

Cost Burden of Cardiovascular Hospitalization and Mortality in ATHENA-Like Patients With Atrial Fibrillation/Atrial Flutter in the United States

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ABSTRACT

Background: The ATHENA trial (A placebo-controlled, double-blind, parallel arm Trial to assess the efficacy of dronedarone 400 mg bid for the prevention of cardiovascular Hospitalization or death from any cause in patiENts with Atrial fibrillation/atrial flutter) demonstrated that dronedarone reduced the risk of cardiovascular (CV) hospitalization/death by 24% ($P < 0.001$) in patients with atrial fibrillation (AF) and atrial flutter (AFL).

Hypothesis: In order to estimate the cost savings associated with dronedarone use, we estimated the costs associated with CV hospitalizations and inpatient mortality in a large cohort of ATHENA-like patients.

Methods: In this retrospective analysis, we evaluated the cost of CV hospitalization/mortality in real-world ATHENA-like patients without heart failure and with employer-sponsored Medicare supplemental insurance in the United States. Patients similar to those in ATHENA (age ≥ 70 years with AF/AFL and ≥ 1 stroke risk factor, without heart failure) who were hospitalized between January 2, 2005, and January 1, 2007, were identified from the MarketScan databases from Thomson Reuters. Health care costs were evaluated during the 12 months following the index hospitalization.

Results: The analysis included 10 200 ATHENA-like patients. Hospitalization for CV causes occurred in 53.9% of patients, with a total of 6700 CV hospitalizations for fatal/nonfatal causes. The most common nonfatal causes of CV hospitalizations were AF/other supraventricular rhythm disorders (20.2% of all CV hospitalizations), congestive heart failure (CHF; 14.3%), and transient ischemic attack (TIA)/stroke (10.7%). Mean costs per CV hospitalization for nonfatal causes were \$10908. Inpatient deaths from CV causes occurred in 264 (2.6%) patients; the most common causes of CV inpatient death were intracranial/gastrointestinal hemorrhage (24.2% of CV deaths), TIA/stroke (17.0%), and CHF (15.9%). Mean hospitalization costs per CV inpatient death were \$18 565.

Conclusions: Health care costs associated with CV hospitalizations and inpatient deaths among ATHENA-like patients in the US are high. Novel antiarrhythmic therapies such as dronedarone, with the potential to reduce CV hospitalizations/mortality in similar patients, could decrease health care costs if adopted in clinical practice.

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Introduction

The prevalence of atrial fibrillation (AF) in the United States is high and predicted to increase over the next 50 years.^{1–3} Patients with AF commonly have cardiovascular (CV) comorbidities and a higher rate of morbidity and mortality than patients without AF.^{1,3–7} In particular, AF is an independent predictor of heart failure (HF) and

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stroke.⁷ Atrial flutter (AFL) is less prevalent than AF, but it frequently leads to AF and is associated with a similar increase in the risk of stroke.^{8,9} Not surprisingly, the costs of managing AF are substantial, with annual costs estimated at \$4700 per patient¹⁰ or \$6.65 billion across the United States,¹¹ largely driven by inpatient hospital admissions.^{11,12}

Although effective treatments are available to maintain and restore sinus rhythm in AF/AFL patients,¹³ these have had little impact on hospitalization rates, which have tended to rise year-on-year.^{4,14,15} Recently, the ATHENA trial (A placebo-controlled, double-blind, parallel arm Trial to assess the efficacy of dronedarone 400 mg bid for the prevention of cardiovascular Hospitalization or death from any cause in patiENts with Atrial fibrillation/atrial flutter) demonstrated that dronedarone, a novel antiarrhythmic therapy, significantly reduced the risk of hospitalization for CV causes or inpatient death from any cause in patients with AF/AFL.¹⁶

There is currently limited information on the real-world cost of hospitalizations or inpatient deaths due to specific CV causes among AF/AFL patients. In order to provide an indication of the potential cost savings associated with dronedarone use in clinical practice, we estimated the current costs associated with CV hospitalizations and inpatient mortality in a large cohort of ATHENA-like patients in the United States.

Methods

Study Design and Databases

This retrospective cohort study used data from January 1, 2004, through December 31, 2007, from the MarketScan Medicare Supplemental and Coordination of Benefits Database from Thomson Reuters. This database is derived from employer-sponsored Medicare-supplemental health care insurance plans and includes information on 21.6 million individuals covered under various fee-for-service and capitated provider reimbursement schemes. MarketScan has formed the basis of more than 250 peer-reviewed publications.^{17,18} In compliance with the Health Insurance Portability and Accountability Act, all patient data were de-identified.

Patient Selection

Patients with AF or AFL were identified by the presence of an AF or AFL diagnosis (International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM] codes 427.31 and 427.32, respectively) on an inpatient admission claim, or ≥ 2 claims on different days for outpatient services other than diagnostic radiology, venipuncture, laboratory, or pathology, between January 1 and December 31, 2005. The first of these claims was designated the index diagnosis.

Patients with transient AF/AFL only were excluded. Transient AF/AFL was identified by a claim with a diagnosis for hyperthyroidism or an outpatient pharmaceutical claim for methimazole or propylthiouracil in the 12 months before the AF/AFL diagnosis, or a solitary AF/AFL diagnosis following recent (< 30 days) cardiac surgery. Patients with an AF/AFL diagnosis indicated solely on an outpatient ECG claim were also excluded.

To be considered "ATHENA-like,"^{16,19} patients had to be age ≥ 70 years and have 1 of the following CV comorbidities in the 12 months before index AF/AFL diagnosis: arterial/pulmonary embolism, arterial hypertension, diabetes, or stroke/transient ischemic attack (TIA). Patients with acute myocarditis, cancer, pregnancy, or end-stage renal disease were excluded in line with ATHENA entry criteria.^{16,19} All comorbidities and other clinical characteristics were identified via ICD-9-CM diagnosis codes or ICD-9-CM and Current Procedure Terminology (CPT) procedure codes.

The ATHENA study excluded patients with New York Heart Association (NYHA) class IV congestive heart failure (CHF), based on possible contraindications to dronedarone in these patients.^{16,19,20} As it was not possible to determine CHF severity in this study using the claims data available, all patients with evidence of CHF were excluded from the primary analysis population. To determine whether exclusion of these patients influenced the cost of CV events, a sensitivity analysis was conducted in the broader group of patients including those with HF in the 12 months before AF/AFL index diagnosis.

To be included in the cost analysis, patients were required to have a hospitalization following the index AF/AFL diagnosis, with an overnight stay covering ≥ 2 consecutive dates between January 2, 2005 and January 1, 2007. This hospitalization had to be followed by ≥ 12 months of continuous enrollment (except for inpatient death). The first hospitalization following the index AF/AFL diagnosis was the index hospitalization.

Study Measures

Patient demographic characteristics at the index AF/AFL diagnosis and clinical characteristics during the 12 months preceding the index diagnosis were recorded. Patients had newly diagnosed AF/AFL if they had no claims with a diagnosis of AF/AFL or for antiarrhythmic agents in the 12 months before the index diagnosis.

The frequency and costs of CV-related hospitalizations were measured during the year following the index hospitalization (including the index hospitalization itself). Expenditures (2006 US\$) represent the sum of all paid claims. Cardiovascular causes were categorized based on the prespecified main causes for CV hospitalization in the ATHENA trial.¹⁹ Costs were also reported separately for hospitalizations resulting in death.



Figure 1. Patient identification.

Results

Patient Characteristics

In total, 15 552 ATHENA-like patients with AF/AFL were identified, of whom 10 200 (65.6%) without prior HF comprised the primary analysis population (Figure 1). Of these, 28.4% were newly diagnosed with AF/AFL. The median postindex follow-up was 12 months (mean [SD], 11.3 [2.6] months).

Patients had a mean age of 79.5 years and 53.2% were female (Table 1). Cardiovascular comorbidities were common: Most patients (91.6%) had hypertension and 28.3% had coronary artery disease (Table 1). Prior to the index AF/AFL diagnosis, more than half of patients had received treatment with warfarin (59.7%), β -blockers (53.4%), and diuretics (54.9%).

Costs of Cardiovascular Hospitalizations

Overall, 38.4% of patients had ≥ 1 readmission following the index hospitalization. Hospitalizations for CV causes occurred in 53.9% of patients, with a total of 6700 CV hospitalizations (fatal or nonfatal causes, including the index hospitalization and readmissions). The most common nonfatal causes of CV hospitalization were AF or other supraventricular rhythm disorders, CHF, and stroke (Table 2). The mean cost per CV hospitalization for which the patient was discharged alive was \$10 908 (Table 2).

Costs of Inpatient Mortality

In total, 736 (7.2%) patients died in hospital during the study. Inpatient death for a CV cause was reported for

Table 1. Patient Characteristics at the Time of First Claim and Preindex Comorbidities

Characteristic	ATHENA-like Patients Without CHF (n = 10 200)	ATHENA-like Patients With/Without CHF (n = 15 552)
Age, y, mean (SD)	79.5 (5.8)	79.8 (5.9)
Age category, y, n (%)		
70–74	2283 (22.4)	3286 (21.1)
75–79	2999 (29.4)	4422 (28.4)
80–84	2874 (28.2)	4476 (28.8)
≥85	2044 (20.0)	3368 (21.7)
Sex, n (%)		
Male	4777 (46.8)	7350 (47.3)
Female	5423 (53.2)	8202 (52.7)
Region, n (%)		
North central	4181 (41.0)	6442 (41.4)
Northeast	1228 (12.0)	1881 (12.1)
South	3012 (29.5)	4476 (28.8)
West	1765 (17.3)	2731 (17.6)
Unknown	14 (0.1)	22 (0.1)
Charlson comorbidity index, ⁴¹ mean (SD)	1.0 (1.1)	1.5 (1.4)
Chronic disease score, ⁴² mean (SD)	8.2 (3.2)	8.7 (3.3)
Comorbidities, n (%)		
Hypertension	9347 (91.6)	14 565 (93.7)
Structural heart disease	3938 (38.6)	8474 (54.5)
CAD	2884 (28.3)	5272 (33.9)
Diabetes	2484 (24.4)	4319 (27.8)
CHF	0	3771 (24.2)
Valvular heart disease	1652 (16.2)	3183 (20.5)
Pulmonary disease	1397 (13.7)	2824 (18.2)
Ischemic stroke	1045 (10.2)	1714 (11.0)

Abbreviations: ATHENA, A Trial With Dronedronone to Prevent Hospitalization or Death in Patients With Atrial Fibrillation; CAD, coronary artery disease; CHF, congestive heart failure; SD, standard deviation; y, years.

264 patients (2.6% of all patients) and accounted for 35.9% of all inpatient deaths. The most common causes of CV-related inpatient death were intracranial or gastrointestinal hemorrhage (24.2% of all CV deaths) and TIA/stroke (17.0%) (Table 3). Each CV-related inpatient death was associated with mean hospitalization costs of \$18565 (Table 3).

Sensitivity Analysis in Patients With or Without Heart Failure

The baseline characteristics of the overall population (ATHENA-like patients with/without HF) were similar to those of the primary analysis population (without HF) (Table 1), as was their duration of postindex follow-up (median 12 months; mean [SD], 11.1 [2.9] months).

Table 2. Frequency and Cost of Hospitalizations for Nonfatal CV Causes

Primary diagnosis for hospitalizations for nonfatal causes	ATHENA-like Patients Without CHF (n = 10 200)			ATHENA-like Patients With/Without CHF (n = 15 552)		
	Patients, n (%)	Hospitalizations, n (% of Total CV Hospitalizations)	Mean Cost per Hospitalization (US\$)	Patients, n (%)	Hospitalizations, n (% of Total CV Hospitalizations)	Mean Cost per Hospitalization (US\$)
AF/other supraventricular rhythm disorders	1251 (12.3)	1355 (20.2)	\$7483	1679 (10.8)	1824 (16.5)	\$7476
CHF	853 (8.4)	960 (14.3)	\$8851	1965 (12.6)	2306 (20.8)	\$8980
TIA/stroke	687 (6.7)	718 (10.7)	\$8015	958 (6.2)	1007 (9.1)	\$8035
Coronary atherosclerosis	600 (5.9)	643 (9.6)	\$16 350	901 (5.8)	960 (8.7)	\$15 845
AMI/ICS	270 (2.6)	281 (4.2)	\$15 450	403 (2.6)	423 (3.8)	\$15 136
BP-related condition (hypertension/hypotension)	258 (2.5)	275 (4.1)	\$5894	464 (3.0)	492 (4.4)	\$6388
Stable angina pectoria/atypical chest pain	202 (2.0)	208 (3.1)	\$4779	290 (1.9)	297 (2.7)	\$4900
Syncope	199 (2.0)	204 (3.0)	\$5587	300 (1.9)	308 (2.8)	\$5538
Implantation of pacemaker/other cardiac device	134 (1.3)	142 (2.1)	\$16 262	228 (1.5)	238 (2.1)	\$21 415
Major bleeding	127 (1.2)	133 (2.0)	\$12 306	178 (1.1)	184 (1.7)	\$11 948
Venous thromboembolism	94 (0.9)	97 (1.4)	\$11 535	143 (0.9)	147 (1.3)	\$11 085
CV surgery	64 (0.6)	64 (1.0)	\$18 897	120 (0.8)	122 (1.1)	\$19 434
Ventricular arrhythmia	52 (0.5)	52 (0.8)	\$12 407	103 (0.7)	107 (1.0)	\$13 569

Table 2. (continued)

	ATHENA-like Patients Without CHF (n = 10 200)			ATHENA-like Patients With/Without CHF (n = 15 552)		
	Patients, n (%)	Hospitalizations, n (% of Total CV Hospitalizations)	Mean Cost per Hospitalization (US\$)	Patients, n (%)	Hospitalizations, n (% of Total CV Hospitalizations)	Mean Cost per Hospitalization (US\$)
Acute/subacute endocarditis	10 (0.1)	11 (0.2)	\$81 121	14 (0.1)	17 (0.2)	\$57 413
Nonfatal cardiac arrest	1 (0.0)	1 (0.0)	\$1961	2 (0.0)	2 (0.0)	\$4260
Other CV ^a	1211 (11.9)	1292 (19.3)	\$15 007	1959 (12.6)	2113 (19.1)	\$15 536
Total CV hospitalizations (patient discharged alive)	5232 (51.3)	6436 (96.1)	\$10 908	8198 (52.7)	10 547 (95.2)	\$11 085
Total CV hospitalizations including inpatient deaths	5496 (53.9)	6700 (100)	NA	8733 (56.2)	11 082 (100)	NA

Abbreviations: AF, atrial fibrillation; AMI, acute myocardial infarction; ATHENA, A Trial With Dronedaron to Prevent Hospitalization or Death in Patients With Atrial Fibrillation; BP, blood pressure; CHF, congestive heart failure; CV, cardiovascular; ICS, intermediate coronary syndrome; NA, not applicable; TIA, transient ischemic attack.

^a CV events not included in the prespecified main causes of CV hospitalizations in the ATHENA trial^{16,19} but meeting criteria for CV hospitalizations defined by the Institute for Clinical Evaluative Sciences.²¹

Table 3. Frequency and Costs of Inpatient Deaths Due to CV Causes

	ATHENA-like Patients Without CHF (n = 10 200)			ATHENA-like Patients With/Without CHF (n = 15 552)		
	Patients, n (%)	Percentage of All Deaths Due to CV Causes	Mean Hospitalization Cost per Death (US\$)	Patients, n (%)	Percentage of All Deaths Due to CV Causes	Mean Hospitalization Cost per Death (US\$)
Primary diagnosis for inpatient deaths						
Intracranial or GI hemorrhage	64 (0.6)	24.2	\$11 861	82 (0.5)	15.3	\$12 131
TIA/stroke	45 (0.4)	17.0	\$10 351	77 (0.5)	14.4	\$9481
CHF	42 (0.4)	15.9	\$11 312	122 (0.8)	22.8	\$13 731
AMI/ICS	33 (0.3)	12.5	\$19 938	68 (0.4)	12.7	\$15 375
CV transcatheter intervention procedure or CV surgical intervention	16 (0.2)	6.1	\$29 873	34 (0.2)	6.4	\$37 067
Pulmonary or arterial embolism	8 (0.1)	3.0	\$22 861	16 (0.1)	3.0	\$21 482
Ventricular arrhythmia	4 (0.0)	1.5	\$6146	14 (0.1)	2.6	\$9880
Other CV ^a	52 (0.5)	19.7	\$35 727	122 (0.8)	22.8	\$25 963
Total inpatient deaths for CV causes	264 (2.6)	100.0	\$18 565	535 (3.4)	100.0	\$17 486

Abbreviations: AMI, acute myocardial infarction; ATHENA, A Trial With Dronedronone to Prevent Hospitalization or Death in Patients With Atrial Fibrillation; CHF, congestive heart failure; CV, cardiovascular; GI, gastrointestinal; ICS, intermediate coronary syndrome; TIA, transient ischemic attack.

^a CV events not included in the prespecified main causes of CV hospitalizations in the ATHENA trial^{16,19} but meeting criteria for CV hospitalizations defined by the Institute for Clinical Evaluative Sciences.²¹

A similar proportion of patients in the overall and primary analysis populations had a CV hospitalization (56.2% vs 53.9%, respectively), although CHF accounted for a higher proportion of nonfatal CV hospitalizations (20.8% vs 14.3%) in the overall population (Table 2). Incidences of inpatient death for CV causes were similar in the 2 populations (3.4% vs 2.6%, respectively) (Table 3). Overall, costs per CV hospitalization were similar in the overall and primary analysis populations, both for nonfatal (\$11 085 vs \$10 908) and fatal (\$17 486 vs \$18 565) causes (Tables 2 and 3).

Discussion

This analysis highlights the high costs associated with hospitalization and inpatient death due to CV causes in a large cohort of real-world ATHENA-like AF/AFL patients with employer-sponsored Medicare supplemental insurance. Overall, the mean per-event cost was \$10 908 for CV hospitalizations and \$18 565 for inpatient deaths due to CV causes.

Patients in this study were well matched in terms of CV comorbidity to those in the ATHENA trial.¹⁶ As in the ATHENA trial, the most common cause of CV hospitalizations in this study was AF or other supraventricular rhythm disorders (responsible for 20.2% of all CV hospitalizations), followed by CHF (14.3%), and stroke (10.7%). Similar findings were reported in a recent United States community-based study, with AF accounting for 26.4% of hospitalizations, CHF 21.7%, coronary/peripheral arterial causes 21.6%, and thromboembolic events 10.5%.⁴ Notably, in both studies, although AF was the most common reason for CV hospitalizations, most hospitalizations were due to other CV conditions.

The most common cause of inpatient death in our study was intracranial or gastrointestinal hemorrhage (24.2% of all deaths), followed by stroke (17.0%), and CHF (15.9%). This high rate of hemorrhage might be related to the relatively high use of warfarin (almost 60% of patients) and the high risk of bleeding complications among elderly patients.

The highest per-event cost in our analysis was hospitalization for acute and subacute endocarditis (\$81 121); however, this was relatively uncommon (11 hospitalizations in total). In terms of both overall frequency of events and cost per event, coronary atherosclerosis was responsible for the greatest proportion of total costs (14.0%), followed by AF/other supraventricular rhythm disorders (13.5%), CHF (12.0%), TIA/stroke (8.3%), and acute myocardial infarction (AMI) or intermediate coronary syndromes (6.7%), which collectively accounted for more than half of all costs. Of the remaining costs, more than half were attributable to "other CV" causes that were not among the prespecified causes of CV hospitalizations in the ATHENA trial,¹⁹ but which met the criteria for CV hospitalizations defined by the Institute for Clinical Evaluative Sciences.²¹

Although it is difficult to compare our data directly with previous cost analyses, the costs of hospitalizations are not dissimilar. For example, an analysis by the Centers for Medicare & Medicaid Services estimated the cost of CHF per discharge at \$7273 (\$8851 in our study), coronary atherosclerosis at \$12 288 (\$16350 in our study), and AMI at \$12 910 (\$15450 in our study).^{22,23} Comorbidities such as AF are predictive of higher costs,^{24,25} which may explain our slightly higher cost estimates.

The costs presented in this study are per event only; total per-patient costs including costs for readmissions and outpatient costs are likely to be much greater. Consistent with this, studies have shown that total per-patient costs associated with CV hospitalizations are generally higher than the per-event costs reported here. For example, annual per-patient costs have been estimated at \$14 000 for patients hospitalized with a primary diagnosis of AF,²⁶ \$14 000 for patients hospitalized with CHF,²⁷ and \$28 500 for patients with stroke (based on Swedish costs).²⁸

Costs of rehospitalization in particular are likely to have contributed to increased overall per-patient costs in our study, with 38.4% of all patients being readmitted over 12 months. This is broadly consistent with the high readmission rates observed previously among patients hospitalized for CV causes.^{29–32} For example, in a study of patients hospitalized for CV events, 38% of those aged ≥ 70 years were readmitted for CV causes within 1 year.²⁹ A recent study also demonstrated that among patients hospitalized with a primary diagnosis of AF, 11% were readmitted for AF over the following year.³²

Patients with NYHA class IV CHF were excluded from the ATHENA trial,²⁰ but 21.2% of the ATHENA population were designated as having NYHA class II or III CHF,^{16,33} which is in line with estimates for the general population.^{34,35} In contrast, all patients with HF were excluded from our primary analysis population. Given that AF patients with CHF are typically in NYHA classes I–III (92.1%),³⁴ a number of patients eligible for ATHENA may have been excluded from our study population. The parallel sensitivity analysis

conducted in the broader population of otherwise eligible ATHENA-like patients, among whom 24.2% had a history of HF (consistent with ATHENA and previous studies^{16,34,35}) indicated, however, that exclusion of patients with HF did not substantially affect our cost estimates. Although this wider patient group experienced a higher proportion of CV hospitalizations and inpatient deaths related to CHF, their per-event costs (\$11 085 for CV hospitalizations and \$17 486 for inpatient deaths) were comparable with those of the primary analysis population (\$10 908 and \$18 565, respectively).

The close similarity in clinical characteristics and causes of hospitalization between our study population and that of the ATHENA trial suggests that the results of ATHENA will be broadly applicable to the wider population of ATHENA-like AF/AFL patients with or without HF across the United States. Of the 100 471 AF/AFL patients in the MarketScan database, almost half (45 504) met the additional criteria for categorization as "ATHENA-like" patients with or without HF (Figure). Given that the inpatient costs of managing AF/AFL in the United States are approximately \$4.88 billion annually (73% of a total of \$6.65 billion),¹¹ the reductions in CV hospitalizations and inpatient mortality observed with dronedarone in ATHENA could potentially result in substantial reductions in health care costs if achieved in this wider population.

Study Limitations

Due to the limited clinical data available in the database and the retrospective nature of the analysis, it was not possible to match patients exactly to the ATHENA cohort. In our analysis, AF/AFL was identified using claim ICD-9-CM codes and was not confirmed with electrocardiography. In addition, it was not possible to distinguish between paroxysmal, persistent, or permanent AF, whereas patients with permanent AF were excluded from the ATHENA trial. Moreover, a higher proportion of CV hospitalizations were related to AF in ATHENA (~55.1%) compared with our study (20.2%), which may be due to differences in the reporting in clinical trials compared with the use of diagnostic codes. Comorbidities and causes of hospitalization were also defined according to ICD-9-CM codes in our study, which may differ from the reporting of events in ATHENA.

Patients in our study were on average slightly older than those in the ATHENA trial (mean 79.5 years vs 71.6 years); the eligibility criterion of age ≥ 70 years was not introduced until partway through ATHENA due to lower than expected mortality rates,¹⁶ whereas all patients in our study met this requirement. An additional limitation is that because the database is restricted to patients with employer-sponsored Medicare supplemental insurance, the results may not be fully representative of all Medicare patients. Information regarding patients' ethnicity was also unavailable.

Conclusion

This study demonstrates the high health care costs associated with common CV causes of hospitalizations and inpatient deaths among ATHENA-like patients in the United States. Although numerous antiarrhythmic drugs have been shown to reduce the frequency of AF recurrences, they have proved ineffective in reducing the burden of CV morbidity and mortality in AF/AFL patients.^{36,37} Post hoc analysis of patients receiving rhythm-control drugs in the Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) study,^{36,38} as well as the sub-cohort receiving amiodarone (who accounted for 62% of antiarrhythmic-treated patients in AFFIRM),³⁹ demonstrated significant worsening of the composite endpoint of CV hospitalization/mortality—in contrast to the effect seen with dronedarone in the ATHENA study.¹⁶ The only encouraging endpoint data obtained prior to the ATHENA findings came from the Danish Investigators of Arrhythmia and Mortality ON Dofetilide (DIAMOND) trials, in which dofetilide reduced HF hospitalizations.⁴⁰ Thus, interest has shifted toward the newer class III antiarrhythmics. If adopted in clinical practice, novel antiarrhythmic therapies with the potential to reduce CV hospitalizations and inpatient mortality in AF patients could lead to substantial reductions in overall health care costs.

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