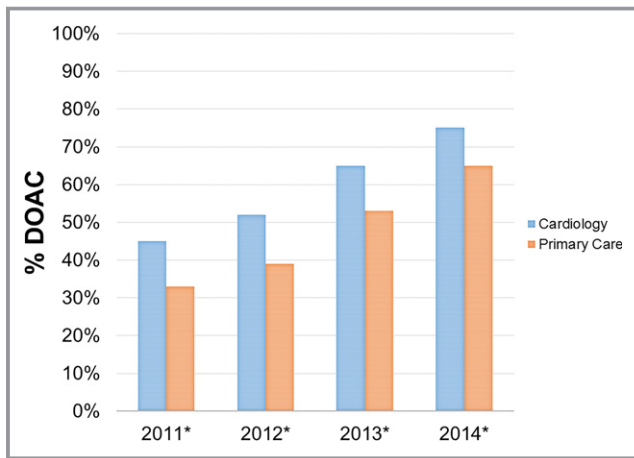
Figure 1. Percentage of direct oral anticoagulant (DOAC) pre‐scriptions among patients with nonvalvular atrial fibrillation who filled oral anticoagulant prescriptions, MarketScan, 2011 to 2014. Values represent the percentage of anticoagulant prescriptions filled that were DOACs. Cochran-Armitage test for trend showed a significant increase for the percentage of DOAC prescriptions filled in patients with atrial fibrillation seen by cardiology ($P<0.001$) and primary care providers ($P<0.001$). Comparison between cardiology and primary care was significant. *$P<0.05$.

Figure 2. Percentage of individual direct oral anticoagulant (DOAC) prescriptions among patients with nonvalvular atrial fibrillation who filled prescriptions, MarketScan, 2011 to 2014. Estimates represent the percentage of total DOAC prescriptions filled by each oral anticoagulant for cardiology (A) and primary care providers (B). Cochran-Armitage tests for trend showed a significant decrease in dabigatran ($P<0.001$) and significant increases in rivaroxaban ($P<0.001$) and apixaban ($P<0.001$) prescription fills across both provider specialties.

reduce morbidity and mortality in this high-risk group through reduction in stroke occurrence.[17] Accordingly, it is of paramount importance for the practicing clinician to consider this key aspect of AF care and possibly consider early involvement of a cardiology specialist shortly after AF diagnosis.

The data in this report also demonstrate that care by outpatient cardiology providers may be linked to lower occurrence of ischemic stroke events in patients with AF. These findings are consistent with data from TREAT-AF, which recently demonstrated that early cardiology specialty care (eg, within 90 days of diagnosis) were associated with a reduced risk of stroke, and this protective benefit possibly was related to an increased likelihood of oral anticoagulant initiation.[5] In comparison with data from TREAT-AF, we were able to show that, despite a higher predilection for patients to initiate oral anticoagulants when seen by a cardiology provider, the risk of bleeding does not increase. The similar rates of bleeding likely were related to the increased use of DOAC agents observed among cardiology compared with primary care providers. In addition, the protective benefit of outpatient cardiology providers was further demonstrated, because the lower risk of ischemic stroke remained when the analysis was limited to patients who filled a prescription for an oral anticoagulant. Possibly, patients who saw an outpatient cardiology provider early in their diagnosis period were more likely to adhere to long-term antithrombotic therapy, and this hypothesis should be explored. Overall, the data presented have important implications about the care for patients with
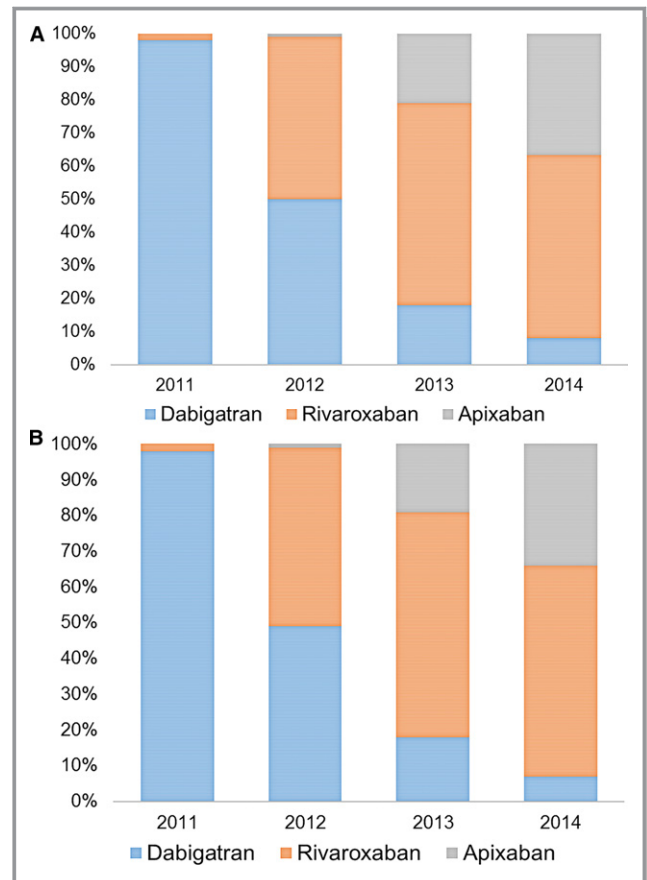
AF, because patients are more likely to initiate oral antico‐agulant therapies when seen by a cardiology outpatient provider shortly after their diagnosis, and they will likely receive therapies with a more favorable bleeding profile.

The findings of this analysis also demonstrated that oral anticoagulant prescriptions are underfilled (and possibly underprescribed), and filling these therapies possibly is influenced by provider specialty. Data from TREAT-AF demon‐strated that filled warfarin prescriptions were present in 54% of the entire cohort, with warfarin prescriptions more often filled among patients seen by cardiology than primary care providers (68.6% versus 48.9%; $P<0.001$).[4] ORBIT-AF reported that the overall use of oral anticoagulants (warfarin or dabigatran) was 73.6% for internal medicine/primary care providers and 76.7% for cardiology providers.[6] The percentage of prescriptions for TREAT-AF are closer to the numbers

Table 4. Association of Provider Specialty With Ischemic Stroke and Major Bleeding Events in Patients With Nonvalvular AF: MarketScan, 2009 to 2014

Variable	Events	Incidence Rate per 1000 Person-Years	HR (95% CI)*	HR (95% CI)†
Stroke				
Primary care	3803	15.7	1 (Reference)	1 (Reference)
Cardiology	5324	12.5	0.90 (0.86–0.94)	0.89 (0.86–0.94)
Major bleeding events				
Primary care	3609	14.9	1 (Reference)	1 (Reference)
Cardiology	5813	13.7	1.03 (0.98–1.07)	1.03 (0.98–1.08)

AF indicates atrial fibrillation; CI, confidence interval; and HR, hazard ratio.

*Results of multivariable Cox regression analysis adjusted for age, sex, heart failure, hypertension, diabetes mellitus, stroke, myocardial infarction, kidney disease, liver disease, bleeding history, alcohol use, antiplatelet agents, angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, calcium channel blockers, diuretics, amiodarone, digoxin, CHA_2DS_2-VASc (congestive heart failure, hypertension, aged ≥75 years, diabetes mellitus, stroke/transient ischemic attack, vascular disease, aged 65 to 75 years, and sex category), and HAS-BLED (hypertension, abnormal renal/liver function, stroke, bleeding history or predisposition, labile international normalized ratio, elderly (aged >65 years).

†Results of 1:1 propensity score–matched analysis. Propensity score was computed using multivariable logistic regression with the following variables: age, sex, heart failure, hypertension, diabetes mellitus, stroke, myocardial infarction, kidney disease, liver disease, bleeding history, alcohol use, antiplatelet agents, angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, calcium channel blockers, diuretics, amiodarone, digoxin, CHA_2DS_2-VASc, and HAS-BLED. Adjusted for all covariates used to derive the propensity-matched cohort (N=292 386).

reported in this analysis (cardiology, 39%; primary care, 27%; $P<0.001$), because these represent filled prescriptions. Although we observed a lower fill rate, the data from TREAT-AF are unique, because they represent AF care to a study population of predominantly men in a single payer system of veterans. Explanations for differences between the current study and ORBIT-AF are attributable to the fact that providers were assessed for anticoagulant prescriptions and the actual fill rates were not reported. Therefore, our data likely are more representative of what occurs in a real-world setting. Barriers (eg, lack of appropriate education) or a period of contemplation possibly exist before filling oral anticoagulant prescriptions among patients with AF, and this merits further attention. Although our analysis was restricted to new-onset cases and we relied on claims data to ascertain AF events in which misclassification bias is possible, our data demonstrated that early outpatient cardiology involvement possibly results in more patients with AF initiating oral anticoagulants. Future work is needed to identify strategies to improve rates of anticoagulation in patients with AF, including the potential benefit of early referral to cardiology specialists.

DOAC use in AF has increased over recent years, and our findings confirm this in a large commercial claims database.[2] In addition, we report trends in the initiation of each DOAC as an initial oral anticoagulant,[3] with reductions in dabigatran use and increases in the use of rivaroxaban and apixaban. The findings in this analysis add to the literature because we have shown that DOACs account for ≈70% of initial oral anticoagulant prescription fills in AF in recent years, and similar trends for each specific DOAC exist between patients seen by cardiology and those managed by primary care providers. Despite increases in the use of DOACs compared with

warfarin, the overall anticoagulation rate remained constant during the study period. A similar observation was reported in a study of residents of Olmsted County, Minnesota, where the overall rate of anticoagulation use was 51% at 1 year after AF diagnosis.[18] In contrast, reports from Europe and Japan have demonstrated that the rates of anticoagulation in AF are increasing, and these increases possibly are attributable to DOACs.[19,20] Therefore, our data suggest that, although patients seen by outpatient cardiology providers have higher anticoagulant prescription fill rates compared with primary care providers, the overall rate of anticoagulation in the United States is suboptimal, identifying an area for practice improvement in AF-related care.

The current analysis should be interpreted in the context of several limitations. *ICD-9-CM* data were used to identify AF cases, comorbid conditions, and AF-related outcomes, and misclassification was possible. We did not separate cases of AF related to secondary precipitants (eg, cardiac surgery), and these cases often are considered transient without a need for long-term anticoagulation. However, recent data have suggested that long-term AF-related stroke and mortality risks are similar between individuals with and without secondary AF precipitants.[21] In addition, we considered cardiology involvement if a patient had a specialty outpatient claim within 3 months before to 6 months after AF diagnosis. Therefore, it is possible that we did not capture all patients seen by an outpatient cardiology provider, or the timing was not optimal for the detection of cardiology involvement. Nonetheless, significant differences in oral anticoagulant prescription fills were observed with the definitions used, suggesting that early outpatient cardiology involvement at the time of AF diagnosis influences oral anticoagulant use. Although we attempted to

account for many patient characteristics in our multivariable model that influenced cardiology involvement and oral anticoagulant prescription fills, we acknowledge that other unmeasured factors (eg, socioeconomic status) possibly influenced our findings. We did not have access to mortality data and were unable to account for the competing risk of death in analyses for stroke and bleeding. Finally, we only had information on prescriptions filled by the patients, not on the medication prescribed by the provider.

In conclusion, early involvement of cardiology outpatient providers positively influences the initiation of oral anticoagulants and DOACs in patients with AF, and their care is associated with a lower risk of stroke without a higher bleeding risk. Further research is needed to better understand barriers to anticoagulation initiation in patients with AF, and early referral to an outpatient cardiology provider should be considered to improve AF-related outcomes.

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Disclosures

None.

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SUPPLEMENTAL MATERIAL

Table S1. ICD-9-CM Codes.

Condition	ICD-9-CM Codes
Heart failure	398.91, 402.01, 402.11, 402.91, 404.01, 404.03, 404.11, 404.13, 404.91, 404.93, 425.4, 425.9, 428
Hypertension	401, 402, 403, 404, 405
Diabetes	250
Stroke	433, 434, 435, 436, 437, 438
Myocardial infarction	410, 412
Peripheral artery disease	440.0, 440.2, 440.9, 443.9
Kidney disease	403.01, 403.11, 403.91, 404.02, 404.03, 404.12, 404.13, 404.92, 404.93, 582, 583.0, 583.1, 583.2, 583.3, 583.4, 583.5, 583.6, 583.7, 585, 586, 588.0, V42.0, V45.1, V56
Liver disease	070.22, 070.23, 070.32, 070.33, 070.44, 070.54, 070.6, 070.9, 456.0, 456.1, 456.2, 570, 571, 572.2, 572.3, 572.4, 572.5, 572.6, 572.7, 572.8, 573.3, 573.4, 573.8, 573.9, V42.7
Intracranial bleeding	430, 431, 432, 852
Gastrointestinal bleeding	455.2, 455.5, 455.8, 456.0, 456.20, 530.7, 530.82, 531.0, 531.2, 531.4, 531.6, 532.0, 532.2, 532.4, 532.6, 533.0, 533.2, 533.4, 533.6, 534.0, 534.2, 534.4, 534.6, 535.01, 535.11, 535.21, 535.31, 535.41, 535.51, 535.61, 537.83, 562.02, 562.03, 562.12, 562.13, 568.81, 569.3, 569.85, 578.0, 578.1, 578.9
Other bleeding	423.0, 459.0, 568.81, 593.81, 599.7, 623.8, 626.6, 719.1, 784.7, 784.8, 786.3
Alcoholism	265.2, 291.1, 291.2, 291.3, 291.5, 291.6, 291.7, 291.8, 291.9, 303.0, 303.9, 305.0, 357.5, 425.5, 535.3, 571.0, 571.1, 571.2, 571.3, 980, V11.3

Table S2. Patient Characteristics at time of Nonvalvular Atrial Fibrillation Diagnosis from 1:1 Propensity Score Matching: MarketScan 2009-2014 (N=292,386)[*]

Characteristic	Cardiology (n=141,193)	Primary Care (n=141,193)	Standardized Difference[†]
Age, mean ± SD, years	69 ± 14	69 ± 15	0.019
Female (%)	43	44	0.0082
Heart failure (%)	24	25	0.018
Hypertension (%)	73	73	0.0092
Diabetes (%)	29	29	0.0040
Stroke (%)	22	22	0.0078
Myocardial infarction (%)	9.5	10	0.019
Peripheral artery disease (%)	2.4	2.5	0.0078
CHA_2DS_2-VASc, mean ± SD	3.3 ± 2.0	3.3 ± 2.0	0.019
Kidney disease (%)	12.5	12.6	0.0016
Liver disease (%)	6.4	6.4	0.0021
Alcohol use (%)	2.7	2.6	0.0058
Bleeding history (%)	20	20	0.0035
Antiplatelet agents (%)	1.8	2.1	0.018
HAS-BLED, mean ± SD	2.0 ± 1.2	2.0 ± 1.2	0.0086
ACE inhibitors (%)	31	31	0.0024
ARB (%)	17.9	18.4	0.015
Beta blockers (%)	54	54	0.0090
Calcium channel blockers (%)	31	31	0.0076
Diuretics (%)	35	35	0.0053
Amiodarone (%)	5.6	5.9	0.016
Digoxin (%)	9.0	9.2	0.0095

[*]Propensity score was computed using multivariable logistic regression with the following variables: age, sex, heart failure, hypertension, diabetes, stroke, myocardial infarction, kidney disease, liver disease, bleeding history, alcohol use, antiplatelet agents, angiotensin converting enzyme inhibitors, angiotensin II receptor blockers, calcium channel blockers, diuretics, amiodarone, digoxin, CHA_2DS_2-VASc, and HAS-BLED.

[superscript]†Standardized differences computed by dividing the difference in mean outcome between groups by the SD of outcome among participants.
ACE=angiotensin-converting-enzyme; ARB=angiotensin II receptor blocker; CHA$_2$DS$_2$-VASc=congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, stroke/transient ischemic attack, vascular disease, age 65–75 years, and sex category; HAS-BLED=hypertension, abnormal renal/liver function, stroke, bleeding history or predisposition, labile international normalized ratio, elderly (age >65 years), drugs/alcohol concomitantly; SD=standard deviation.