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# **Clinical Research**

# Temporal Trends in Population Rates of Incident Atrial Fibrillation and Atrial Flutter Hospitalizations, Stroke Risk, and Mortality Show Decline in Hospitalizations

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#### **ABSTRACT**

Background: Hospitalization for nonvalvular atrial fibrillation (NVAF) is common and results in substantial cost burden. Current national data trends for the incidence, stroke risk profiles, and mortality of hospitalization for NVAF and atrial flutter (AFL) are sparse.

Methods: The Canadian Institute of Health Information Discharge Abstract Database was used to identify patients ≥ 20 years with incident NVAF/AFL (NVAF, ICD-9 code 427.3 or ICD-10 I48) in any diagnosis field from 2006 to 2015 in Canada, except Québec. National and provincial trends in rate over time (rate ratio, 95% confidence interval [CI]) were calculated for age-sex standardized hospitalizations. Trends in stroke risk profiles and in-hospital mortality rates adjusted for stroke risk factors were also calculated.

Results: A total of 578,947 patients were hospitalized with incident NVAF/AFL. The median age was 77 years (interquartile range: 68-84),

## RÉSUMÉ

Introduction: Les hospitalisations en raison de fibrillation auriculaire non valvulaire (FANV) sont fréquentes et aboutissent à un fardeau considérable des coûts. Les tendances nationales des données actuelles sur l'incidence, les profils de risque d'accidents vasculaires cérébraux (AVC) et la mortalité lors d'hospitalisation en raison de FANV et de flutter auriculaire (FLA) sont limitées.

Méthodes: Nous avons utilisé la base de données sur les congés des patients de l'Institut canadien d'information sur la santé pour trouver les patients ≥ 20 ans qui avaient reçu un diagnostic de FANV/FLA (FANV, CIM-9 code 427.3 ou CIM-10 I48) dans tout champ de diagnostic de 2006 à 2015 au Canada, à l'exception du Québec. Nous avons évalué les tendances nationales et provinciales dans les taux au fil du temps (ratio des taux, intervalle de confiance [IC] à 95 %) en fonction des hospitalisations standardisées par âge et par sexe. Nous

Atrial fibrillation (AF) is the most common sustained rhythm disorder. Many patients with AF are hospitalized, either for management of symptoms, other consequences such as heart failure or thromboembolic events, or as a result of complications of therapy. Older studies from Europe and North

reported high rates of hospitalizations due to AF, with trends increasing over time. Hospitalizations represent the largest proportion of direct AF-related health care costs. 10-12

America, including the only estimates from Canada, have

The number of persons with AF is expected to rise significantly because of an aging population, increasingly adverse lifestyles, and cardiovascular risk factors that predispose to development of AF. Given the symptomatic and episodic nature of AF, the higher burden of illness may lead to more and costly admissions. On the other hand, there may be a shift to outpatient management of AF or more patients with AF being discharged from emergency departments instead of hospitalized. To ensure cost containment and guide resource

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82% were  $\geq$  65 years, 54% were men, 54% had a CHADS2  $\geq$  2, and 69% had a CHA2DS2-Vasc  $\geq$  3. The overall age- and sex-standardized rate of NVAF/AFL hospitalization was 315 per 100,000 population and declined by 2% per year (P < 0.001). There was an annual rate decline in NVAF/AFL hospitalizations in every province. The majority of hospitalized patients are at high risk of stroke, and this risk remained unchanged. The average adjusted in-hospital mortality was 8.80 per 100 patients 95% CI, 8.80-8.81 with a 2% annual decline in rate (P < 0.001).

Conclusion: Between 2006 and 2015, we found national and provincial hospitalization rates for incident NVAF/AFL are declining. The majority of patients are at high risk for stroke. In-hospital mortality has declined but remains substantial.

allocation, understanding trends in the prevalence rates of incident AF hospitalizations, the clinical characteristics of patients, and their prognosis in a contemporary era are needed.

Accordingly, we evaluated trends in prevalence rates of incident nonvalvular atrial fibrillation (NVAF) and atrial flutter (AFL) hospitalizations, stroke-risk profiles, and associated in-hospital mortality rates using the Canadian Institute of Health Information Discharge Abstract Database for the years between 2006 and 2015 in Canada.

## **Methods**

The Canadian Institute of Health Information (CIHI) Discharge Abstract Database (DAD), which contains information for all hospitalizations in Canada except Québec, was used to identify patients ≥ 20 years with AF/AFL using International Classification of Diseases, 9th revision clinical modification ICD-9-CM codes 427.3 or ICD-10 code I48, in any diagnostic field, from April 1, 2006 to March 31, 2015. 13 Data from Québec are submitted to CIHI directly by the ministère de la Santé et des Services sociaux du Québec in a different database and format that is not consistent with other provinces. To further identify patients with incident NVAF/ AFL, we excluded patients who had index hospitalizations with NVAF/AFL in the 2 years before the start of the study (April 2004 to March 2006), in addition to valvular heart disease, those residing in Québec, outside of Canada, or with unidentified gender. In the case of multiple hospitalizations over the study period, the first hospitalization with NVAF/ AFL was defined as the index hospitalization. In a secondary analysis, we evaluated incident hospitalizations with AF/AFL as the primary diagnosis.

Demographics were assessed at the time of the incident NVAF/AFL, and data on the presence of stroke risk factors avons aussi évalué les profils de risque d'AVC et les tendances des taux de mortalité intrahospitalière ajustés selon les facteurs de risque d'AVC.

Résultats: Un total de 578 947 patients ont été hospitalisés en raison d'un nouveau diagnostic de FANV/FLA. L'âge médian était de 77 ans (écart interquartile : 68-84), 82 % avaient  $\geq$  65 ans, 54 % étaient des hommes, 54 % avaient un CHADS2  $\geq$  2, et 69 % avaient un CHA2DS2-Vasc  $\geq$  3. Le taux global standardisé par âge et par sexe des hospitalisations en raison de FANV/FLA était de 315 sur 100 000 dans la population et déclinait de 2 % par année (P<0,001). Toutes les provinces montraient un déclin du taux annuel des hospitalisations en raison de FANV/FLA. La majorité des patients hospitalisés sont exposés à un risque élevé d'AVC, et ce risque demeurait le même. La mortalité moyenne intrahospitalière ajustée était de 8,80 par 100 patients, IC à 95 %, 8,80-8,81 avec un déclin annuel du taux de 2 % (P<0,001).

Conclusion: Entre 2006 et 2015, nous avons observé que les tendances nationale et provinciales des taux d'hospitalisations en raison d'un nouveau diagnostic FANV/FLA sont en déclin. La majorité des patients sont exposés à un risque élevé d'AVC. La mortalité intrahospitalière avait décliné, mais demeurait importante.

(ie, components of congestive heart failure, hypertension, age ≥ 75, diabetes, previous stroke or systemic embolism [CHADS2] and congestive heart failure, hypertension, age 65 to 74 or ≥ 75 years, diabetes, previous stroke or systemic embolism and arterial vascular disease and female sex [CHA2DS2VASc]) were obtained from the same CIHI DAD database if the conditions were present in the 2 years before the incident diagnosis of NVAF/AFL. The outcome measure was in-hospital death during index hospitalization.

## Statistical analysis

Baseline characteristics were summarized as median with interquartile range for continuous variables and absolute number with proportion for categorical variables. Cochrane-Armitage trend was performed to explore trend over time for categorical data, and nonparametric Kruskal-Wallis test was done for continuous data. The unit of analysis was patients with NVAF/AFL. Crude rate was calculated as the number of patients with incident NVAF/AFL in a given fiscal year (FY) divided by the Canadian population estimate of that FY. Similarly, provincial rates for incident NVAF were calculated as the number of patients with incident NVAF/ AFL receiving inpatient care in a given province, in a given FY, divided by the provincial population estimate of that FY. Age- and sex-standardized rate was calculated per 100,000 of the population, with a direct standardization approach using the 2016 census population of Canada as the reference population. Patients and Canadian population were grouped by sex and in age groups starting from 20 to 80 years with 5-year age increments and finally > 80 years. Poisson regression analysis or negative binomial in case of overdispersion was done to assess the trend in rate over time or differences in rates across provinces. All analyses were performed in SAS 9.4 version (SAS Institute, Cary, NC).

Table 1. Cohort characteristics overall and by year

Variable Value	Total	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	P value for trend
Patients N	578,947	598,46	56,657	56,302	56,000	56,593	57,696	58,754	58,771	59,670	58,658	
Age (years), median	77.0	77	77	77	77	78	78	78	77	78	77	< 0.001
(IQR)	(68, 84)	(69, 84)	(68, 84)	(68, 84)	(68, 84)	(68, 84)	(68, 85)	(68, 85)	(68, 85)	(68, 85)	(68, 85)	
Age group												
< 65 years	105,011	10,419	10136	10,196	10,423	10,436	10,476	10,829	10,741	10,614	10,741	< 0.001
	(18.1)	(17.4)	(1,7.9)	(18.1)	(18.6)	(18.4)	(18.2)	(18.4)	(18.3)	(17.8)	(18.3)	
65 < 75 years	131,981	13,405	12,754	12,612	12,451	12,547	13,024	13,369	13,633	13,849	14,337	
	(22.8)	(22.4)	(22.5)	(22.4)	(22.2)	(22.2)	(22.6)	(22.8)	(23.2)	(23.2)	(24.4)	
$\geq$ 75 years	341,955	36,022	33,767	33,494	33,126	33,610	34,196	34,556	34,397	35,207	33,580	
	(59.1)	(60.2)	(59.6)	(59.5)	(59.2)	(59.4)	(59.3)	(58.8)	(58.5)	(59.0)	(57.2)	
Sex												
Female patients	265,918	27,699	26,340	25807	25866	26254	26416	26964	26687	27179	26706	< 0.001
	(45.9)	(46.3)	(46.5)	(45.8)	(46.2)	(46.4)	(45.8)	(45.9)	(45.4)	(45.5)	(45.5)	
Male patients	313,029	32,147	30,317	30,495	30,134	30,339	31,280	31,790	32,084	32,491	31,952	
	(54.1)	(53.7)	(53.5)	(54.2)	(53.8)	(53.6)	(54.2)	(54.1)	(54.6)	(54.5)	(54.5)	
CHADS2 score												
0-1	264,626	28,996	27,150	26,206	25,758	25,440	25,667	26,157	25,976	26,464	26,812	< 0.0001
	(45.7)	(48.5)	(47.9)	(46.6)	(46.0)	(45.0)	(44.5)	(44.5)	(44.2)	(44.4)	(45.7)	
$\geq 2$	314,321	30,850	29,507	30,096	30,242	31,153	32,029	32,597	32,795	33,206	31,846	
	(54.3)	(51.6)	(52.1)	(53.5)	(54.0)	(55.1)	(55.5)	(55.5)	(55.8)	(55.7)	(54.3)	
CHA2DS2VSc												
score												
0-1	82,446	8713	8183	8086	8064	7983	8030	8241	8336	8256	8554	0.017
	(14.2)	(14.6)	(14.4)	(14.4)	(14.4)	(14.1)	(13.9)	(14.0)	(14.2)	(13.8)	(14.6)	
$\geq 2$	496,501	51,133	48,474	48,216	47,936	48,610	49,666	50,513	50,435	51,414	50,104	
	(85.8)	(85.4)	(85.6)	(85.6)	(85.6)	(85.9)	(86.1)	(86.0)	(85.8)	(86.2)	(85.4)	
Comorbidities												
Heart failure	154,243	16,977	15,693	15,615	15,014	14,912	14,757	14,929	15,286	15,746	15,314	< 0.001
	(26.6)	(28.4)	(27.7)	(27.7)	(26.8)	(26.3)	(25.6)	(25.4)	(26.0)	(26.4)	(26.1)	
Hypertension	254,205	22,041	21,872	23,164	24,153	25,694	27,164	27,689	28,025	27,849	26,554	< 0.001
	(43.9)	(36.8)	(38.6)	(41.1)	(43.1)	(45.4)	(47.1)	(47.1)	(47.7)	(46.7)	(45.3)	
Diabetes	150,628	14,177	13,898	14,162	14,301	14,741	15,337	15,796	15,986	16,188	16,042	< 0.001
	(26.0)	(23.7)	(24.5)	(25.2)	(25.5)	(26.0)	(26.6)	(26.9)	(27.2)	(27.1)	(27.3)	
Vascular disease	163,845	19,072	17,554	17,223	16,281	16,152	16,201	15,832	15,510	15,333	14,687	< 0.001
	(28.3)	(31.9)	(31.0)	(30.6)	(29.1)	(28.5)	(28.1)	(26.9)	(26.4)	(25.7)	(25.0)	
Coronary artery	120,961	14,266	13,122	12,756	12,086	11,970	11,951	11,556	11,407	11,158	10,689	< 0.001
disease	(20.9)	(23.8)	(23.2)	(22.7)	(21.6)	(21.2)	(20.7)	(19.7)	(19.4)	(18.7)	(18.2)	
Stroke/TIA	56,001	5629	5324 (9.4)	5486	5459	5595	5671	5778 (9.8)	5604	5782	5673	0.034
	(9.7)	(9.4)		(9.7)	(9.7)	(9.9)	(9.8)		(9.5)	(9.7)	(9.7)	

TIA, transient ischemic attack.

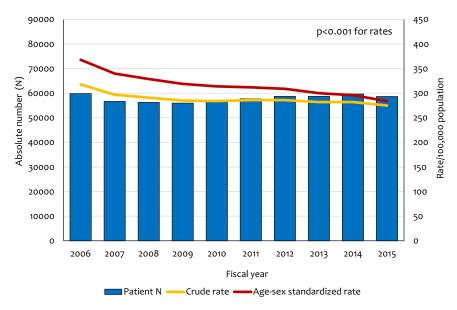


Figure 1. Absolute number, crude, and age-sex standardized rate of incident atrial fibrillation/atrial flutter hospitalizations from 2006 to 2015 in Canada.

## **Results**

#### Cohort characteristics

There was a total of 632,343 patients with incident AF/ AFL identified over a 10-year period. After excluding patients with valvular heart disease (n = 51,248) and those residing in Québec, outside of Canada, or with unidentified gender (n = 2148), a total of 578,947 patients with incident NVAF/AFL comprised the final study cohort. The median age was 77 years (interquartile ratio [IQR]: 68-84), and 54% were men (Table 1).

## AF/AFL hospitalization rates

The overall crude and age-sex standardized hospitalization rates for incident NVAF/AFL were 288 per 100,000 population (95% confidence interval [CI], 287-289 per 100,000 population) and 315 per 100,000 population (95% CI, 315-316 per 100,000 population). The absolute number, crude, and age-sex standardized hospitalization rates for incident NVAF/AFL from 2006 to 2015 are shown in Figure 1. The age-and sex-standardized incidence of hospitalization for AF in any diagnostic field declined overall from 368 to 284 per 100,000 population over the study period, representing a 2% (rate ratio [RR]: 98%, 97%-99%) annual rate decline (P < 0.001).

The overall crude and age-sex standardized hospitalization rates for incident NVAF/AFL as the primary diagnosis were 58.1 per 100,000 population (95% CI, 57.7-58.4 per 100,000 population) and 63.1 per 100,000 population (95% CI, 62.2-63.5 per 100,000 population, Table 2). The age-and sex-standardized incidence of hospitalization as the primary diagnosis declined from 77.9 to 54.3 per 100,000 population over the study period, representing a 4% (RR: 0.96, 0.94-0.99) annual rate decline (P = 0.005).

The overall age-sex standardized hospitalization rates for incident NVAF/AFL across the provinces and territories is shown in Figure 2. For this analysis, 5104 patients, who did not receive inpatient care in their residential provinces, were excluded. The lowest rate was in the territories (263 per 100,000 population), and the highest was in Saskatchewan (338 per 100,000 population. There was a decrease in the crude and age-sex standardized incident NVAF/AFL rates across all the provinces over time (Table 3). The annual rate decline ranged from 0.6% in Ontario and Nova Scotia to 3.5% in Saskatchewan. The annual rate decline in age-sex standardized rate ranged from 5.0% in Manitoba to 14.2% in New Brunswick.

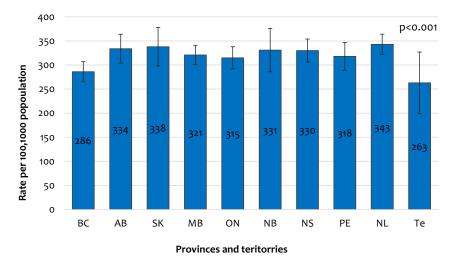
# Stroke-risk profile

The majority of the hospitalized NVAF/AFL cohort was at high risk of stroke. Overall, 82% of hospitalized patients with

Table 2. National crude and age-sex standardized rate of incident atrial fibrillation/atrial flutter hospitalizations as a primary diagnosis by study year

Rate	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	Rate ratio	P value
Crude rate	68.1 (66.9-69.2)	63.7 (62.5-64.8)	60.3 (59.2-61.4)	59.1 (58.0-60.1)	58.8 (57.8-59.9)	57.1 (56.1-58.2)	55.6 (54.6-56.7)	54.5 (53.5-55.5)	52.7 (51.8-53.7)	52.7 (51.8-53.7)	0.97 (0.97-0.98)	< 0.001
(95% CI) Age-sex	77.9	72.2	67.7	65.6	64.6	62.0	59.7	57.7	55.2	54.3	0.96	0.005
standardized rate (95% CI)	(76.6-79.3)	(70.9-73.5)	(66.4-68.9)	(64.4-66.8)	(63.5-65.8)	(60.9-63.1)	(58.6-60.8)	(56.6-58.8)	(54.2-56.2)	(53.3-55.3)	(0.94-0.99)	

CI, confidence interval.



**Figure 2.** Overall age-sex standardized rates of incident atrial fibrillation/atrial flutter hospitalizations across the provinces and territories. AB, Alberta; BC, British Columbia; MB, Manitoba; NB, New Brunswick; NFL, Newfoundland; NS, Nova Scotia, ON, Ontario; PEI, Prince Edward Island; SK, Saskatchewan; Te, Territories.

NVAF/AFL were  $\geq$  65 years, 54% had CHADS2  $\geq$  2, and 69% had a CHA2DS2-Vasc  $\geq$  3 (Table 1). Age category of 65 to < 75 years significantly increased from 22.4% to 24.4% (a relative 8.9% increase), whereas the proportion of patients  $\geq$  75 years of age decreased from 60.2% to 57.2% (a relative 5.0% decrease). The proportion of patients with CHADS2  $\geq$  2 increased over time from 51.6% to 54.3%, with a relative increase of 5.2%, whereas the proportion of patients with CHA2DS2VASc scores  $\geq$  2 remained stable (Table 1). Over time, the proportion of patients with histories of hypertension (23.1%) and diabetes (15.2%) increased, whereas histories of heart failure (8.1%), arterial vascular disease (21.6%), and stroke/transient ischemic attack (3.2%) decreased (Figs. 3 and 4).

## In-hospital mortality

The overall rate of death during incident hospitalization for NVAF/AFL was 9.4% (95% CI, 9.3%-9.5%; n=54,527). The absolute number, crude, and adjusted rates of death are shown in Table 4. The crude death rate ranged from 8.69 (95% CI, 8.45-8.93) in 2015 to 10.00 (95% CI, 9.75-10.27) in 2008, and adjusted death rate ranged from 9.50 (95% CI, 9.25-9.75) in 2007 to 8.09 (95% CI, 7.87-8.32) in 2015.

Over the study period, there was a 1% to 13% relative decrease in rate with a 2% annual rate decline. In-hospital mortality rate by provinces is shown in Figure 5.

## **Discussion**

Between 2006 and 2015, we found that national and provincial age- and sex-standardized rates of hospitalizations for incident NVAF/AFL as any diagnosis and as a primary diagnosis have declined over time. Regardless of the applied stroke-risk scheme, the majority of patients hospitalized are at high risk. Of the known stroke risk factors, age category of 65 to <75 years, hypertension, diabetes, and heart failure have increased over the study period. In-hospital mortality remains high and has had only declined by 2% annually.

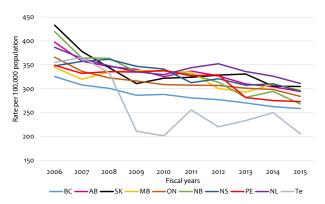
high and has had only declined by 2% annually.

Previous studies<sup>6-9</sup> from several countries from the early 1980s to early 2000s have consistently reported that population rates of all AF-related hospitalizations have increased over time, yet little is known regarding trends in the incidence of AF hospitalizations. A population-based cohort study from Denmark<sup>6</sup> found a 60% (95% CI, 30%-100%) increase in first-ever hospitalization for AF from early 1980s and early 1990s. Contrary to that report, our data, which include more

Table 3. Changes in crude and age-sex standardized rates of hospitalizations for incident atrial fibrillation/atrial flutter over time

Provinces	Crude rate: average change per year	P value	Age-sex standardized rate: average change per year	P value
Pitt Cl. It				
British Columbia	1.2% decrease	< 0.001	6.7% decrease	< 0.001
Alberta	1.8% decrease	< 0.001	9.2% decrease	< 0.001
Saskatchewan	3.5% decrease	< 0.001	10.1% decrease	< 0.001
Manitoba	1.5% decrease	< 0.001	5.0% decrease	< 0.001
Ontario	0.6% decrease	< 0.001	6.9% decrease	< 0.001
New Brunswick	2.5% decrease	< 0.001	14.2% decrease	< 0.001
Nova Scotia	0.6% decrease	0.009	7.2% decrease	< 0.001
Prince Edward Island	1.4% decrease	0.02	8.4% decrease	< 0.001
Newfoundland	0.25% increase	0.41	5.7% decrease	< 0.001

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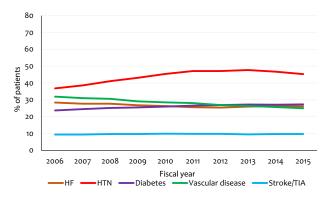


**Figure 3.** Yearly age-sex standardized rates of incident atrial fibrillation/atrial flutter hospitalizations across provinces. AB, Alberta; BC, British Columbia; MB, Manitoba; NB, New Brunswick; NFL, Newfoundland; NS, Nova Scotia, ON, Ontario; PEI, Prince Edward Island; SK, Saskatchewan; Te, Territories.

recent years, found the rate of admission to hospital for incident NVAF/AFL has declined by 2% annually. Furthermore, we found admissions for NVAF/AFL as a primary diagnosis decreased even more than overall AF admissions. Our findings are supported by the only other study<sup>14</sup> that has reported on incidence rates for any AF hospitalization, which demonstrated a 1.1% annual downward trend from 1995 to 2010 in Western Australia. Although these are modest declines, given the high cost burden associated with AF-related hospitalizations, <sup>15</sup> any rate reduction will translate into a meaningful difference.

There are several possible explanations for the observed decline in the national and provincial rates of incident NVAF/AFL hospitalizations. First, the threshold for admission has likely increased, given the growing demands on a limited number of inpatient beds. Second, physicians in emergency departments have become more comfortable initiating rate or rhythm strategies (ie, cardioversion), thereby alleviating patient symptoms and need for admission. 16 Third, a downward trend in the incidence of NVAF/AFL hospitalization may be offset by increases seen in other health care settings. In a population-based study performed in the province of Alberta, age- and sex-standardized AF inpatient incidence rates decreased 21% between 2000 and 2005 but rose 50% in the outpatient setting.<sup>17</sup> Another study performed in all Ontario emergency departments found the annual number of ED visits for AF increased by 29%, whereas hospital admissions decreased by almost 10% over the 8-year period. 16 Similarly, an analysis from the Nationwide Emergency Department Sample for 2007 to 2014 found a significant increase in the annual ED visits for AF of 31.7% (P for trend = 0.008), whereas rates of admission decreased by 11.4% (P for trend 0.017) during this study period. 18 In addition, further investigations are needed evaluating whether changes in AF risk factors, ED practice patterns, admission standards, and burden of outpatient AF care may be some of the reasons for the decline seen within each of the provinces.

Determining risk of stroke for patients with NVAF/AFL has been a cornerstone guideline recommendation <sup>19-21</sup> and an identified performance measure among several professional



**Figure 4.** Temporal trends in baseline characteristics. HF, heart failure; HTN, hypertension; TIA, transient ischemic attack.

societies. <sup>13,22</sup> The Canadian Cardiovascular Society (CCS) AF/AFL quality indicator (QI) group recently published an update on clinically important QIs to determine standard quality of care, and measuring the proportion of patients with NVAF/AFL according to stroke-risk strata (CHADS2, CHA2DS2VASc) has remained a priority QI. <sup>13</sup> Using the CIHI database, in which risk of stroke could only be assessed with relevant elements of the scores obtained from administrative data and then calculated, we provide the first national data on this AF QI, demonstrating that the majority of hospitalized patients would be categorized as high risk for stroke and continue to be over time.

At present, we were not able to abstract whether patients with NVAF/AFL and incident hospitalization were already taking oral anticoagulant (OAC) therapy, had it prescribed in hospital or if a contraindication to stroke prevention therapy was present. Although previous work has found less than 50% of hospitalized high-risk patients were on warfarin within 90 days of discharge,8 further research is needed on the impact of non-vitamin K antagonists, 23,24 which are safer and easier to use than warfarin. The hospital setting provides a distinct opportunity to review the use of strokeprevention therapy. A Danish study of 108,791 newly diagnosed AF found that the prescription rate for OAC therapy after discharge increased from 29.8% to 43.5% from 1995 to 2004.<sup>25</sup> Among a similar cohort, a Canadian study found prescriptions for OAC therapy increased from 51% to 64.5% after hospital discharge over a 9-year period ending in 2006.<sup>26</sup>

The in-hospital mortality for patients with an incident hospitalization for NVAF/AFL of 9.4% was high and likely reflects the older age and comorbidities of hospitalized patients. However, the main analysis included anyone with a diagnosis of AF, and, in most cases, this may have been an incidental comorbidity. Regardless, it was encouraging to find a significant 2% annual decline (or relative decrease of 11% to 13%) in the hospital mortality rate even after adjusting for confounders over the study period. Although data from the Nationwide Inpatient Sample (NIS) database also demonstrated that in-hospital mortality decreased for hospitalizations with AF as the primary diagnosis (1.2% in 2010 to 0.9% in 2010, relative 29% decrease), the mortality rates were much lower than observed in our study.<sup>27</sup> The

'able 4. Yearly crude and adjusted death rates during index hospitalization for atrial fibrillation/atrial flutter

In-hospital death during index hospitalization number	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	Rate ratio (95% CI) P value
Absolute number of deaths	5838	0995	5632	5480	5618	5235	5436	5210	5322	9609	
Crude	9.76	66.6	10.00	9.79		9.07		8.86	8.92		86.0
	(9.51-10.01)	(9.73-10.25)	(9.75-10.27)	(9.53-10.05)	(9.67-10.19)	(8.83 - 9.32)	(9.01 - 9.50)	(8.63-9.11)	(8.68 - 9.16)	(8.45-8.93)	(0.98-0.99)
											P < 0.001
CHADS2 adjusted	9.31	9.50	9.40	9.16	9.21	8.39	8.56	8.19	8.24	8.09	0.98
	(9.07 - 9.55)	(9.25 - 9.75)	(9.15 - 9.65)	(8.92-9.41)	(8.97-9.46)	(8.16 - 8.62)	(8.33-8.79)	(7.97 - 8.41)	(8.02 - 8.46)	(7.87 - 8.32)	(0.97-0.98)
											P < 0.001
CHA2DS2VAc	9.06	9.28	9.23	9.05	9.12	8.33		8.17	8.23	8.10	0.98
adjusted	(8.83 - 9.30)	(9.04 - 9.53)	(8.99 - 9.48)	(8.81-9.29)	(8.89-9.37)	(8.10 - 8.56)	(8.30 - 8.76)	(7.95 - 8.40)	(8.01 - 8.46)	(7.88-8.33)	(0.98-0.99)
											P < 0.001
CI, confidence interval.	al.										

only comparable in-hospital mortality rate (8.2%) was seen for patients hospitalized for AF and a history of heart failure, which had a prevalence of 0.3% to 1.2% in the NIS database. In contrast, heart failure was a comorbid condition in at least a quarter of patients in our study. Understanding the clinical-risk profiles for patients hospitalized with incident AF may further explain provincial differences in mortality rates. If a province admits a higher proportion of sicker patients it will be reflected in a higher mortality rate compared with another province that does not. This further stresses the importance of both preventive measures for NVAF/AFL and the comorbid conditions that predispose to it, as well as early treatment interventions as indicated for management of AF.

#### Limitations

There are several limitations of our analyses that warrant further discussion. First, administrative data can be subject to misclassification; however, the administrative code for AF and many of the comorbidities have been previously validated. 13 Second, the CIHI does not capture lifestyle, anthropometric, laboratory, imaging, or symptom status, which may provide further insight into patient profiles that prompted admission. Third, CIHI does not possess data on out-of-hospital mortality or specific cause of death. Fourth, data are limited to hospitalizations, and therefore trends in ED and outpatient visits over this period could not be reported. Finally, and perhaps most importantly, this study underscores the importance of having a rigourous and sustainable mechanism to measure QIs to capture NVAF/ AFL care fully across Canada and trends over time. In particular, data from non-hospital settings in which management is large and increasing, improving cohort accuracy—as ICD codes were not designed to define NVAF—and combing provinces into regions to address subgroups with relative small numbers, making estimates uncertain. CCS QI AF/AFL work could address these and other gaps.

### **Conclusion**

In this contemporary study, we found that both the crude and age- and sex-standardized rates of hospitalizations for incident NVAF/AFL are declining, both nationally and across provinces. The majority of hospitalized patients with NVAF/AFL were at high risk of stroke, and this remained consistent over time. In-hospital mortality was high even though the rate declined annually.

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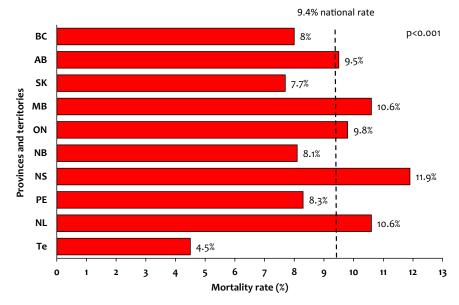


Figure 5. In-hospital mortality rates according to province over the study period. AB, Alberta; BC, British Columbia; MB, Manitoba; NB, New Brunswick; NFL, Newfoundland; NS, Nova Scotia, ON, Ontario; PEI, Prince Edward Island; SK, Saskatchewan; Te, Territories.

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#### References

- Chugh SS, Havmoeller R, Narayanan K, et al. Worldwide epidemiology of atrial fibrillation: a Global Burden of Disease 2010 Study. Circulation 2014;129:837-47.
- Dorian P, Jung W, Newman D, et al. The impairment of health-related quality of life in patients with intermittent atrial fibrillation: implications for the assessment of investigational therapy. J Am Coll Cardiol 2000;36: 1303-9.
- Singh SN, Tang XC, Singh BN, et al. Quality of life and exercise performance in patients in sinus rhythm versus persistent atrial fibrillation: a Veterans Affairs Cooperative Studies Program Substudy. J Am Coll Cardiol 2006;48:721-30.
- Thrall G, Lane D, Carroll D, Lip GY. Quality of life in patients with atrial fibrillation: a systematic review. Am J Med 2006;119:448.
- Kang Y. Relation of atrial arrhythmia-related symptoms to health-related quality of life in patients with newly diagnosed atrial fibrillation: a community hospital-based cohort. Heart Lung 2006;35:170-7.
- Friberg J, Buch P, Scharling H, Gadsbphioll N, Jensen GB. Rising rates of hospital admissions for atrial fibrillation. Epidemiology 2003;14: 666-72.

- Stewart S, MacIntyre K, MacLeod MM, Bailey AE, Capewell S, McMurray JJ. Trends in hospital activity, morbidity and case fatality related to atrial fibrillation in Scotland, 1986-1996. Eur Heart J 2001;22: 693-701.
- Humphries KH, Jackevicius C, Gong Y, et al. Population rates of hospitalization for atrial fibrillation/flutter in Canada. Can J Cardiol 2004;20:869-76.
- Wattigney WA, Mensah GA, Croft JB. Increasing trends in hospitalization for atrial fibrillation in the United States, 1985 through 1999: implications for primary prevention. Circulation 2003;108:711-6.
- Ball J, Carrington MJ, McMurray JJ, Stewart S. Atrial fibrillation: profile and burden of an evolving epidemic in the 21st century. Int J Cardiol 2013;167:1807-24.
- Coyne KS, Paramore C, Grandy S, Mercader M, Reynolds M, Zimetbaum P. Assessing the direct costs of treating nonvalvular atrial fibrillation in the United States. ValueHealth 2006;9:348-56.
- O'Reilly DJ, Hopkins RB, Healey JS, et al. The burden of atrial fibrillation on the hospital sector in Canada. Can J Cardiol 2013;29:229-35.
- Sandhu RKWS, Cruz J, Atzema CL, et al. An update on the development and feasibility assessment of Canadian quality indicators for atrial fibrillation and atrial flutter. Can J Cardiol Open 2019;1:198-204.
- Briffa T, Hung J, Knuiman M, et al. Trends in incidence and prevalence of hospitalization for atrial fibrillation and associated mortality in Western Australia, 1995-2010. Int J Cardiol 2016;208:19-25.
- Meyre P, Blum S, Berger S, et al. Risk of hospital admissions in patients with atrial fibrillation: a systematic review and meta-analysis. Can J Cardiol 2019;35:1332-43.
- Atzema CL, Austin PC, Miller E, Chong AS, Yun L, Dorian P. A population-based description of atrial fibrillation in the emergency department, 2002 to 2010. Ann Emerg Med 2013;62:570-577.e577.
- Sandhu RK, Bakal JA, Ezekowitz JA, McAlister FA. The epidemiology of atrial fibrillation in adults depends on locale of diagnosis. Am Heart J 2011;161:986-992.e981.

- Rozen G, Hosseini SM, Kaadan MI, et al. Emergency department visits for atrial fibrillation in the United States: trends in admission rates and economic burden from 2007 to 2014. J Am Heart Assoc 2018;7.
- January CT, Wann LS, Calkins H, et al. 2019 AHA/ACC/HRS focused update of the 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation. J Am Coll Cardiol 2019;74:104-32.
- Kirchhof P, Benussi S, Kotecha D, et al. 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS. Eur Heart J 2016;37:2893-962.
- Verma A, Cairns JA, Mitchell LB, et al. 2014 focused update of the Canadian Cardiovascular Society Guidelines for the management of atrial fibrillation. Can J Cardiol 2014;30:1114-30.
- Heidenreich PA, Solis P, Estes NAM 3rd, et al. 2016 ACC/AHA clinical performance and quality measures for adults with atrial fibrillation or atrial flutter. J Am Coll Cardiol 2016;68:525-68.

- Dentali F, Riva N, Crowther M, Turpie AG, Lip GY, Ageno W. Efficacy and safety of the novel oral anticoagulants in atrial fibrillation: a systematic review and meta-analysis of the literature. Circulation 2012;126: 2381-91.
- Ruff CT, Giugliano RP, Braunwald E, et al. Comparison of the efficacy and safety of new oral anticoagulants with warfarin in patients with atrial fibrillation: a meta-analysis of randomised trials. Lancet 2014;383: 955-62.
- Hansen ML, Gadsboll N, Gislason GH, et al. Atrial fibrillation pharmacotherapy after hospital discharge between 1995 and 2004: a shift towards beta-blockers. Europace 2008;10:395-402.
- Pilote L, Eisenberg MJ, Essebag V, et al. Temporal trends in medication use and outcomes in atrial fibrillation. Can J Cardiol 2013;29:1241-8.
- Patel NJ, Deshmukh A, Pant S, et al. Contemporary trends of hospitalization for atrial fibrillation in the United States, 2000 through 2010: implications for healthcare planning. Circulation 2014;129:2371-9.