



Clinical Research

Comparison of Readmission and Death Among Patients With Cardiac Disease in Northern vs Southern Ontario

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ABSTRACT

Background: Geographic factors may influence cardiovascular disease outcomes in Canada. Circulatory diseases are a major reason for higher population mortality rates in Northern Ontario, but it is unknown if hospitalized patients with cardiovascular disease experience differential outcomes compared with those in the South.

Methods: We examined 30-day and 1-year mortality and readmissions for patients hospitalized with acute myocardial infarction (AMI), heart failure (HF), atrial fibrillation (AF), or stroke in Northern compared with Southern Ontario, using the Canadian Institute for Health Information Discharge Abstract Database (2005-2016). Northern patients were defined as those residing and hospitalized in the Northwest or North-east Local Health Integration Network regions. We used multiple Cox

RÉSUMÉ

Contexte : Des facteurs géographiques peuvent influencer sur l'issue de maladies cardiovasculaires au Canada. Les maladies du système circulatoire constituent une raison majeure du taux de mortalité élevé dans le nord de l'Ontario, mais on ne sait pas si les patients hospitalisés pour une maladie cardiovasculaire connaissent des issues différentes par rapport aux personnes vivant dans le sud.

Méthodologie : Nous avons examiné les taux de mortalité et de readmissions à 30 jours et à 1 an des patients hospitalisés pour un infarctus aigu du myocarde (IAM), une insuffisance cardiaque (IC), une fibrillation auriculaire (FA) ou un accident vasculaire cérébral (AVC) dans le nord de l'Ontario comparativement à ceux observés dans le sud de la province, à partir de la base de données sur les congés des pa-

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See page 350 for disclosure information.

Cardiovascular disease (CVD) is a leading cause of death and hospitalizations globally.¹ There are approximately 950,000 deaths in North America and 70,000 deaths in Canada due to CVD every year.^{2,3} CVD is also a major reason for hospitalization, with more than 5.5 million admissions in North America and approximately 360,000 admissions in Canada occurring annually.^{4,5} Recently, there has been increasing interest in hospital readmissions as

proportional hazards regression analysis for time-to-first event and Prentice-Williams-Peterson method to evaluate repeat and multiply admitted patients.

Results: A total of 47,745 Northern and 465,353 Southern patients hospitalized with AMI ($n = 182,158$), HF ($n = 130,770$), AF ($n = 72,326$), or stroke ($n = 127,844$) were studied. Rates of first readmission were higher among Northern patients for AMI (adjusted hazard ratio [HR], 1.32), HF (HR, 1.16), AF (HR, 1.21), and stroke (HR, 1.27) compared with Southern patients (all $P < 0.001$). Repeat readmission rates among Northern patients for AMI (HR, 1.23), HF (HR, 1.13), AF (HR, 1.18), and stroke (HR, 1.22) were also increased (all $P < 0.001$ vs Southern). Thirty-day mortality did not differ significantly between Northern and Southern patients.

Conclusions: Readmissions were increased in those residing and hospitalized in the North. To reduce readmissions in the North, the quality of postacute transitional care should be examined further.

potential indicators of quality of acute or transitional post-discharge care. Furthermore, readmissions may be preventable with better ambulatory care and systemic preventive care strategies.

Earlier studies reported that there are variations in CVD outcomes across Canada, with an increasing incidence of CVD in Eastern compared with Western provinces. This is largely due to an increased burden of cardiac risk factors. However, within provinces, access to care may differ with a South to North gradation, partly due to greater rurality in the North when compared with the South. In part, compared with higher physician concentrations in the South, there may be reduced access to physicians and other care providers, and differential access to hospital-based care in the North.⁶ Indeed, in an earlier study, rural hospitals had lower initial admission rates for patients who presented to the emergency department with heart failure (HF), but there were higher rates of subsequent emergency visits and hospitalizations.⁷

A report from Health Quality Ontario (HQP) found that age-standardized mortality rates for the population of Northern Ontario were higher compared with the South, and circulatory diseases were the major causes of death in the North.⁸ In the face of these concerning statistics, it is unknown if the outcomes of patients who were recently hospitalized with CVD also differ in the North. In this study, we compared death and readmission risks of patients admitted with acute myocardial infarction (AMI), HF, stroke, and atrial fibrillation (AF) in Northern vs Southern Ontario. We hypothesized that readmission rates and mortality rates would be higher in the North, with a concomitant reduction in postacute processes of care because repeat hospital admissions are ambulatory care sensitive.

tients de l'Institut canadien d'information sur la santé (2005-2016). Les patients du nord étaient ceux qui résidaient et étaient hospitalisés dans les régions nord-ouest et nord-est du réseau local d'intégration des services de santé (RLISS). Nous avons fait appel à la méthode de régression multiple à risque proportionnel de Cox pour calculer le temps écoulé avant le premier événement et à la méthode Prentice-Williams-Peterson pour évaluer les patients hospitalisés de façons répétées ou plusieurs fois.

Résultats : Un total de 47 745 patients du nord et 465 353 patients du sud hospitalisés pour un IAM ($n = 182\ 158$), une IC ($n = 130\ 770$), une FA ($n = 72\ 326$) ou un AVC ($n = 127\ 844$) ont été inclus dans l'étude. Les taux de première réadmission ont été plus élevés chez les patients du nord pour l'IAM aigu (rapport des risques instantanés corrigé [RRI], 1,32), l'IC (RRI, 1,16), la FA (RRI, 1,21) et l'AVC (RR, 1,27) comparativement aux patients du sud ($p < 0,001$ dans tous les cas). Les taux de réadmissions répétées des patients du nord pour l'IAM (RRI, 1,23), l'IC (RRI, 1,13), la FA (RRI, 1,18) et l'AVC (RRI, 1,22) étaient également élevés ($p < 0,001$ vs sud dans tous les cas). La mortalité à trente jours n'était pas considérablement différente entre le nord et le sud.

Conclusions : Les réadmissions étaient accrues chez les patients résidents et hospitalisés dans le nord. Pour réduire les réadmissions dans le nord, la qualité des soins transitionnels après un épisode aigu devrait être examinée davantage.

Methods

Data sources

We examined the Canadian Institute for Health Information Discharge Abstract Database (CIHI-DAD) for all index hospitalizations and readmissions from April 1, 2005, to March 31, 2015. Mortality was determined via the Registered Persons Database. Physician specialty was determined using the Institute for Clinical Evaluative Sciences (ICES) Physicians Database, and physician consultations or visits were determined using the Ontario Health Insurance Program (OHIP) database. We used the Canadian Institute for Health Information Discharge Abstract Database, Canadian Institute for Health Same Day Surgery, and OHIP databases to determine whether cardiac procedures (eg, echocardiogram, stress testing, or cardiac catheterization) were performed as previously described.⁹ Performance of brain imaging via computed tomography or magnetic resonance imaging was determined using Canadian Classification of Intervention codes 3AN20WA, 3AN20WC, 3AN20WE, 3AN40WA, and 3AN40WC or OHIP codes X400, X401, and X421. Hospital teaching status was defined by the Ontario Ministry of Health and Long-Term Care (MOHLTC), and distances from the patients' homes to the hospital were determined from great circle distances using latitude and longitude mapping databases at ICES. Socioeconomic status was determined by neighbourhood income derived from the Canadian Census. Population estimates were determined using Statistics Canada population data files, which are updated annually. The number of hospital beds were determined using the Institution information system, which contains information about health care institutions funded by the Ontario MOHLTC. Costs of care during admission and after discharge from the hospital were determined from the perspective of the

MOHLTC. These included all hospital-based costs, dialysis clinics, physician claims, drugs provided through Ontario drug benefit, rehabilitation, home care, long-term care, adult mental health services, chemotherapy, and assisted device program if applicable. The use of data in this project was authorized under section 45 of Ontario's Personal Health Information Protection Act, which does not require review by a Research Ethics Board.

Patients

Northern patients were defined as those living in the Northeast or Northwest Local Health Integration Networks (described at www.lhins.on.ca), using the forward sortation address of the home postal code. Southern patients were those living in all other Ontario Local Health Integration Networks. Patients aged ≥ 18 years were included if their index hospitalization for AMI, HF, AF, or stroke occurred in their Northern or Southern region of residence (ie, Northern residents were included if their index hospitalization occurred at a hospital in the North, and Southern residents were included if they were hospitalized in the South). The International Classification of Diseases 10th Edition (ICD-10) codes were used to identify those hospitalized with AMI (ICD-10 codes I21, I22), HF (ICD-10 codes I50, I11.0, I13.0, I13.2), AF (ICD-10 code I48), or stroke (ICD-10 codes I60, I61, I62, I63, I64, I69.3, I69.4, H34.1). We excluded those aged > 105 years or those ineligible for Ontario MOHLTC coverage and non-Ontario residents. Since we examined 4 diseases of interest analyzed separately, a unique patient could have been included in the AMI, HF, AF, and stroke cohorts, but only their first disease-specific hospitalization was classified as the index hospital admission.

Outcomes

The primary outcome was hospital readmission, which was determined from the date of hospital discharge ($t = 0$), and could have occurred at any hospital in Ontario, irrespective of North or South location. All-cause mortality was the co-primary outcome assessed from the date of index hospital admission.

Covariates for adjustment

We examined many concomitant variables and comorbidities as factors for multivariate adjustment that have been shown to be associated with mortality and readmission.^{10,11} We used a 3-year window for identification of comorbidities before the index hospitalization date, using the ICD-10 codes shown in [Supplemental Table S1](#). These factors included cardiac risk factors (hypertension, diabetes, hyperlipidemia), prior myocardial infarction, prior unstable angina, chronic atherosclerosis, history of cigarette smoking, AF, prior HF hospitalization, any HF (ambulatory or in-hospital diagnosis), peripheral vascular disease, cerebrovascular disease, pericarditis, endocarditis, cardiomyopathy, myocarditis, and left bundle-branch block. Hypertension, diabetes, and HF were identified using ICES-derived databases that have been validated in prior studies,¹²⁻¹⁴ and smoking status was determined using previously described methods.¹⁵ We also adjusted for prior cardiac procedures: coronary artery bypass graft surgery, percutaneous coronary

intervention procedures, implantable cardioverter defibrillator, and permanent pacemaker implantation. In addition to all noncardiac comorbidities shown in [Table 1](#), we also adjusted for pulmonary vascular disease, other respiratory disease, thyroid disease, and the Johns Hopkins Aggregated Diagnosis Group comorbidity index. We also adjusted for demographic factors: age, sex, socioeconomic status income quintile, and distance from the patients' home to the nearest hospital. We adjusted for temporal factors including year and season of hospitalization (winter, spring, summer, autumn), and hospital characteristics including annual AMI, HF, AF, and stroke volume divided into tertiles.^{16,17} Because hospital length of stay can affect readmission outcomes,¹⁸ we also adjusted for index hospital length of stay. To determine if any North-South differences could be accounted for by rurality, we stratified our analyses using the Rurality Index of Ontario, which has been used previously to identify urban vs rural (Rurality Index of Ontario index < 40 vs ≥ 40) hospitals.⁷ We performed similar analyses stratified by presence of on-site multidisciplinary HF clinics as previously identified.¹⁹

Statistical analyses

Continuous variables were reported as medians and interquartile ranges (IQRs) and compared using the Kruskal-Wallis test. Categorical variables were reported as proportions and compared using the chi-square statistic. Unadjusted event rates per person-time were compared using a Poisson regression model with Northern vs Southern Ontario residence status as the exposure variable and with the log of follow-up person-years as offset. We used multivariable Cox regression analysis to examine the hazard of the occurrence of a first event (ie, death, first readmission, physician consultation or visit, and diagnostic procedure) adjusting for the aforementioned variables. The proportional hazards assumption was tested by introducing interaction terms between time and each covariate. If the interactions were not significant, the proportional hazards assumption was treated as valid. For the mortality analyses, subjects were censored after 1 year of follow-up or on the last follow-up date of March 31, 2016, whichever came first. For the readmission analyses, subjects were followed until death or the last follow-up date. To account for the possibility of a subject having multiple readmissions, we used Prentice-Williams-Peterson models for repeated events, which are not limited to the first rehospitalization, but include the possibility of multiple events occurring in the same patient over follow-up.²⁰ The incidence of death and first readmission over time were estimated using cumulative incidence functions and compared using the log-rank test (death) or Gray's test (cumulative incidence functions). A nominal P value < 0.05 was deemed statistically significant. All analyses were performed using SAS version 9.4.3 (SAS Institute, Inc., Cary, NC).

Results

Cohort characteristics

From 699,479 index patient hospitalizations initially identified, we excluded those that were nonindex (ie, not the

Table 1. Overall cohort characteristics[†]

	Northern	Southern	Standardized difference	P value
Total N	47,745	465,353		
Patient demographics				
Age, y	74 (62-82)	75 (63-83)	0.060	< 0.001
Sex, men	26,330 (55.1%)	256,147 (55.0%)	0.002	0.665
Socioeconomic status*				
1 (low)	13,736 (28.8%)	100,320 (21.6%)	0.167	< 0.001
2	9799 (20.5%)	98,383 (21.1%)	0.015	
3	9182 (19.2%)	92,078 (19.8%)	0.014	
4	7656 (16.0%)	89,353 (19.2%)	0.083	
5 (high)	6929 (14.5%)	83,417 (17.9%)	0.093	
Residence [‡]				
Rural	16,066 (33.6%)	32,720 (7.0%)	0.916	< 0.001
Urban	26,932 (56.4%)	431,301 (92.7%)	0.701	
Cardiac conditions				
Prior MI	4367 (9.1%)	37,773 (8.1%)	0.037	< 0.001
Chronic atherosclerosis	14,814 (31.0%)	137,750 (29.6%)	0.031	< 0.001
AF	9124 (19.1%)	93,101 (20.0%)	0.023	< 0.001
Prior HF	21,371 (44.8%)	211,969 (45.6%)	0.016	< 0.001
CABG surgery	904 (1.9%)	8924 (1.9%)	0.002	0.712
PCI	5727 (12.0%)	59,012 (12.7%)	0.021	< 0.001
Implantable defibrillator	232 (0.5%)	4208 (0.9%)	0.050	< 0.001
Pacemaker	1486 (3.1%)	12,789 (2.7%)	0.022	< 0.001
PVD	2110 (4.4%)	18,855 (4.1%)	0.018	< 0.001
Cerebrovascular disease	2362 (4.9%)	23,681 (5.1%)	0.007	0.179
HTN	37,670 (78.9%)	368,965 (79.3%)	0.010	0.046
Diabetes	18,880 (39.5%)	177,177 (38.1%)	0.030	< 0.001
Hyperlipidemia	2440 (5.1%)	30,368 (6.5%)	0.061	< 0.001
Noncardiac comorbidities				
Respiratory disease	6344 (13.3%)	43,448 (9.3%)	0.125	< 0.001
Rheumatologic disease	6768 (14.2%)	57,031 (12.3%)	0.057	< 0.001
Peptic ulcer disease	431 (0.9%)	4270 (0.9%)	0.002	0.745
Renal disease	6063 (12.7%)	67,194 (14.4%)	0.051	< 0.001
Cancer	3311 (6.9%)	31,700 (6.8%)	0.005	0.311
Dementia	1617 (3.4%)	15,433 (3.3%)	0.004	0.414
Trauma	1936 (4.1%)	18,851 (4.1%)	< 0.001	0.967
Anemia/blood disease	5823 (12.2%)	53,972 (11.6%)	0.019	< 0.001
Depression	1044 (2.2%)	8698 (1.9%)	0.023	< 0.001
Hospital characteristics				
No. of teaching hospitals, n (%)	< 6	26 (16.8%)	0.409	0.036
Distance to nearest hospital, km	3.2 (1.4-9.8)	3.3 (1.8-6.4)	0.007	0.133
Average annual hospitalization volume				
AMI	13 (7-37)	61 (20-221)	0.702	< 0.001
HF	14 (7-32)	65 (24-236)	0.873	< 0.001
AF	8 (4-22)	35 (10-89)	0.672	< 0.001
Stroke	6 (2-18)	35 (10-146)	0.844	< 0.001
Length of hospital stay				
AMI	4 (2-7)	4 (2-7)	0.103	< 0.001
HF	6 (3-11)	6 (3-11)	0.004	0.642
AF	4 (2-7)	3 (1-6)	0.155	< 0.001
Stroke	7 (3-14)	7 (4-14)	0.047	< 0.001
No. of beds per 1000 population				
Overall	2.50	1.25	0.029	0.003
Rural	2.41	1.54	0.020	0.033
Urban	2.54	1.24	0.030	0.057

AF, atrial fibrillation; AMI, acute myocardial infarction; CABG, coronary artery bypass grafting; HF, heart failure; HTN, hypertension; MI, myocardial infarction; PCI, percutaneous coronary intervention; PVD, peripheral vascular disease.

* Socioeconomic status data missing in 443 (0.9%) Northern and 1802 (0.4%) Southern patients.

[†] Continuous data are shown as median (interquartile range [IQR]).

[‡] Residence information missing in 4747 (9.9%) Northern patients and 1332 (0.3%) Southern patients.

first hospital admission for the disease of interest for the patient) hospitalizations (n = 176,450). After applying exclusion criteria (Fig. 1), the final cohort consisted of 47,745 Northern and 465,353 Southern index patient hospitalizations. Patient characteristics showed small absolute differences in comorbidities and condition-specific length of stay between North and South (Table 1). Larger differences

between the North and South were observed in hospital volumes, teaching status, and rurality. The distribution of Johns Hopkins Aggregated Diagnosis Group, which was adjusted for in the model, is shown for the diagnosis-specific cohorts in Supplemental Tables S2-S5. The number of beds per 1000 population was higher in Northern than Southern Ontario (Table 1).

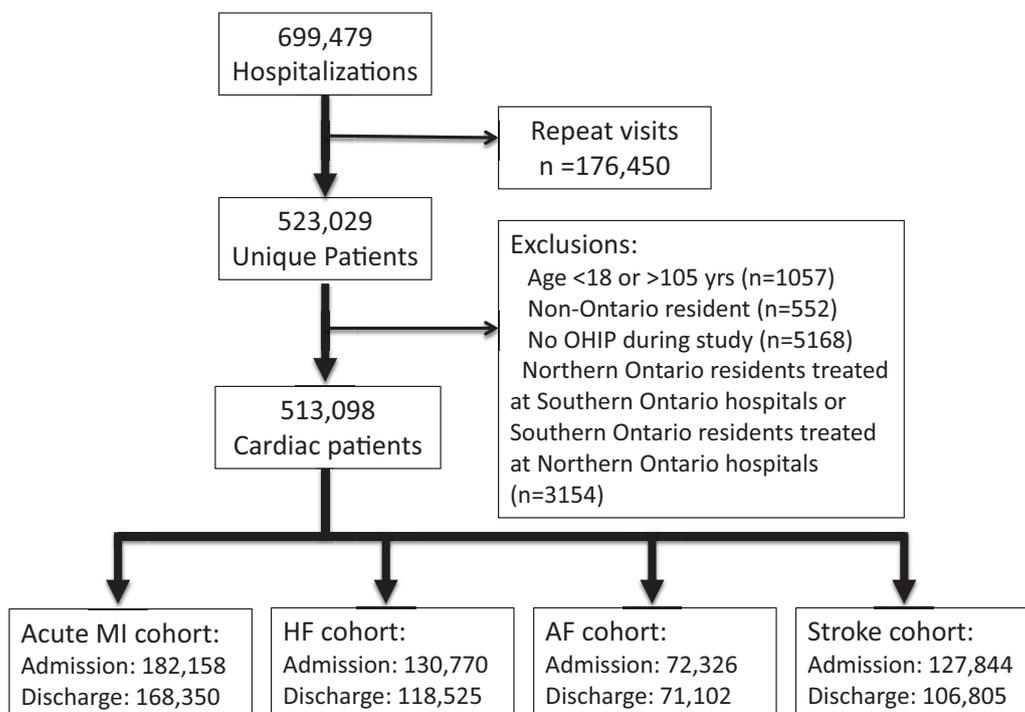


Figure 1. Participant flow chart. AF, atrial fibrillation; HF, heart failure; MI, myocardial infarction; OHIP, Ontario Health Insurance Program.

Myocardial infarction

There were 182,158 patients with AMI, of whom 18,374 were Northern (median age, 69 years [IQR, 58-80], 61.5% were men) and 163,784 were Southern (median age, 69 years [IQR, 57-80], 64.3% were men). Characteristics of the index AMI cohort are shown in [Supplemental Table S2](#). Northern patients with AMI had a marginally higher prevalence of diabetes (37.4% vs 35.5%, $P < 0.001$), whereas Southern patients had higher rates of prior percutaneous coronary intervention (29.3% vs 23.7%, $P < 0.001$) as detailed in [Supplemental Table S2](#). Among 16,939 Northern and 151,411 Southern patients discharged alive after index AMI, crude readmission rates were higher in the North ([Table 2](#)). Crude 1-year mortality ([Table 3](#)) and cumulative incidence of readmission were significantly higher in the North ([Fig. 2](#)).

Table 2. Crude rate of readmission at 30 days and 1 year by cardiovascular diagnosis

	Northern rate	Southern rate	P value
AMI			
Per 100 person-mo	21.7	15.9	< 0.001
Per 100 person-y	89.5	63.5	< 0.001
HF			
Per 100 person-mo	28.3	23.6	< 0.001
Per 100 person-y	162.3	133.7	< 0.001
AF			
Per 100 person-mo	19.1	15.4	< 0.001
Per 100 person-y	93.0	73.7	< 0.001
Stroke			
Per 100 person-mo	12.8	10.8	< 0.001
Per 100 person-y	76.0	57.1	< 0.001

AF, atrial fibrillation; AMI, acute myocardial infarction; HF, heart failure.

After multivariable adjustment, 1-year mortality ([Table 3](#)) first readmission, and any readmissions were higher (all $P < 0.001$) in the North ([Table 4](#)).

Heart failure

Among 130,770 patients with HF, 11,717 were Northern (median age, 78 years [IQR, 69-85], 51.4% were men) and 119,053 (median age, 80 years [IQR, 71-86], 49.8% were men) were Southern. Characteristics of the index HF cohort are shown in [Supplemental Table S3](#). Northern patients were more likely to have respiratory disease (26.3% vs 18.5%, $P < 0.001$), and Southern patients had higher rates of renal disease (27.4% vs 23.9%, $P < 0.001$) as shown in [Supplemental Table S3](#). Of 10,605 Northern and 107,920 Southern patients discharged alive after index HF hospitalization, crude readmission rates were again higher in the North ([Table 2](#)). Crude mortality rates did not differ ([Table 3](#)), but cumulative incidence of readmissions was significantly higher in the North ([Fig. 3](#)).

In adjusted analyses, there was no difference in mortality ([Table 3](#)), but both first and repeat readmissions (both $P < 0.001$, [Table 4](#)) were significantly higher among patients with HF discharged from Northern hospitals.

Atrial fibrillation

There were 72,326 patients with AF, of whom 7530 were Northern (74 years [IQR, 64-82], 49.4% were men) and 64,796 were Southern (75 years [IQR, 64-83], 49.7% were men). Southern patients had more renal disease, but Northern patients had more respiratory disease ([Supplemental Table S4](#)). There were 7430 Northern and 63,672 Southern patients discharged alive after AF hospitalization, and again,

Table 3. Mortality outcomes after multivariable adjustment*

	Northern	Southern	P value
AMI			
Crude mortality rates			
30 d	8.9%	8.6%	0.153
1 y	17.9%	17.0%	0.002
Adjusted HR (95% CI)			
30 d	1.05 (1.00-1.11)	Reference	0.062
1 y	1.05 (1.01-1.09)	Reference	0.007
HF			
Crude mortality rates			
30 d	11.2%	11.4%	0.462
1 y	33.8%	34.2%	0.457
Adjusted HR (95% CI)			
30 d	0.97 (0.91-1.03)	Reference	0.288
1 y	0.99 (0.96-1.03)	Reference	0.739
AF			
Crude mortality rates			
30 d	2.5%	3.0%	0.012
1 y	12.7%	13.4%	0.101
Adjusted HR (95% CI)			
30 d	0.87 (0.74-1.01)	Reference	0.066
1 y	0.95 (0.88-1.02)	Reference	0.138
Stroke			
Crude mortality rates			
30 d	17.7%	17.3%	0.284
1 y	28.4%	28.8%	0.347
Adjusted HR (95% CI)			
30 d	1.03 (0.98-1.08)	Reference	0.239
1 y	0.99 (0.95-1.03)	Reference	0.560

AF, atrial fibrillation; AMI, acute myocardial infarction; CI, confidence interval; HF, heart failure; HR, hazard ratio.

* Multivariable models adjusted for hypertension, diabetes, prior MI, unstable angina, chronic atherosclerosis, smoking history, AF, prior HF, prior HF hospitalization, prior CABG surgery, prior PCI, implantable defibrillator, pacemaker, peripheral vascular disease, cerebrovascular disease, respiratory disease, rheumatologic disease, peptic ulcer disease, renal disease, cancer, trauma, anemia/blood disease, depression, Johns Hopkins Aggregated Diagnosis Group, hyperlipidemia, other respiratory disease, dementia, thyroid disease, pulmonary vascular disease, pericarditis, endocarditis, cardiomyopathy, myocarditis, left bundle-branch block, socioeconomic status, distance from the nearest hospital to home, year of admission, season (winter, spring, summer, fall), and hospital volume tertile (low, intermediate, high).

crude readmission rates were higher in the North (Table 2). Again, the cumulative incidence of death did not differ, but readmissions were significantly higher in the North (Fig. 4). AF readmissions, both first and repeat events, were significantly higher in the North after multivariable adjustment (both $P < 0.001$, Table 4).

Stroke

There were 127,844 patients admitted with stroke, of whom 10,124 were Northern (median age, 75 years [IQR, 64-82], 52.2% were men) and 117,720 were Southern (median age, 76 years [IQR, 64-84], 50.4% were men) (Supplemental Table S5). There were 8358 patients with stroke who were discharged from the North and 98,447 patients discharged from the South, and again, unadjusted rates of readmission were higher in Northern Ontario (Table 2). Crude mortality (Table 3) and cumulative incidence of death did not differ, but the probability of readmission was significantly higher in the North (Fig. 5). After multivariable adjustment, readmissions after acute stroke were significantly

increased in multivariable-adjusted analyses for both first and repeat events (Table 4).

Medical care

Within 30 days of admission for AMI, HF, or AF, patients hospitalized in the North were significantly less likely to be attended by a consultant cardiologist (Table 5). Patients admitted with acute stroke were also less likely to be attended by a consultant neurologist in the North (Table 5). Key procedures were also less likely to be performed within 30 days, including cardiac catheterization or stress testing for AMI, echocardiogram for HF or AF, and brain computed tomography or magnetic resonance imaging for acute stroke (Table 5).

Stratification by rurality index. Stratified analyses of rural patients in the North vs rural patients in the South are shown in Supplemental Tables S6-S10. Readmission rates remained higher in the rural North than in the rural South (Supplemental Table S9). Likewise, analyses of urban patients in the North vs urban patients in the South are shown in Supplemental Tables S11-S15. Readmission rates continued to be higher in the North vs the South among those in urban areas (Supplemental Table S14). Access to specialists and key procedures remained lower in the North compared with the South irrespective of rural vs urban region of residence (Supplemental Tables S10 and S15). Length of stay in hospital differed only minimally but tended to be longer in the North than the South, even after stratification by rurality (Supplemental Table S16). Finally, we conducted analyses stratified by rural or urban hospital with or without on-site multidisciplinary HF clinics, and the readmission risks remained significantly higher in the North compared with the South (data not shown).

Costs. Overall costs for the index hospital admission, 30-day postdischarge transition period, and 1-year postdischarge are shown in Supplemental Table S17. In-hospital costs and 30-day postdischarge costs were lower in the North. However, 1-year costs tended to be higher for HF and AF and were significantly higher for myocardial infarction in the North (Supplemental Table S17). One-year stroke costs remained significantly lower in the North.

Discussion

We found that patients admitted with acute cardiovascular conditions at hospitals in Northern Ontario had significantly higher rates of readmission after their index hospital discharge. The hazards of both first readmission and repeat readmissions were higher in the North for all conditions evaluated. In contrast, mortality rates were largely similar in both regions, with the only signal for higher risk observed after AMI in the North at 1 year. Early access to specialized physician care, cardiac testing, and brain imaging were lower in the North. The in-hospital and 30-day postdischarge costs were lower for all conditions in the North. At 1 year, however, costs in the North were higher for AMI, slightly higher for HF or AF, and lower for stroke.

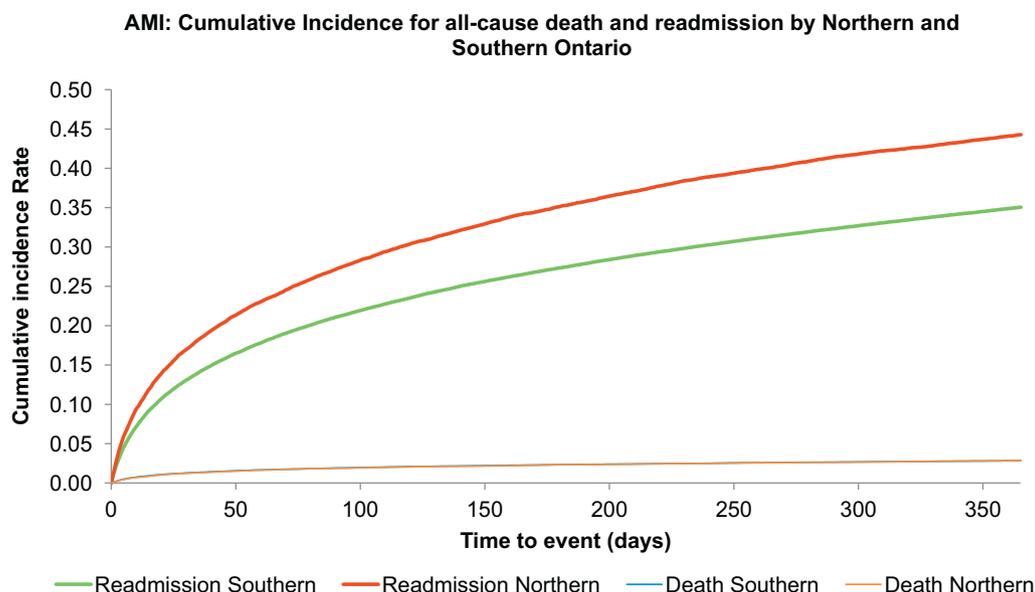


Figure 2. Acute myocardial infarction (AMI): cumulative incidence for all-cause death and readmission by Northern and Southern Ontario.

There is a paucity of studies that comprehensively examine regional outcomes of CVD. Since our analysis found that more than one-third of Northern patients lived in rural regions, we anticipated that prior studies comparing rural and urban residence on mortality could be informative. However, although we found minimal differences in mortality between Northern and Southern Ontario, data from the United States exhibited variability. Patients in rural Maine had no difference

in coronary mortality after AMI, despite reduced access to interventional cardiology services.²¹ In a large study of critical access hospitals serving persons who live in rural areas of the United States, mortality for hospitalized rural patients was 70% higher after AMI and 28% higher after HF admission compared with urban regions.²² Favourable trends in coronary heart disease mortality rates were found in urban but not in rural regions, resulting in worse coronary disease survival in rural areas.²³

The impact of rurality on CVD readmissions has also been understudied, but published studies have found variable impacts on readmissions. Outpatients with chronic, stable HF living in rural areas of the United States had significantly lower risk of readmissions or emergency department visits than those in urban areas.²⁴ At critical access hospitals providing surgical care to Medicare beneficiaries, there was only an approximately 1% absolute increase in 30-day readmissions at rural hospitals.²⁵ Our study adds to the current literature with the finding that geographic factors may be of greater importance for readmission outcomes than rurality, because all cardiovascular conditions exhibited higher readmission rates in both rural and urban regions in the North.

Among the multiple potential reasons for the high readmission rates in Northern Ontario, reduced access to care is one potential explanation. The **Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients With Heart Failure (OPTIMIZE-HF)** and the **Get With The Guidelines-Heart Failure (GWTG-HF)** registries found that those living in hospital referral regions where there was higher physician concentration were 29% more likely to undergo early follow-up.²⁶ The lack of specialized physician involvement may have had an impact because specialist care has been associated with improved outcomes and reduced readmissions for patients with acute coronary syndromes,²⁷⁻³⁰ HF,⁹ AF,³¹ and stroke.³² We found that rurality, hospital volume, length of hospital stay, patient comorbidities, distance to the hospital, or the presence of multidisciplinary HF clinics did not explain our

Table 4. Readmission outcomes at 1 year after multivariable adjustment*

	Northern	Southern	P value
AMI	HR (95% CI)	HR (95% CI)	
First readmission	1.32 (1.29-1.35)	Reference	< 0.001
Repeat readmissions	1.23 (1.21-1.26)	Reference	< 0.001
HF	HR (95% CI)	HR (95% CI)	
First readmission	1.16 (1.13-1.19)	Reference	< 0.001
Repeat readmissions	1.13 (1.11-1.15)	Reference	< 0.001
AF	HR (95% CI)	HR (95% CI)	
First readmission	1.21 (1.17-1.26)	Reference	< 0.001
Repeat readmissions	1.18 (1.14-1.21)	Reference	< 0.001
Stroke	HR (95% CI)	HR (95% CI)	
First readmission	1.27 (1.22-1.31)	Reference	< 0.001
Repeat readmissions	1.22 (1.18-1.25)	Reference	< 0.001

AF, atrial fibrillation; AMI, acute myocardial infarction; CI, confidence interval; HF, heart failure; HR, hazard ratio.

* Multivariable models adjusted for hypertension, diabetes, prior MI, unstable angina, chronic atherosclerosis, AF, smoking history, prior HF, prior HF hospitalization, prior CABG surgery, prior PCI, implantable defibrillator, pacemaker, peripheral vascular disease, cerebrovascular disease, respiratory disease, rheumatologic disease, peptic ulcer disease, renal disease, cancer, trauma, anemia/blood disease, depression, Johns Hopkins Aggregated Diagnosis Group, hyperlipidemia, other respiratory disease, dementia, thyroid disease, pulmonary vascular disease, pericarditis, endocarditis, cardiomyopathy, myocarditis, left bundle-branch block, socioeconomic status, distance from the nearest hospital to home, year of admission, season (winter, spring, summer, fall), hospital volume tertile (low, intermediate, high), and length of stay during index hospital admission.

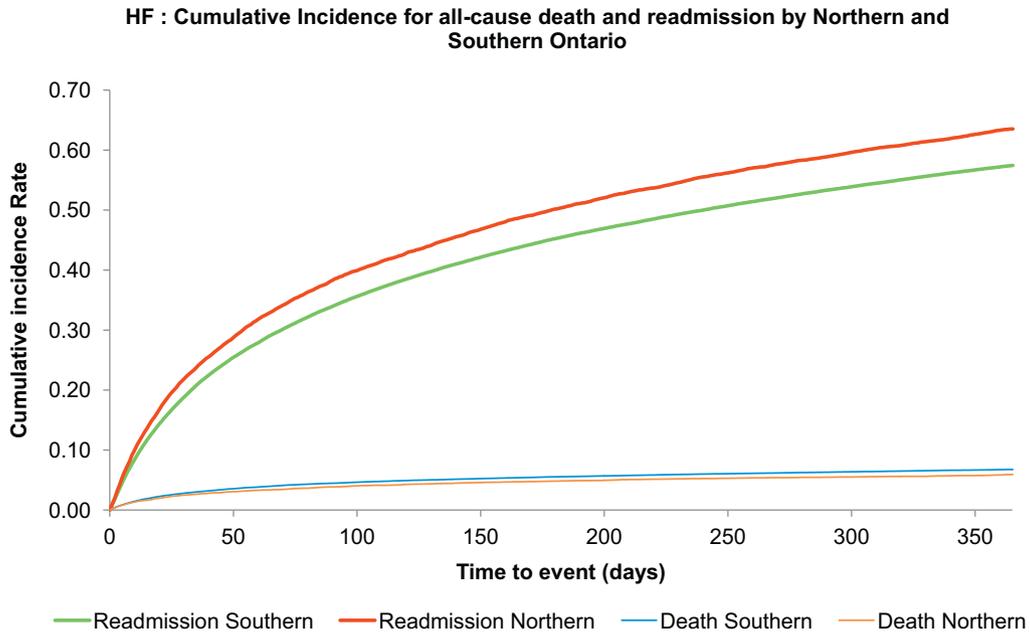


Figure 3. Heart failure (HF): cumulative incidence for all-cause death and readmission by Northern and Southern Ontario.

findings, because an increased readmission risk was observed despite accounting for these factors. Finally, the number of hospital beds per capita was higher in the North, and thus bed availability also did not explain our observations.

Our study suggests that there is greater need to understand why readmissions are higher in Northern Ontario. Readmissions are costly to the healthcare system and may have contributed to the late increases in costs for patients with myocardial infarction, HF, and AF. Prior studies have found

that hospital readmissions are explained, in part, by reduced access to transitional care, with early, specialized postdischarge care leading to reduced repeat hospitalizations.³³ Improved access to postdischarge specialized care may be of even greater importance because the complexity of medical care is increasing. Examples of this complexity include new drug therapies (eg, sacubitril/valsartan, ivabradine), implantable devices for HF, interventional procedures for AF or valvular heart disease management, and polypharmacy (eg, P2Y12

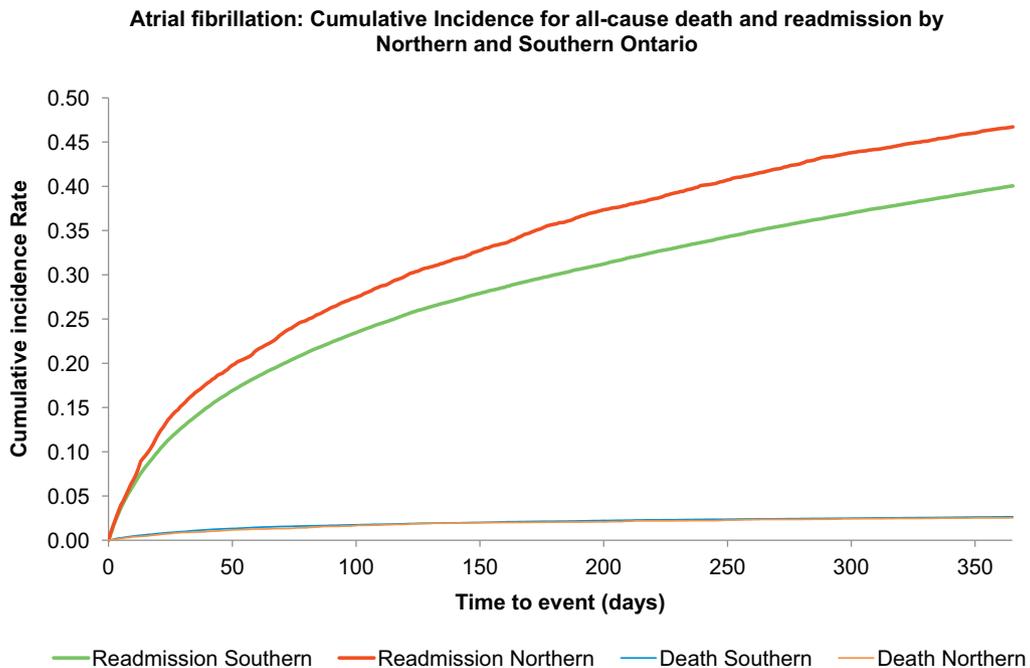


Figure 4. Atrial fibrillation (AF): cumulative incidence for all-cause death and readmission by Northern and Southern Ontario.

Stroke: Cumulative Incidence for all-cause death and readmission by Northern and Southern Ontario

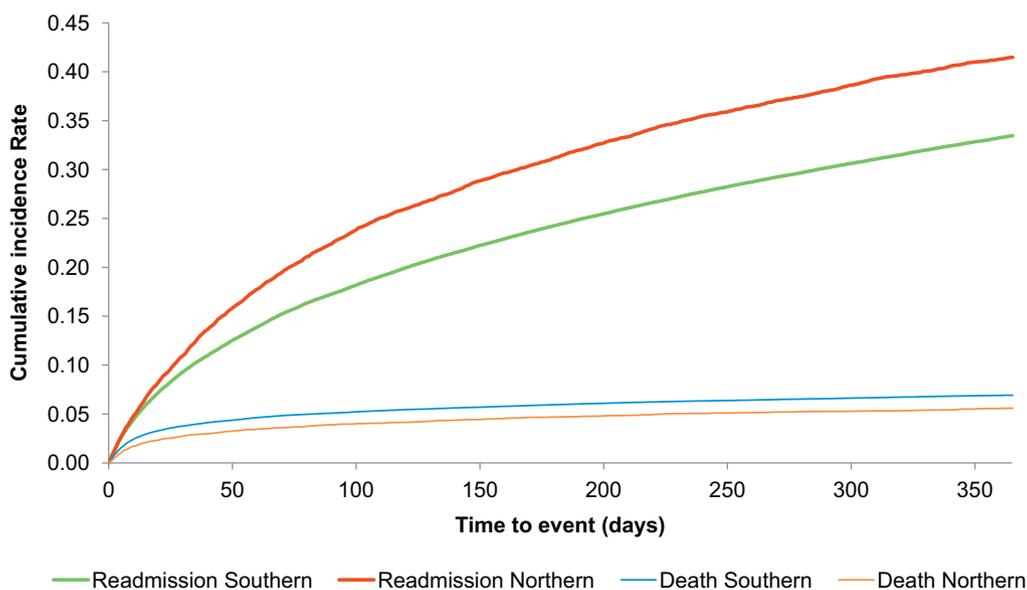


Figure 5. Stroke: cumulative incidence for all-cause death and readmission by Northern and Southern Ontario.

inhibitors and novel anticoagulants for combined coronary disease and AF). In addition to these, other factors, such as improved patient education and access to community and primary care, also may be important in reducing readmissions.

The higher Northern cardiovascular mortality found by HQO despite similar mortality rates after discharge for HF, AF, and stroke in this study suggests the possibility that more people are dying of CVD in the North before coming to medical

Table 5. Access to specialist care and diagnostic testing within 30 days of hospital admission*

	Adjustment	Northern	Southern	P value
AMI		HR (95% CI)[†]	HR (95% CI)	
Cardiology	Age and sex	0.66 (0.65-0.67)	Reference	< 0.001
	Multivariable	0.71 (0.70-0.72)	Reference	< 0.001
Cardiac catheterization or stress test	Age and sex	0.77 (0.75-0.78)	Reference	< 0.001
	Multivariable	0.80 (0.79-0.82)	Reference	< 0.001
HF		HR (95% CI)[†]	HR (95% CI)	
Cardiology	Age and sex	0.58 (0.56-0.59)	Reference	< 0.001
	Multivariable	0.68 (0.66-0.70)	Reference	< 0.001
Echocardiogram	Age and sex	0.76 (0.74-0.78)	Reference	< 0.001
	Multivariable	0.88 (0.86-0.91)	Reference	< 0.001
AF		HR (95% CI)[†]	HR (95% CI)	
Cardiology	Age and sex	0.60 (0.58-0.62)	Reference	< 0.001
	Multivariable	0.67 (0.65-0.69)	Reference	< 0.001
Echocardiogram	Age and sex	0.79 (0.77-0.82)	Reference	< 0.001
	Multivariable	0.85 (0.82-0.88)	Reference	< 0.001
Stroke		HR (95% CI)[†]	HR (95% CI)	
Neurologist	Age and sex	0.48 (0.47-0.50)	Reference	< 0.001
	Multivariable	0.59 (0.57-0.62)	Reference	< 0.001
Brain CT or MRI	Age and sex	0.75 (0.73-0.77)	Reference	< 0.001
	Multivariable	0.87 (0.84-0.89)	Reference	< 0.001

AF, atrial fibrillation; AMI, acute myocardial infarction; CI, confidence interval; CT, computed tomography; HF, heart failure; HR, hazard ratio; MI, myocardial infarction; MRI, magnetic resonance imaging.

* Multivariable models adjusted for hypertension, diabetes, prior MI, unstable angina, chronic atherosclerosis, smoking history, AF, prior HF, prior HF hospitalization, prior CABG surgery, prior PCI, implantable defibrillator, pacemaker, peripheral vascular disease, cerebrovascular disease, respiratory disease, rheumatologic disease, peptic ulcer disease, renal disease, cancer, trauma, anemia/blood disease, depression, Johns Hopkins Aggregated Diagnosis Group, hyperlipidemia, other respiratory disease, dementia, thyroid disease, pulmonary vascular disease, pericarditis, endocarditis, cardiomyopathy, myocarditis, left bundle-branch block, socioeconomic status, distance from the nearest hospital to home, year of admission, season (winter, spring, summer, fall), hospital volume tertile, and length of stay during index hospital admission.

[†] An adjusted HR < 1.0 indicates reduced likelihood of cardiology consultation after hospital admission for AMI, HF, or AF or reduced likelihood of neurology evaluation after admission for stroke. An adjusted HR < 1.0 indicates reduced likelihood of cardiac stress testing or cardiac catheterization after admission for AMI, echocardiogram after HF hospitalization or AF, and brain CT or MRI after stroke admission.

attention.⁸ In our study, there was reduced access to consultant physicians within 30 days of discharge, and the findings of the HQO report may have been contributed by difficulty in visiting primary care providers or specialists on the same or next day because of lack of physician availability or transportation challenges.⁸ To improve health care for people in the North, programs have been started to address these issues, including the Ontario Telemedicine Network, mobile health services, and travel grants. Finally, future studies could examine the drivers of the lower in-hospital and 30-day costs of care in the North, which may inform how efficiencies in care might be realized in the South.

Study limitations

Our study should be interpreted in light of potential limitations. Although associations between Northern residence and care processes were observed, we cannot infer that these were causally related. Indeed, the underlying reasons for our observations remain undefined. Finally, we did not account for care delivered to indigenous persons and those living on reserve, who may be represented to a greater extent in Northern Ontario and may exhibit poor CVD outcomes.

Conclusions

Patients hospitalized for cardiovascular conditions in Northern Ontario were at substantially higher risk of first readmission and repeat readmissions compared with those in the South. However, 30-day mortality was not significantly different despite lower in-hospital costs for all of these conditions in the North. Higher overall rates of cardiovascular mortality and rates of readmission in the North suggest that access to physicians and other facets of postdischarge transitional care could influence these potentially ambulatory care-sensitive outcomes. Our study highlights the need for studies to further evaluate the care and outcomes of those living in the North.

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Disclosures

The authors have no conflicts of interest to disclose.

References

1. GBD Causes of Death Collaborators. Global, regional, and national age-sex specific mortality for 264 causes of death, 1980-2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet* 2017;390:1151-210.
2. Statistics Canada. Statistics Canada Table 102-0551: deaths and mortality rate, by selected group causes, age group and sex, Canada, CANSIM database. Available at: <http://www5.statcan.gc.ca/cansim/a26?lang=eng&id=1020551>. Accessed August 18, 2018.
3. Roth GA, Johnson C, Abajobir A, et al. Global, regional, and national burden of cardiovascular diseases for 10 causes, 1990 to 2015. *J Am Coll Cardiol* 2017;70:1-25.
4. Centers for Disease Control and Prevention. Healthcare Cost and Utilization Project (HCUP): National Inpatient Survey. Updated February 27, 2018. Available at: <https://chronicdata.cdc.gov/Heart-Disease-Stroke-Prevention/Healthcare-Cost-and-Utilization-Project-HCUP-Natio/ntny-77fx>. Accessed August 18, 2018.
5. Tu JV, Nardi L, Fang J, et al; Canadian Cardiovascular Outcomes Research Team. National trends in rates of death and hospital admissions related to acute myocardial infarction, heart failure and stroke, 1994-2004. *CMAJ* 2009;180:E118-25.
6. Glazier R, Gozdyra P, Yeritsyan N. Geographic access to primary care and hospital services for rural and northern communities: report to the Ontario Ministry of Health and Long-Term Care. Toronto: ICES, 2011.
7. Bhatia RS, Austin PC, Stukel TA, et al. Outcomes in patients with heart failure treated in hospitals with varying admission rates: population-based cohort study. *BMJ Qual Saf* 2014;23:981-8.
8. Health Quality Ontario. Health in the North: a report on geography and health of people in Ontario's two northern regions. August 13, 2017. Toronto: Health Quality Ontario, 2016.
9. Lee DS, Stukel TA, Austin PC, et al. Improved outcomes with early collaborative care of ambulatory heart failure patients discharged from the emergency department. *Circulation* 2010;122:1806-14.
10. Krumholz HM, Wang Y, Mattera JA, et al. An administrative claims model suitable for profiling hospital performance based on 30-day mortality rates among patients with heart failure. *Circulation* 2006;113:1693-701.
11. Keenan PS, Normand SL, Lin Z, et al. An administrative claims measure suitable for profiling hospital performance on the basis of 30-day all-cause readmission rates among patients with heart failure. *Circ Cardiovasc Qual Outcomes* 2008;1:29-37.
12. Tu K, Campbell NR, Chen ZL, Cauch-Dudek KJ, McAlister FA. Accuracy of administrative databases in identifying patients with hypertension. *Open Med* 2007;1:e18-26.

13. Hux JE, Ivis F, Flintoft V, Bica A. Diabetes in Ontario: determination of prevalence and incidence using a validated administrative data algorithm. *Diabetes Care* 2002;25:512-6.
14. Schultz SE, Rothwell DM, Chen Z, Tu K. Identifying cases of congestive heart failure from administrative data: a validation study using primary care patient records. *Chronic Dis Inj Can* 2013;33:160-6.
15. Tu JV, Chu A, Rezaei MR, et al. The incidence of major cardiovascular events in immigrants to Ontario, Canada: The CANHEART Immigrant Study. *Circulation* 2015;132:1549-59.
16. Goldraich L, Austin PC, Zhou L, et al. Care setting intensity and outcomes after emergency department presentation among patients with acute heart failure. *J Am Heart Assoc* 2016;5:e003232.
17. Joynt KE, Orav EJ, Jha AK. The association between hospital volume and processes, outcomes, and costs of care for congestive heart failure. *Ann Intern Med* 2011;154:94-102.
18. Sud M, Yu B, Wijesundera HC, et al. Associations between short or long length of stay and 30-day readmission and mortality in hospitalized patients with heart failure. *JACC Heart Fail* 2017;5:578-88.
19. Wijesundera HC, Trubiani G, Wang X, et al. A population-based study to evaluate the effectiveness of multidisciplinary heart failure clinics and identify important service components. *Circ Heart Fail* 2013;6:68-75.
20. Braga JR, Tu JV, Austin PC, et al. Recurrent events analysis for examination of hospitalizations in heart failure: insights from the Enhanced Feedback for Effective Cardiac Treatment (EFFECT) trial. *Eur Heart J Qual Care Clin Outcomes* 2018;4:18-26.
21. Rhudy JP Jr, Alexandrov AW, Hyrkas KE, et al. Geographic access to interventional cardiology services in one rural state. *Heart Lung* 2016;45:434-40.
22. Joynt KE, Harris Y, Orav EJ, Jha AK. Quality of care and patient outcomes in critical access rural hospitals. *JAMA* 2011;306:45-52.
23. Kulshreshtha A, Goyal A, Dabhadkar K, Veledar E, Vaccarino V. Urban-rural differences in coronary heart disease mortality in the United States: 1999-2009. *Public Health Rep* 2014;129:19-29.
24. Wu JR, Moser DK, Rayens MK, et al. Rurality and event-free survival in patients with heart failure. *Heart Lung* 2010;39:512-20.
25. Ibrahim AM, Hughes TG, Thumma JR, Dimick JB. Association of hospital critical access status with surgical outcomes and expenditures among Medicare beneficiaries. *JAMA* 2016;315:2095-103.
26. Kociol RD, Greiner MA, Fonarow GC, et al. Associations of patient demographic characteristics and regional physician density with early physician follow-up among Medicare beneficiaries hospitalized with heart failure. *Am J Cardiol* 2011;108:985-91.
27. Ayanian JZ, Landrum MB, Guadagnoli E, Gacione P. Specialty of ambulatory care physicians and mortality among elderly patients after myocardial infarction. *N Engl J Med* 2002;347:1678-86.
28. Radzimanowski M, Gallowitz C, Muller-Nordhorn J, Rieckmann N, Tenckhoff B. Physician specialty and long-term survival after myocardial infarction - A study including all German statutory health insured patients. *Int J Cardiol* 2018;251:1-7.
29. Czarnecki A, Chong A, Lee DS, et al. Association between physician follow-up and outcomes of care after chest pain assessment in high-risk patients. *Circulation* 2013;127:1386-94.
30. O'Neill DE, Southern DA, Norris CM, et al. Acute coronary syndrome patients admitted to a cardiology vs non-cardiology service: variations in treatment & outcome. *BMC Health Serv Res* 2017;17:354.
31. Atzema CL, Dorian P, Ivers NM, Chong AS, Austin PC. Evaluating early repeat emergency department use in patients with atrial fibrillation: a population-based analysis. *Am Heart J* 2013;165:939-48.
32. Smith MA, Liou JI, Frytak JR, Finch MD. 30-day survival and rehospitalization for stroke patients according to physician specialty. *Cerebrovasc Dis* 2006;22:21-6.
33. Feltner C, Jones CD, Cene CW, et al. Transitional care interventions to prevent readmissions for persons with heart failure: a systematic review and meta-analysis. *Ann Intern Med* 2014;160:774-84.

Supplementary Material

To access the supplementary material accompanying this article, visit the online version of the *Canadian Journal of Cardiology* at www.onlinecjc.ca and at <https://doi.org/10.1016/j.cjca.2019.01.004>.