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Original Article

Sex Differences in High-Cost Users of Healthcare for Atrial Fibrillation

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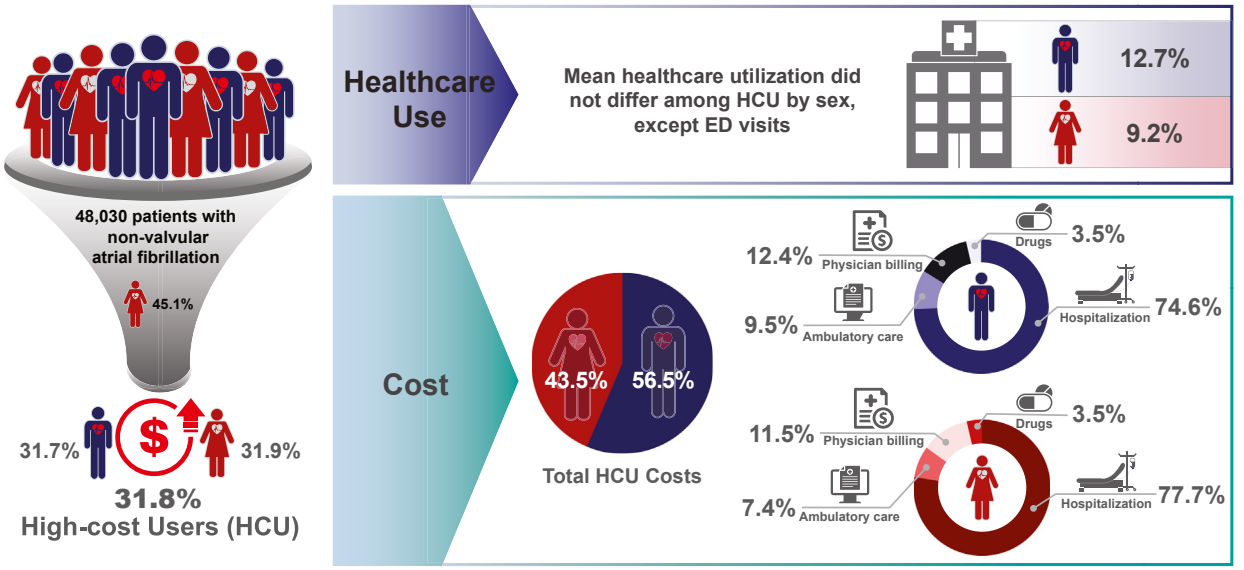

ABSTRACT

Background: Healthcare resource use for atrial fibrillation (AF) is high, but it may not be equivalent across all patients. We examined whether sex differences exist for AF high-cost users (HCUs), who account for the top 10% of total acute care costs.

Methods: All patients aged ≥ 20 years who presented to the emergency department (ED) or were hospitalized with AF were identified in Alberta, Canada, between 2011 and 2015. The cohort was categorized by sex into HCUs and non-HCUs. Healthcare utilization was defined as ED, hospital, and physician visits, and costs included those for hospitalization, ambulatory care, physician billing, and drugs. All costs were inflated to 2022 Canadian dollars (CAD$).

RÉSUMÉ

Contexte : L'utilisation des ressources en santé est élevée pour la fibrillation auriculaire (FA), mais elle n'est pas forcément équivalente pour tous les patients. Nous avons examiné s'il existait des différences entre les sexes pour ce qui est des cas très coûteux de FA, qui représentent les 10 % supérieurs des coûts totaux de soins de courte durée.

Méthodologie : Tous les patients âgés de 20 ans et plus qui se sont présentés au service des urgences ou qui ont été hospitalisés pour une FA ont été répertoriés en Alberta, au Canada, entre 2011 et 2015. La cohorte a été divisée par sexe en fonction des utilisateurs très coûteux et des autres utilisateurs. L'utilisation des soins de santé était définie

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Results: Among 48,030 AF patients, 45.1% were female. Of these, 31.8% were HCUs, and the proportions of female and male patients were equal (31.9% vs 31.7%). Female HCUs were older, more likely to have hypertension and heart failure, and had a higher stroke risk than male HCUs. Mean healthcare utilization did not differ among HCUs by sex, except for number of ED visits, which was higher in male patients (12.7% vs 9.2%, $P < 0.0001$). Overall, HCUs accounted for 65.8% of the total costs (CAD$3.4 billion). Almost half of total HCU costs were attributable to female HCUs (CAD$966.1 million). Significant differences were present in the distributions of HCU-related costs (male patients: 74.6% hospitalization, 9.5% ambulatory care, 12.4% physician billing, 3.5% drugs; female patients: 77.7% hospitalization, 7.4% ambulatory care, 11.5% physician billing, 3.5% drugs, $P < 0.0001$).

Conclusions: Despite having a lower AF prevalence, female patients represent an equal proportion of HCUs, and account for almost half the total HCU costs. Interventions targeted at reducing the number of AF HCU are needed, particularly for female patients.

Résultats : Parmi les 48 030 patients atteints de FA, 45,1 % étaient des femmes et 31,8 % étaient des utilisateurs très coûteux, en proportions égales entre les femmes et les hommes (31,9 % *vs* 31,7 %). Parmi les utilisateurs très coûteux, les femmes étaient plus âgées, plus susceptibles de présenter de l'hypertension et une insuffisance cardiaque, et leur risque d'AVC était plus élevé comparativement aux hommes. L'utilisation moyenne des soins de santé n'affichait pas de différences chez les utilisateurs très coûteux selon le sexe, à l'exception des consultations aux urgences, qui étaient plus fréquentes chez les hommes (12,7 % *vs* 9,2 %, $p < 0{,}0001$). Dans l'ensemble, les utilisateurs très coûteux représentaient 65,8 % des coûts totaux, qui étaient de 3,4 milliards de dollars canadiens. Les femmes représentaient par ailleurs près de la moitié du total des utilisations très coûteuses (966,1 millions de dollars canadiens). Des différences significatives ont été observées quant à la répartition des coûts liés aux utilisateurs très coûteux (hommes : hospitalisations [74,6 %], soins ambulatoires [9,5 %], honoraires des médecins [12,4 %], médicaments [3,5 %]; femmes : hospitalisations [77,7 %], soins ambulatoires [7,4 %], honoraires des médecins [11,5 %], médicaments [3,5 %], $p < 0{,}0001$).

Conclusions : Bien que la FA soit moins fréquente chez les femmes que chez les hommes, celles-ci représentent une proportion tout aussi importante des utilisations très coûteuses et comptent pour presque la moitié des coûts totaux attribuables aux utilisateurs très coûteux. Des interventions visant à réduire les utilisations très coûteuses pour la FA sont donc nécessaires, particulièrement chez les femmes.

Lay Summary

Atrial fibrillation, the most common type of irregular heartbeat, is costly to the healthcare system and may vary by sex. Between 2011 and 2015, we examined sex differences in the use of healthcare services, with a focus on high-cost users, who account for the top 10% of total healthcare costs. Even though female patients made up less than half the cases of atrial fibrillation, they were an equal proportion of high-cost users, and accounted for almost half of total costs.

A widely recognized finding is that a small proportion of patients account for a disproportionate amount of healthcare spending in developed countries. In any given year, patients who account for the top 1% of healthcare spending also account for 25%-40% of total healthcare expenditure in North America.[1,2] A recent analysis found that cardiovascular disease was prevalent in 75% of high-cost users (HCUs) and accounted for an estimated 80% of total HCU costs.[3] Atrial fibrillation (AF), the most common sustained cardiac rhythm disorder,[4] is responsible for a considerable amount of healthcare utilization and cost.[5-11]

Prior studies have demonstrated that female patients with AF experience more symptoms, and more functional impairment,[12-17] and are more likely to suffer from AF-related clinical consequences compared to male patients,[18] a difference that may explain, in part, female patients' higher rates of acute care visits.[19,20] The extent to which AF occurs among HCUs, particularly with respect to sex, and their impact on healthcare resource use, is unknown. Addressing this evidence gap is important in targeted management and resource allocation efforts.

Accordingly, we used the Canadian Institute for Health Information (CIHI) "dynamic cohort of complex, high system users" (defined as the top 10% of total acute care costs) to examine sex differences in the prevalence, clinical profiles, healthcare utilization (emergency department [ED], hospital, physician office visits), and cost (hospitalization, ambulatory care, physician billing, drugs) for AF patients who met the CIHI criteria for being an HCU in Alberta, Canada.

Methods

Our population-level cohort from the province of Alberta, Canada consisted of all patients aged $\geq$ 20 years with an ED or hospitalization record with AF, using the International Classification of Diseases Tenth Revision (ICD-10) code I48 in any diagnosis field, between April 1, 2011 and March 31, 2015. Patients with valvular AF, defined as those with aortic, tricuspid, or pulmonary valve disease or valve procedures

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See page 414 for disclosure information.

(administrative codes are given in Supplemental Table S1) were excluded.

This cohort was further categorized into HCU and non-HCU patients. The HCU patients were identified using the CIHI "dynamic cohort" HCU flag, which consists of patients for fiscal years (FYs) 2011-2012 to FY 2014-2015 (April 1, 2011 to March 31, 2015) whose cumulative annual acute care hospitalization costs during a specific FY were in the top 10% for the province.[3]

We linked the following Alberta Ministry of Health administrative databases for the AF cohort for FY 2011-2012 to FY 2014-2015: (i) Discharge Abstract Database (DAD) of all acute care hospitalizations, which includes the primary or most responsible diagnosis and up to 24 secondary diagnoses; (ii) National Ambulatory Care Reporting System (NACRS) of all ambulatory care, including ED visits, hospital-based specialist outpatient visits, and day procedures; (iii) the Practitioner Claims Database, which captures physician billing, including fee-for-service and shadow-billed claims; (iv) Alberta Blue Cross (ABC) and Pharmaceutical Information Network (PIN) for pharmaceutical costs and dispenses, respectively; and (v) the Population Registry, which captures demographic and geographic information.

We identified comorbidities (heart failure, hypertension, diabetes, stroke and/or transient ischemic attack, peripheral artery disease [PAD], coronary artery disease [CAD], myocardial infarction [MI], renal disease, dementia, cancer, anemia, CHA_2DS_2-VASc score (**C**ongestive Heart Failure, **H**ypertension, **A**ge [$\geq$ 75 Years] [doubled], **D**iabetes Mellitus, **S**troke [doubled], **V**ascular Disease, **A**ge [65-74] Years, **S**ex **C**ategory [Female]), and $CHADS_2$ score (**C**ongestive Heart Failure, **H**ypertension, **A**ge $\geq$ 75, **D**iabetes, and Prior **S**troke/Transient Ischemic Attack [doubled]) as present using validated ICD codes, if they were documented in any of the aforementioned databases during the 5 years prior to incident AF diagnosis using validated ICD, ninth revision (ICD-9) and ICD-10 codes. [21] The following management strategies were assessed for each patient during the study period: oral anticoagulant use (oral anticoagulant [OAC], warfarin, apixaban, dabigatran, edoxaban, and rivaroxaban); rhythm control (propafenone, flecainide, procainamide, sotalol, dronedarone, disopyramide, amiodarone, and catheter ablation); rate control (verapamil, diltiazem, digoxin, and beta-blockers); and catheter ablation and cardioversion (Supplemental Table S2).

Healthcare utilization was defined as visits to the hospital, ED, and physician office over the study period, and costs included those for hospitalization, ambulatory care, drugs, and physician billing. For hospitalization and ambulatory care settings, we assessed the cost per record by multiplying the Alberta provincial average "cost of a standard hospital stay" by the resource intensity weight (RIW) assigned to that record. Alberta Health calculated and assigned inpatient RIWs using CIHI's case mix groups plus (CMG+) grouping methodology, and ambulatory RIWs using CIHI's Comprehensive Ambulatory Classification System.[22] The data on cost of a standard hospital stay for the years of the study are available from the CIHI.[23,24] We assigned drug price data to the PIN by deriving the median cost per unit by drug identification number and FY from the Alberta Blue Cross claims data. Our method assigns costs to 91% of the drug identification numbers in the PIN. Unit costs of dronedarone were extracted from published literature. The cost per patient record was determined by multiplying the price per drug unit by the amount dispensed. For physician billing, the practitioner claims dataset was used to identify the amount paid for fee-for-service physicians, and for non-fee-for-service care, an estimate of the value of shadow billing claims were used. All costs were inflated to 2022 Canadian dollars (CAD$).

Descriptive statistics are reported as means and standard deviations for continuous variables, and as counts and proportions for categorical variables. Comparisons between HCU and non-HCU groups by sex were conducted using the χ^2 test for categorical variables, and *t*-tests for continuous variables. For comparison of average healthcare visits between groups, a 2-sample test was used, under a negative binomial distribution for visits. Total healthcare costs were estimated as the sum of the costs identified due to hospitalization, ambulatory care, physician billing, and drug dispensation. The total healthcare costs were divided by the total number of patients in each group, to arrive at the average healthcare cost per patient in the 4-year period. For comparisons of average healthcare costs between groups, a 2-sample test was used, under a Tweedie distribution for costs. All analyses were carried out using SAS 9.4 (SAS Institute, Cary, NC). This study was approved by the University of Alberta Research Ethics Board (Pro00082215).

Results

Baseline characteristics

During the 4-year study period, a total of 48,030 patients had AF. Among this cohort, we identified 15,280 patients (31.8%) in the HCU group using the CIHI "dynamic cohort" flag. The proportions of female and male AF patients who were HCUs were equal (31.9% vs 31.7%). Compared to male HCUs, the female HCU group members were older (mean age 80.7 $\pm$ 10.8 years vs 75.5 $\pm$ 11.8 years; 91.6% vs 82.2% age $\geq$ 65 years; $P < 0.001$), more likely to have hypertension and heart failure, and at higher risk for stroke (CHA_2DS_2-Vasc $\geq$ 2; 98.6% vs 91.7%, $P < 0.001$; Table 1).

During the 4-year study period, the HCU group was less likely to have OAC therapy (50.8% vs 58.1%, $P < 0.0001$), rhythm control (8.9% vs 12.9%, $P < 0.0001$), rate control (68.4% vs 69.9%, $P = 0.0008$), catheter ablation (0.8% vs 2.1%, $P < 0.0001$), and cardioversion, compared to the non-HCU group (6.8% vs 12.3%, $P < 0.0001$; Table 1). No sex differences were present in the HCU group, with respective to OAC use. However, sex differences were demonstrated for rhythm and rate control, catheter ablation, and cardioversion. Female HCU patients, in comparison to male HCU patients, were more likely to receive rate control (69.2% vs 67.7%, $P = 0.049$) and less likely to receive rhythm control (6.7% vs 10.8%, $P < 0.0001$), catheter ablation (0.4% vs 1.0%, $P < 0.0001$), and cardioversion (4.6% vs 8.6%, $P < 0.0001$). No sex differences were present in management for female vs male patients in the non-HCU group.

Healthcare utilization

Healthcare utilization as a proportion of total use among the HCUs and non-HCUs with AF, according to sex, is shown in Figure 1. Overall, the HCU group was responsible

Table 1. Baseline characteristics of non-HCUs and HCUs for AF, stratified by sex

Characteristic	Total	Non-HCUs for AF				HCUs for AF			
		Female patients	Male patients	Non-HCU total	Female vs male non-HCUs; *P*	Female patients	Male patients	HCU total	Female vs male HCUs; *P*
Total patients	48,030	14,767 (45.1)	17,983 (54.9)	32,750		6923 (45.3)	8357 (54.7)	15,280	
Age, mean (SD), y	74.5 (14.0)	76.9 (13.1)	69.8 (15.1)	73.0 (14.7)	< 0.0001	80.7 (10.8)	75.5 (11.8)	77.8 (11.6)	< 0.0001
Age 65+ y	37,640 (78.4)	12,353 (83.7)	12,078 (67.2)	24,431 (74.6)	< 0.0001	6340 (91.6)	6869 (82.2)	13,209 (86.4)	< 0.0001
Stroke and/or TIA	7634 (15.9)	2283 (15.5)	2256 (12.5)	4539 (13.9)	< 0.0001	1475 (21.3)	1620 (19.4)	3095 (20.3)	0.003
Peripheral arterial disease	4823 (10.0)	999 (6.8)	1459 (8.1)	2458 (7.5)	< 0.0001	910 (13.1)	1455 (17.4)	2365 (15.5)	< 0.0001
Coronary artery disease	16,351 (34.0)	3756 (25.4)	6226 (34.6)	9982 (30.5)	< 0.0001	2342 (33.8)	4027 (48.2)	6369 (41.7)	< 0.0001
Prior myocardial infarction	5239 (10.9)	1076 (7.3)	1671 (9.3)	2747 (8.4)	< 0.0001	913 (13.2)	1579 (18.9)	2492 (16.3)	< 0.0001
Heart failure	15,604 (32.5)	4103 (27.8)	4704 (26.2)	8807 (26.9)	0.0010	3186 (46.0)	3611 (43.2)	6797 (44.5)	0.001
Hypertension	36,369 (75.7)	11,343 (76.8)	12,213 (67.9)	23,556 (71.9)	< 0.0001	5993 (86.6)	6820 (81.6)	12,813 (83.9)	< 0.0001
Diabetes	13,984 (29.1)	3406 (23.1)	4920 (27.4)	8326 (25.4)	< 0.0001	2305 (33.3)	3353 (40.1)	5658 (37.0)	< 0.0001
Renal	5873 (12.2)	1295 (8.8)	1608 (8.9)	2903 (8.9)	0.59	1243 (18.0)	1727 (20.7)	2970 (19.4)	< 0.0001
Dementia	5534 (11.5)	1721 (11.7)	1209 (6.7)	2930 (8.9)	< 0.0001	1387 (20.0)	1217 (14.6)	2604 (17.0)	< 0.0001
Cancer	8057 (16.8)	1841 (12.5)	2734 (15.2)	4575 (14.0)	< 0.0001	1305 (18.9)	2177 (26.1)	3482 (22.8)	< 0.0001
Anemia	4296 (8.9)	1184 (8.0)	1004 (5.6)	2188 (6.7)	< 0.0001	1093 (15.8)	1015 (12.1)	2108 (13.8)	< 0.0001
$CHADS_2$ score									
0	5739 (11.9)	1635 (11.1)	3395 (18.9)	5030 (15.4)	< 0.0001	205 (3.0)	504 (6.0)	709 (4.6)	< 0.0001
1	8916 (18.6)	2801 (19.0)	4122 (22.9)	6923 (21.1)		738 (10.7)	1255 (15.0)	1993 (13.0)	
2+	33,375 (69.5)	10,331 (70.0)	10,466 (58.2)	20,797 (63.5)		5980 (86.4)	6598 (79.0)	12,578 (82.3)	
CHA_2DS_2-VASc score									
0	2693 (5.6)	0 (0.0)	2443 (13.6)	2443 (7.5)	< 0.0001	0 (0.0)	250 (3.0)	250 (1.6)	< 0.0001
1	3729 (7.8)	1039 (7.0)	2152 (12.0)	3191 (9.7)		98 (1.4)	440 (5.3)	538 (3.5)	
2+	41,608 (86.6)	13,728 (93.0)	13,388 (74.4)	27,116 (82.8)		6825 (98.6)	7667 (91.7)	14,492 (94.8)	
Treatment management strategies									
OACs	26,805 (55.8)	8518 (57.7)	10,519 (58.5)	19,037 (58.1)	0.1386	3543 (51.2)	4225 (50.6)	7768 (50.8)	0.4448
Rate control	33,338 (69.4)	10,547 (71.4)	12,343 (68.6)	22,890 (69.9)	< 0.0001	4790 (69.2)	5658 (67.7)	10,448 (68.4)	0.0493
Rhythm control	5600 (11.7)	1575 (10.7)	2660 (14.8)	4235 (12.9)	< 0.0001	461 (6.7)	904 (10.8)	1365 (8.9)	< 0.0001
Catheter ablation	808 (1.7)	205 (1.4)	488 (2.7)	693 (2.1)	< 0.0001	31 (0.4)	84 (1.0)	115 (0.8)	< 0.0001
Cardioversion	5070 (10.6)	1290 (8.7)	2741 (15.2)	4031 (12.3)	< 0.0001	319 (4.6)	720 (8.6)	1039 (6.8)	< 0.0001

Values are n (%), unless otherwise indicated.

$CHADS_2$, **C**ongestive Heart Failure, **H**ypertension, **A**ge ≥ 75, **D**iabetes, and Prior **S**troke/Transient Ischemic Attack (doubled); CHA_2DS_2-VASc, **C**ongestive Heart Failure, **H**ypertension, **A**ge (≥ 75 Years) (doubled), **D**iabetes Mellitus, **S**troke (doubled), **V**ascular Disease, **A**ge (65-74) Years, **S**ex **C**ategory (Female); HCU, high-cost user; OAC, oral anticoagulant; TIA, transient ischemic attack.

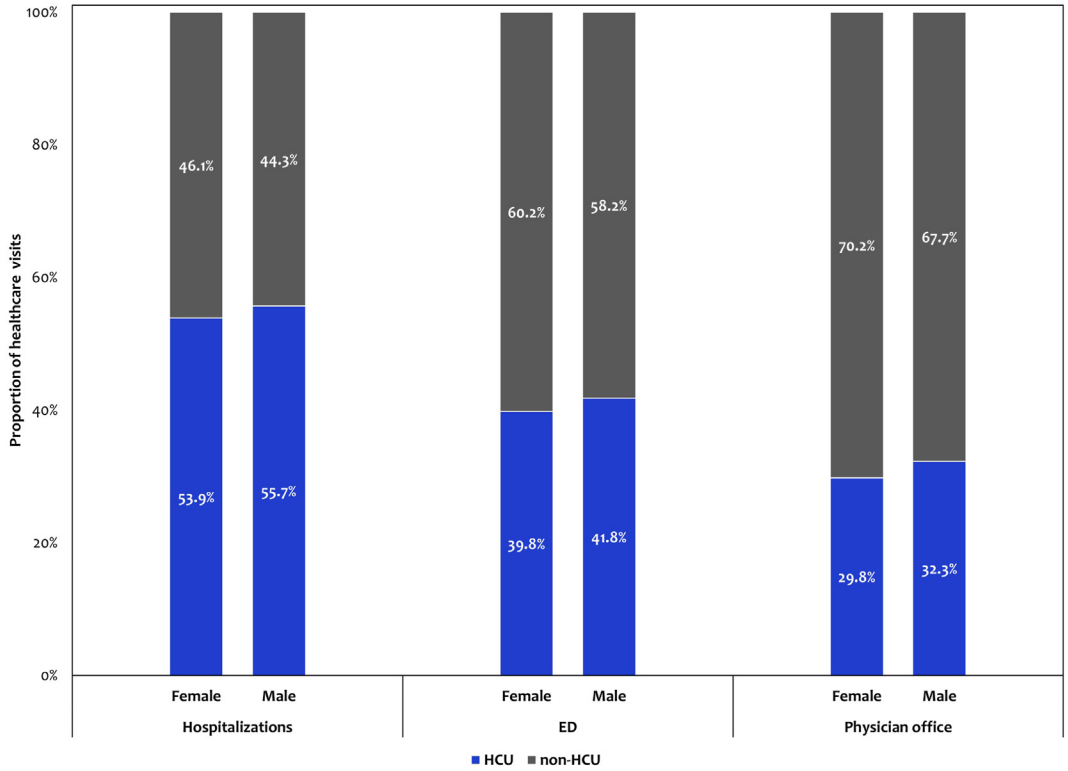

Figure 1. Healthcare utilization as a proportion of total use among non-HCUs and HCUs, stratified by sex and visit type. ED, emergency department; HCU, high-cost user.

for 54.9% of total hospital visits, 31.1% of total physician office visits, and 40.9% of total ED visits, in comparison to the non-HCU group (Table 2; Supplemental Fig. S1). The HCUs had significantly higher average numbers of acute care visits, compared to non-HCUs (ED: 8.4 vs 5.6; hospital: 4.5 vs 1.7; $P < 0.0001$, respectively), but fewer physician office visits (61.4 vs 63.4, $P < 0.0001$). The male HCUs had a significantly higher average number of acute care visits, compared to male non-HCUs (ED: 8.7 vs 5.6; hospital: 4.5 vs 1.7; $P < 0.0001$, respectively), and the average numbers of physician office visits were slightly higher (61.7 vs 60.1, $P = 0.0152$; Table 2; Supplemental Fig. S1). The female HCUs had a significantly higher average number of acute care visits, compared to the female non-HCUs (ED: 8.0 vs 5.7; hospital: 4.5 vs 1.8; $P < 0.0001$, respectively), but fewer physician office visits (61.1 vs 67.4, $P < 0.0001$). Mean healthcare utilization did not differ among HCUs by sex, except for ED visits, the number of which was higher in male patients (12.7% vs 9.2%, $P < 0.0001$; Table 2; Supplemental Fig. S1).

Costs

The HCU group accounted for CAD$3.4 billion (65.8%) of the total healthcare costs (Table 3; Supplemental Fig. S2). Specifically, the HCU group was responsible for 75.0% of total hospitalization costs, 54.9% of total physician billing costs, 45.2% of total ambulatory care costs, and 35.2% of total drug costs, in comparison to the non-HCU group. Healthcare costs, as a proportion of total use among the HCUs and non-HCUs with AF, according to sex, are shown in Figure 2. The average cost per patient for HCUs was 4.1 times higher than that of non-HCUs (CAD$145,280 vs CAD$35,273 per person, $P < 0.0001$; Table 4). The male HCUs accounted for CAD$2.2 billion (56.5%) of the total HCU costs (Table 3; Supplemental Fig. S2). Significant differences were present in the distributions of HCU-related costs for each sex (male patients: 74.6% hospitalization, 9.5% ambulatory care, 12.4% physician billing, 3.5% drugs; female patients: 77.7% hospitalization, 7.4% ambulatory care, 11.5% physician billing, 3.5% drugs; $P < .0001$; Table 3; Supplemental Fig. S2).

The average HCU cost per patient was higher for male than for female patients (CAD$150,024 vs CAD$139,554, $P < 0.0001$; Table 4), and the average non-HCU cost per patient for male patients was lower than that for female patients (CAD$34,703 vs CAD$35,967, $P < 0.0001$).

Discussion

To our knowledge, this study is the first to demonstrate both the extent of healthcare utilization and cost among AF patients who account for the top 10% of total acute care costs, and the impact of sex. Our study found that almost one-third of AF patients are HCUs and account for two-thirds of the total healthcare costs. Most HCU cost was attributed to hospitalization. Although the AF prevalence was lower among female patients overall, they represented an equal proportion of HCUs. No sex differences were present in healthcare utilization among HCUs, except for number of ED visits, which was higher for male patients. Costs were significantly higher

Table 2. Total and mean healthcare utilization of non-HCUs and HCUs with AF, stratified by sex and visit type

Variable	Total	AF non-HCU				AF HCU			
		Female patients	Male patients	Non-HCU total	Female vs male non-HCUs; *P*	Female patients	Male patients	HCU total	Female vs male HCUs; *P*
Patients, n (%)	48,030 (100.0)	14,767 (45.1)	17,983 (54.9)	32,750		6923 (45.3)	8357 (54.7)	15,280	
Hospitalization									
Total	125,373	26,425	30,147	56,572		30,905	37,896	68,801	
Mean (SD)	2.6 (2.6)	1.8 (1.6)	1.7 (1.6)	1.7 (1.6)	< 0.0001	4.5 (3.1)	4.5 (3.2)	4.5 (3.2)	0.14
ED visits									
Total	313,812	84,037	101,384	185,421		55,576	72,815	128,391	
Mean (SD)	6.5 (9.3)	5.7 (8.3)	5.6(8.0)	5.7 (8.1)	0.36	8.0 (9.2)	8.7 (12.7)	8.4 (11.2)	< 0.0001
Physician office visits									
Total	3,015,254	995,803	1,080,764	2,076,567		422,847	515,840	938,687	
Mean (SD)	62.8 (50.6)	67.4 (52.2)	60.1 (49.4)	63.4 (50.8)	< 0.0001	61.1 (49.5)	61.7 (50.5)	61.4 (50.1)	0.43

AF, atrial fibrillation; HCU, high-cost user; ED, emergency department; SD, standard deviation.

for male HCUs than for female HCUs. Almost half of the total HCU cost of CAD$2.2 billion was attributable to female HCUs.

Several explanations are possible for our findings that, despite having a lower AF prevalence, female AF patients represent an equal proportion of HCUs, and almost half of the HCU cost, compared to male HCU patients with AF. First, female patients with AF are older and have a higher cardiovascular comorbid burden (ie, hypertension, heart failure with preserved ejection fraction) than men.[25,26] Second, female patients with AF experience more symptoms, more functional impairment, and worse quality of life, in comparison to men,[12-17] resulting in higher rates of acute care visits.[19,20] The **O**utcomes **R**egistry for **B**etter **I**nformed **T**reatment of **A**trial **F**ibrillation (ORBIT-AF) reported that women experience a higher frequency of palpitations, exertional dyspnea, effort intolerance, lightheadedness, dyspnea at rest, fatigue, and chest discomfort than men.[12] Third, for symptomatic AF patients, catheter ablation is an effective strategy for maintaining sinus rhythm, improving symptoms, and improving quality of life. Compared to male patients, female patients are treated preferentially with antiarrhythmic drug therapy, which has been shown to be associated with a higher risk of torsade de pointes and other drug-related adverse events.[27-29] When female patients are referred for catheter ablation, they have higher-risk clinical profiles, and their AF is more advanced.[30,31] Despite evidence that early rhythm control of AF results in fewer adverse cardiovascular outcomes, the magnitude in reduction is numerically larger in female patients than it is in male patients (28% vs 17%),[32] and that catheter ablation in particular reduces AF progression and lowers the number of hospitalizations,[33] treatment gaps between the sexes persist. Our data demonstrate that female patients were less likely to receive rhythm control (antiarrhythmic drugs or catheter ablation), catheter ablation, or cardioversion, compared to men, in the HCU group. Strategies to address this gap require an improved understanding of barriers.

Consistent with analyses from other countries, we also found that the largest proportion of healthcare costs were attributable to hospitalizations for AF HCU patients, irrespective of sex. On a per-patient basis, the direct annual cost of AF has been estimated at USD$22,462 (in 2020 USD$s) per AF patient, compared with USD$5518 (in 2020 USD$s) for patients without AF.[8] Our data further demonstrate a per person cost that is about 4 times higher in the HCU group, compared to that for all other AF patients. A better understanding of physician decision-making for admission is needed. Prior work has suggested that many AF patients may be admitted for "rule out" diagnosis or therapeutic interventions that could be performed in an outpatient setting.[34-36] Implementing a standardized decision-making tool in the ED may be one method to lower admission rates. A prior report found that instituting guideline recommendations in the ED reduced hospitalization from 74% to 38% without affecting clinical outcomes.[37] Such application of recommendations not only may reduce the proportion of admissions overall for AF but also may identify the high-risk patients among the HCU group that requires hospitalization.

ED visits are another major contributor to cost. Although hospital admission rates in a national survey from the US found a decline in hospital admission rates for a primary diagnosis of AF, to 62% in 2014 from 70% (2007-2011), the annual AF hospitalization volume increased 16% from 2007 to 2014 because of an increase in the total annual number of ED visits for AF.[38] A nationwide study from Canada also

Table 3. Total healthcare costs of atrial fibrillation for non-HCUs and HCUs stratified by sex and cost source

Variable	Total costs	Female patients	Male patients	Non-HCU total	Female patients	Male patients	HCU total
Patients, n	48,030	14,767	17,983	32,750	6923	8357	15,280
Hospitalization	2.2 B	270.7 M (51.0)	292.5 M (46.9)	563.2 M (48.8)	750.6 M (77.7)	935.8 M (74.6)	1.7 B (76.0)
Ambulatory care	420.8 M	95.8 M (18.0)	135.0 M (21.6)	230.8 M (20.0)	71.2 M (7.4)	118.8 M (9.5)	190.0 M (8.6)
Physician billing	219.5 M	63.9 M (19.0)	78.3 M (18.9)	142.2 M (19.0)	33.7 M (11.5)	43.7 M (12.4)	77.3 M (12.0)
Drug	485.1 M	100.8 M (12.0)	118.2 M (12.6)	219.0 M (12.3)	110.7 M (3.5)	155.4 M (3.5)	266.1 M (3.5)
All costs	3.4 B	531.1 M	624.1 M	1.2 B (100)	966.1 M	1.3 B	2.2 B

Values are Canadian $s, unless otherwise indicated. Values in parentheses are % of all costs.
B, billion; HCU, high-cost user; M, million.

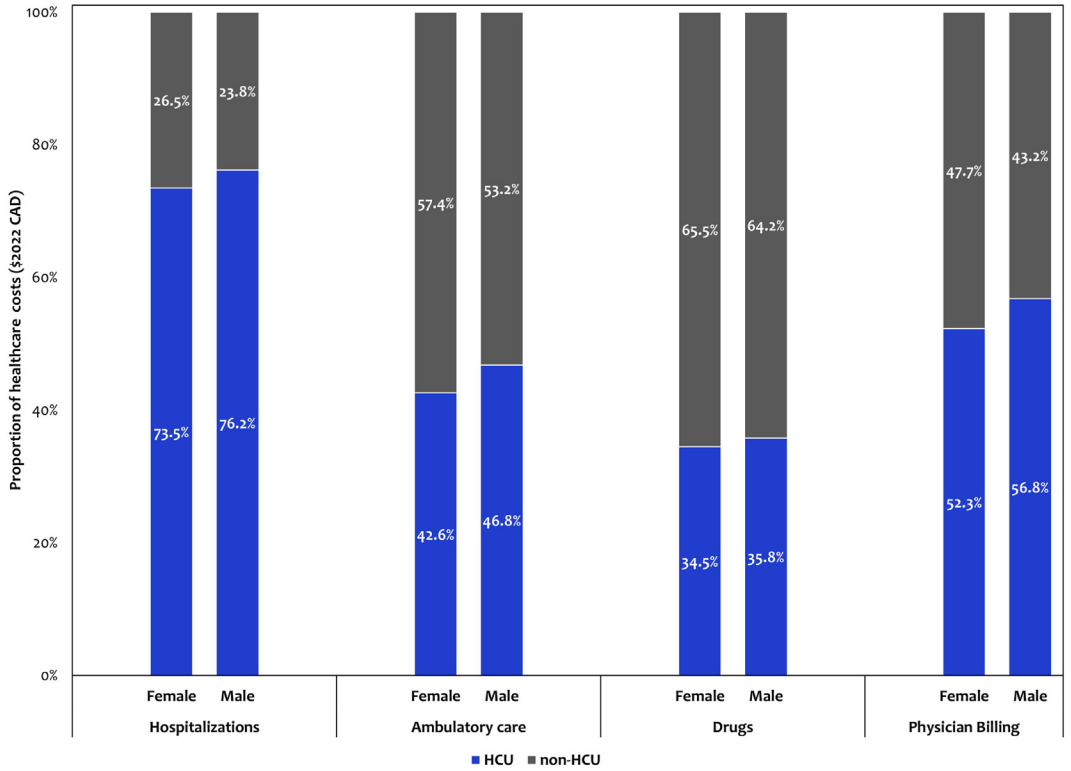

Figure 2. Healthcare costs as a proportion of total use among non-HCUs and HCUs, stratified by sex and visit type. CAD, Canadian $s; HCU, high-cost user.

found a 2% decline in incident nonvalvular AF hospitalization between 2006 to 2015, but data from an Ontario-based study found that although hospital admissions decreased by 8% over an 8-year period, the annual number of ED visits for AF increased by 29%.

Several strategies may reduce the high volume and large resource use associated with the HCUs presenting to the ED. Systematic screening for and treatment of modifiable AF risk factors in clinical practice is needed.[39,40] An aggressive approach may be needed, particularly after a new AF diagnosis. A study from Denmark evaluating the 3-year total and attributable costs for AF found that costs were highest during the first year after a new diagnosis.[41] To address the complexities involved in AF management, an integrated, structured approach to AF care has been proposed which includes patient involvement and a multidisciplinary team including primary care providers, specialists, and allied health professionals to support lifestyle interventions and treatment of risk factors, along with AF-specific therapy.[40,42] This model of an "AF centre of excellence" has resulted in reductions in all of the following factors: wait times for specialist assessment, number of ED visits, hospitalizations, and mortality.[43] More research is needed to assess whether an AF centre-of-excellence model is associated with significant reductions in healthcare costs. Leveraging large and comprehensive health data and applying novel methods, such as machine learning, may provide further opportunity for the early identification of potential HCUs for nonvalvular AF healthcare.

An important finding is that in order to evaluate the impact of initiatives aimed at reducing the number of patients

Table 4. Mean healthcare costs per person of AF non-HCU and HCU stratified by sex and cost source

	Total AF non-HCU costs				Total AF HCU costs			
Variable Label	Female patients	Male patients	Non-HCU total	Female vs male non-HCUs; *P*	Female patients	Male patients	HCU total	Female vs male HCUs; *P*
Patients, n	14,767	17,983	32,750		6923	8357	15,280	
Hospitalization	18,330	16,268	17,197	< 0.0001	108,425	111,983	110,371	0.0073
Ambulatory care	6489	7506	7047	< 0.0001	10,279	14,219	12,434	< 0.0001
Physician billing	6824	6574	6687	< 0.0001	15,989	18,594	17,414	< 0.0001
Drug	4325	4355	4341	0.6120	4861	5227	5061	0.0004
All costs	35,967	34,703	35,273	0.0006	139,554	150,024	145,280	< 0.0001

Values are Canadian $, unless otherwise indicated.
AF, atrial fibrillation; HCU, high-cost user.

who comprise the HCU group, enhanced surveillance, including standardized collection, tracking, and reporting of data, is needed.[44,45]

Limitations

Several limitations of our analyses warrant further discussion. First, the CIHI "dynamic HCU cohort" accounts for only the top 10% of acute care (hospitalization) costs and not for total healthcare costs. Furthermore, this cohort captured data for only a limited period, and how the HCU group may have changed over contemporary years is unclear. Evidence to suggest comorbidity burden among incident AF patients has increased over time and represents a sicker population with more interactions with the healthcare system. Second, the diagnosis of AF, and comorbidities, was based upon validated ICD codes[46,47]; however; under-coding or misclassification errors may exist. Third, unmeasured confounders may cause the observed baseline differences between sexes in both the HCU and the non-HCU groups. Fourth, we were unable to capture diagnostic imaging—that is, echocardiogram data from the database—and therefore could not estimate whether sex differences existed in management of heart failure with preserved and reduced ejection fraction. Fifth, our total costs were underestimated, as we were unable to estimate costs related to laboratory tests, diagnostic imaging, or other community-based providers—that is, pharmacists and social workers who may be involved in patient care. Sixth, the pharmaceutical data apply only to community settings and do not include in-hospital pharmaceutical data. In addition, drug costs do not include dispensing fees. Seventh, our inpatient and ambulatory costs are based on provincial averages (not facility level), and they may underestimate or overestimate true costs. Lastly, these results may not be generalizable to other geographic areas.

Conclusion

In this population-based study, we found that almost one-third of all AF patients are HCUs and are responsible for two-thirds of total healthcare costs. Despite having a lower AF prevalence, female patients represent an equal proportion of HCUs and account for almost half the total HCU costs. To ensure future cost containment, prevention and early treatment are necessary to reduce the AF HCU burden on the healthcare system.

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Data Statement

The data underlying this article were provided by the Government of Alberta under the terms of a research agreement. Inquiries regarding access to the data can be made to health.resdata@gov.ab.ca.

Ethics Statement

This study was approved by the University of Alberta Research Ethics Board (Pro00082215).

Patient Consent

The authors confirm that patient consent is not applicable to this article because this analysis is based on de-identified administrative data and therefore the institutional review board did not require consent from the patient.

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Supplementary Material

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