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ORIGINAL RESEARCH

Impact of Atrial Fibrillation Burden on Health Care Costs and Utilization

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ABSTRACT

BACKGROUND Integrating patient-specific cardiac implantable electronic device (CIED)-detected atrial fibrillation (AF) burden with measures of health care cost and utilization allows for an accurate assessment of the AF-related impact on health care use.

OBJECTIVES The goal of this study was to assess the incremental cost of device-recognized AF vs no AF; compare relative costs of paroxysmal atrial fibrillation (pAF), persistent atrial fibrillation (PeAF), and permanent atrial fibrillation (PermAF) AF; and evaluate rates and sources of health care utilization between cohorts.

METHODS Using the de-identified Optum Clinformatics U.S. claims database (2015-2020) linked with the Medtronic CareLink database, CIED patients were identified who transmitted data ≥6 months postimplantation. Annualized per-patient costs in follow-up were analyzed from insurance claims and adjusted to 2020 U.S. dollars. Costs and rates of health care utilization were compared between patients with no AF and those with device-recognized pAF, PeAF, and PermAF. Analyses were adjusted for geographical region, insurance type, CHA_2DS_2-VASc score, and implantation year.

RESULTS Of 21,391 patients (mean age 72.9 ± 10.9 years; 56.3% male) analyzed, 7,798 (36.5%) had device-recognized AF. The incremental annualized increased cost in those with AF was $12,789 ± $161,749 per patient, driven by increased rates of health care encounters, adverse clinical events associated with AF, and AF-specific interventions. Among those with AF, PeAF was associated with the highest cost, driven by increased rates of inpatient and outpatient hospitalization encounters, heart failure hospitalizations, and AF-specific interventions.

CONCLUSIONS Presence of device-recognized AF was associated with increased health care cost. Among those with AF, patients with PeAF had the highest health care costs. Mechanisms for cost differentials include both disease-specific consequences and physician-directed interventions. (J Am Coll Cardiol EP 2024;■:■-■) © 2024 by the American College of Cardiology Foundation.

Atrial fibrillation (AF) is the most common sustained arrhythmia, with increasing prevalence, and associated cost, worldwide.[1-3] To date, the majority of studies comparing health care costs between AF and non-AF cohorts have relied on administrative claims data to categorize presence of AF or have been isolated to patients in a clinical trial setting.[1,4-11] However, clinical categorization of AF

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ABBREVIATIONS AND ACRONYMS

AAD = antiarrhythmic drug

AF = atrial fibrillation

CDM = Clinformatics Data Mart

CIED = cardiac implantable electronic device

CRT-D = cardiac resynchronization therapy defibrillator

CRT-P = cardiac resynchronization therapy pacemaker

HF = heart failure

ICD = implantable cardioverter-defibrillator

ICM = implantable cardiac monitor

OAC = oral anticoagulant

MACE = major adverse cardiac event

pAF = paroxysmal atrial fibrillation

PeAF = persistent atrial fibrillation

PermAF = permanent atrial fibrillation

PPM = permanent pacemaker

diagnosis is prone to error, selection bias, and underdiagnosis of asymptomatic AF.[8,12-16] In addition, many of the prior studies on cost associated with AF were completed before the institution of current AF practice patterns and have not assessed the incremental cost associated with AF burden, a metric that has been shown to correlate strongly with multiple outcomes.[17,18] More precise characterization of the true incremental cost of, and health care utilization associated with, presence of AF and varying degrees of AF burden would provide valuable data regarding the financial impact of AF on the health care system and individual patients.

Cardiac implantable electronic devices (CIEDs) can provide long-term continuous rhythm monitoring that is highly sensitive and specific for the diagnosis of AF and characterization of AF burden.[12,19] The goals of the present analysis were to determine the following: 1) annualized cost associated with presence of device-recognized AF and differences in cost between patients with and without AF; 2) annualized cost associated with varying degrees of AF burden and differences in cost between patients with device-recognized paroxysmal atrial fibrillation (pAF), persistent atrial fibrillation (PeAF), and permanent atrial fibrillation (PermAF) AF; and 3) rates and cost of health care utilization between cohorts to provide mechanistic insight into observed differences.

METHODS

SAMPLE SELECTION. The de-identified Medtronic CareLink data warehouse and de-identified Optum Clinformatics Data Mart (CDM) claims database were used for this analysis. The Optum CDM is derived from a database of administrative health claims for members of large commercial and Medicare Advantage health plans, including approximately 19 million annual covered lives across all 50 states.

All patients in the Optum CDM (2015-2020) database with a Medtronic cardiac resynchronization therapy-pacemaker (CRT-P), cardiac resynchronization therapy-defibrillator (CRT-D), dual-chamber implantable cardioverter-defibrillator (ICD), dual-chamber permanent pacemaker (PPM), or implantable cardiac monitor (ICM) implanted between October 1, 2016, and September 30, 2019, were eligible for inclusion. Patients who had a prior CIED implanted, whose CIED did not have AF-monitoring capability, or whose device did not have ≥95% observable monitoring days and ≥95% nonmissing AF data during the 6 months postimplantation were excluded from analysis. Only those patients who had effective insurance enrollment at the time of implantation and continuous insurance enrollment for at least 6 months postimplantation were included in the final analytic cohort (Supplemental Figure 1).

DATA SET CONSTRUCTION. Study design. Heart rhythm data from the Medtronic CareLink database were evaluated and characterized in the first 6 months after device implantation (baseline period) to classify patients according to AF status. The index date for outcomes evaluation in the Optum CDM claims database (including health care cost and utilization) was set at 6 months postimplantation of the device, and patients were followed up through the end of continuous insurance eligibility, death, or a censoring date of December 31, 2020 (Supplemental Figure 2).

Classification of AF status. The presence of AF and degree of AF burden during the first 6 months postimplantation of the CIED were evaluated based on previously validated detection algorithms embedded within the CIEDs.[12-14,16] AF was defined as "present" if a device engaged automatic mode switching (dual chamber or CRT CIED) for ≥6 minutes, or if an atrial tachycardia/AF episode ≥6 minutes was detected on an ICM, in accordance with prior and ongoing studies that have used and validated similar thresholds for device-detected AF.[18,20-23] AF burden was defined as the proportion of the monitored time that a patient was in AF and was characterized based on prior literature as follows: pAF, at least 1 day with ≥6 minutes of AF but <7 days with >23 hours of AF; PeAF, at least 7 consecutive days with >23 hours of AF; and PermAF, all days with >23 hours of AF or >95% AF burden.[16]

Outcome variables. The Optum CDM claims database was linked with the de-identified Medtronic CareLink database to obtain patient-specific demographic, cost, and health care utilization data. Overall and patient-incurred health care costs, the number and cost of health care encounters at specific sites of service, inpatient hospitalization days, AF-specific interventions during follow-up (AF ablation, cardioversion, oral anticoagulant [OAC] prescription, antiarrhythmic drug [AAD] prescription, and hospitalization for AAD initiation), and adverse events associated with AF (major adverse cardiac events [MACE] and heart failure [HF] hospitalization) during follow-up were ascertained from the claims data (2016-2020) and identified by using the International

Classification of Diseases-Tenth Revision diagnosis and procedure codes, Current Procedural Terminology codes, and Healthcare Common Procedure Coding system codes.

Hospitalization for AAD initiation was defined as patients with no prior evidence of AAD in their claims history who started any AAD within 7 days before or after a hospitalization. MACE was defined as presence of: 1) myocardial infarction in a primary diagnosis position; 2) stroke in primary diagnosis position; or 3) all-cause death.[24] AF- or HF-related visits and costs were defined as claims with a primary diagnosis of AF or HF. Direct patient-incurred costs were defined as the sum of the patient deductible, copay, and coinsurance amounts as measured from the Optum CDM claims database.[25]

STUDY ENDPOINTS. The primary endpoints of the present study were the annualized health care cost associated with the presence of device-recognized AF and adjusted differences in cost between patients with and without AF. Secondary endpoints included the annualized cost and adjusted overall and patient-incurred cost differentials between patients with different degrees of AF burden and annualized cost by type of CIED implanted. To provide mechanistic insight into differences observed, further secondary endpoints included rates of health care utilization (number and cost of encounters in various health care settings and number of inpatient hospitalization days), AF-related interventions, and AF-related adverse events between groups.

STATISTICAL ANALYSIS. Patient characteristics during the baseline period were compared between cohorts by using chi-square or Fisher exact tests to compare categorical variables, and paired sample *t*-tests, Student's *t*-tests, or Mann-Whitney *U* tests to compare continuous variables as appropriate. Repeated measures analysis of variance procedures were used to test associations between demographic criteria and AF burden. Cost ratios were estimated by using a generalized linear model with a Tweedie distribution. Incidence rate ratios of health care utilization metrics were calculated from multivariable Poisson regression models. Incidence rate ratios of inpatient hospital days were estimated by using a generalized linear model with a gamma distribution. The ORs of AF-specific medications according to degree of AF burden were calculated by using logistic regression analysis. Incidence rate ratios of clinical events associated with AF were calculated by using multivariate Cox regression models. To evaluate for the incremental impact of AF and AF burden on overall health care cost and utilization, all analyses were adjusted for CHA_2DS_2-VASc score, geographical region of the patient at time of device implantation, insurance type (commercial vs Medicare Advantage), and CIED implantation year.

Numerical results are reported as mean ± SD, median (Q1-Q3), or number (%). All tests were 2-sided, and $P < 0.05$ was considered significant. Statistical computations were performed by using R version 4.0.5 (R Foundation for Statistical Computing) and SAS version 9.4 (SAS Institute, Inc).

The Institutional Review Board at Northwestern University has previously determined that the use of these data conforms to the guidelines set forth in the Declaration of Helsinki (as revised in 2013), does not constitute human research, and that no approval was indicated. In addition, the protocol was reviewed by WCG IRB and granted exemption status with The Health Insurance Portability and Accountability Act of 1996 full waiver of authorization for the use and access of protected health information under 45 CFR § 46.104(d).[4] Due to contractual arrangements between Medtronic and Optum, the raw data cannot be made available to other researchers.

RESULTS

PATIENT CHARACTERISTICS. Of 427,688 patients who had a Medtronic CIED implanted between October 1, 2015, and September 30, 2019, a total of 21,391 patients (mean age 72.9 ± 10.9 years; 56.3% male) were included in the analysis (Supplemental Figure 1, **Table 1**). Among these, 2,985 (14.0%) had a CRT-D, 765 (3.6%) had a CRT-P, 3,464 (16.2%) had an ICD, 7,415 (34.7%) had a PPM, and 6,762 (31.6%) had an ICM. The most common indications for CIED placement are listed in Supplemental Table 1, and baseline characteristics stratified according to type of CIED are listed in Supplemental Table 2.

AF DETECTION. There were 7,798 (36.5%) patients who had AF during the 6 months after CIED implantation. Those with AF were older; more likely to have Medicare Advantage insurance; and had higher rates of hypertension, mitral valve disease, HF, diabetes, pulmonary disease, vascular disease, and obstructive sleep apnea, along with a lower rate of prior stroke. The cohort of patients with AF had a higher baseline CHA_2DS_2-VASc score than those patients without AF (**Table 1**).

Of the patients with AF, 5,966 (76.5%) had pAF (average burden: 2.9% ± 8.6%), 1,145 (14.7%) had PeAF (average burden: 47.2% ± 29.9%), and 687 (8.8%) had PermAF (average burden 99.3% ± 0.7%) (**Table 1**).

TABLE 1 Demographic Characteristics According to Presence of Device-Recognized AF

	Total (N = 21,391)	No AF (n = 13,593)	AF (n = 7,798)	*P* Value	pAF (n = 5,966)	PeAF (n = 1,145)	PermAF (n = 687)	*P* Value
Age, y	72.9 ± 10.9	71.9 ± 11.4	74.8 ± 9.7	<0.001	74.22 ± 10.0	75.99 ± 8.5	77.24 ± 8.2	<0.001
Male	12,046 (56.3)	7,611 (56.0)	4,435 (56.9)	0.216	3,239 (54.3)	739 (64.5)	457 (66.5)	<0.001
Region of CIED implantation								
Midwest	4,502 (21.1)	2,817 (20.7)	1,685 (21.6)	0.127	1,244 (20.9)	277 (24.2)	164 (23.9)	0.014
Northeast	2,757 (12.9)	1,723 (12.7)	1,034 (13.3)	0.220	821 (13.8)	122 (10.7)	91 (13.2)	0.018
South	9,887 (46.3)	6,406 (47.2)	3,481 (44.7)	<0.001	2,677 (44.9)	516 (45.1)	288 (41.9)	0.325
West	4,230 (19.8)	2,638 (19.4)	1,592 (20.4)	0.073	1,220 (20.5)	228 (19.9)	144 (21.0)	0.880
Medicare Advantage	19,465 (91.0)	12,191 (89.7)	7,274 (93.3)	<0.001	5,526 (92.6)	1,086 (94.8)	662 (96.4)	<0.001
Medicaid dual-enrollment	1,028 (4.8)	690 (5.1)	338 (4.3)	0.016	256 (4.3)	54 (4.7)	28 (4.1)	0.763
CIED implantation year								
2015	635 (3.0)	410 (3.0)	225 (2.9)	0.587	158 (2.6)	40 (3.5)	27 (3.9)	0.068
2016	3,057 (14.3)	2,043 (15.0)	1,014 (13.0)	<0.001	746 (12.5)	157 (13.7)	111 (16.2)	0.020
2017	4,205 (19.7)	2,726 (20.1)	1,479 (19.0)	0.054	1,139 (19.1)	198 (17.3)	142 (20.7)	0.179
2018	7,245 (33.9)	4,544 (33.4)	2,701 (34.6)	0.072	2,077 (34.8)	400 (34.9)	224 (32.6)	0.502
2019	6,249 (29.2)	3,870 (28.5)	2,379 (30.5)	0.002	1,846 (30.9)	350 (30.6)	183 (26.6)	0.068
CIED type								
Cardiac resynchronization therapy-defibrillator	2,985 (14.0)	2,184 (16.1)	801 (10.3)	<0.001	454 (7.6)	191 (16.7)	156 (22.7)	<0.001
Cardiac resynchronization therapy-pacemaker	765 (3.6)	483 (3.6)	282 (3.6)	0.841	153 (2.6)	65 (5.7)	64 (9.3)	<0.001
Dual-chamber defibrillator	3,464 (16.2)	2,407 (17.7)	1,057 (13.6)	<0.001	741 (12.4)	188 (16.4)	128 (18.6)	<0.001
Implantable cardiac monitor	6,762 (31.6)	4,352 (32.0)	2,410 (30.9)	0.096	2,230 (37.4)	136 (11.9)	44 (6.4)	<0.001
Dual-chamber pacemaker	7,415 (34.7)	4,167 (30.7)	3,248 (41.7)	<0.001	2,388 (40.0)	565 (49.3)	295 (42.9)	<0.001
Comorbidities								
Hypertension	18,249 (86.4)	11,457 (85.3)	6,792 (88.2)	<0.001	5,151 (87.4)	1,040 (91.8)	601 (88.9)	<0.001
Coronary artery disease	10,598 (50.1)	6,705 (49.9)	3,893 (50.5)	0.391	2,845 (48.3)	668 (59.0)	380 (56.2)	<0.001
Mitral valve disease	3,822 (18.1)	2,123 (15.8)	1,699 (22.1)	<0.001	1,157 (19.6)	369 (32.6)	173 (25.6)	<0.001
Heart failure	9,381 (44.4)	5,850 (43.6)	3,531 (45.8)	0.001	2,332 (39.6)	726 (64.1)	473 (70.0)	<0.001
Cardiomyopathy	7,692 (36.4)	5,159 (38.4)	2,533 (32.9)	<0.001	1,682 (28.5)	500 (44.1)	351 (51.9)	<0.001
Diabetes	8,181 (38.7)	5,316 (39.6)	2,865 (37.2)	<0.001	2,145 (36.4)	455 (40.2)	265 (39.2)	0.03
Pulmonary disease	5,271 (24.9)	3,146 (23.4)	2,125 (27.6)	<0.001	1,583 (26.9)	348 (30.7)	194 (28.7)	0.023
Prior stroke	6,165 (29.2)	4,024 (30.0)	2,141 (27.8)	<0.001	1,703 (28.9)	291 (25.7)	147 (21.7)	<0.001
Vascular disease	3,743 (17.7)	2,221 (16.5)	1,522 (19.8)	<0.001	1,136 (19.3)	264 (23.3)	122 (18.0)	0.004
Thyroid disease	5,310 (25.1)	3,301 (24.6)	2,009 (26.1)	0.016	1,532 (26.0)	309 (27.3)	168 (24.9)	0.50
Sleep apnea	4,852 (23.0)	2,938 (21.9)	1,914 (24.9)	<0.001	1,407 (23.9)	332 (29.3)	175 (25.9)	<0.001
Prior MI	4,145 (19.6)	2,684 (20.0)	1,461 (19.0)	0.077	1,087 (18.4)	251 (22.2)	123 (18.2)	0.012
CHA_2DS_2-VASc score	4.33 (1.78)	4.27 (1.78)	4.44 (1.77)	<0.001	4.38 (1.78)	4.70 (1.73)	4.60 (1.65)	<0.001
Oral anticoagulation prescription	6,488 (30.3)	2,448 (18.0)	4,040 (51.8)	<0.001	2,802 (47.0)	789 (68.9)	449 (65.4)	<0.001

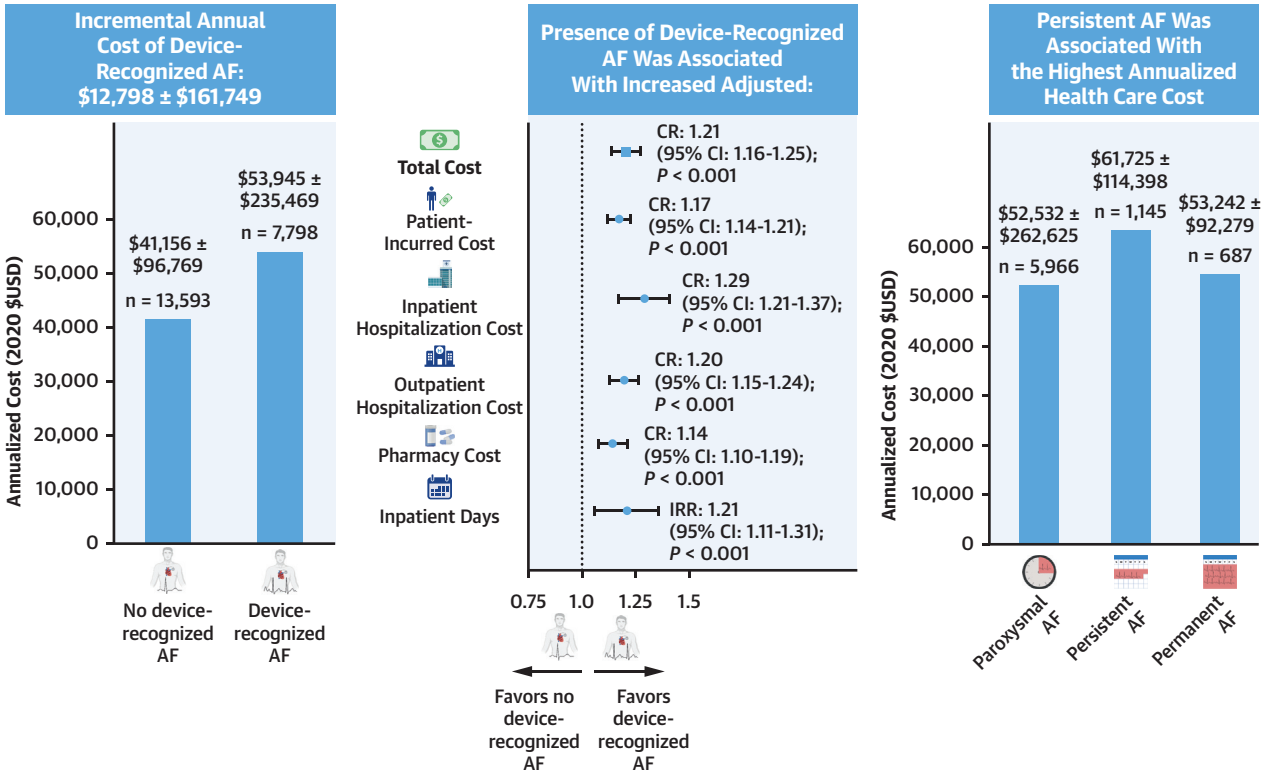
Values are mean ± SD or n (%).

AF = atrial fibrillation; CIED = cardiac implantable electronic device; MI = myocardial infarction; pAF = paroxysmal atrial fibrillation; PeAF = persistent atrial fibrillation; PermAF = permanent atrial fibrillation.

OVERALL COST ASSOCIATED WITH DEVICE-RECOGNIZED AF. The average annualized health care cost during follow-up in the overall cohort was $45,817 ± $161,861 (median: $18,166 [Q1-Q3: $7,497-$45,813]). Patients with AF ($53,945 ± $235,469; median: $21,308 [Q1-Q3: $9,148-$52,665]) had higher overall unadjusted total health care costs than those without AF ($41,156 ± $96,769; median: $16,481 [Q1-Q3: $6,741-$41,861]) (cost ratio: 1.22 [95% CI: 1.18-1.26; $P < 0.001$]). The incremental annualized cost in those with AF was $12,789 ± $161,749 per patient (Central Illustration, Figure 1). After adjustment for geographical region of the patient at time of device implantation, insurance type, implantation year, and CHA_2DS_2-VASc score, patients with AF continued to have significantly higher overall health care costs than those without AF.

The average annualized costs of pAF, PeAF, and PermAF are displayed in Figure 1. The adjusted annualized costs in patients with pAF, PeAF, and PermAF were all greater than in patients with no AF (for all, $P < 0.001$). Adjusted analysis further showed that the annualized cost of PeAF was higher than that of pAF and PermAF and that the annualized cost of PermAF was higher than that of pAF (Central Illustration, Figure 1).

CENTRAL ILLUSTRATION Impact of AF Burden on Health Care Costs and Utilization



Impact of Persistent AF, Adjusted for Comorbidities

Total Cost
CR vs pAF: 1.21 (95% CI: 1.16-1.25); P < 0.001
CR vs PermAF: 1.15 (95% CI: 1.03-1.29); P = 0.01

Inpatient hospitalization encounters
IRR vs pAF: 1.32 (95% CI: 1.25-1.40); P < 0.001
IRR vs PermAF: 1.12 (95% CI: 1.03-1.22); P = 0.01

Outpatient hospitalization encounters
IRR vs pAF: 1.18 (95% CI: 1.16-1.20); P < 0.001
IRR vs PermAF: 1.03 (95% CI: 1.002-1.05); P = 0.03

Heart failure hospitalization
IRR vs pAF: 1.77 (95% CI: 1.49-2.11); P < 0.001
IRR vs PermAF: 1.41 (95% CI: 1.15-1.73); P = 0.001

Rates of AF Interventions

Antiarrhythmic drug prescription
OR vs pAF: 1.28 (95% CI: 1.11-1.46); P < 0.001
OR vs PermAF: 3.13 (95% CI: 2.49-3.92); P < 0.001

Cardioversion
OR vs pAF: 2.60 (95% CI: 2.16-3.13); P < 0.001
OR vs PermAF: 3.56 (95% CI: 2.49-3.92); P < 0.001

Hospitalization for AAD initiation
OR vs pAF: 1.54 (95% CI: 1.21-1.95); P < 0.001
OR vs PermAF: 2.79 (95% CI: 1.72-4.52); P < 0.001

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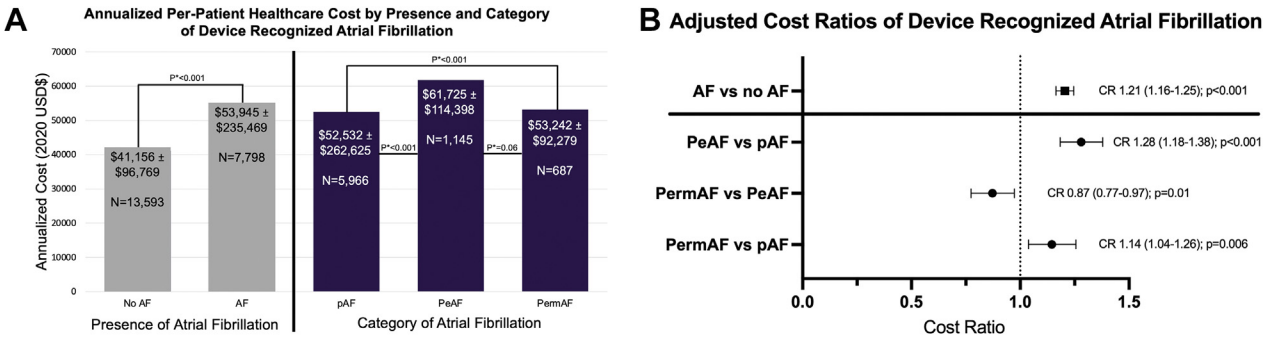
AF = atrial fibrillation; CR = cost ratio; IRR = incidence rate ratio; pAF = paroxysmal atrial fibrillation; PermAF = permanent atrial fibrillation.

FIGURE 1 Annualized Per-Patient Health Care Cost According to Presence and Category of Device-Recognized AF

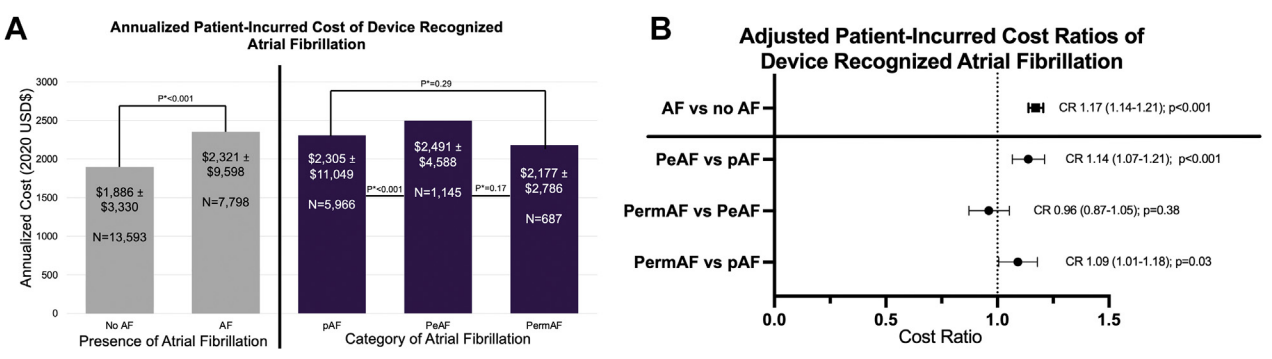


Presence, compared with absence, of device-recognized atrial fibrillation (AF) was associated with increased absolute (A) and adjusted (B) annualized health care costs. The incremental annualized cost in those with AF was $12,789 ± $161,749 per patient. As shown in B, among those with AF, persistent AF (PeAF) was associated with the highest adjusted costs. CR = cost ratio; pAF = paroxysmal atrial fibrillation; PermAF = permanent atrial fibrillation; USD = U.S. dollars.

Cost incurred by patients. Patients with AF had higher annualized patient-incurred health care costs than those without AF (**Central Illustration**, **Figure 2**). The annual incremental patient-incurred cost in those with AF was $290 ± $4,126 per patient. Patients with AF, pAF, PeAF, and PermAF all had higher patient-incurred adjusted health care costs than those without AF (for all, $P < 0.001$). Among those with AF, patients with PeAF and PermAF had higher adjusted patient-incurred costs than patients with pAF; however, there was no statistically significant difference in costs between patients with PeAF and PermAF (**Figure 2**).

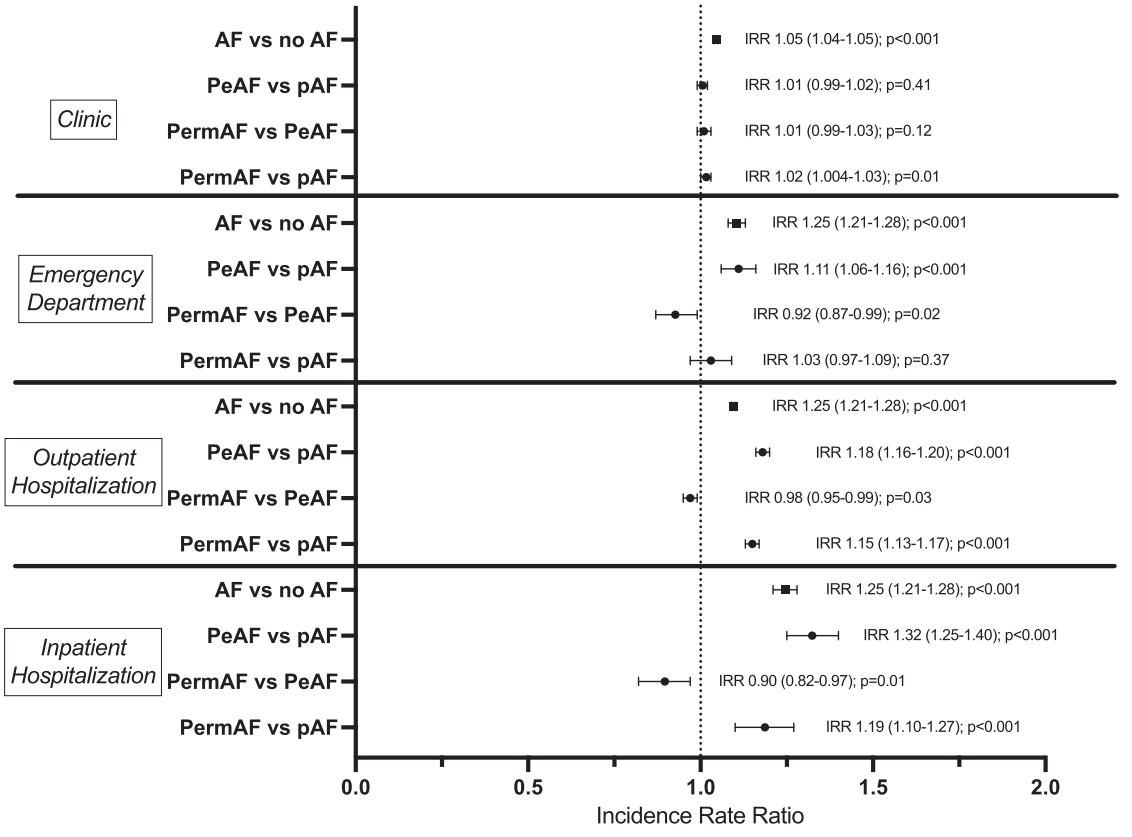
Cost by device type. The annualized costs according to device type and AF burden category are listed in Supplemental Table 3. In all subcohorts based on type of CIED implanted, patients with AF had higher adjusted annualized costs than those without AF (Supplemental Figure 3). Within the cohort of patients with a PPM, patients with PeAF or PermAF had higher annualized adjusted costs than those with pAF. There were no differences in costs between PPM patients with PermAF and PeAF. Among patients with CRT-Ds and ICMs, those with PeAF had higher annualized costs than those with pAF. No differences were observed in annualized costs between CRT-D or ICM patients with PermAF and pAF, or PermAF and PeAF. There were no differences in adjusted annualized health care costs according to AF burden category among the subcohorts with CRT-P or ICDs.

FIGURE 2 Annualized Per-Patient Patient-Incurred Health Care Cost According to Presence and Category of Device-Recognized AF



Presence, compared with absence, of device-recognized AF was associated with increased unadjusted (A) and adjusted (B) patient-incurred health care costs, with an annual incremental patient-incurred cost of $290 ± $4,126 per patient. As shown in B, presence of PeAF and PermAF were associated with higher annual patient-incurred costs than pAF. Abbreviations as in **Figure 1**.

FIGURE 3 Adjusted IRRs of Health Care Encounters According to Site of Service



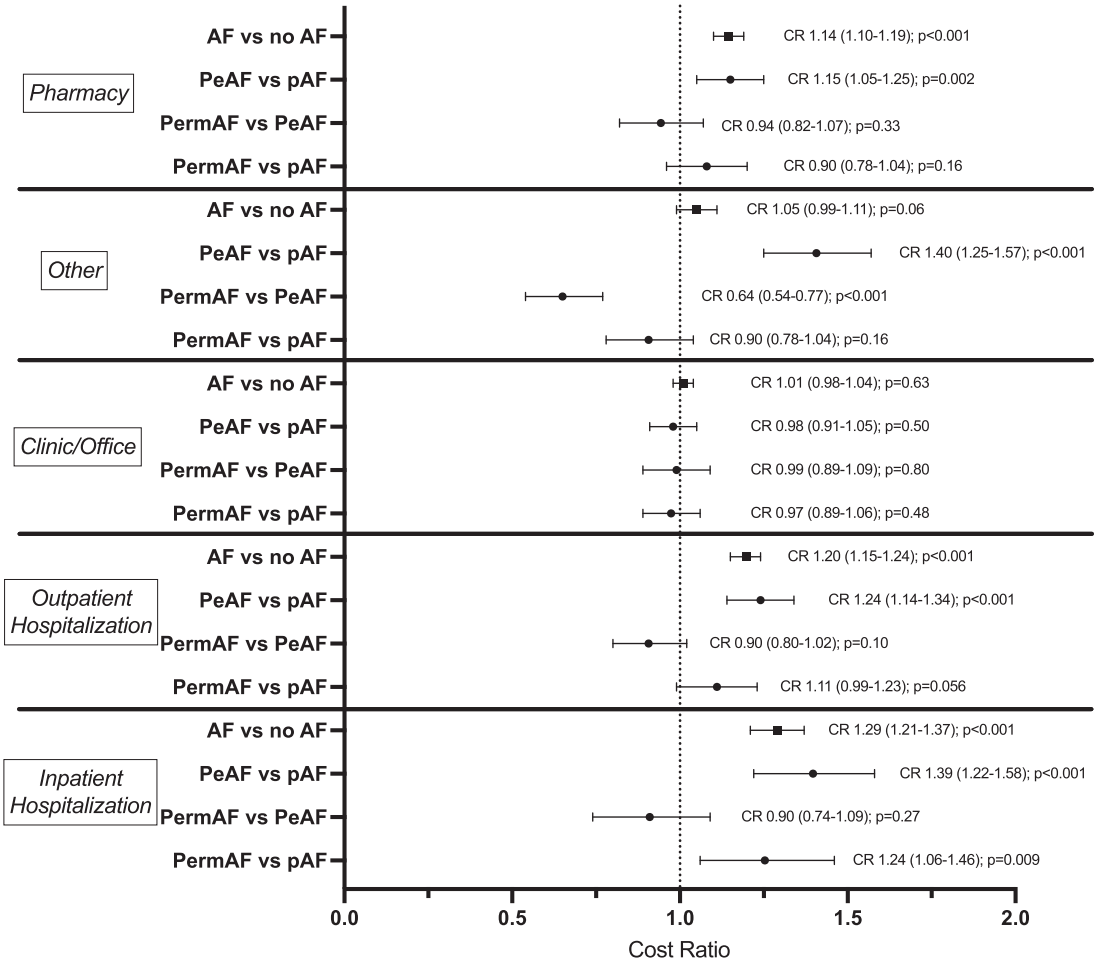
Presence, compared with absence, of device-recognized AF was associated with increased adjusted rates of clinic, emergency department, and inpatient/outpatient hospitalization encounters. Among patients with AF, those with PeAF had a higher adjusted rate of emergency department, outpatient hospitalization, and inpatient hospitalization encounters. IRR = incidence rate ratio; other abbreviations as in Figure 1.

HEALTH CARE UTILIZATION ASSOCIATED WITH DEVICE-RECOGNIZED AF. Health care encounters. In the overall cohort, patients had an average of 0.74 ± 3.7 inpatient hospitalizations, 8.1 ± 15.4 outpatient hospitalizations, 1.3 ± 6.5 emergency department visits, and 16.7 ± 49.7 clinic encounters per year. Presence of AF, pAF, PeAF, and PermAF were each associated with increased adjusted incidence rate ratios of inpatient hospitalizations, outpatient hospitalizations, emergency department visits, and clinic encounters compared with no AF (for all, $P < 0.001$). Among those with AF, patients with PeAF had higher adjusted incidence rate ratios of inpatient hospitalizations, outpatient hospitalizations, and emergency department visits than patients with pAF and PermAF (**Central Illustration**, **Figure 3**).

Inpatient hospitalization days. Patients in the entire cohort averaged 8.7 ± 55.1 inpatient hospitalization days per year. Presence of AF, PeAF, and PermAF were each associated with an increased adjusted number of inpatient hospitalization days per year compared with no AF (for all, $P < 0.001$). There was no difference in the adjusted number of annualized inpatient hospitalization days between patients with pAF and no AF (incidence RR: 1.06 [95% CI: 0.99-1.13]; $P = 0.098$). Patients with PeAF had a higher number of annualized inpatient hospitalization days than patients with pAF, but there was no difference between the number of annualized inpatient hospitalization days between patients with PeAF and PermAF (Supplemental Figure 4).

Cost at sites of service. Annualized costs according to site of service and category of AF burden are listed in Supplemental Table 4. Presence of AF, pAF, PeAF, and PermAF were each associated with increased adjusted inpatient hospitalization, outpatient hospitalization, and pharmacy costs,

FIGURE 4 Adjusted CRs According to Site of Service



Presence, compared with absence, of device-recognized AF was associated with increased adjusted costs in the pharmacy, outpatient hospitalization, and inpatient hospitalization settings. Among patients with AF, those with PeAF had higher adjusted pharmacy, outpatient hospitalization, and inpatient hospitalization costs than those with pAF. Abbreviations as in Figure 1.

compared with no AF (for all, $P < 0.001$). Relative to patients with pAF, those with PeAF had higher annualized inpatient hospitalization, outpatient hospitalization, and outpatient pharmacy costs. Although there was a trend toward higher annualized costs for patients with PeAF compared with those with PermAF at these locations, the observed difference did not reach statistical significance (Figure 4).

Rhythm control and stroke prevention interventions. During follow-up, 4.5%, 5.2%, and 5.1% of the patients with AF underwent an ablation, cardioversion, or admission for initiation of a new AAD, respectively. In addition, there were 2,193 (28.1%) patients who had a prescription for an AAD and 4,609 (59.1%) patients with a prescription for an OAC during follow-up. In total, the mean annualized cost of AF-specific treatments was $8,316, which accounts for 65.03% of the incremental increased cost attributed to AF in the cohort.

The rates of ablations, cardioversions, hospitalizations for AAD initiation, and use of AADs and OAC according to degree of AF burden are listed in Table 2. Patients with PeAF had a higher adjusted annualized rate of cardioversions, hospitalizations for new AAD initiation, and AAD prescriptions than patients with pAF and PermAF. Those with PeAF also had a higher adjusted rate of OAC prescription than patients with pAF and a higher adjusted rate of ablations than those with PermAF. Patients with PermAF had a lower

adjusted rate of ablation, hospitalization for new AAD initiation, and AAD prescription but a higher rate of OAC prescription than those with pAF (Central Illustration, Figure 5).

The mean annualized costs of AF-specific treatments among patients with pAF, PeAF, and PermAF were $8,892, $7,488, and $4,819, respectively. The cost of AF-specific treatments accounted for 78.2% of the incremental cost associated with pAF, 36.4% of the incremental cost associated with PeAF, and 39.9% of the incremental cost associated with PermAF.

Rates of and cost associated with MACE and HF hospitalization. In the entire cohort, the annual incidence rates of MACE and HF hospitalizations during follow-up were 16.2% and 7.7%, respectively. Patients with AF had a higher adjusted rate of MACE and HF hospitalizations than those without AF. Among those with AF, patients with PeAF had higher incidence rates of HF hospitalization than those with pAF and PermAF (Central Illustration, Figure 6). Although the incidence rate of MACE was higher among patients with PeAF compared with those with pAF, rates were similar between patients with PeAF and PermAF (Figure 6). There was no difference in annualized cost per HF hospitalization between patients with and without AF (AF: $28,527 ± $70,394; no AF: $26,521 ± 61,858; adjusted cost ratio: 1.09 [95% CI: 0.93-1.28]; $P = 0.29$).

TABLE 2 AF-Specific Treatments During Follow-Up

	AF (n = 7,798)	pAF (n = 5,966)	PeAF (n = 1,145)	PermAF (n = 687)
AF ablation	348 (4.5)	272 (4.6)	61 (5.3)	15 (2.2)
Cardioversion	406 (5.2)	261 (4.4)	123 (10.7)	22 (3.2)
Hospitalization for new antiarrhythmic drug initiation	394 (5.1)	287 (4.8)	87 (7.6)	20 (2.9)
Antiarrhythmic drug prescription	2193 (28.1)	1724 (28.9)	392 (34.2)	77 (11.2)
Oral anticoagulation prescription	4609 (59.1)	3318 (55.6)	808 (70.6)	483 (70.3)

Values are n (%).
Abbreviations as in Table 1.

DISCUSSION

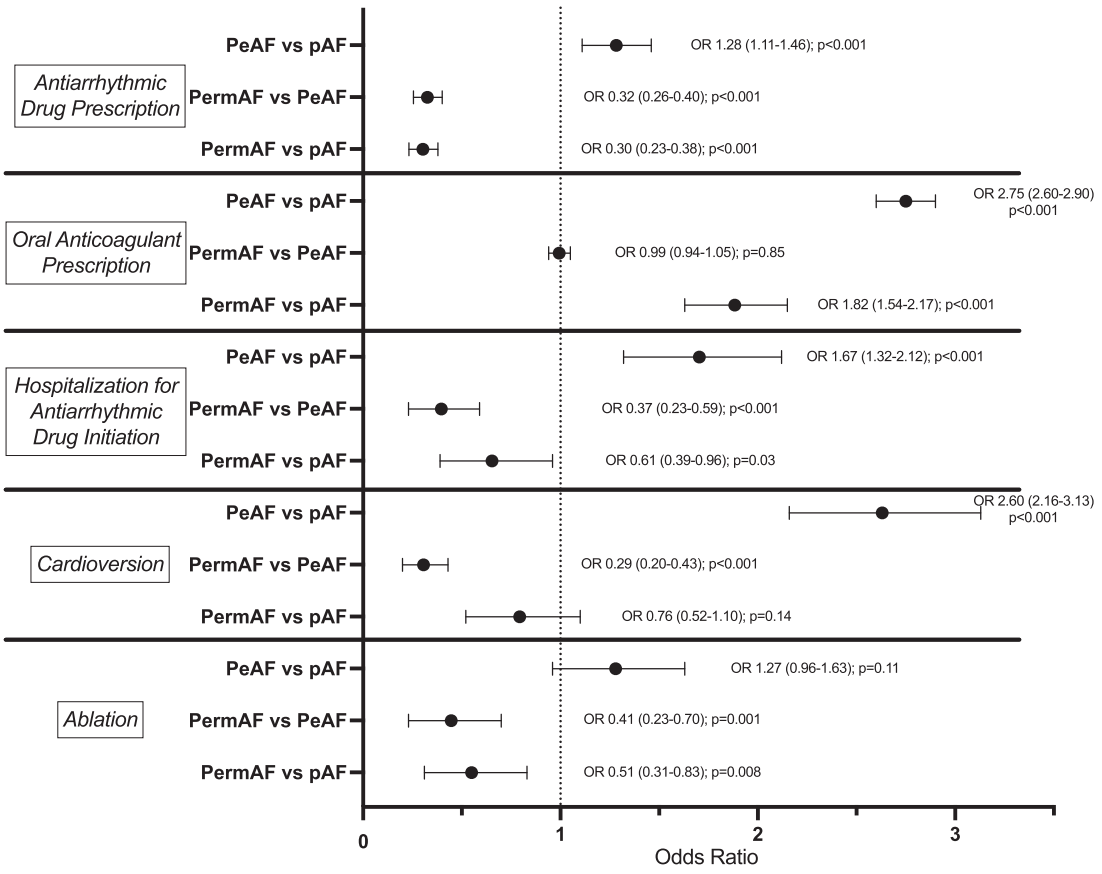
DEGREE OF INCREASED COST ASSOCIATED WITH DEVICE-RECOGNIZED AF AND AF BURDEN. The present study evaluated the degree and mechanisms of increased cost associated with device-recognized AF in a large national sample of patients with CIEDs. The incremental annualized increased cost in those with AF was $12,789 ± $161,749 per patient compared to those without AF. After adjustment for demographic and clinical covariates, presence of device-recognized AF remained associated with greater health care costs compared with no AF. These results were durable irrespective of type of CIED implanted.

Prior analyses have attributed variable costs to AF diagnosis, ranging from $4,000 to $27,896.[1,7,10,11,26,27] However, these studies relied on clinical diagnosis of AF, rather than AF detected by using high-fidelity implantable devices. Clinical diagnosis of AF may miss asymptomatic and pAF episodes that have a significant impact on a patient's health and subsequent health care utilization. By using device-recognized AF to categorize AF, the present study allows for a more precise estimation of the cost and health care utilization associated with true presence of arrhythmia. Furthermore, methods of matching patients with and without AF were variable in prior studies and oftentimes did not include common medical comorbidities. By controlling for CHA_2DS_2-VASc score, which encompasses many of the comorbidities and disease-modifying factors prevalent in patients with AF, the present analysis provides a comprehensive estimation of the independent impact of AF on health care cost.[28]

The results of our study suggest higher overall health care costs among patients with AF than another cost analysis of AF in CIED patients, all of whom had a Medicare claims diagnosis of pAF.[29] Although this prior study found that higher burdens of pAF were associated with increased health care costs, the present analysis differs in a number of fundamental ways. Specifically, the present study provides additional data on the incremental cost of AF among a large cohort of patients and confirms that presence of AF is associated with increased both total and direct patient-incurred health care costs. In addition, the present study specifically assesses patients with PeAF and PermAF, rather than just pAF. Because PeAF and PermAF are considered unique disease processes, with different risk factors, associated conditions, and treatment strategies, defining the increased cost associated with PeAF has significant implications.[30,31]

HEALTH CARE UTILIZATION. Health care encounters. The rates and associated costs of health care encounters according to site of service among patients with and without AF provide valuable mechanistic data into the observed overall cost differentials. Indeed, results from the present analysis add to existing data on mechanisms of increased cost associated with AF diagnosis by showing that the increased cost associated with AF is driven by higher annualized costs in the inpatient, outpatient, and pharmacy settings, and a greater number of annualized inpatient hospitalization days.[1,5,8,9,32]

FIGURE 5 Adjusted ORs of Interventions Among Patients With Device-Recognized AF



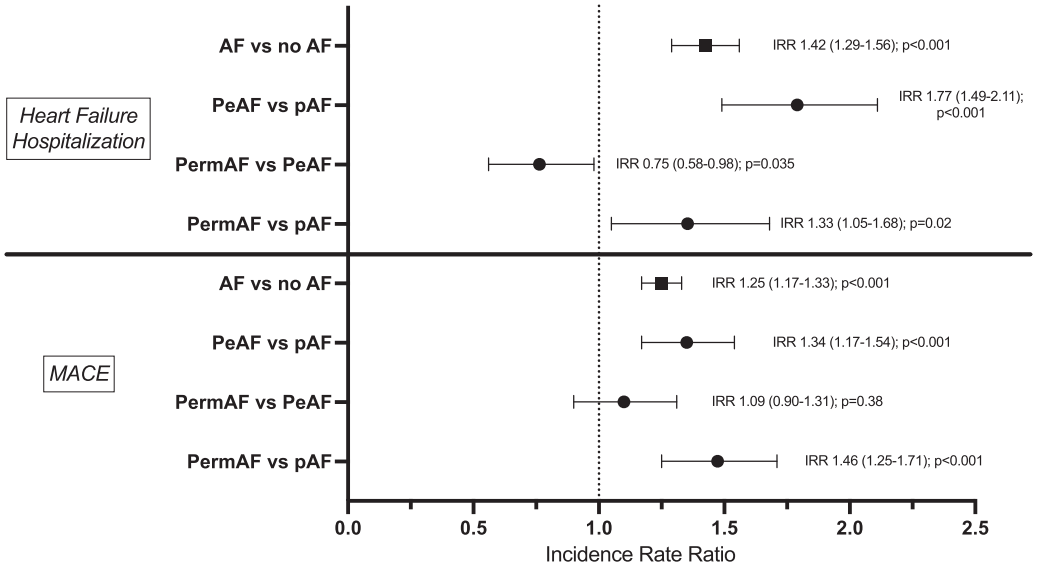
Among those with device-recognized AF, patients with PeAF had a higher adjusted rate of cardioversion and hospitalization for antiarrhythmic drug initiation than patients with pAF and PermAF. In addition, patients with PeAF also had higher adjusted rates of ablation and antiarrhythmic drug prescription than those with PermAF. Abbreviations as in Figure 1.

Specifically, among patients with AF, our results show that patients with PeAF had a higher number of annualized inpatient hospitalization, outpatient hospitalization, and emergency department encounters than those with pAF and PermAF. These findings align with those from the prospective CIRCA-DOSE (Cryoballoon vs Irrigated Radiofrequency Catheter Ablation: Double Short vs Standard Exposure Duration) trial, which found that significant reduction in AF burden after ablation led to substantial decreases in emergency department visits and inpatient hospitalizations among patients with continuous rhythm monitors.[33]

Clinical endpoints. To date, few studies have evaluated the impact of AF-related clinical events on total health care cost and utilization among patients with and without AF. Our results show that patients with AF had a higher adjusted rate of MACE and HF hospitalizations compared to patients without AF. Among those with AF, patients with PeAF also had a higher rate of HF hospitalization than those with pAF and PermAF and a higher rate of MACE than those with pAF. Taken together with the cost differentials observed, these findings suggest that the downstream disease-specific consequences of AF significantly contribute to the increased health care costs incurred by patients with AF (compared to those without AF) or PeAF (compared to those with pAF or PermAF).

AF-specific physician-driven interventions. To the best of our knowledge, the present study is the first to report different rates of AF-specific interventions among cohorts with pAF, PeAF, and PermAF.[29] As expected, among those with AF, patients with PeAF had a higher adjusted rate of cardioversions and hospitalizations for AAD initiation than patients with pAF and PermAF. Furthermore,

FIGURE 6 Adjusted Rate Ratios of AF-Related Adverse Events According to Category of Device-Recognized AF



Patients with device-recognized AF had a higher adjusted rate of major adverse cardiac events (MACE) and heart failure hospitalizations than those without AF. Among those with AF, patients with PeAF had higher incidence rates of heart failure hospitalization than those with pAF and PermAF. The incidence rate of MACE was higher among patients with PeAF compared with those with pAF. Abbreviations as in Figures 1 and 3.

patients with PeAF also had higher adjusted rates of ablations and AAD prescriptions than those with PermAF, another anticipated finding, as rhythm control interventions are often abandoned in patients with PermAF. Despite patients with PeAF having increased rates of AF-specific, physician-driven interventions compared to those with pAF and PermAF, the cost of those AF-specific interventions accounted for the greatest proportion of incremental costs in patients with pAF. This is likely due to the cost of other downstream clinical endpoints that were more prevalent in patients with PeAF.

In sum, results from the present analysis suggest that presence of AF, and specifically PeAF, is associated with increased cost and health care utilization among patients with CIEDs. The increased system and individual costs associated with PeAF speak to the incremental financial impact of increased AF burden, and are hypothesis generating to suggest a potential monetary benefit of strategies to prevent AF onset and specifically PeAF. Furthermore, although prior research shows that thresholds of sustained AF duration >24 hours are necessary to correlate with clinical endpoints such as stroke, the present results, indicating increased health care cost and utilization among patients with pAF compared with no AF, suggest that even low burdens of AF may be associated with deleterious health outcomes and increased health care utilization.[17] Finally, recent data suggest that anticoagulation for device-recognized atrial high rate episodes ≥6 minutes to 24 hours, in the absence of a clinical diagnosis for AF, decreases the rate of stroke, and increases the risk of major bleeding.[23] Taken together with the present results, which show that episodes of device-recognized AF are associated with increased health care costs (which are partially driven by physician-driven interventions, including OAC prescription), further large-scale analyses are necessary to evaluate the cost efficacy of AF-specific, physician-driven interventions.

STUDY LIMITATIONS. The generalizability of the present study may be limited by exclusive enrollment of patients with CIEDs, as this represents a sample with a unique demographic and comorbidity profile. Specifically, our sample had a higher percentage of patients with HF than prior cohorts evaluated for a similar purpose, which may partially explain variability in results between studies. Because AF was defined as any presence of AF during the 6 months after device implantation, AF-specific interventions before the monitoring period may have affected costs and health care utilization in follow-up.

Furthermore, because AF was defined as "present" if a dual-chamber device engaged automatic mode switching ≥6 minutes, or if AF was detected on an ICM for ≥6 minutes, some short episodes of CIED mode switching or ICM-detected AF may be due to atrial tachycardia and would therefore be miscategorized as AF. However, prior studies have shown that ≥6 minutes of device-recognized AF is a reliable threshold for defining AF,[20-23] and even among patients with pAF in the present study, the average burden of AF greatly exceeded 6 consecutive minutes.

Despite the covariates in the adjusted model encompassing many of the relevant clinical and demographic variables that could bias results, there are potentially additional variables excluded from our model that could affect findings.[32,34-40] It is possible that not accounting for "crossover days" may have miscategorized patients with PeAF or PermAF; however, given the large sample size, the authors do not expect these rare cases to significantly affect results. Finally, PermAF was defined as all days with >23 hours of AF or >95% AF burden. However, in clinical practice, permanent AF is a diagnosis which indicates that rhythm control strategies have been abandoned, a designation that can only be made by a treating physician. Indeed, there was likely a subcohort of patients with high enough degrees of AF burden to qualify them as "permanent" but were not categorized as permanent by their physicians, and accordingly continued to undergo AF rhythm control strategies.

CONCLUSIONS

In the present study of 21,391 patients with CIEDs, presence, compared to absence, of device-recognized AF was associated with significantly higher health care costs. Among those with AF, patients with PeAF had the highest degrees of health care cost and utilization. Cost differences were largely driven by differential rates of hospitalization, inpatient length of stay, emergency department encounters, adverse clinical events associated with AF, and AF-specific interventions between cohorts.

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PERSPECTIVES

COMPETENCY IN SYSTEMS-BASED PRACTICE 1: Presence, compared with absence, of device-recognized AF is associated with increased annualized total and patient-incurred health care cost. Cost differentials are driven by increased rates of health care encounters, adverse clinical events associated with AF, and AF-specific interventions.

COMPETENCY IN SYSTEMS-BASED PRACTICE 2: Among those with device-recognized AF, patients with PeAF have the highest health care costs, driven by increased rates of inpatient and outpatient hospitalization encounters, HF hospitalizations, and AF-specific interventions.

COMPETENCE IN PATIENT CARE AND PROCEDURAL SKILLS: Preventing the onset of AF, and specifically PeAF, may reduce total and patient-incurred health care costs.

TRANSLATIONAL OUTLOOK: The present study, which uses highly sensitive implantable devices to define presence of AF and degree of AF burden, found that: 1) presence of AF is associated with increased health care costs and utilization; and 2) among those with device-recognized AF, PeAF is associated with the highest cost and health care utilization. Further studies are needed to assess the impact of AF prevention and treatment strategies on overall health care utilization using high-fidelity methods of AF burden detection.

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APPENDIX For supplemental figures and tables, please see the online version of this paper.