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Pharmacotherapy in Medicare Beneficiaries With Atrial Fibrillation

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Abstract

Background—There are limited data regarding national patterns of pharmacotherapy for atrial fibrillation (AF) among older patients. Drug exposure data are now captured for Medicare beneficiaries enrolled in prescription drug plans.

Objective—To describe pharmacotherapy for AF among Medicare beneficiaries.

Methods—Using a 5% national sample of Medicare claims data, we compared demographic characteristics, comorbidity, and treatment patterns according to Medicare Part D status among patients with prevalent AF in 2006 and 2007.

Results—In 2006, 27,174 patients (29.3%) with prevalent AF were enrolled in Medicare Part D. In 2007, enrollment increased to 45,711 (49.1%). Most enrollees were taking rate control agents (74.0% in 2007). β -Blocker use was higher in those with concomitant AF and heart failure and increased with higher CHADS₂ scores ($P < .001$). Antiarrhythmic use was 18.7% in 2006 and 19.1% in 2007, with amiodarone accounting for more than 50%. Class Ic drugs were used in 3.2% of patients in 2007. Warfarin use was less than 60% and declined with increasing stroke risk ($P < .001$).

Conclusion—Pharmacotherapy for AF varied according to comorbidity and underlying risk. Amiodarone was the most commonly prescribed antiarrhythmic agent. Postmarketing surveillance using Medicare Part D claims data linked to clinical data may help inform comparative safety, effectiveness, and net clinical benefit of drug therapy for AF in older patients in real-world settings.

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Keywords

Adrenergic beta-Antagonists; Anti-Arrhythmia Agents; Anticoagulants; Atrial Fibrillation; Calcium Channel Blockers; Drug Therapy

Introduction

Atrial fibrillation (AF) is a pervasive public health problem; prevalence doubles with each decade of life and continues to increase.^{1, 2} There are 3 therapeutic goals in the care of patients with AF: prevention of stroke, rate control, and rhythm control. During the past several years, new therapies have emerged, including both pharmacologic and nonpharmacologic interventions.³⁻⁶ The Institute of Medicine recently ranked treatment for AF among the highest-priority topics for comparative effectiveness research.⁴ Accordingly, we investigated patterns of pharmacotherapy for AF in the US Medicare population. We assessed the comparability of Medicare beneficiaries with AF with and without Medicare Part D prescription drug coverage. We also investigated pharmacotherapy for AF across risk strata, including medications for stroke prophylaxis, rate control, and rhythm control.

Methods

Using administrative claims data for a nationally representative 5% sample of Medicare beneficiaries, we compared patient-level characteristics of patients with AF according to whether they were enrolled in a standalone Medicare Part D plan. Medicare Part D is a comprehensive prescription drug plan established in January 2006. In the first year, 55.9% of Medicare beneficiaries were enrolled.⁷

We identified 2 cohorts of patients with prevalent AF for the analysis: (1) patients with prevalent AF as of January 1, 2006, and (2) patients with prevalent AF as of January 1, 2007. We defined prevalence as the presence of an AF diagnosis (International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM] code 427.31) in any position on an inpatient claim or 2 outpatient or carrier claims during the previous calendar year (eg, in 2005 for the 2006 cohort). We required patients to be enrolled in fee-for-service Medicare and to have 12 months of prior claims data (ie, patients were 66 years as of January 1 of the cohort year). We used Medicare denominator files to ascertain enrollment in Medicare Part D.

We used the cohorts described above to describe pharmacotherapy for AF in the study population. We required that patients be enrolled in Medicare Part D on January 1 of the cohort year and to be alive and continuously enrolled through at least April 30 of the cohort year, to provide adequate time for prescription event ascertainment.

We used the Medicare denominator files to ascertain baseline demographic characteristics, including age, race, sex, and US geographic region. We used the Medicare inpatient, outpatient, and carrier claims files to collect data about comorbid conditions during the 12 months preceding the cohort date. We used previously validated algorithms^{8,9} to identify comorbid conditions, including cancer (ie, metastatic solid tumor), cerebrovascular disease, chronic obstructive pulmonary disease, heart failure, dementia, diabetes mellitus, hypertension, ischemic heart disease, peripheral vascular disease, and renal disease. We also searched for instances of the use of implantable cardioverter-defibrillators (Current Procedural Terminology codes 33245, 33246, 33249, G0297, G0298, G0299, and G0300) and pacemakers (33206, 33207, and 33208). We defined CHADS₂ scores as reported by Gage et al.¹⁰

Prespecified pharmacotherapies of interest included antithrombotic therapy (ie, warfarin, clopidogrel, and enoxaparin), rate control agents, and guideline-recommended antiarrhythmic drugs.¹¹ We searched the Red Book to identify National Drug Codes (NDCs) associated with the generic names of the drugs of interest and searched for prescriptions in the Medicare Part D event file using the NDCs. The ascertainment period for medications was the first 4 months of each calendar year. We considered a patient to be using a medication if the patient had 1 prescription claim for the medication during the ascertainment period. We defined the use of each medication as a binary variable.

In the statistical analysis, we described patients' baseline characteristics by Medicare Part D enrollment status, using proportions for categorical variables and means or medians for continuous variables. To enable comparisons with previously published rates, we calculated both unadjusted and age- and sex-adjusted rates of the use of rate control, rhythm control, and anticoagulant medications relevant to the management of patients with AF by study cohort. We calculated *P* values on the basis of unequal variances between the cohorts, and we used standard normal *z* tests to test differences in medication use between the cohorts given the large sample sizes. We used SAS version 9.2 for all analyses (SAS Institute Inc, Cary, North Carolina). The institutional review board of the Duke University Health System approved the study.

Results

Of 92,819 Medicare beneficiaries with prevalent AF in 2006, 27,174 (29.3%) were enrolled in Medicare Part D. Enrollment increased to 45,711/93,112 (49.1%) in 2007. Patients with and without Medicare Part D coverage were similar in age; however, women and black patients were more likely to be enrolled in Medicare Part D (Table 1). In general, Medicare Part D enrollees had greater comorbidity. For example, in 2006, heart failure was more frequent among enrollees (56% vs 47%; *P* < .001). CHADS₂ scores were also higher among enrollees. Use of implantable cardiac rhythm devices was similar between enrollees and nonenrollees. There were no significant clinical differences between enrolled and nonenrolled patients by geographic region. However, the prevalence of AF was greatest in the Eastern North Central (15%) and South Atlantic regions (21%).

Tables 2 and 3 show unadjusted and adjusted rates of medication use. Most patients took some form of rate control medication (73.0% in 2007), most commonly β -blockers (52.8% in 2007). The rate of digoxin use was 30%. Among patients receiving β -blockers, metoprolol was the most commonly prescribed. Overall profiles of rate control agents, including all 3 classes of atrioventricular nodal blocking agents, were comparable between the 2006 and 2007 cohorts.

Membrane-active antiarrhythmic medications (Vaughan Williams classes I and III) were used in 18.7% of patients in 2006 and in 19.1% in 2007 (Table 3). Class III agents were the most commonly used therapy, accounting for nearly 80% of antiarrhythmic drug prescriptions in 2007. Amiodarone was the most commonly used single antiarrhythmic agent, representing 51.3% of antiarrhythmic agents used in 2006 and 49.4% in 2007. Sotalol was the second most commonly used agent, representing 26.1% of antiarrhythmic agents used in 2006 and 26.5% in 2007. Class Ic agents were used in 3% of patients in the 2006 cohort and 3.2% in the 2007 cohort.

Use of antithrombotic agents is also shown in Table 3. Warfarin was used in 56.5% of patients in 2006 and in 59.0% of patients in 2007. Enoxaparin use was low (1.0%) in the outpatient setting. In 2007, antiplatelet therapy with clopidogrel was used in 9.1% of

patients, and combination therapy with clopidogrel and warfarin was used in 2.3% of patients. Aspirin is not captured in Medicare Part D claims.

Table 4 shows age- and sex-adjusted rates of medication use by heart failure status. Patients with AF and heart failure had a higher frequency of β -blocker therapy, including greater use of carvedilol. Overall, the frequency of antiarrhythmic therapy was similar among patients with and without heart failure, though class Ic therapy was less common (2% vs 5%) and amiodarone was more common (12% vs 8%) among those with heart failure. Oral anticoagulation was comparable between the groups (57 vs 59%), whereas antiplatelet therapy was more frequent among those with heart failure (11 vs 7%).

As shown in Table 5, after adjustment for age and sex, medication use varied significantly by CHADS₂ score. β -Blocker therapy increased with higher CHADS₂ scores (42% among patients with CHADS₂ score of 0; 60% with CHADS₂ score of 6). Antiarrhythmic medication use decreased with increasing CHADS₂ scores ($P < .001$ for trend). Anticoagulation therapy was less frequent with increasing CHADS₂ scores ($P < .001$), and antiplatelet therapy increased with CHADS₂ scores ($P < .001$).

Discussion

Drug therapy is essential in AF for achieving multiple therapeutic goals, including prevention of stroke and ventricular rate control.¹¹ Outpatient pharmacy charges for AF in the United States approach \$600 million annually.¹² In this analysis of more than 70,000 patients in a nationally representative cohort of Medicare beneficiaries with AF, patients enrolled in Medicare Part D were more likely to be women and black. Enrollees also had greater comorbidity, including a higher frequency of heart failure. These differences have implications for the interpretation of comparative effectiveness studies that include data on medication use from Medicare Part D data. The differences may also confer some advantages for researchers, given the underrepresentation of minorities in randomized trials of AF pharmacotherapy.

Rate control with β -blockers or nondihydropyridine calcium channel blockers is a class I guideline recommendation for the management of patients with AF.¹³ More than 75% of patients in the Medicare Part D cohort received a rate control agent. Use of rate control agents increased with comorbidity and risk. Among patients receiving a rate control agent, more than half were taking a β -blocker. Given that more than 50% of the cohort had heart failure and 60% had ischemic heart disease, it is surprising that β -blocker use was not higher. When we examined medication use by heart failure status and CHADS₂ score, β -blocker therapy was more frequent among patients with concomitant AF and heart failure and those with greater stroke risk.

Less than 1 in 5 Medicare Part D enrollees were receiving antiarrhythmic drug therapy, substantially lower than rates observed in large AF registries, which often exceed 50%.^{14,15} This finding likely reflects the greater comorbidity in this older population, higher prevalence of persistent and permanent AF, and preferences for rate control. Among patients treated with antiarrhythmic drugs, amiodarone was the most commonly prescribed. Because amiodarone is often considered a drug of last resort for AF, the preponderance of amiodarone use may relate to age and lack of response to other agents. Physicians may also prescribe amiodarone earlier in older patients. Greater use of amiodarone use can be explained in part by the higher prevalence of heart failure in this cohort of older patients. In Medicare Part D, amiodarone use was greater among patients with AF and heart failure, also consistent with guidelines.¹³ Furthermore, high use of amiodarone highlights the importance of comparative effectiveness studies in AF. Although amiodarone is effective in the

maintenance of sinus rhythm, it is associated with end-organ complications, including thyroid, liver, and pulmonary toxicities.^{16,17} Because data from contemporary, randomized, active-comparator studies are limited, comparative effectiveness and safety data in large populations using Medicare Part D data have the potential to refine estimates of net clinical benefit for older patients.¹⁸

With respect to stroke prevention, warfarin use was less than 60%. This finding reiterates the well-recognized underuse of oral anticoagulation in patients with AF.^{19,20} Although many patients may have had contraindications to warfarin or insufficient risk to warrant therapy, more than half of the beneficiaries had heart failure, one-third had diabetes, and more than 30% had cerebrovascular disease. Consistent with other studies,²¹ we observed a risk-treatment paradox, in which oral anticoagulation decreased with increasing stroke risk. Although increased use of clopidogrel may reflect therapeutic strategies to prevent bleeding, randomized trial data have not shown that dual antiplatelet therapy leads to decreased bleeding compared with warfarin.²² Improving the use of stroke prevention therapy remains an important goal for quality improvement in the care of patients with AF.

Our study has several limitations. First, prevalence estimates from Medicare claims data are not directly comparable to estimates from medical record review. However, Medicare Part D claims report actual prescriptions filled (ie, exposures). In addition, claims for AF on the basis of *ICD-9-CM* codes have a sensitivity of 73% and a specificity of 99%.²³ Second, due to its over-the-counter status, we could not study the use of aspirin, an important antithrombotic agent for patients with AF. Third, our analysis of medication use focused on prescriptions filed in the first 4 months of the calendar year, and we were unable to ascertain longitudinal adherence. Therefore, our utilization rates are estimates insofar as they represent a sample of AF medication claims. On the other hand, given the large, nationally representative sample, our findings are unlikely to be spurious. Fourth, these data reflect use of antiarrhythmic and antithrombotic agents before the availability of dronedarone and the novel oral anticoagulants; therefore, they may not reflect current prescribing trends. Finally, we cannot comment on patient-level appropriateness with administrative data. However, utilization estimates have some bearing at the population-level, particularly when comorbid conditions are known.

Conclusion

Medication use for AF varies according to underlying risk and comorbid disease. In older patients, rate control strategies dominate. Among patients treated with antiarrhythmic therapy, amiodarone remains the most commonly used agent. The risk-treatment paradox observed with stroke prevention therapy in older Medicare Part D enrollees highlights the challenges of treatment decisions and reinforces the need for large comparative effectiveness studies in older patients.

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Abbreviations

AF	atrial fibrillation
ICD-9-CM	International Classification of Diseases, Ninth Revision, Clinical Modification

References

1. Wolf PA, Benjamin EJ, Belanger AJ, Kannel WB, Levy D, D'Agostino RB. Secular trends in the prevalence of atrial fibrillation: the Framingham Study. *Am Heart J*. 1996; 131:790–795. [PubMed: 8721656]
2. Benjamin EJ, Levy D, Vaziri SM, D'Agostino RB, Belanger AJ, Wolf PA. Independent risk factors for atrial fibrillation in a population-based cohort. The Framingham Heart Study. *JAMA*. 1994; 271:840–844.
3. Connolly SJ, Eikelboom J, Joyner C, et al. Apixaban in patients with atrial fibrillation. *N Engl J Med*. 2011; 364:806–817. [PubMed: 21309657]
4. Institute of Medicine. Initial National Priorities for Comparative Effectiveness Research. IOM; Washington, DC: 2009.
5. Piccini JP, Lopes RD, Kong MH, Hasselblad V, Jackson K, Al-Khatib SM. Pulmonary vein isolation for the maintenance of sinus rhythm in patients with atrial fibrillation: a meta-analysis of randomized, controlled trials. *Circ Arrhythm Electrophysiol*. 2009; 2:626–633. [PubMed: 20009077]
6. Piccini JP, Lopes RD, Mahaffey KW. Oral factor Xa inhibitors for the prevention of stroke in atrial fibrillation. *Curr Opin Cardiol*. 2010; 25:312–320. [PubMed: 20520539]
7. Centers for Medicare & Medicaid Services. [Accessed April 6, 2012] Part D Claims Data. <https://www.cms.gov/Medicare/Prescription-Drug-Coverage/PrescriptionDrugCovGenIn/PartDDData.html>
8. Birman-Deych E, Waterman AD, Yan Y, Nilasena DS, Radford MJ, Gage BF. Accuracy of ICD-9-CM codes for identifying cardiovascular and stroke risk factors. *Med Care*. 2005; 43:480–485. [PubMed: 15838413]
9. Quan H, Sundararajan V, Halfon P, et al. Coding algorithms for defining comorbidities in ICD-9-CM and ICD-10 administrative data. *Med Care*. 2005; 43:1130–1139. [PubMed: 16224307]
10. Gage BF, Waterman AD, Shannon W, Boechler M, Rich MW, Radford MJ. Validation of clinical classification schemes for predicting stroke: results from the National Registry of Atrial Fibrillation. *JAMA*. 2001; 285:2864–2870. [PubMed: 11401607]
11. Wann LS, Curtis AB, January CT, et al. 2011 ACCF/AHA/HRS Focused Update on the Management of Patients With Atrial Fibrillation (Updating the 2006 Guideline): A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2011; 123:104–123. [PubMed: 21173346]
12. Kim MH, Johnston SS, Chu BC, Dalal MR, Schulman KL. Estimation of total incremental health care costs in patients with atrial fibrillation in the United States. *Circ Cardiovasc Qual Outcomes*. 2011; 4:313–320. [PubMed: 21540439]
13. European Heart Rhythm Association; Heart Rhythm Society. , Fuster V, et al. ACC/AHA/ESC 2006 guidelines for the management of patients with atrial fibrillation--executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the European Society of Cardiology Committee for Practice Guidelines (Writing Committee to Revise the 2001 Guidelines for the Management of Patients With Atrial Fibrillation). *J Am Coll Cardiol*. 2006; 48:854–906. [PubMed: 16904574]
14. Le Heuzey JY, Breithardt G, Camm J, et al. The RecordAF study: design, baseline data, and profile of patients according to chosen treatment strategy for atrial fibrillation. *Am J Cardiol*. 2010; 105:687–693. [PubMed: 20185018]
15. Nieuwlaat R, Capucci A, Camm AJ, et al. Atrial fibrillation management: a prospective survey in ESC Member Countries: The Euro Heart Survey on Atrial Fibrillation. *Eur Heart J*. 2005; 26:2422–2434. [PubMed: 16204266]

16. Mason JW. Amiodarone. *N Engl J Med*. 1987; 316:455–466. [PubMed: 3543680]
17. Piccini JP, Hasselblad V, Peterson ED, Washam JB, Califf RM, Kong DF. Comparative efficacy of dronedarone and amiodarone for the maintenance of sinus rhythm in patients with atrial fibrillation. *J Am Coll Cardiol*. 2009; 54:1089–1095. [PubMed: 19744618]
18. Piccini JP, Kong DF. Mixed treatment comparisons for atrial fibrillation: evidence network or bewildering entanglement? *Europace*. 2011; 13:295–296. [PubMed: 21345924]
19. Birman-Deych E, Radford MJ, Nilasena DS, Gage BF. Use and effectiveness of warfarin in Medicare beneficiaries with atrial fibrillation. *Stroke*. 2006; 37:1070–1074. [PubMed: 16528001]
20. Go AS, Hylek EM, Borowsky LH, Phillips KA, Selby JV, Singer DE. Warfarin use among ambulatory patients with nonvalvular atrial fibrillation: the anticoagulation and risk factors in atrial fibrillation (ATRIA) study. *Ann Intern Med*. 1999; 131:927–934. [PubMed: 10610643]
21. Sandhu RK, Bakal JA, Ezekowitz JA, McAlister FA. Risk stratification schemes, anticoagulation use and outcomes: the risk--treatment paradox in patients with newly diagnosed non-valvular atrial fibrillation. *Heart*. 2011; 97:2046–2050. [PubMed: 22076011]
22. ACTIVE Writing Group of the ACTIVE Investigators. Connolly S, Pogue J, et al. Clopidogrel plus aspirin versus oral anticoagulation for atrial fibrillation in the Atrial fibrillation Clopidogrel Trial with Irbesartan for prevention of Vascular Events (ACTIVE W): a randomised controlled trial. *Lancet*. 2006; 367:1903–12. [PubMed: 16765759]
23. Kokotailo RA, Hill MD. Coding of stroke and stroke risk factors using International Classification of Diseases, Revisions 9 and 10. *Stroke*. 2005; 36:1776–1781. [PubMed: 16020772]

Table 1
Baseline Characteristics of the Study Population by Medicare Part D Enrollment Status

Characteristic	2006 Cohort			2007 Cohort		
	Without Part D Enrollment (n = 65,645)	With Part D Enrollment (n = 27,174)	P Value	Without Part D Enrollment (n = 47,401)	With Part D Enrollment (n = 45,711)	P Value
Age, mean (SD), y	79.3 (7.1)	80.0 (7.6)		79.3 (7.0)	80.0 (7.5)	
Age, median (IQR), y	79.0 (74.0-84.0)	80.0 (74.0-86.0)		79.0 (74.0-84.0)	80.0 (74.0-85.0)	
Age, min-max, y	66-105	66-107		66-106	66-108	
Age group, No. (%)			<.001			<.001
67-69 y	6416 (9.8)	2668 (9.8)		4630 (9.8)	4486 (9.8)	
70-74 y	11,220 (17.1)	4518 (16.6)		8081 (17.0)	7282 (15.9)	
75-79 y	15,602 (23.8)	5842 (21.5)		11,108 (23.4)	9962 (21.8)	
80-84 y	16,480 (25.1)	6208 (22.8)		11,964 (25.2)	10,775 (23.6)	
85-89y	10,777 (16.4)	4754 (17.5)		8043 (17.0)	8138 (17.8)	
90 y	5150 (7.8)	3184 (11.7)		3575 (7.5)	5068 (11.1)	
Male sex, No. (%)	33,236 (50.6)	9979 (36.7)	<.001	25,776 (54.4)	17,796 (38.9)	<.001
White race, No. (%)	62,960 (95.9)	24,126 (88.8)	<.001	45,491 (96.0)	41,810 (91.5)	<.001
Comorbid conditions, No. (%)						
Cancer	12,387 (18.9)	4415 (16.2)	<.001	9202 (19.4)	7759 (17.0)	<.001
Cerebrovascular disease	18,724 (28.5)	9157 (33.7)	<.001	13,724 (29.0)	14,712 (32.2)	<.001
Congestive Heart failure	30,978 (47.2)	15,227 (56.0)	<.001	21,914 (46.2)	23,937 (52.4)	<.001
COPD	23,673 (36.1)	11,324 (41.7)	<.001	16,942 (35.7)	17,826 (39.0)	<.001
Dementia	4375 (6.7)	3905 (14.4)	<.001	3117 (6.6)	5347 (11.7)	<.001
Diabetes mellitus	20,852 (31.8)	10,503 (38.7)	<.001	15,708 (33.1)	16,703 (36.5)	<.001
Hypertension	55,624 (84.7)	23,864 (87.8)	<.001	40,670 (85.8)	40,169 (87.9)	<.001
ICD	1141 (1.7)	389 (1.4)	<.001	746 (1.6)	580 (1.3)	<.001
Ischemic heart disease	38,622 (58.8)	16,706 (61.5)	<.001	28,004 (59.1)	27,275 (59.7)	.07
Pacemaker	2508 (3.8)	1031 (3.8)	.85	1761 (3.7)	1751 (3.8)	.36
Peripheral vascular disease	18,388 (28.0)	9274 (34.1)	<.001	13,703 (28.9)	14,812 (32.4)	<.001
Renal disease	8278 (12.6)	4476 (16.5)	<.001	7745 (16.3)	8466 (18.5)	<.001

Characteristic	2006 Cohort			2007 Cohort		
	Without Part D Enrollment (n = 65,645)	With Part D Enrollment (n = 27,174)	P Value	Without Part D Enrollment (n = 47,401)	With Part D Enrollment (n = 45,711)	P Value
US geographic region, No. (%) [*]			<.001			<.001
East North Central	12,248 (18.7)	4884 (18.0)		9156 (19.3)	7581 (16.6)	
East South Central	3966 (6.0)	2030 (7.5)		2582 (5.4)	3377 (7.4)	
Middle Atlantic	10,494 (16.0)	3848 (14.2)		7953 (16.8)	6424 (14.1)	
Mountain	3447 (5.3)	995 (3.7)		2475 (5.2)	2007 (4.4)	
New England	4333 (6.6)	1907 (7.0)		3181 (6.7)	3252 (7.1)	
Pacific	6418 (9.8)	2805 (10.3)		4569 (9.6)	4849 (10.6)	
South Atlantic	14,048 (21.4)	5503 (20.3)		10,413 (22.0)	9181 (20.1)	
West North Central	4659 (7.1)	2387 (8.8)		2737 (5.8)	4366 (9.6)	
West South Central	6032 (9.2)	2815 (10.4)		4335 (9.1)	4674 (10.2)	
CHADS ₂ score, mean (SD)	2.6 (1.3)	2.9 (1.4)	<.001	2.6 (1.3)	2.8 (1.4)	<.001
CHADS ₂ score, No. (%)			<.001			<.001
0	2023 (3.1)	581 (2.1)		1309 (2.8)	1028 (2.2)	
1	10,987 (16.7)	3442 (12.7)		7903 (16.7)	6298 (13.8)	
2	22,263 (33.9)	8038 (29.6)		16,333 (34.5)	14,369 (31.4)	
3	15,344 (23.4)	6775 (24.9)		11,069 (23.4)	11,087 (24.3)	
4	9198 (14.0)	4552 (16.8)		6527 (13.8)	7297 (16.0)	
5	4382 (6.7)	2642 (9.7)		3245 (6.8)	4008 (8.8)	
6	1448 (2.2)	1144 (4.2)		1015 (2.1)	1624 (3.6)	

Abbreviations: ICD, implantable cardioverter-defibrillator; IQR, interquartile range.

^{*} New England includes Connecticut, Maine, Massachusetts, New Hampshire, Rhode Island, and Vermont. Middle Atlantic includes New Jersey, New York, and Pennsylvania. South Atlantic includes Delaware, District of Columbia, Florida, Georgia, Maryland, North Carolina, South Carolina, Virginia, and West Virginia. East South Central includes Alabama, Kentucky, Mississippi, and Tennessee. West South Central includes Arkansas, Louisiana, Oklahoma, and Texas. East North Central includes Illinois, Indiana, Michigan, Ohio, and Wisconsin. West North Central includes Iowa, Kansas, Minnesota, Missouri, Nebraska, North Dakota, and South Dakota. Mountain includes Arizona, Colorado, Idaho, Montana, Nevada, New Mexico, Utah, and Wyoming. Pacific includes Alaska, California, Hawaii, Oregon, and Washington.

Table 2

Unadjusted Rates of Medication Use for Atrial Fibrillation

Medication	2006 Cohort (n = 19,523)	2007 Cohort (n = 38,671)	P Value *
Rate-control medications, No. (%)	14,041 (71.9)	28,249 (73.0)	.004
β-Blocker	9695 (49.7)	20,420 (52.8)	< .001
Atenolol	2073 (10.6)	4116 (10.6)	.93
Carvedilol	1678 (8.6)	3455 (8.9)	.17
Metoprolol	5722 (29.3)	12,344 (31.9)	< .001
Other	392 (2.0)	771 (2.0)	.91
Digoxin	6001 (30.7)	11,453 (29.6)	.006
Diltiazem	2879 (14.7)	5656 (14.6)	.70
Verapamil	585 (3.0)	1100 (2.8)	.31
Antiarrhythmic agents, No. (%)	3424 (17.5)	6823 (17.6)	.75
Class Ia	99 (0.5)	152 (0.4)	.06
Disopyramide	45 (0.2)	76 (0.2)	.41
Procainamide	15 (0.1)	17 (0.0)	.14
Quinidine	40 (0.2)	59 (0.2)	.17
Class Ic	602 (3.1)	1235 (3.2)	.47
Flecainide	260 (1.3)	556 (1.4)	.30
Propafenone	348 (1.8)	686 (1.8)	.94
Class III	2758 (14.1)	5480 (14.2)	.89
Amiodarone	1820 (9.3)	3547 (9.2)	.56
Dofetilide	81 (0.4)	167 (0.4)	.77
Sotalol	884 (4.5)	1799 (4.7)	.50
Anticoagulation agents, No. (%)	10,983 (56.3)	22,678 (58.6)	< .001
Enoxaparin	181 (0.9)	369 (1.0)	.75
Warfarin	10,952 (56.1)	22,605 (58.5)	< .001
Antiplatelet agents, No. (%)	1879 (9.6)	3611 (9.3)	.27
Clopidogrel	1879 (9.6)	3611 (9.3)	.27
Clopidogrel and warfarin, No. (%)	421 (2.2)	915 (2.4)	.11

* From χ^2 tests

Table 3

Rates of Medication Use for Atrial Fibrillation After Adjustment for Age and Sex

Medication	2006 Cohort (n = 19,523)	2007 Cohort (n = 38,671)	P Value *
Rate-control medications, No. (%)	14,136 (72.4)	28,632 (74.0)	< .001
β-Blocker	9802 (50.2)	20,765 (53.7)	< .001
Atenolol	2114 (10.8)	4257 (11.0)	.51
Carvedilol	1658 (8.5)	3396 (8.8)	.24
Metoprolol	5806 (29.7)	12,583 (32.5)	< .001
Other	402 (2.1)	795 (2.1)	.97
Digoxin	5936 (30.4)	11,356 (29.4)	.01
Diltiazem	2969 (15.2)	6004 (15.5)	.31
Verapamil	621 (3.2)	1201 (3.1)	.63
Antiarrhythmic agents, No. (%)	3646 (18.7)	7381 (19.1)	.23
Class Ia	102 (0.5)	162 (0.4)	.09
Disopyramide	50 (0.3)	90 (0.2)	.57
Procainamide	17 (0.1)	17 (0.0)	.06
Quinidine	36 (0.2)	54 (0.1)	.21
Class Ic	705 (3.6)	1510 (3.9)	.08
Flecainide	314 (1.6)	701 (1.8)	.07
Propafenone	399 (2.0)	819 (2.1)	.54
Class III	2885 (14.8)	5763 (14.9)	.69
Amiodarone	1874 (9.6)	3652 (9.4)	.54
Dofetilide	90 (0.5)	187 (0.5)	.73
Sotalol	955 (4.9)	1963 (5.1)	.34
Anticoagulation agents, No. (%)	11,058 (56.6)	22,868 (59.1)	< .001
Enoxaparin	196 (1.0)	404 (1.0)	.67
Warfarin	11,027 (56.5)	22,797 (59.0)	< .001
Antiplatelet agents, No. (%)	1847 (9.5)	3535 (9.1)	.21
Clopidogrel	1847 (9.5)	3535 (9.1)	.21
Clopidogrel and warfarin, No. (%)	420 (2.2)	907 (2.3)	.14

* From χ^2 tests

Table 4

Rates of Medication Use for Atrial Fibrillation by Heart Failure Status After Adjustment for Age and Sex

Medication	Without Heart Failure (n = 29,557)	With Heart Failure (n = 28,637)	P Value*
Rate-control medications, No. (%)	20,641 (69.8)	22,202 (77.5)	< .001
β-Blocker	14,022 (47.4)	16,633 (58.1)	< .001
Atenolol	3810 (12.9)	2495 (8.7)	< .001
Carvedilol	681 (2.3)	4560 (15.9)	< .001
Metoprolol	8921 (30.2)	9451 (33.0)	< .001
Other	763 (2.6)	426 (1.5)	< .001
Digoxin	7455 (25.2)	9965 (34.8)	< .001
Diltiazem	4713 (15.9)	4254 (14.9)	< .001
Verapamil	1092 (3.7)	712 (2.5)	< .001
Antiarrhythmic agents, No. (%)	5756 (19.5)	5226 (18.2)	< .001
Class Ia	152 (0.5)	112 (0.4)	.02
Disopyramide	85 (0.3)	57 (0.2)	.04
Procainamide	12 (0.0)	24 (0.1)	.04
Quinidine	58 (0.2)	31 (0.1)	.007
Class Ic	1507 (5.1)	632 (2.2)	< .001
Flecainide	719 (2.4)	253 (0.9)	< .001
Propafenone	801 (2.7)	382 (1.3)	< .001
Class III	4154 (14.1)	4525 (15.8)	< .001
Amiodarone	2265 (7.7)	3336 (11.6)	< .001
Dofetilide	136 (0.5)	143 (0.5)	.50
Sotalol	1787 (6.0)	1087 (3.8)	< .001
Anticoagulation agents, No. (%)	17,485 (59.2)	16,438 (57.4)	< .001
Enoxaparin	274 (0.9)	331 (1.2)	.006
Warfarin	17,439 (59.0)	16,379 (57.2)	< .001
Antiplatelet agents, No. (%)	2173 (7.4)	3259 (11.4)	< .001
Clopidogrel	2173 (7.4)	3259 (11.4)	< .001
Clopidogrel and warfarin, No. (%)	500 (1.7)	851 (3.0)	< .001

* From χ^2 tests

Table 5
Rates of Medication Use for Atrial Fibrillation by CHADS₂ Score after Adjustment for Age and Sex

Medication	CHADS ₂ Score						P Value [*]
	0 (n = 1508)	1 (n = 8801)	2 (n = 19,161)	3 (n = 13,859)	4 (n = 8668)	5 (n = 4560)	6 (n = 1637)
Rate-control medications, No. (%)	413 (64.3)	5950 (67.6)	14,181 (74.0)	10,607 (76.5)	6387 (73.7)	3457 (75.8)	719 (76.4)
β-Blocker	267 (41.6)	3742 (42.5)	10,034 (52.4)	7791 (56.2)	4782 (55.2)	2607 (57.2)	568 (60.3)
Atenolol	69 (10.7)	901 (10.2)	2318 (12.1)	1373 (9.9)	855 (9.9)	370 (8.1)	66 (7.0)
Carvedilol	25 (3.9)	383 (4.3)	1368 (7.1)	1846 (13.3)	909 (10.5)	659 (14.5)	166 (17.6)
Metoprolol	167 (26.0)	2308 (26.2)	6035 (31.5)	4425 (31.9)	2940 (33.9)	1566 (34.3)	331 (35.2)
Other	7 (1.1)	186 (2.1)	444 (2.3)	283 (2.0)	181 (2.1)	71 (1.6)	14 (1.5)
Digoxin	170 (26.5)	2562 (29.1)	5772 (30.1)	4488 (32.4)	2530 (29.2)	1404 (30.8)	306 (32.5)
Diltiazem	79 (12.4)	1321 (15.0)	3096 (16.2)	2191 (15.8)	1260 (14.5)	624 (13.7)	114 (12.1)
Verapamil	24 (3.7)	321 (3.6)	646 (3.4)	404 (2.9)	188 (2.2)	129 (2.8)	15 (1.6)
Antiarrhythmic agents, No. (%)	165 (25.8)	1758 (20.0)	3748 (19.6)	2468 (17.8)	1380 (15.9)	712 (15.6)	117 (12.4)
Class Ia	5 (0.8)	57 (0.7)	103 (0.5)	52 (0.4)	23 (0.3)	5 (0.1)	3 (0.3)
Disopyramide	3 (0.5)	28 (0.3)	55 (0.3)	28 (0.2)	13 (0.2)	3 (0.1)	1 (0.1)
Procainamide	0 (0.0)	4 (0.0)	16 (0.1)	11 (0.1)	2 (0.0)	1 (0.0)	1 (0.1)
Quinidine	2 (0.3)	26 (0.3)	32 (0.2)	13 (0.1)	7 (0.1)	1 (0.0)	1 (0.1)
Class Ic	62 (9.6)	461 (5.2)	663 (3.5)	363 (2.6)	233 (2.7)	90 (2.0)	7 (0.8)
Flecainide	36 (5.6)	244 (2.8)	259 (1.3)	166 (1.2)	79 (0.9)	31 (0.7)	2 (0.2)
Propafenone	27 (4.1)	224 (2.5)	412 (2.2)	198 (1.4)	155 (1.8)	59 (1.3)	5 (0.6)
Class III	101 (15.8)	1257 (14.3)	3015 (15.7)	2083 (15.0)	1137 (13.1)	618 (13.5)	108 (11.4)
Amiodarone	54 (8.4)	701 (8.0)	1884 (9.8)	1437 (10.4)	810 (9.3)	442 (9.7)	84 (8.9)
Dofetilide	6 (1.0)	45 (0.5)	103 (0.5)	48 (0.3)	19 (0.2)	19 (0.4)	1 (0.1)
Sotalol	41 (6.4)	522 (5.9)	1046 (5.5)	610 (4.4)	317 (3.7)	163 (3.6)	23 (2.4)
Anticoagulation agents, No. (%)	398 (62.1)	5431 (61.7)	11,527 (60.2)	8014 (57.8)	4797 (55.3)	2398 (52.6)	469 (49.8)
Enoxaparin	6 (1.0)	81 (0.9)	198 (1.0)	148 (1.1)	106 (1.2)	60 (1.3)	10 (1.0)
Warfarin	398 (62.1)	5423 (61.6)	11,497 (60.0)	7990 (57.7)	4779 (55.1)	2375 (52.1)	465 (49.4)
Antiplatelet agents, No. (%)	20 (3.1)	420 (4.8)	1394 (7.3)	1502 (10.8)	1282 (14.8)	813 (17.8)	160 (17.0)

Medication	CHADS ₂ Score						P Value*
	0 (n = 1508)	1 (n = 8801)	2 (n = 19,161)	3 (n = 13,859)	4 (n = 8668)	5 (n = 4560)	6 (n = 1637)
Clopidogrel	20 (3.1)	420 (4.8)	1394 (7.3)	1502 (10.8)	1282 (14.8)	813 (17.8)	160 (17.0)
Clopidogrel and warfarin, No. (%)	8 (1.3)	97 (1.1)	386 (2.0)	388 (2.8)	308 (3.6)	166 (3.6)	37 (4.0)
							< .001
							< .001

* From χ^2 tests.