

Estimation of Total Incremental Health Care Costs in Patients With Atrial Fibrillation in the United States

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Background—Detailed information on the cost burden of atrial fibrillation (AF) is limited. To provide an up-to-date estimate of the national cost of AF, we conducted a retrospective, observational cohort study using administrative claims from the MarketScan Commercial and Medicare Supplemental research data bases, 2004 to 2006.

Methods and Results—Patients aged ≥ 20 years with ≥ 1 inpatient or ≥ 2 outpatient AF diagnoses in 2005 (first diagnosis=index) and ≥ 12 months' enrollment before and after index were selected. AF patients were propensity score-matched (1:1) with non-AF control subjects. Medical costs (2008 US\$), including AF costs, other cardiovascular, and noncardiovascular costs, were examined over 1 year after index. National incremental costs of AF were based on age-/sex-specific AF prevalence projections for 2010. In total, 89 066 AF patients were matched to non-AF control subjects. Over 1 year, 37.5% of AF versus 17.5% of control subjects were hospitalized and 2.1% versus 0.1% died during hospitalization. For AF versus control subjects, mean annual inpatient costs per patient were \$7841 versus \$2622 (incremental cost, \$5218), outpatient medical costs were \$9225 versus \$5629 (\$3596), and outpatient pharmacy costs were \$3605 versus \$3714 ($-\$109$) (all $P < 0.001$). The total incremental cost of AF was \$8705 per patient. The national incremental cost of AF was \$26.0 billion (AF, \$6.0 billion; other cardiovascular, \$9.9 billion; noncardiovascular, \$10.1 billion). Cardiovascular costs were based on claims with a primary disease diagnosis and may be underestimates.

Conclusions—On the basis of current US age- and sex-specific prevalence data, the national incremental AF cost is estimated to range from \$6.0 to \$26.0 billion. (*Circ Cardiovasc Qual Outcomes*. 2011;4:313-320.)

Key Words: atrial fibrillation ■ health care costs ■ incremental costs ■ national cost burden

Atrial fibrillation (AF) is the most common manifestation of cardiac arrhythmia, and, as the population ages, the prevalence of the disease is expected to increase substantially.¹ Currently there are an estimated 3.0 million adults with AF in the United States, and this figure is projected to at least double in the next 25 years.^{1,2} Patients with AF typically have other cardiovascular comorbidities and are at elevated risk of cardiovascular and cerebrovascular events and mortality compared with individuals without the condition.³ Hospitalizations and deaths associated with AF have risen steadily in the United States since the 1980s.^{2,4,5} Currently, hospitalizations with AF as the primary diagnosis exceed 460 000 each year, and AF is estimated to contribute to more than 80 000 annual deaths.⁶ Because hospitalization is the primary cost driver in the management of the disease,^{7,8} the economic burden of AF on the health care system is likely to continue to grow.

Although several previous US-based studies have examined the cost of AF,^{7,9-11} their findings may not be readily generalized nationwide. Recent changes in the management of AF mean that older studies may not reflect contemporary

treatment practice, whereas studies based on small patient samples¹⁰ or limited to younger AF patients⁹ may be unrepresentative of the larger AF population. From a methodological perspective, few studies have calculated the incremental costs of AF by comparing costs in AF patients with matched control subjects without this condition,^{7,9,12-14} and even fewer have projected these costs nationally.

The purpose of this study was to use a large, national data base to provide a comprehensive and up-to-date estimate of the national incremental costs incurred by patients with AF and to explore the relative contribution of cardiovascular and noncardiovascular components of their care.

Methods

Study Design

This retrospective observational cohort study used health care data collected from the MarketScan *Commercial Claims and Encounters* and *Medicare Supplemental and Coordination of Benefits* research data bases from Thomson Reuters for the period January 1, 2004, through December 31, 2006. These data bases represent the health services of approximately 38 million employees, dependents, and retirees in the United States, with commercial, primary, or Medicare

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supplemental coverage through privately insured, employer-sponsored health plans.¹⁵ Both the Commercial and Medicare data bases include individuals covered under a variety of fee-for-service, point of service, and capitated reimbursement schemes. The Commercial and Medicare Supplemental data bases comprise a nonprobability convenience sample; however, nearly half of all US health plans, including many of the larger ones, contribute to these data bases. Compared with the 2006 Medical Expenditure Panel Survey, a US-based probability sample that reflects the population with employer-sponsored insurance, the 2007 MarketScan Commercial and Medicare Supplemental data bases contain a slightly lower proportion of individuals in the 18- to 64-year age group (68.2% versus 71.8%), and a higher proportion of individuals in the North Central and South US Census Bureau regions (74.8% versus 53.2%).^{16,17}

WHAT IS KNOWN

- There are an estimated 3.0 million adults with atrial fibrillation in the United States, and this figure is projected to at least double in the next 25 years.
- Hospitalizations with atrial fibrillation as the primary diagnosis exceed 460 000 each year, and atrial fibrillation contributes to >80 000 annual deaths.
- Hospitalization is the primary cost driver in the management of atrial fibrillation.

WHAT THE STUDY ADDS

- This study, based on a large, national, multipayer data set of approximately 90 000 atrial fibrillation patients, is the first to project the national incremental cost of atrial fibrillation using propensity-matching techniques.
- Total direct medical costs were estimated to be 73% higher in atrial fibrillation patients than in matched control subjects, representing a net incremental cost of \$8705 per patient per annum (2008 values); based on current US age- and sex-specific prevalence data, the national incremental cost of atrial fibrillation is estimated to range between \$6.0 and \$26.0 billion.

By covering a heterogeneous patient population represented by a mix of payers rather than a single payer, the MarketScan data bases lend themselves to large-scale observational studies because their findings can be more readily extrapolated to the “real-world” setting. The MarketScan data bases have formed the basis of >300 peer-reviewed publications, including several prevalence and trending studies.¹⁸ The data bases complied with all aspects of the Health Insurance Portability and Accountability Act of 1996 and the study data were deidentified and therefore exempt from Institutional Review Board approval.

Patient Identification

Men and women who were identified as having ≥ 1 inpatient or ≥ 2 outpatient diagnoses of AF (*International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM]* diagnosis code 427.31) in any diagnosis position on nondiagnostic claims between January 1, 2005, and December 31, 2005, and who were ≥ 20 years of age at the time of diagnosis, were eligible for inclusion. The first qualifying AF diagnosis was designated the index diagnosis. Patients were required to have ≥ 12 months of continuous enrollment and complete data availability for the period immediately before and after the index diagnosis (other than in cases of inpatient death). Preexisting AF was signified by the presence of an AF claim ≤ 12

months before the index date. Patients considered to have transient AF, as signified by (1) an *ICD-9-CM* diagnosis code for hyperthyroidism or an outpatient prescription claim for methimazole or propylthiouracil in the 12-month period before the index diagnosis, or (2) a single AF diagnosis after recent (within 30 days) cardiac surgery, were excluded.

For comparison, patients aged ≥ 20 years without AF or atrial flutter or who were not receiving antiarrhythmic drugs were randomly selected from the data base, in the ratio of 40 comparison patients for every AF patient, to obtain a large pool of potential matches. Patients were excluded from this pool if they had any claim with an *ICD-9-CM* diagnosis code for AF (*ICD-9-CM* 427.31) or atrial flutter (*ICD-9-CM* 427.32) between January 1, 2004, and December 31, 2006. Index dates were assigned to potential comparison patients to replicate the distribution of index dates for AF patients. Comparison (control) patients were required to have ≥ 12 months of continuous enrollment and prescription data immediately before and after the index date (except in cases of inpatient death).

Propensity Score Matching

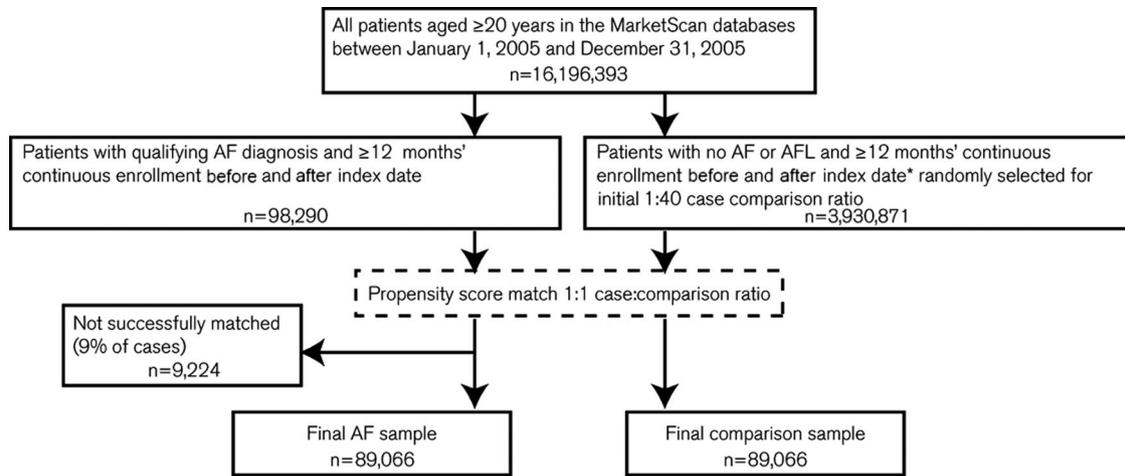
Propensity score matching techniques documented to minimize the impact of selection bias in observational studies¹⁹ were used to select control patients from the pool of comparison patients who shared similar demographic and clinical characteristics to the cohort of AF patients. Propensity score was computed using a logistic regression model, with the dependent variable comprising membership of the AF cohort and independent variables (covariates) including baseline demographics (age, sex, US Census Bureau geographic region, payer type, and index date) and cardiovascular comorbidities such as coronary artery disease, cardiomyopathies, mitral valve disease, other valvular disease, congestive heart failure, peripheral vascular disease, diabetes, hypertension and other clinical conditions such as thyroid disease, and pulmonary disease, as well as the Charlson-Deyo Comorbidity Index,²⁰ and Chronic Disease Score.²¹ Each patient in the AF cohort was matched with his/her closest control using a 1:1 “nearest neighbor matching” technique, with a caliper of $0.25 \times$ standard deviation of the estimated propensity score.²²

The discriminative power of the propensity score model was evaluated using the area under the receiver operating characteristic curve, or *C*-statistic. Potential overfitting was avoided through use of a variance inflation factor and correlation matrix for all included variables.²³ The success of propensity score matching was assessed by comparing the prematch and postmatch balance of identified covariates.^{19,22} A standardized difference between the 2 cohorts (mean difference expressed as a percentage of the average standard deviation of the variable’s distribution across the AF and control cohorts) of <10% was considered indicative of good balance.²⁴

Outcome Measures

Direct costs (in US\$ at 2008 values) for inpatient and outpatient medical services and pharmacy prescriptions were determined for each patient cohort over 12 months after the index (or until inpatient death). Health care expenditures covered plan-insured costs, coordination of benefits, patient copayments, deductibles, and coinsurance payments. The MarketScan data bases provided comprehensive prescription data coverage for all patients in the analysis, including outpatient pharmacy costs for Medicare patients in fee-for-service programs. Medical costs were categorized as AF-related costs (antiarrhythmic drug prescriptions and claims with a primary AF diagnosis), other cardiovascular costs (for claims with other primary cardiovascular diagnoses or procedures), and noncardiovascular costs (all other claims). Cardiovascular-specific medical expenditures were identified using a set of cardiovascular *ICD-9-CM* diagnosis and procedure codes and cardiovascular-specific pharmaceutical costs were determined from the RedBook Therapeutic Group 7 (cardiovascular system) drug list. Expenditures were quantified for hospitalizations (including inpatient deaths), emergency department visits, physician visits, laboratory services, other outpatient services, and outpatient drug prescriptions.

Costs for services provided under capitated arrangements were estimated using a Thomson Reuters algorithm that computes a



*Index dates were assigned to potential control patients to replicate the distribution of index dates among AF patients
AF, atrial fibrillation; AFL, atrial flutter

Figure 1. Patient identification.

payment “proxy” for health care services used, based on the average payments for noncapitated claims at the procedure level within the MarketScan data bases. This algorithm has been widely used in the published health-economic literature for multiple disease areas, including cardiovascular disease.

For determination of national cost projections, paired AF patients and control subjects were allocated to 1 of 16 combined sex- and age-specific strata (male/female, 20 to 54, 55 to 59, 60 to 64, 65 to 69, 70 to 74, 75 to 79, 80 to 84, and ≥ 85 years). Within each stratum, costs of control patients were subtracted from those of AF patients, and the mean (95% confidence interval) cost difference, representing the incremental cost of AF per capita, was calculated. Mean (95% confidence interval) stratum-specific incremental costs were multiplied by the stratum-specific estimated national prevalence of AF, based on age- and sex-specific projections for 2010.¹ Resulting costs were summed across strata to generate the estimated total national direct cost burden of AF for 2010.

The sensitivity of per-capita cost estimates to multivariable adjustment was evaluated using second-stage multivariable regression analysis.²⁵ The variables used in calculating the propensity score were included in either an ordinary least squares regression model with log-transformed costs or a two-part model, where appropriate, to adjust for any small residual covariate imbalance between the two cohorts after propensity score matching.

Statistical Analysis

Data management and statistical analyses were conducted using STATA 9.2 (Stata Corp, College Station, TX) for propensity score matching and SAS version 9.1.3 (SAS Institute Inc., Cary, NC) for all other analyses. Student *t* test and the Maentel-Haenszel χ^2 test were used for comparison of continuous and categorical variables, respectively. A probability value of <0.05 was considered statistically significant.

Results

Study Population

Of an initial sample of 98 290 identified AF patients, 89 066 (90.6%) were successfully matched to an identical number of control patients without AF (Figure 1). The 2 cohorts were well balanced with regard to sex, age, and comorbidity covariates (standardized difference $<10\%$) after matching (Table 1). The logistic regression model used to generate the propensity score showed excellent discriminative power (*C*-

statistic=0.93), indicating that the model readily distinguished AF patients from control patients. The high *C*-statistic probably was due in part to the marked age difference between the initial (prematch) AF patient pool (mean, 71.9 years) and the comparison patient pool (mean, 48.5 years).

The postmatch study population was of mean age 71 years at baseline (27% of patients were <65 years), with a male:female balance of 55%:45% and was drawn predominantly from the North Central and Southern regions of the United States. Medicare was the primary payer for most (75%) of the study population. The mean duration of follow-up for the AF and control groups was 360 and 365 days, respectively.

Among the AF patient cohort, 19.5% had newly diagnosed AF and 80.5% had preexisting AF, whereas 5% had coexisting atrial flutter. Common baseline comorbidities included hypertension and structural heart disease (Table 1). Overall, 22.0% of AF patients were receiving rhythm-control therapy, 73.5% rate-control therapy, and 57.2% warfarin. By design, no patients in the control group received rhythm-control therapy, but 54.6% received rate-control therapy, and 5.8% warfarin. Similar proportions of patients in the AF and control groups were receiving cardiovascular pharmacotherapy (88.4% versus 86.2%).

Hospitalizations and Inpatient Deaths

During the 12-month period after the index date, twice as many AF patients as control patients were hospitalized for any reason (37.5% versus 17.5%; $P<0.001$), and 3 times as many AF patients as control subjects had multiple hospitalizations (11.1% versus 3.3%; $P<0.001$). Moreover, AF patients were 4 times more likely to undergo cardiovascular hospitalization compared with control patients (21.3% versus 5.4%; $P<0.001$) and 8 times more likely than control patients to have multiple cardiovascular hospitalizations (4.1% versus 0.5%; $P<0.001$). Among AF patients, 7.2% had ≥ 1 inpatient admission with AF as the primary diagnosis, and 10.3% of

Table 1. Patient Demographics and Comorbidities (Before and After Matching)

Characteristics	Prematch			Postmatch		
	AF Patient Pool (n=98 290)	Comparison Patient Pool (n=3 930 871)	Standardized Difference (%) Between Cohorts*	AF Patients (n=89 066)	Medically Matched Control Patients (n=89 066)	Standardized Difference (%) Between Cohorts*
Sex, n (%)						
Male	54 833 (55.8)	1 818 326 (46.3)	19.1	49 190 (55.2)	49 746 (55.9)	-1.3
Female	43 457 (44.2)	2 112 545 (53.7)	-19.1	39 876 (44.8)	39 320 (44.1)	1.3
Age, mean (SD)	71.9 (11.7)	48.5 (14.8)	175.8	71.3 (11.8)	71.5 (11.5)	-2.3
Age category, y, n (%)						
20-54	8212 (8.4)	2 614 304 (66.5)	-150.3	8121 (9.1)	7266 (8.2)	3.4
55-59	7462 (7.6)	481 474 (12.2)	-15.6	7298 (8.2)	7170 (8.1)	0.5
60-64	9396 (9.6)	308 645 (7.9)	6.1	8988 (10.1)	8996 (10.1)	0.0
65-69	10 148 (10.3)	165 973 (4.2)	23.7	9567 (10.7)	10 593 (11.9)	-3.6
70-74	15 524 (15.8)	143 466 (3.6)	41.9	14 150 (15.9)	14 751 (16.6)	-1.8
75-79	19 182 (19.5)	111 158 (2.8)	54.9	17 061 (19.2)	16 832 (18.9)	0.7
80-84	16 889 (17.2)	67 731 (1.7)	54.8	14 464 (16.2)	13 513 (15.2)	2.9
≥85	11 477 (11.7)	38 120 (1.0)	45.1	9417 (10.6)	9945 (11.2)	-1.9
Geographic region, n (%)						
North Central	34 559 (35.2)	1 095 669 (27.9)	15.7	31 272 (35.1)	31 692 (35.6)	-1.0
Northeast	9957 (10.1)	373 626 (9.5)	2.1	8950 (10.0)	8638 (9.7)	1.2
South	29 550 (30.1)	1 599 090 (40.7)	-22.3	26 972 (30.3)	26 743 (30.0)	0.6
West	23 477 (23.9)	816 644 (20.8)	7.5	21 185 (23.8)	20 632 (23.2)	1.5
Unknown	747 (0.8)	45 842 (1.2)	-4.2	687 (0.8)	1361 (1.5)	-7.1
Payer type, n (%)						
Commercial	23 423 (23.8)	3 369 569 (85.7)	-158.8	22 844 (25.6)	21 627 (24.3)	3.2
Medicare	74 867 (76.2)	561 302 (14.3)	158.8	66 222 (74.4)	67 439 (75.7)	-3.2
Comorbidities, n (%)						
Hypertension	80 632 (82.0)	906 146 (23.1)	146.4	71 555 (80.3)	73 783 (82.8)	-6.5
Structural heart disease	47 448 (48.3)	161 977 (4.1)	116.3	38 339 (43.0)	33 744 (37.9)	10.5
Coronary artery disease	28 097 (28.6)	112 474 (2.9)	75.5	22 548 (25.3)	21 827 (24.5)	1.9
Mitral valve disease	11 762 (12.0)	30 557 (0.8)	47.1	8235 (9.2)	7299 (8.2)	3.7
Congestive heart failure	19 175 (19.5)	15 722 (0.4)	67.3	12 057 (13.5)	9320 (10.5)	9.5
Cardiomyopathy	4997 (5.1)	5731 (0.1)	31.3	3048 (3.4)	2384 (2.7)	4.3
Diabetes	21 637 (22.0)	290 976 (7.4)	42.2	18 998 (21.3)	19 088 (21.4)	-0.2
Pulmonary disease	14 683 (14.9)	125 170 (3.2)	41.8	11 687 (13.1)	11 007 (12.4)	2.3
Ischemic stroke	8630 (8.8)	28 235 (0.7)	38.6	7163 (8.0)	5066 (5.7)	9.3
Peripheral vascular disease	5341 (5.4)	19 943 (0.5)	29.3	4188 (4.7)	4112 (4.6)	0.4
Thyroid disease	4400 (4.5)	78 700 (2.0)	14.0	3706 (4.2)	3502 (3.9)	1.2
CCI, mean (SD)	1.5 (1.8)	0.3 (0.8)	85.6	1.3 (1.7)	1.3 (1.7)	2.6
CDS, mean (SD)	7.5 (3.7)	2.0 (2.8)	168.0	7.1 (3.6)	7.2 (3.6)	-3.2

AF indicates atrial fibrillation; CCI, Charlson-Deyo Comorbidity Index; SD, standard deviation; and CDS, Chronic Disease Score.

*A standardized difference <10% was considered indicative of a good balance in covariates between cohorts.²⁴

these patients had ≥1 readmission with AF as the primary diagnosis. The proportion of AF patients who died during hospitalization was higher than that of control patients (2.1% versus 0.1%; $P<0.001$). Deaths during cardiovascular-related admissions were also more frequent among AF patients than control subjects (0.8% versus 0.0%; $P<0.001$).

Annual Direct Costs Per Patient

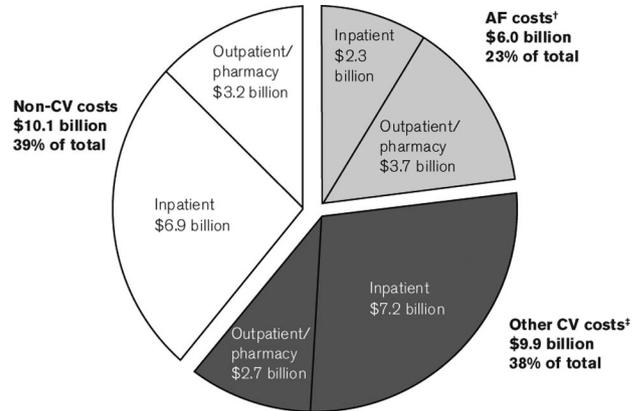
Total direct costs per patient over the 12-month period after the index date were (mean) \$20 670 in the AF group and \$11 965 in the control group, a net incremental cost of \$8705 ($P<0.001$). The principal driver of this cost difference was inpatient services (mean, \$7841 for AF patients versus \$2622

Table 2. Per-Patient Medical Costs in AF and Matched Control Patients

	Per-Patient Cost in AF Patients (US\$) (n=89 066)	Per-Patient Cost in Medically Matched Control Subjects (US\$) (n=89 066)	Incremental Per-Patient Cost in AF Patients (US\$)
Total costs	20 670	11 965	8705*
AF‡	1945	...	1945*
Other CV§	5824	2613	3211*
Non-CV	12 901	9352	3550*
Inpatient costs	7841	2622	5218*
AF‡	780	...	780*
Other CV§	3155	835	2321*
Non-CV	3905	1787	2118*
Outpatient medical¶	9225	5629	3596*
AF‡	972	...	972*
Other CV§	1576	678	898*
Non-CV	6677	4951	1726*
Outpatient pharmacy	3605	3714	-109*
AF‡	193	...	193*
Other CV§	1093	1101	-8†
Non-CV	2319	2613	-294*

AF indicates atrial fibrillation; CV, cardiovascular.
 * $P < 0.001$, intercohort comparison.
 † $P > 0.05$, intercohort comparison.
 ‡Only includes costs for claims with a primary AF diagnosis or claims for antiarrhythmic drugs.
 §Includes costs for claims with a primary CV diagnosis, excluding AF.
 ||Covers hospitalization (including inpatient deaths).
 ¶Covers emergency department visits, physician visits, laboratory services, and other outpatient services.

for control subjects; \$5218 increment; $P < 0.001$), followed by office visits (mean, \$966 for AF patients versus \$655 for control subjects; \$311 increment; $P < 0.001$) and emergency room services (mean, \$371 for AF patients versus \$168 for control subjects; \$203 increment; $P < 0.001$). The difference in cardiovascular-specific expenditure (mean \$7769 for AF patients versus \$2613 for control subjects; \$5156 increment; $P < 0.001$) exceeded that for noncardiovascular expenditure (mean \$12 901 for AF patients versus \$9352 for control subjects; \$3550 increment; $P < 0.001$). The major contributor to inflation of cardiovascular-specific costs among AF patients was cardiovascular-specific inpatient expenditure (mean, \$3935 for AF patients versus \$835 for control subjects; \$3100 increment; $P < 0.001$). Lower outpatient pharmacy costs for AF patients compared with control patients (mean, \$3605 versus \$3714; \$109 decrement; $P < 0.001$) were attributable to reduced expenditure on noncardiovascular drugs (mean, \$2319 versus \$2613; \$294 decrement; $P < 0.001$). In contrast, overall cardiovascular drug costs (mean, \$1219 versus \$556; \$663 increment), including anticoagulant/antiplatelet drug costs (mean, \$219 versus \$148; \$71 increment), were higher for AF patients than for control patients (both $P < 0.001$). In terms of expenditure type, the overall incremental cost of AF (mean, \$8705) comprised (mean) AF-related costs (ie, for care provided in connection with a



*Includes costs for claims with a primary AF diagnosis and claims for antiarrhythmic drugs
 †Includes costs for claims with a primary cardiovascular diagnosis (excluding AF) and claims for non-antiarrhythmic cardiovascular drugs
 AF, atrial fibrillation; CV, cardiovascular; OP, outpatient

Figure 2. Breakdown of national incremental costs in patients with atrial fibrillation.

primary diagnosis of AF) of \$1945, incremental “other cardiovascular” costs of \$3211 and incremental noncardiovascular costs of \$3550 (Table 2).

Sensitivity analysis indicated that propensity score matching addressed bias related to identified preindex demographic and clinical differences between the 2 cohorts, although the potential for residual bias from unmeasured confounders remains. Second-stage multivariable adjustment had a minimal and bidirectional effect on cost estimates: total inpatient expenditure fell by (mean) \$297 from the unadjusted, propensity match-based estimate of \$5218, whereas cardiovascular-specific inpatient expenditure rose by \$479 from the unadjusted estimate of \$3101. Accordingly, the cost estimates generated from the primary analysis were considered robust.

National Cost Projections

Extrapolation of the cohort cost findings (2008 values) to an estimated 3.5 million cases of AF in 2010, based on US Census Bureau projections of the age and sex distribution of the US population,¹ yielded an incremental cost in AF patients versus control patients of \$26.0 billion over a 12-month period. AF-specific costs constituted \$6.0 billion (23%), of which \$2.3 billion (38%) comprised inpatient admissions with a primary diagnosis of AF and \$3.1 billion (52%) comprised outpatient medical care. Other cardiovascular costs constituted \$9.9 billion (38%), arising from an estimated 700 000 additional cardiovascular-specific inpatient admissions and 3.2 million additional hospital days, whereas noncardiovascular costs constituted \$10.1 billion (39%) (Figure 2). Outpatient medical/pharmacy costs accounted for the majority of AF-specific costs (62%), whereas inpatient costs accounted for the majority of other cardiovascular (73%) and noncardiovascular (68%) costs. At the individual level, costs tended to be higher among patients younger than 65 years than in older patients, whereas at the national level the cost burden was greatest among men in the 60- to 64-year age group (Figure 3).

Discussion

The results of this study, based on a large, national, multi-payer data set of ≈90 000 AF patients, provide comprehen-

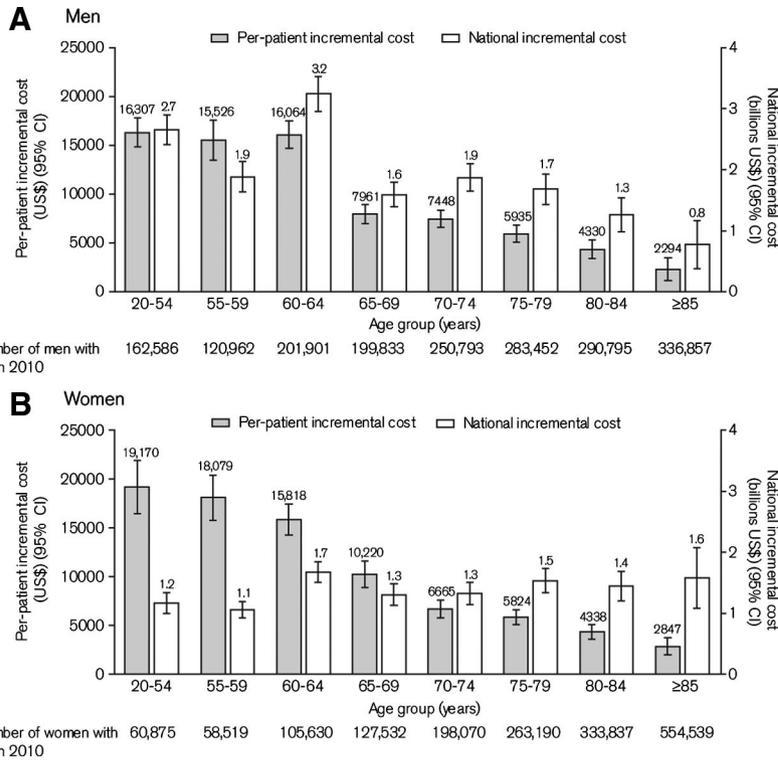


Figure 3. Incremental health care costs in men (A) and women (B) with atrial fibrillation (AF), stratified by age. CI indicates confidence interval.

sive and up-to-date information on the incremental cost burden of AF in the US. An estimated 57% of the US population receives health care insurance through employer-sponsored arrangements,¹⁵ and these individuals represent a large mix of payers. Use of the MarketScan data bases has the advantage of capturing the reimbursement policies and practices of multiple payers, and the study findings are therefore more likely to reflect the collective heterogeneities of the highly complex US health care system. Moreover, this is the first study to project the national incremental cost of AF using propensity-matching techniques to adjust for residual non-AF disease differences.

The study indicated that total annual direct medical costs were 73% higher in AF patients than in control subjects, representing a net incremental AF cost of \$8705 per patient (2008 values). This figure compares with previous estimates of \$12 349 (2002 values) obtained from a small study (n=3944) of relatively young (mean age, 55 years) AF patients,⁹ and \$14 199 (2004 values) from a larger study (n=55 260) of elderly Medicare patients with AF.¹⁴ Likewise, our national incremental cost projections of \$6.0 billion (AF-related costs alone) and \$26.0 billion (AF-related costs plus other cardiovascular costs and noncardiovascular costs) per annum are generally consistent with previously published estimates, despite notable differences in study design.^{7,13} A US survey based on 2001 data collected from 3 federally funded data bases, covering hospital inpatient stays, physician office visits, emergency department visits, and hospital outpatient visits, estimated AF-related direct medical expenditure (ie, costs specific to the diagnosis and treatment of AF) to be \$6 to \$7 billion annually at 2005 values.⁷ However, these cost estimates were on the conservative side because this cross-sectional study did not capture the full costs of AF

as a secondary (comorbid) discharge diagnosis, whereas the hospital sampling data omitted charges for hospital-based physician services.⁷ Moreover, the study data bases did not provide the actual costs of the reported services; instead, an average charge-to-cost ratio was applied uniformly across all hospitalizations, whereas resource use items pertaining to office, emergency room, and hospital outpatient visits were assigned unit costs.⁷ A later study, based on a sample of 35 255 managed-care patients and using the same national prevalence projections that we used, estimated total annual AF-related costs at ≈\$12.7 billion in 2005 and \$13.9 billion in 2010.¹³ However, this study did not use propensity matching techniques, and the patient cohorts differed in prevalence of cardiovascular comorbidity; moreover, this managed-care population was notably younger (mean age, 64 years) than our AF population (mean age, 71 years).¹³

The propensity matching techniques used in our study produced an AF cohort and a control cohort that were well matched with respect to sex, age, and most cardiovascular comorbidities. Furthermore, the proportions of patients receiving cardiovascular pharmacotherapy were similarly high in the AF and control groups (88.4% versus 86.2%). More than half of the control patients (55%) received rate-control therapy. Although this finding may initially appear anomalous, these medications were probably used for the treatment of cardiovascular conditions other than AF, such as hypertension, coronary artery disease, and congestive heart failure, all of which were prevalent in control patients.

Our finding of a higher incremental cost of AF in patients in the under-65 age group is not unexpected, given that suspected AF may be investigated more extensively in the under-65s and, once diagnosed, it may be treated more aggressively than in the elderly. Patients under the age of 65

years may also be presenting with symptomatic cardiovascular disease for the first time and therefore likely to be evaluated more extensively than older patients with existing disease. Examination of sex- and age-group-specific costs for procedures such as radiofrequency catheter ablation, atrioventricular node ablation, pacemaker insertion, surgical maze procedure, and electric cardioversion revealed that, with the exception of pacemaker insertion, mean expenditure on these interventions declined substantially with advancing age in both males and females, suggesting that they are employed less frequently in older patients, including the Medicare age group. Furthermore, the under-65 age group is covered by private, commercial insurance plans, which have higher reimbursement fees than the government-funded Medicare program. Clinical treatment of the under-65s may involve greater emphasis on rhythm control strategies such as curative AF ablation or antiarrhythmic drug therapy because the data on AF ablation are more applicable to this cohort and the results of the Atrial Fibrillation Follow-Up Investigation of Rhythm Management (AFFIRM) study²⁶ cannot be confidently extrapolated to these younger populations.

At the national level, the incremental cost burden of AF was greater in men under 65 years of age than in those over 65 years, despite the low prevalence of AF in this younger age group. In contrast, for women, the national incremental burden showed minimal variation with age. Although sex-related differences in longevity may be expected to shift the demographic burden of AF toward a lower median age among men, this is unlikely to account for the disproportionately high national cost burden projected for men in the 20- to 64-year age category. Rather, the data would suggest that, among the AF population in the United States, men of working age receive the most generous health care provision for diagnosis and treatment of this condition.

This retrospective, nonrandomized, observational study has a number of limitations. Clinical characteristics were determined using *ICD-9-CM* diagnosis codes on nondiagnostic claims, thereby potentially introducing error from coding inaccuracy. Additionally, there is scope for misclassification of expenditure across the various cost subcategories. The unexpectedly large noncardiovascular cost component of the overall incremental cost of AF may have been due to a noncardiovascular condition being inadvertently coded in the primary position for billing purposes when instead treatment was provided for a cardiovascular condition or the patient's condition was exacerbated by underlying cardiovascular morbidity. Despite good balance in baseline characteristics between the 2 patient cohorts, possible bias due to imbalance in nonidentified covariates cannot be excluded. Moreover, the closely matched comorbidity rates suggested by *ICD-9-CM* diagnostic coding may conceal clinically important differences in disease severity between the 2 cohorts. The use of certain medications for multiple purposes/indications can also complicate the comparison of costs between AF and control patients. Limitations concerning the recording and identification of mortality data should also be considered. For example, deaths occurring outside the inpatient setting were not recorded. Therefore, the mortality findings reported here are not comparable with other studies of mortality in AF patients.³

Furthermore, the study data constitute a sample of convenience and the patients and practice patterns in the constituent health care organizations may not be fully representative of the nation as a whole. Additionally, the prevalence of AF and its comorbidities may differ from that of other payer populations and the uninsured. The assumption of 3.5 million AF cases in 2010 that supported the national cost projections was based on a single study, and published AF prevalence projections for 2010 range from 2.7 to 6.7 million AF cases.^{2,27} Finally, AF- and cardiovascular-related costs were defined solely on the basis of claims with a primary diagnosis of AF or cardiovascular disease, which may result in their underestimation, and indirect costs associated with AF, such as lost productivity, were not considered in this analysis.

Conclusion

This study indicates that direct medical costs are substantially higher in AF patients than in medically matched non-AF control subjects—primarily because of higher inpatient costs (due to more frequent hospitalization/mortality) and outpatient medical costs associated with AF. Less than one-quarter of the total incremental AF costs were related primarily to AF care; of the remainder, incremental costs were equally divided between cardiovascular (non-AF-related) and noncardiovascular care. Based on current US age- and sex-specific prevalence data, the national incremental cost of AF is estimated to range from a low of \$6.0 billion (AF-related costs alone) to a high of \$26.0 billion (including other cardiovascular costs plus noncardiovascular costs).

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Disclosures

Dr Kim is a research consultant to Sanofi-Aventis and is also on the Sanofi-Aventis Speakers Bureau and Advisory Board. Dr Dalal is an employee of Sanofi-Aventis. Stephen Johnston, Dr Chu, and Kathy Schulman are employees of Thomson Reuters, which has a research consulting agreement with Sanofi-Aventis, US.

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