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Avoidable Acute Care Use by Persons with Rheumatoid Arthritis: A Population-Based Study

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Avoidable Acute Care Use by Persons with Rheumatoid Arthritis: A Population-Based Study

by

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ABSTRACT

Rheumatoid Arthritis (RA) is Canada's most common chronic inflammatory joint disease, affecting 1.2% of Canadians 16 years and older, and is more prevalent among females. People with RA have an increased risk of mortality compared to the general population due to comorbidities such as cardiovascular disease, depression, and osteoporosis. The presence of these comorbidities can lead to increased healthcare utilization, including hospitalizations. Most healthcare interactions for treating and monitoring RA occur in the outpatient setting, usually with a family physician or a rheumatologist.

Ambulatory Care Sensitive Conditions (ACSCs) were thus derived as a list of conditions where appropriate ambulatory care would prevent or reduce the need for hospital admission. The objective of this thesis is to estimate incidence rates of avoidable acute care use by persons with RA relative to the general population.

The RA cohort was established by identifying individuals meeting a validated case definition for RA based on ICD-9-CM and ICD-10-CA codes in years 2002-2023. Four general population controls were matched to each RA case by age, sex, and date of diagnosis. Acute care use for ACSCs including grand mal seizures, chronic lower respiratory diseases, asthma, diabetes, heart failure and pulmonary edema, hypertension, and angina from 2007-2023 were identified by established diagnostic codes. Incidence rate ratios were calculated using a multivariable regression model adjusting for age, sex, and location of residence. A Cox proportional hazards model was used to identify predictors of avoidable hospitalizations among RA patients.

RA cases had a 14% higher risk of hospitalization and a 6% higher rate of ED visits for any ACSC compared those without RA. Significant predictors of ACSC hospitalizations for RA

cases were increasing age, prolonged exposure to corticosteroids, being from a rural location, and having comorbid conditions, especially if the comorbid condition is an ACSC.

Persons with RA are at a higher risk of potentially avoidable acute care use compared to those without RA. Improved ambulatory care access and quality, inclusive of primary care and contributing role of subspecialty care, is proposed to prevent unnecessary hospitalizations and reduce burden on the acute care system.

PREFACE

This manuscript-based thesis consists of five chapters.

Chapter 1 introduces the background, motivation, research objectives and related literature.

Chapter 2 discusses the methods and statistical analyses used.

Chapter 3 is a co-authored manuscript submitted under review in a peer-reviewed journal (Arthritis Care & Research).

Chapter 4 is a co-authored manuscript submitted to the Canadian Journal of Emergency Medicine.

Finally, Chapter 5 discusses the results, implications, future directions, and significance of this master's thesis.

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Palangga ko kamo tanan (I love you all).

DEDICATION

To Kailey.

Everything I do is for you.

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LIST OF ABBREVIATIONS

ACR: American College of Rheumatology

ACPA: Anti-Citrullinated Protein Antibody

ACPAC: Advanced Clinical Practitioner in Arthritis Care

ACSC: Ambulatory Care Sensitive Condition

AHCIP: Alberta Health Care Insurance Plan

AHRQ: Agency for Healthcare Research and Quality

AIC: Akaike Information Criterion

bDMARD: Biologic disease-modifying anti-rheumatic drug

CCDSS: Canadian Chronic Disease Surveillance System

CCI: Charlson Comorbidity Index

CI: Confidence Interval

CIHI: Canadian Institute for Health Information

CMA: Canadian Medical Association

COPD: Chronic Obstructive Pulmonary Disease

CPAR: Central Patient Attachment Registry

CRA: Canadian Rheumatology Association

CRP: C-reactive Protein

csDMARD: Conventional synthetic disease-modifying anti-rheumatic drug

CTAS: Canadian Triage and Acuity Scale

CVD: Cardiovascular diseases

DAD: Discharge Abstract Database

DMARD: Disease-modifying anti-rheumatic drug

ED: Emergency Department

EULAR: European League Against Rheumatism

FFS: Fee-for-Service

FN: First Nation

GBD: Global Burden of Diseases

GC: Glucocorticoids

GP: General Practitioners

HSP: Health System Performance

HR: Hazard Ratio

IA: Inflammatory Arthritis

ICD: International Classification of Diseases

IQR: Interquartile Range

IRR: Incidence Rate Ratio

JAK: Janus Kinase

MTX: Methotrexate

NACRS: National Ambulatory Care Reporting System

NPV: Negative Predictive Value

PCP: Primary Care Provider

PHC: Primary Health Care

PIN: Pharmaceutical Information Network

PPV: Positive Predictive Value

RA: Rheumatoid Arthritis

RF: Rheumatoid Factor

SD: Standard Deviation

T2T: Treat-to-Target

TNF: Tumor Necrosis Factor

tsDMARD: Targeted synthetic disease-modifying anti-rheumatic drug

ULI: Unique Lifetime Identifier

Chapter 1 – INTRODUCTION

1.1 Rheumatoid Arthritis

Rheumatoid arthritis (RA) is a chronic systemic inflammatory disease characterized by pain, swelling and stiffness of articular joints, commonly of the hands and feet. Systemic manifestations of RA can include fatigue and fever (1). The contributing causes that lead to RA development are still being elucidated, but many studies have identified that there is an interplay between genetic and environmental risk factors. For example, specific genetic factors that increase risk include the human leukocyte antigen (HLA)-DRB1 alleles, while acquired environmental risks including smoking, and viral or bacterial infectious triggers have also been described (2, 3).

1.2 RA comorbidities

People with RA may also have other co-occurring conditions that can arise due to the effects of chronic systemic inflammation, consequences of treatment, as well as overlapping risks between RA and other conditions. As patients try to navigate the healthcare system for the diagnosis and treatment of RA, they also have the additional burden of managing other comorbid conditions. In a cross-sectional study conducted in Germany that used patient-reported outcomes with claims data, a cohort of 96,921 persons with RA and age- and sex-matched controls were examined to determine the prevalence of comorbidities (4). Researchers found hypertension, osteoarthritis, depression, and osteoporosis as the most prevalent conditions comorbid to RA, and were much more prevalent among those with RA compared to controls. The authors acknowledged that the diagnoses in the claims data have not been validated.

In a multinational, cross-sectional study of 3,920 individuals with RA across 17 countries, the prevalence of comorbidities was estimated by self-report. The most common comorbidity was depression, with a mean prevalence of 15%, but with high variability among countries (5). Approximately 6% had a history of cardiovascular diseases (CVD) such as myocardial infarction or stroke (5). There was also a high prevalence of risk factors related to CVD in this cohort: approximately 43% had a high Framingham Risk, which is used to determine one's risk of developing CVD, 40% had hypertension, and 32% had high cholesterol.

In a 15-year cohort study conducted in the Netherlands examining mortality among those with RA vs the general population, the observed mortality was approximately 54% higher among those with RA and was especially pronounced for cardiovascular, respiratory, and musculoskeletal diseases (6).

There is an increased risk of developing comorbidities that may result from chronic inflammation from RA.

1.3 Epidemiology of RA

1.3.1 Overall population rates

The Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) estimates that in 2020, 17.6 million people live with RA (95% CI 15.8, 20.3) (7). The age-standardized prevalence was estimated at 208.8 per 100,000, with a higher prevalence in low- and middle-income countries (4).

The Canadian Chronic Disease Surveillance System (CCDSS) is a collaborative network of provincial and territorial surveillance systems, that generates national estimates and trends for

over 20 chronic diseases and conditions (8). Provincial and territorial databases use validated diagnostic codes and algorithms to define a disease or condition and use unique personal identifiers to corresponding physician claims, hospitalization discharge abstract records, and prescription information. Altogether, it is estimated that in 2020-2021, more than 450,000 individuals in Canada 16 years and older had RA (8).

1.3.2 Variations in RA Prevalence by Sex

RA is more prevalent among women (7). In 2020, RA cases globally were two times more prevalent among females than males, with an age-standardized prevalence of 293.5 per 100,000 females (95% CI 262.7, 336.3) vs 119.8 per 100,000 males (95% CI 106.3, 140.0) (7).

In Canada, the CCDSS estimated that in 2020-2021, the national prevalence of RA for females was 1.62% (95% CI 1.62, 1.63), 0.79% (95% CI 0.79, 0.80) for males, and 1.22% for both sexes (8). The overall prevalence has increased by 22% over time for both sexes, where the prevalence of RA among females in 2007-2008 was 1.32% (95% CI 1.32, 1.33), 0.66% (95% CI 0.65, 0.66) for males, and 1.00% (95% CI 1.00, 1.01) for both sexes. The age-standardized incidence rate of RA is also twice as high among females, with a rate of 107 per 100,000 (95% CI 106, 109) in 2020-2021, compared to 58 per 100,000 (95% CI 57, 59) among males. For both sexes, the incidence rate is 83 per 100,000 (95% CI 82, 84) in that same year. A study conducted in the United States using a population-based registry estimated the lifetime risk, defined as the percentage of people who develop the disease from any age, was 3.6% for women and 1.7% for men (9).

1.3.3 Variations in RA Prevalence by Age

The onset of this condition is typically later in life, usually between 30 to 50 years (3, 10), but it can occur at any age (3). In Canada for fiscal year 2007-2008, the crude incidence rate for both sexes was highest among those aged 80 and older, at 264 per 100,000 (95% CI 255, 273) and lowest among those aged 16-34 at 19 per 100,000 (95% CI 18, 19). In 2021-2022, the incidence rate is still the highest among those 80 and older, but the rate has decreased by 28% to 191 per 100,000 (95% CI 185, 198), and increased by 21% among those aged 16-34 at 23 per 100,000 (95% CI 22, 24) (8).

1.3.4 Variations in RA Prevalence by Ethnicity

The prevalence of RA is disproportionally higher in certain populations, such as among the Indigenous peoples in North America and Australia. As summarized in a systematic review examining the prevalence and/or incidence of arthritis conditions among Indigenous peoples in Australia, Canada, New Zealand, and the USA, the prevalence of RA is high, especially among the Chippewa in the USA at 6.8%, the Blackfeet at 3.9%, and the Kwakiutl District Council and Yakima both at 3.4% (11). This review showed the persistent disparities in disease prevalence among Indigenous populations, noting that certain populations experience higher disease burden and are of particular importance when considering interventions for disease monitoring and management.

A cross-sectional study in the United States examined differences in patient-reported outcomes of disability, pain, and global health of over 4,000 RA patients of different ethnic backgrounds, and found that members of the African American and Hispanic communities had significantly

poorer outcomes in all three domains compared to white counterparts, with African American patients having the worst outcome of the three groups (12). Another US study examined differences in the use of disease-modifying anti-rheumatic drugs (DMARDs) among RA patients from 1998-2005 (13). African American persons had lower odds of receiving DMARDs compared to white people, while Hispanic persons had higher odds of receiving biologic DMARDs compared to white people. The authors suggest that this may be due to physicians suspecting higher disease severity or faster disease progression for Hispanic RA patients, but disease severity was not collected nor examined (14). Other studies found similar patterns of disparities among various ethnic groups compared to white RA patients: Hispanic patients had consistently higher disease activity at baseline, and minority ethnic groups reported worse functional status compared to white patients (11, 12).

1.3.5 Mortality Rates

A systematic review and meta-analysis in 2013 examined trends in mortality among persons with RA from 1966 to 2010, encompassing 44 years (13). The authors included studies which reported incident and standardized mortality rates (IMR and SMR, respectively) and found that there was a significant decrease in IMR, from a pooled IMR of 4.7 per 100 person-years (95% CI 4.0-5.4) in studies conducted before 1970, to 3.0 per 100 person-years (95% CI 2.3, 4.0) in studies conducted between 1970 and 1980, to 2.0 per 100 person-years (95% CI 1.3, 2.8) in studies after 1983. However, there was significant heterogeneity in all of these studies, specifically among those done after 1983.

In Canada, the all-cause mortality rates decreased among those with RA (14). A recent study found that the RA mortality rate decreased by 27% between 1990 to 2019 (15). While mortality remains high compared to those without RA, the CCDSS estimates that mortality rates decreased for both sexes, from 1259 per 100,000 in 2007-2008 to 1138 per 100,000 in 2021-2022, with male RA patients having a higher mortality rate than females (Figure 1—1) (8).

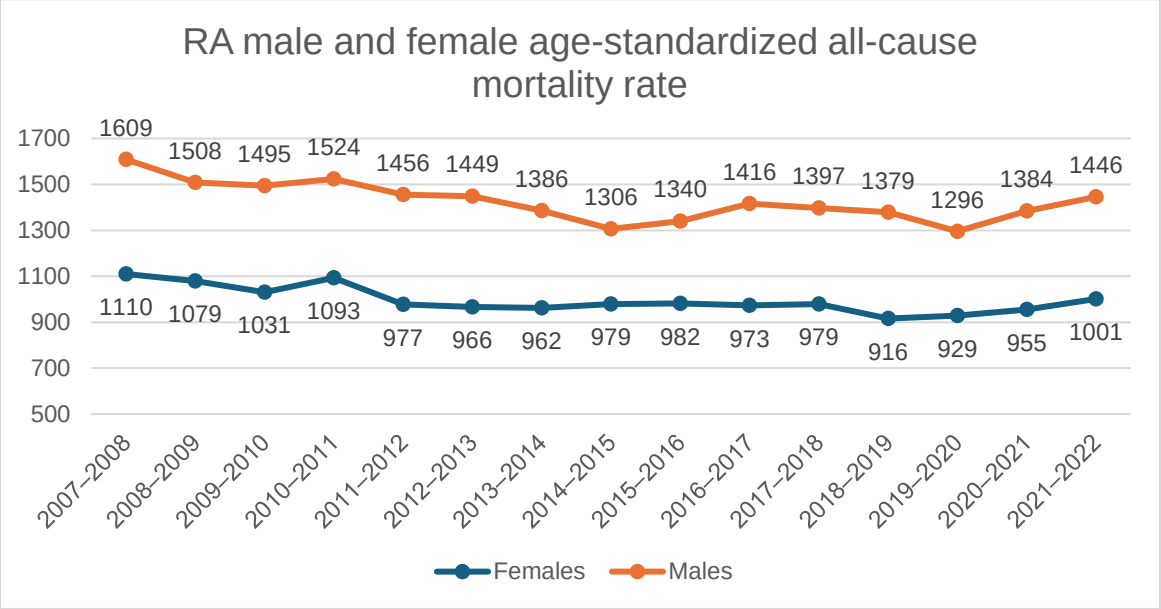

Figure 1—1. Male vs female RA age-standardized all-cause mortality rate, by 100,000, aged 16 and older. Source: Canadian Chronic Disease Surveillance System data files provided by provinces and territories, as of September 2023. Public Health Agency of Canada, Health Infobase (8).

1.4 RA Diagnosis

The gold standard for the diagnosis of RA is a clinical diagnosis by a rheumatologist based on patient symptoms, physical examinations, and supporting laboratory and diagnostic imaging

results. In research, a verified RA diagnosis by a rheumatologist can be used as an inclusion criterion in the study design. There are many ways that persons who likely have RA can be classified if access to the gold standard is not available, namely, using validated classification criteria and case definitions.

1.4.1 RA Classification Criteria

Disease classification criteria are standardized definitions used to create well-defined homogenous cohorts in clinical research (16). In 2010, the American College of Rheumatology (ACR) and the European League Against Rheumatism (EULAR) revised existing classification criterion for RA. This is a score-based criteria, where a patient with a score of 6 and over are classified as having "definite RA". The criteria include a history of symptom duration, thorough joint evaluation, and at least one serological test (rheumatoid factor (RF) or anti-citrullinated protein antibody (ACPA)) and one acute-phase response measure (erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP)) (16).

The target population, that is, people who should be tested for RA, are those who either have 1) at least one joint with definite swelling (synovitis) or 2) with swelling not attributed to another disease (differential diagnoses such as systemic lupus erythematosus, psoriatic arthritis, gout, and juvenile idiopathic arthritis in those <18 years old). As RA is typically found more in "small" joints (i.e., metacarpophalangeal, proximal interphalangeal, second to fifth metatarsophalangeal, thumb interphalangeal joints, and wrists) than "large" joints of the shoulders, elbows, hips, knees, and ankles, clinicians should assign higher scores if there are more small joints affected by swelling. Additionally, high-positive RF or ACPA, and either abnormal CRP or ESR are

given a score of 3 and 1 respectively. Finally, symptom duration should be more than 6 weeks (Table 1—1).

Table 1—1. Classification criteria for Rheumatoid Arthritis (2010) by the American College of Rheumatology/European League Against Rheumatism.

Who should be tested? Patients who: 1) Have at least 1 joint with definite swelling (synovitis)* 2) With joint swelling not better explained by another disease**	
Classification criteria (add scores of categories A-D, ≥6/10 means patient has definite RA)	Score
A. Joint involvement	
1 large joint	0
2-10 large joints	1
1-3 small joints (with/out involvement of large joints)	2
4-10 small joints (with/out involvement of large joints)	3
>10 joints (at least 1 small joint)	5
B. Serology	
Negative RF **and** negative ACPA	0
Low-positive RF **or** low-positive ACPA	2
High-positive RF **or** high-positive ACPA	3
C. Acute-phase reactants (at least 1 result needed for classification)	
Normal CRP **and** normal ESR	0
Abnormal CRP **or** abnormal ESR	1

D. Duration of symptoms	
<6 weeks	0
≥6 weeks	1

*This is aimed at classifying newly presenting patients

**Differential diagnoses can include conditions such as systemic lupus erythematosus, psoriatic arthritis, and gout

Adapted from Aletaha et al. (2010) with permission under BMJ Publishing Group Ltd. and Copyright Clearance Center.

1.4.2 RA Case definition

Defining RA can be challenging in cohort studies that leverage registries, physician claims, and other administrative data sources. These databases contain information on physician visits and billings, emergency department (ED) visits, hospital discharges, and medications prescribed and dispensed. Algorithms to define RA in administrative databases follow diagnostic codes from the International Classification of Diseases, Ninth or Tenth Editions (ICD-9/ICD-10). Validation of these algorithms is usually done in comparison to the gold standard, which is a diagnosis by a rheumatologist. For example, MacLean defined RA cases as someone with two physician visits for RA (identified by ICD-9 codes 714.X and ICD-10 codes M05-M05.9, M06.0, M06.8, and M06.9) at least 2 months apart (17). Many variations exist within the literature, and researchers have their own preferences on which case definitions to use depending on the research question. Ideally, maximizing the tradeoff between sensitive and specific case definitions is able to identify true positive RA cases and exclude false positives or people who have a different inflammatory arthritis condition.

1.5 Treatment and management of RA

There have been significant pharmacological advances in the treatment of RA in the last few decades. The goal of treating RA has changed from managing pain to reducing disease activity and achieving remission. Historically, anti-inflammatories, corticosteroids and injectable gold were used to treat various illnesses, including RA. Methotrexate, a type of conventional synthethic disease-modifying anti-rheumatic drug (csDMARD) was introduced in the 1950s, and remains the first line therapy for treatment initiation. The revolutionary change in rheumatology therapy occurred in the 1990s with the introduction of biologic DMARDS (bDMARDs). Combined with early diagnosis and initiation of pharmacotherapy and continuous titration to achieve remission, rheumatologists have many tools to apply to optimize health outcomes.

1.5.1 RA "Window of Opportunity"

For patients with suspected or newly diagnosed RA, the ideal course of action is to get a confirmation and initiate treatment as early as possible. The rationale behind this is that initiation of treatment relatively early in the disease course could prevent further joint damage that may otherwise be irreversible. Several randomized controlled trials have shown that the window of opportunity for therapeutic initiation is within the first 2 years following disease onset, where earlier treatment led to lower levels of radiographic joint damage and slower disease progression (18). The perception of the window of opportunity has evolved over time, with studies looking at even the pre-clinical phase to find ways to prevent RA development.

1.5.2 Therapeutic advances

Corticosteroids were the original approach to treating rheumatoid arthritis, especially effective at controlling inflammation. However, long-term use has deleterious side effects such as weight gain, increased blood pressure, and a high risk of osteoporosis (19). Steroids are now primarily used for the short-term only, as a bridge strategy to control inflammation while awaiting the effects of DMARDs. Methotrexate (MTX), as monotherapy or in combination with other DMARDs, became the mainstay approach. Approximately 70% of people respond to first-line therapy (20), but those who do not respond well need to advance to other therapeutic strategies. Tumor necrosis factor (TNF) inhibitors, also known as anti-TNF agents, were first introduced in 1999 and directly block cytokines that mediate joint damage (19). Additional therapeutic targets were eventually introduced, including B-cell depletion, interleukin-6 inhibitors (anti-IL6 therapy), T-cell costimulation reduction, and Janus Kinase (JAK) inhibitors that interfere with cellular transcription. ACR recommends the following treatment guidelines (21) based on patient disease activity:

1. In DMARD-naïve patients with moderate-to-high disease activity:
    a. MTX monotherapy:
        i. strongly recommended over hydroxychloroquine, sulfasalazine, bDMARD or targeted synthetic DMARD (tsDMARD) monotherapy, MTX plus TNF-inhibitor bMARD or
        ii. conditionally recommended over dual/triple csDMARD, leflunomide, MTX plus TNF-inhibitor bDMARD/tsDMARD
    b. csDMARD without short-term (< 3 months) glucocorticoids (GCs) over csDMARD with short-term GCs

c. csDMARD without long-term (≥ 3 months) GCs over csDMARD with long-term GCs

2. In DMARD-naïve patients with low disease activity:
    a. Hydroxychloroquine is conditionally recommended over other csDMARDs
    b. Sulfasalazine is conditionally recommended over MTX
    c. MTX is conditionally recommended over leflunomide
3. In patients with moderate-to-high disease activity who have been treated with csDMARDs excluding MTX
    a. MTX monotherapy is conditionally recommended over MTX plus bDMARD/tsDMARD

1.5.3 Treat to target (T2T) recommendations

In 2010, an expert task force of rheumatologists developed a consensus on recommendations to improve the management of RA (Table 1—2, Figure 1—2). They established that the primary goal is to treat RA with the target of achieving remission, thus preventing further damage and disease progression (22).

Table 1—2. T2T recommendations for RA. Reproduced with permission. © 2010. BMJ. All rights reserved.

Treat-to-Target Recommendations
1. The primary target for treatment of RA should be clinical remission.

2. Clinical remission is defined as the absence of significant inflammatory disease activity.
3. While remission is the primary target, low disease activity may also be an alternative target.
4. Until target is reached, drug therapy should be adjusted at least every 3 months.
5. Disease activity should be documented regularly: ideally, monthly for those with moderate/high disease activity, or every 3-6 months among those with low disease activity or those in remission.
6. Validated composite measures of disease activity, including joint assessments, are needed in clinical practice to guide treatment decisions.
7. In addition to composite measures of disease activity, structural changes and impairment should be considered when deciding treatment options.
8. The desired treatment target should be maintained for the remaining disease course.
9. Patient factors, medication-related complications, and comorbid conditions should be taken into consideration when choosing the composite measures of disease activity.
10. The patient should be appropriately informed about the treatment target and strategies to reach it.

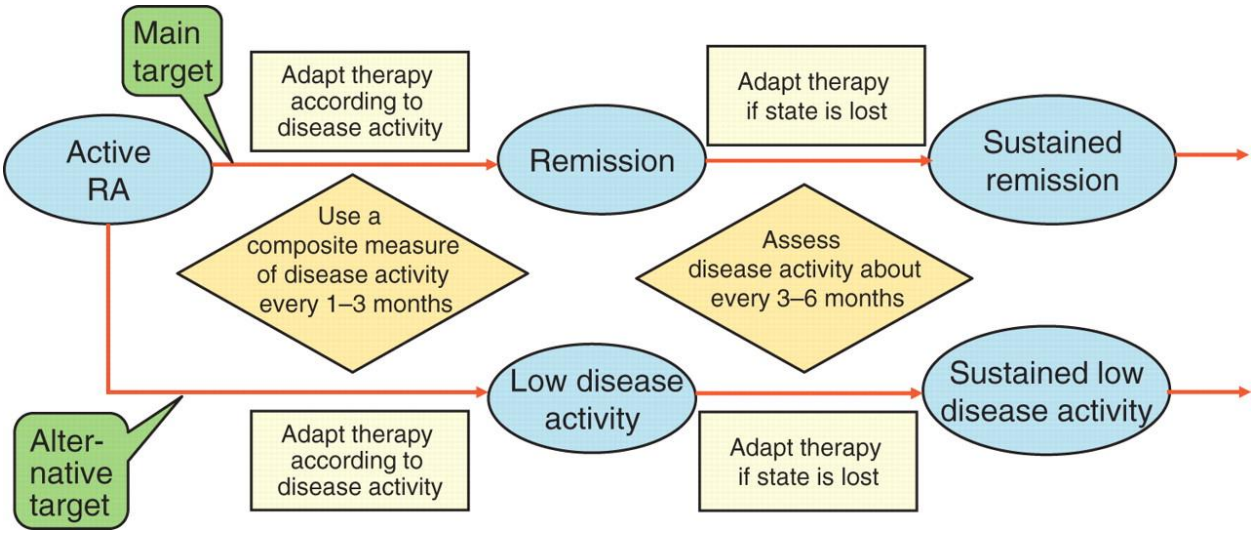

Figure 1—2. Algorithm for T2T in RA. Reproduced with permission. © 2010. BMJ. All rights reserved.

With T2T as the guiding principle, ACR developed guidelines for pharmacological treatment of RA patients based on patient disease activity, and taking into account specific patient populations (e.g., patients with comorbid conditions such as cardiovascular and pulmonary diseases, and Hepatitis B infection) (21). For example, for RA patients with moderate-to-high disease activity, a monotherapy of MTX is recommended over other DMARDs such as hydroxychloroquine or sulfasalazine.

1.5.4 Access to rheumatology care

The time-sensitive nature of RA requires early diagnosis and pharmacotherapy initiation, as well as regular follow-ups with the rheumatologist to assess response to treatment and escalate it if needed. However, specialist access and treatment delays are still too common (23-25).

System-level performance measures were developed to evaluate care for patients with inflammatory arthritis, and the indicators include waiting times for a rheumatology consult for patients with new-onset IA, the percentage of patients seen by a rheumatologist, and the percentage of patients seen by a rheumatologist for annual follow-ups (23). Based on these indicators, the quality of the rheumatology care system can be evaluated throughout the country. In Ontario, only 50% of patients diagnosed with RA were seen by a rheumatologist within the accepted benchmark of 3 months from when the diagnosis is suspected by a family physician and initiated a rheumatology referral; the frequency of initial consultations occurring within 6 and 12 months from referral has been increasing over time (24). In Alberta in fiscal year 2012/13 through 2015/16, only 63% of persons with RA had access to a rheumatologist within one year of disease onset, and the proportion of patients with a minimum of an annual follow-up with a rheumatologist varied between 73-80% (23).

The current rheumatology care systems not meeting established benchmarks of care can be attributed in part to a shortage of rheumatologists in Canada, which may only worsen within the next decade. In 2017, the Canadian Rheumatology Association (CRA) surveyed rheumatologists across Canada as part of a national rheumatology workforce survey that was launched in 2015 and found that there was an estimated 0 to 0.8 full-time rheumatologists per 75,000 population per province (26). The results of this 2017 survey found a deficit of approximately 1 to 77 full-time rheumatologists per province/territory in Canada. The workforce was surveyed again from 2020 to 2021 to update demographic and practice information, pandemic effects, and burnout among Canadian rheumatologists and found that, when using a benchmark of one full-time equivalent rheumatologist per 75,000 people, there is an estimated deficit of 194 rheumatologists

nationwide (27). About 51% of the respondents reported burnout, specifically rheumatologists who are female and younger had higher odds of reporting burnout.

Another factor contributing to delays in assessment and treatment is related to a growing cohort of patients requiring specialty care follow-up. Improved pharmacological management of RA has decreased mortality and increased the chance of achieving low disease activity, remission, and a better quality of life. In a population-based cohort study conducted in British Columbia, Canada, the mortality risk in RA patients, relative to controls, differed between incident cohorts from 1996-2000 and 2001-2006, where the former had a 39% increase in all-cause mortality compared to the latter cohort (28). This was also observed in the United Kingdom, where RA patients diagnosed between 1999 to 2006 had higher mortality than those diagnosed from 2007 to 2014 (17.0 vs 12.9 deaths per 1000 years) (29). This improvement in mortality means that people with these conditions require a longer duration of follow-up from rheumatologists. A large portion of medical care by RA patients is also provided by primary care physicians (30), but they too face significant service provision challenges due to a growing physician shortage, and increasingly medically-complex patients who often require more time to properly assess and manage. Added to administrative work, there is simply no more room in a physician's daily schedule to accommodate urgent concerns that come up. At other times, concerns that need attention cannot be dealt with because the physician cannot be accessed.

With the shortage of both rheumatologists and primary care physicians comes the problem of trying to address care for a growing number of people with suspected RA. On the other hand, persons with RA face a difficult situation when trying to address concerns related to their disease, treatment, or complications through ambulatory care options. Consequently, urgent care centres or emergency departments become the default locations for individuals with urgent

concerns. Even worse, if concerns were not properly addressed early on, patients may present to the ED with a more severe disease course, which may require hospitalization.

1.6 Acute Care Use by Persons with RA

1.6.1 Hospitalizations

Many studies have examined healthcare utilization, specifically hospitalizations, by persons with RA. As early as the 1960s, researchers in Sweden examined hospital care utilization by those with RA from 1967 to 1980. Results showed that those with RA had 38.3 hospital admissions per 100 person-years (for all ages) compared to 15.1 per 100 person-years in controls (31). 34% of those with RA were hospitalized for disorders in the circulatory system, and 26% were for disorders of the musculoskeletal system (31). This study also reported that RA itself was the most frequently responsible diagnosis for hospitalizations, and had 13.6 hospital days per 100 person-years in the rheumatology department, likely due to flares, rehabilitation, or pain management.

1.6.2 All-cause hospitalizations

A Spanish study describing hospitalizations by RA patients from 2002-2017, found that the overall hospitalization rate during the study period was 4.1 per 100,000 RA patients (95% CI 4.0, 4.2), with RA as the main diagnosis, and 39.7 per 100,000 RA patients (95% CI 39.6, 39.8) when RA was a comorbidity upon admission (32). Researchers noted that 19% (N = 54,123) of the hospitalizations were considered diseases of the circulatory system, and 17.5% were diseases of

the respiratory system, excluding hospital encounters where RA was the main diagnosis. These hospitalizations were not compared to the general population.

In the United States, a cohort study examining all-cause hospitalizations for patients with and without RA from 1987 to 2012 found that RA patients had a higher risk of hospitalization compared to those without RA (risk ratio [RR] 1.51, 95% CI 1.42, 1.59) (33). They also found that those with RA had a 2.45 times risk of being hospitalized for diabetes compared to those without RA (RR 2.45, 95% CI 1.34, 4.89), and male RA patients had a significantly higher risk of being hospitalized for depression compared to males without RA (RR 7.16, 95% CI 2.78, 30.67). However, the authors did not find temporal changes in hospitalizations after the introduction of biologics.

In Nova Scotia, Canada, a population-based cohort study examined physician encounters, ED visits, and hospitalizations by RA patients for 13 years, and found that those with RA had significantly higher odds of hospitalizations compared to controls (odds ratio 1.55, 95% CI 1.48-1.62) (34). The hospitalizations by those with RA do decrease a few years after being diagnosed, likely due to improved disease control as appropriate treatment strategies were initiated.

1.6.3 Emergency Department Visits

ED visits by persons with RA have been examined in Alberta, Canada. In a province of 4.6 million, the prevalence of RA was approximately 1.1%, yet in 2017, approximately 2.1% of all ED visits were by persons with RA (35). Nearly half of these visits were triaged as less or non-urgent, and males and those living in urban areas were more likely to be admitted to hospital.

Compared to the general population controls, RA patients in Nova Scotia, Canada, visited the ED more frequently, especially earlier in the disease course (34).

1.7 Ambulatory Care Sensitive Conditions

Ambulatory Care Sensitive Conditions (ACSCs) are defined as conditions where appropriate and timely ambulatory care could prevent complications, a more severe disease course, or hospital admissions. Different countries and health organizations have developed their lists of ACSCs. The first list of ACSCs (then ACS) was developed in 1993 and was comprised of acute (bacterial pneumonia, cellulitis, kidney/urinary tract infections) and chronic ACSCs (asthma, diabetes, hypertension) (36). In Canada, the Canadian Institute for Health Information (CIHI) developed a list of ACSCs which include: grand mal status and other epileptic convulsions, chronic lower respiratory diseases, asthma, diabetes, heart failure and pulmonary edema, hypertension, and angina (37). The Manitoba Centre for Health Policy has adapted the list developed by Billings et al. (1993) which listed other conditions such as dental conditions, ear-nose-throat infections, and pelvic inflammatory disease (38). The Agency for Healthcare Research and Quality (AHRQ) in the USA has developed its own list of ACSCs which include conditions such as dehydration, urinary tract infection (UTI), and low birth weight (39). The Swedish National Board of Health and Welfare defined several chronic and acute conditions that are indicators of avoidable conditions, which include anemia, asthma, heart failure, bleeding ulcers, and diarrhea (40).

1.7.1 ACSCs as health system performance indicators

In health services research, health system performance indicators are useful in assessing the effectiveness of the health care system. Health system performance indicators usually have desired directions (e.g., lower rates are better), and are assessed based on dimensions of quality, which focus on aspects of the patient experience (41).

CIHI has created a framework to measure health system performance (41). The Health System Performance (HSP) Measurement Framework provides an overview of key dimensions for measures and indicators that can be used to monitor the health care system performance. One of the four quadrants of the HSP framework examines health system outputs, such as access to, quality, and value of health care services (41). As such, the health care system can be considered appropriate and effective if it can provide care to only those who could benefit, specifically reducing the incidence, duration, intensity, and consequences of health problems (41). Examples of CIHI health system performance indicators include surgical patients readmitted to the hospital, hospitalizations entirely caused by alcohol, and ambulatory care sensitive conditions.

1.7.2 ACSC rates in Canada

As a measure of access to ambulatory care, national and provincial estimates of ACSCs are reported by CIHI for each fiscal year. These are calculated using the formula:

$$\frac{\text{Total number of acute care hospitalizations for ACSCs in patients} < 75}{\text{Total mid} - \text{year population} < 75} \text{x}100000$$

CIHI reports that the number of ACSC hospitalizations in Alberta in 2022-23 was approximately 287 per 100,000, slightly higher than the national average of 275 per 100,000. Among Canadian

provinces and territories, Nunavut has the highest rate of ACSC hospitalizations, with approximately 1211 per 100,000 in 2022-23. Since 2013-14, ACSC rates in Alberta have been consistently higher than the national average, and while the gap narrowed, especially during COVID-19, there is still some discrepancy with the high rates of avoidable hospitalizations (Figure 1—3).

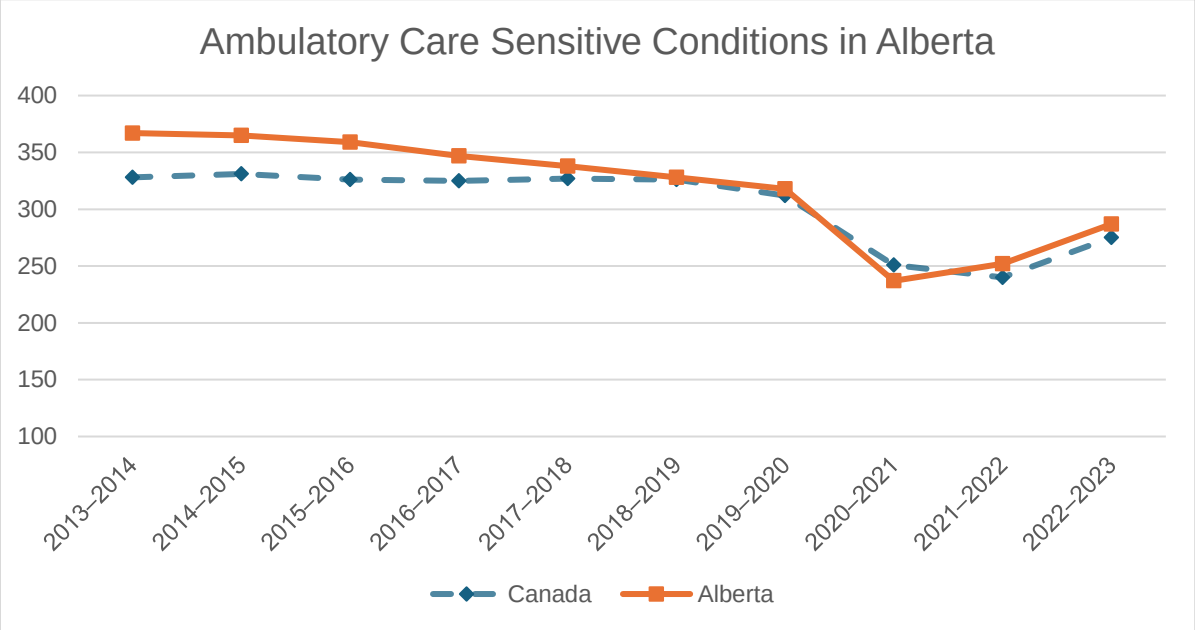

Figure 1—3. ACSCs in Alberta and Canada. Rates are calculated per 100,000. Source: Canadian Institute for Health Information (42).

1.7.3 Ambulatory care access reduces ACSC rates

Reflective of the ACSC definition, a systematic review in 2012 demonstrated that patients with greater access to primary care have lower rates of ACSC hospitalizations (42), highlighting previous work done in the USA and Australia showing an inverse relationship between physician supply and ACSC hospitalizations. “Access” to primary care was defined in multiple ways, namely, the number of general practitioners (GPs) per 1000 residents, the availability and

presence of community health centres or the number of primary health care centres in an area of residence, the number of GP or specialist visits, and access to enhanced primary health care programs.

A study in Ontario, Canada examined trends in primary care provider (PCP) attachment over time from 2008 to 2018 and noted and while there was an increase in the number of attached patients, there were still a significant proportion of patients not attached to PCPs with frequent contact with emergency departments (about 25%) and hospitalizations (10-12%) (43). Attachment was also found to be lower among those with low comorbidity, high material deprivation, living in rural areas, and recently immigrated.

In 2023, a cross-sectional study examined the family physician workforce and service provisions in Ontario and Alberta from fiscal years 2005-2006 to 2007-2018 and found a decrease in the average number of service days in both provinces (44). They also noted a low increase in physician count in rural and remote areas, with a 30% decrease in average service days per physician. In 2022, CIHI estimates that there are 119 family physicians per 100,000 population in Alberta (46). Provinces of Ontario, Quebec, and Alberta also had the highest number of family medicine residency positions unfilled in the country (45). With the growing demand for primary care increasing each year, patients struggle with prevention and early intervention for otherwise avoidable conditions, which can lead to an increase in ACSC hospitalizations.

1.7.4 RA and ACSCs

There is little literature available estimating admissions for ACSCs in persons with RA. A study published in 2020 examined the risk of “preventable” hospitalizations among those with RA

relative to matched controls in Taiwan (46). The authors adapted the AHRQ's definition of ACSCs, namely: diabetes short-term complications, diabetes long-term complications, chronic obstructive pulmonary disease (COPD), asthma, hypertension, heart failure, dehydration, bacterial pneumonia, urinary tract infection, uncontrolled diabetes, and lower-extremity amputation, but they excluded low birth weight and perforated appendix. They found that, for overall ACSCs, those with RA had higher odds of being hospitalized for any of the mentioned ACSCs compared to controls (OR 1.61, 95% CI 1.51, 1.71) after adjusting for various covariates. For specific ACSCs, they found significantly higher odds of avoidable hospitalizations for COPD, asthma, bacterial pneumonia, and UTI among those with RA relative to controls.

1.8 Thesis Aims

Thus, this project aims to examine the rates of avoidable acute care use, inclusive of hospitalizations and ED use, by persons with RA in one of Canada's largest provinces, and potential contextual factors that explain variations in the data, such as sex, location of residence, exposure to medication and access to care.

1.8.1 Research Objectives

The primary objective of this master's thesis is to estimate avoidable acute care use by persons with rheumatoid arthritis (RA) related to selected health conditions compared to the general population. "Avoidable" conditions are defined to be Ambulatory Care Sensitive Conditions (ACSCs), conditions where appropriate access to ambulatory or primary care could prevent

complications, a more severe disease course, or the need for hospitalization. The objectives of this research are as follows:

1. Estimate the incidence of ACSC-related acute care use by persons with RA relative to the general population.
2. Describe ACSC-related acute care use by persons with RA and examine temporal trends.
3. Identify predictors of ACSC-related acute care use by persons with RA.

Importantly, this will also help physicians and other care providers identify conditions that should be taken into consideration when trying to enhance service delivery to minimize and prevent avoidable acute care use.

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Chapter 2 – METHODS

2.1 Study Design

We conducted a retrospective cohort study using population-level administrative data. In Alberta, a province of 4.6 million people with universal access to healthcare, all health administrative data are maintained by Alberta Health for the Alberta Health Care Insurance Plan (AHCIP) and Alberta Health Services, a single-payer health system. The administrative datasets represent patient interactions with the healthcare system at all sources (ambulatory care with primary care physicians and specialists; emergency department and urgent care use; hospital admissions; pharmacy dispensations). These datasets can be linked using a Unique Lifetime Identifier (ULI) assigned to each patient, allowing linkage for cohort creation and outcome ascertainment.

2.2 Datasets

For this thesis, five datasets were accessed (See Table 2—1): the Discharge Abstract Database (DAD; hospitalizations, April 2007-March 2023), Practitioner Claims (inpatient/outpatient physician visits, April 2007-March 2023), National Ambulatory Care Reporting System (NACRS; emergency department and urgent care centre visits, April 2007-March 2023), Pharmaceutical Information Network (PIN; pharmacy dispensations, April 2007-March 2023) and Provincial Registry (demographic information, April 2002-March 2023).

Table 2—1. List of Administrative Datasets for cohort creation and outcomes analysis.

Dataset	Time Period	Description	Purpose
Practitioner Claims	April 2007-March 2023	Diagnostic codes from physician services, including fee-for-service and shadow-billed claims	Cohort creation AND Outcomes analysis
Inpatient/Discharge Abstract Database	April 2007-March 2023	Diagnostic codes from hospitalizations	Cohort creation AND Outcomes analysis
Provincial Registry	April 2002-March 2023	Demographic and geographic location	Outcomes analysis by biological sex, location of residence
Ambulatory Care	April 2007-March 2023	Emergency department and urgent care centre visits, Day procedures	Outcomes analysis
Pharmaceutical Information Network (PIN)	April 2007-March 2023	Medication exposure	Covariate in outcomes analysis

2.3 Participants

This study included identification of cases meeting a prespecified definition for RA, and controls without RA.

2.3.1 RA Cases

Cases were identified using a validated case definition for RA and extracted from datasets using an algorithm with diagnostic codes from the International Classification of Diseases Ninth Revision (ICD-9) for Practitioner Claims, or Tenth Revision (ICD-10) for NACRS and DAD. Persons meeting the case definition had one hospitalization or two physician visits within two years, but at least 8 weeks apart. The algorithm has been validated across multiple Canadian provinces relative to a diagnosis by a rheumatologist, which is the gold standard. In Manitoba, authors noted poor agreement between survey and administrative data: using a single year of data, this algorithm showed high specificity at 99.9%, the negative predictive value (NPV) and positive predictive values were 92.2% and 78.1%, but the sensitivity was low (5.4%) (1). In Ontario, this algorithm had 97% sensitivity, 77% specificity, 67% PPV, and 98% NPV among patients ≥20 years (2). This algorithm has also been adopted by the Canadian Chronic Disease Surveillance System (CCDSS) (3), and has been used widely throughout Canada.

A five-year period was established to wash out all prevalent cases and identify the incident cohort.

2.3.2. General Population Controls

Four controls matched by age and sex were identified for every case. The index date, defined as the date of first RA code, was applied to corresponding matched controls.

For the second objective, general population controls were not included in the hazard ratio model (See 2.4.2).

2.4 Outcomes

2.4.1 Primary Outcome

The primary outcomes were incidence rates for acute care use, using DAD and NACRS, for overall and individual ACSCs, reported as incidence rate ratios (IRR) (95% CI) for cases relative to controls. The most responsible diagnosis was identified using ICD-10-CA/CM codes for each ACSC following the Canadian Institute for Health Information (CIHI) methodology (Table 2—2) (4).

Table 2—2. ICD codes for ACSCs, as defined by CIHI.

Ambulatory Care Sensitive Conditions	**Diagnostic codes**
Grand mal status and other epileptic convulsions	ICD-9/9-CM: 345 ICD-10-CA: G40, G41
Chronic lower respiratory diseases (except asthma)	ICD-9/9-CM: 491, 492, 494, 496 ICD-10-CA: J41, J42, J43, J44, J47 **OR** MRDx[1] of acute lower respiratory infection, only when a secondary diagnosis[2] of J44 in

	ICD-10-CA or 496 in ICD-9/9-CM is also present ICD-9/9-CM: 466, 480–486, 487.0 ICD-10-CA: J10.0, J11.0, J12–J16, J18, J20, J21, J22
Asthma	ICD-9/9-CM: 493 ICD-10-CA: J45
Diabetes	ICD-9: 250.0, 250.1, 250.2, 250.7 ICD-9-CM: 250.0, 250.1, 250.2, 250.8 ICD-10-CA: E10.0, E10.1, E10.63, E10.64, E10.9, E11.0, E11.1, E11.63, E11.64, E11.9, E13.0, E13.1, E13.63, E13.64, E13.9, E14.0, E14.1, E14.63, E14.64, E14.9
Heart failure and pulmonary edema[3]	ICD-9/9-CM: 428, 518.4 ICD-10-CA: J81 (MRDx), I50 (MRDx), I50 as diagnosis type (1) when I11 is MRDx
Hypertension[3]	ICD-9/9-CM: 401.0, 401.9, 402.0, 402.1, 402.9 ICD-10-CA: I10 (MRDx), I11 as MRDx when I50 as diagnosis type (1) is not present
Angina[3]	ICD-9: 411, 413 ICD-9-CM: 411.1, 411.8, 413 ICD-10-CA: I20, I23.82, I24.0, I24.8, I24.9
Diagnostic codes of cardiac procedure for exclusion	CCP: 47XX, 480X–483X, 489.1, 489.9, 492X–495X, 497X, 498X ICD-9-CM: 336, 35XX, 36XX, 373X, 375X, 377X, 378X, 379.4–379.8

	CCI codes beginning with: 1HA58, 1HA80, 1HA87, 1HB53, 1HB54, 1HB55, 1HB87, 1HD53, 1HD54, 1HD55, 1HH59, 1HH71, 1HJ76, 1HJ82, 1HM57, 1HM78, 1HM80, 1HN71, 1HN80, 1HN87, 1HP76, 1HP78, 1HP80, 1HP82, 1HP83, 1HP87, 1HR71, 1HR80, 1HR84, 1HR87, 1HS80, 1HS90, 1HT80, 1HT89, 1HT90, 1HU80, 1HU90, 1HV80, 1HV90, 1HW78, 1HW79, 1HX71, 1HX78, 1HX79, 1HX80, 1HX83, 1HX86, 1HX87, 1HY85, 1HZ53, 1HZ54, 1HZ55, 1HZ56, 1HZ57, 1HZ59, 1HZ80, 1HZ85, 1HZ87, 1IF83, 1IJ50, 1IJ55, 1IJ57, 1IJ76, 1IJ80, 1IK57, 1IK80, 1IK87, 1IN84, 1LA84, 1LC84, 1LD84, 1IJ86 **AND** not equal to (1HZ53LAKP, 1HZ55LAKP) **AND** not equal to abandoned at onset

[1]MRDx = Most responsible diagnosis

[2]Secondary diagnosis = diagnosis other than MRDx

[3]Excluding cases with cardiac procedures. Exclusionary codes are listed.

2.4.2 Secondary Outcome

The secondary outcome was potential predictors for an ACSC hospitalization amongst RA cases, reported using hazard ratios (HR) (95% CI).

2.4.2.1 Predictor Variables

Potential predictors for ACSC acute care use were sex, age at visit/admission, geographic location of residence (binary characterization of urban or rural using the second character of the forward sortation area) (5), attachment to an ambulatory care physician, continuous exposure to disease-modifying anti-rheumatic drugs (DMARDs), continuous corticosteroid exposure, the burden of comorbidities as defined by the Charlson comorbidity index scores (6) excluding RA in the score calculation, and whether the comorbid conditions are themselves ACSCs (Table 2—4). The variables for outcomes analysis are as follows:

- Sex (Categorical: Male/Female) from Practitioner Claims, NACRS, DAD, PIN
- Age (Numerical: Continuous) from NACRS, DAD
- Geographic location (Categorical: Urban/Rural) from DAD
- Attachment to an ambulatory care physician (Categorical: Defined as a visit to a family physician or rheumatologist at least once a year after index date (7)) from Practitioner Claims
- Exposure to DMARDs (Categorical: Defined as having a disease-appropriate drug (See Table 2—3) dispensed for ≥70% eligible days in a fiscal year (2)) from PIN
- Exposure to corticosteroids (Categorical: Defined as having a corticosteroid dispensed for ≥30 days in a fiscal year, every year after index date) from PIN

Table 2—3. Disease Modifying Anti-Rheumatic Drugs and associated Anatomical Therapeutic Chemical codes.

Medications	**ATC Codes**
Sulfasalazine	A07EC01
Methotrexate	L01BA01
Rituximab	L01XC02
Leflunomide	L04AA13
Abatacept	L04AA24
Tofacitinib	L04AA29
Baricitinib	L04AA37
Upadacitinib	L04AA44
Etanercept	L04AB01
Infliximab	L04AB02
Adalimumab	L04AB04
Certolizumab	L04AB05
Golimumab	L04AB06
Tocilizumab	L04AC07
Sarilumab	L04AC14
Hydroxychloroquine	P01BA02
Prednisone[1]	H02AB07

[1] Corticosteroid

- Charlson Comorbidity Index Score (Numerical: Continuous composite scoring (6).

  Rheumatic diseases were excluded from the calculation) from Practitioner Claims

- ACSC as a comorbidity (Categorical: Defined as whether a comorbid condition is also considered an ACSC derived from Practitioner Claims)

Table 2—4. ICD-10 codes for comorbid conditions that are also considered ACSCs.

ICD-10 Code	ACSC	Condition
G40	Grand mal status and other epileptic convulsions	Epilepsy
G41		Status epilepticus
J41*	Chronic lower respiratory diseases (except asthma)	Simple and mucopurulent chronic bronchitis
J42*		Unspecified chronic bronchitis
J43*		Emphysema
J44*		Other chronic obstructive pulmonary disease
J47*		Bronchiectasis
J45*	Asthma	Asthma
E100*	Diabetes	Type 1 diabetes mellitus with coma
E101*		Type 1 diabetes mellitus with acidosis
E1063		Type 1 diabetes mellitus with hypoglycaemia
E1064		Type 1 diabetes mellitus with poor control, so described

E109*		Type 1 diabetes mellitus without (mention of) complication
E110*		Type 2 diabetes mellitus with coma
E111*		Type 2 diabetes mellitus with acidosis
E1163		Type 2 diabetes mellitus with hypoglycaemia
E1164		Type 2 diabetes mellitus with poor control, so described
E119		Type 2 diabetes mellitus without (mention of) complication
E130*		Other specified diabetes mellitus with coma
E131*		Other specified diabetes mellitus with acidosis
E1363		Other specified diabetes mellitus with hypoglycaemia
E1364		Other specified diabetes mellitus with poor control, so described
E139*		Other specified diabetes mellitus without (mention of) complication

E140*		Unspecified diabetes mellitus with coma
E141*		Unspecified diabetes mellitus with acidosis
E1463		Unspecified diabetes mellitus with hypoglycaemia
E1464		Unspecified diabetes mellitus with poor control, so described
E149		Unspecified diabetes mellitus without (mention of) complication
J81	Heart failure and pulmonary edema	Pulmonary oedema
I50*		Heart failure
I10	Hypertension	Essential (primary) hypertension
I11		Hypertensive heart disease
I20	Angina	Angina pectoris
I2382		Postmyocardial infarction angina as current complication following acute myocardial infarction
I240		Coronary thrombosis not resulting in myocardial infarction

I248		Other forms of acute ischaemic heart disease
I249		Acute ischaemic heart disease, unspecified

*Indicates codes that are also present in the Charlson Comorbidity Index (6), the comorbidities were defined by Charlson in 1987 (8).

2.5 Statistical analysis

Statistical analyses were performed using R version 4.4.0. Descriptive statistics were used to report the cohort characteristics of ED visits and hospitalizations from 2007 to 2023 for cases and controls. This included frequency and proportions and means and standard deviations.

The IRRs were calculated using a zero-inflated Poisson regression model. Poisson regression is a generalized linear model used to model count variables (e.g., number of ACSC ED visits/hospitalizations three and five years from index date). The counts of ACSC hospitalizations five years from index date (Figure 2—1) follow a Poisson distribution, with an excess of zeros.

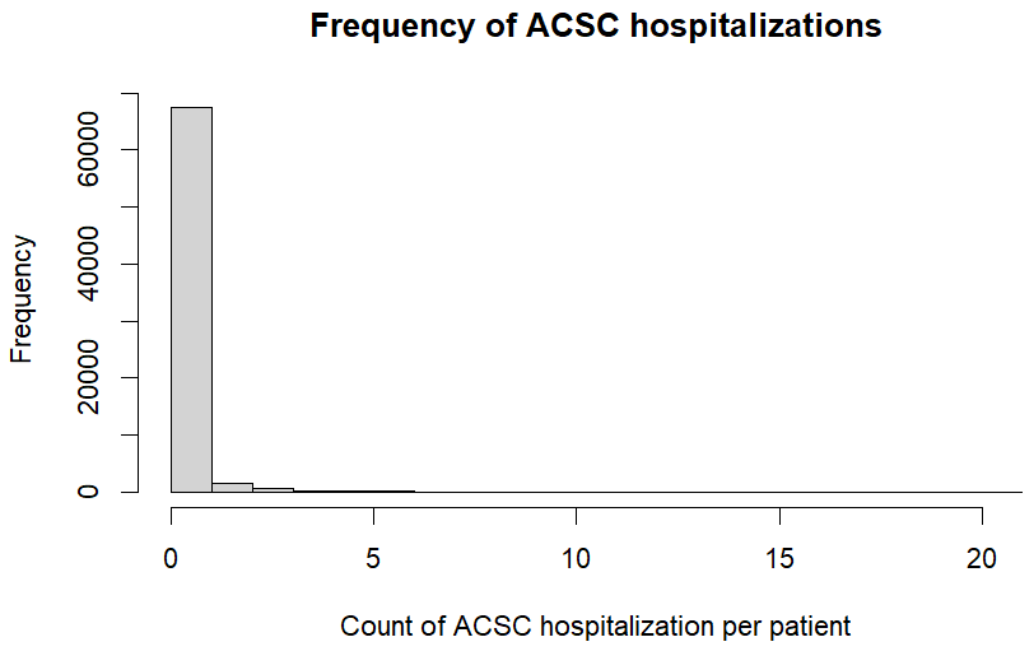

Figure 2—1. A histogram showing the frequency of ACSC hospitalizations.

The number of zeros in Figure 2—1 implied two things: 1) those who were hospitalized, but not for ACSCs, and 2) those who had no hospitalizations during the time period. Thus, the excess zeros were generated by a separate process. To confirm that this was the best Poisson regression model to be used for analysis, the zero-inflated model was tested against two other models: a Poisson regression model, and a negative binomial model. Comparing the Akaike information criterion (AIC) for model selection (6) between these three models, with the lowest AIC being the best model fit, the zero-inflated Poisson regression was determined to be the best model for this analysis.

We used survival analysis techniques to identify predictors of ACSC-related hospitalizations. The event of interest was the first ACSC-related acute care use among those with RA over a 16-

year period (2007-2023). People with RA are "censored" when the event has not occurred during the follow-up time, or when patients die while admitted in hospital or during an ED visit. Survival analysis techniques such as Kaplan-Meier curves and Log-Rank tests cannot account for multiple predictor variables. A Cox proportional hazards model is advantageous for this objective as it can adjust for multiple variables and is especially useful for staggered entry (patients entering the study at different time points, i.e., different index dates) (9). Using this model, the dependent variables are "hazards" instead of the survival time, which is the probability of the event happening given that the patients survived up to a given point in time (10). The model can be written as:

$$h(t) = h_0(t) \times e^{b_1x_1+b_2x_2+\cdots+b_kx_k}$$

where h(t) is the expected hazard at a given time t, and $h_0(t)$ is the baseline hazard when all the predictors x_1, $x_2 \ldots x_k$ are equal to zero (11).

A Cox proportional hazards model was used to identify predictors of avoidable ED visits and hospitalizations in the RA cohort, considering the covariates listed above. This model was chosen as it can examine the relationship between the outcome of interest (i.e., the first ACSC acute care use among RA cases and multiple potential predictors within a time period). It is especially useful when dealing with both categorical and numerical variables. Multiple events were not considered, as previous literature showed that it was already a significant predictor of future hospitalizations, especially if prior hospitalization occurred in the previous year (12). Predictors were assessed to be statistically significant at a level of $p < 0.05$.

2.6 Chapter 2 References

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Chapter 3 – MANUSCRIPT: Avoidable Hospitalizations in Persons with Rheumatoid Arthritis:

A Population-Based Study Using Administrative Data

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3.1 Abstract

Objective: We estimated incidence rates of avoidable hospitalizations by persons with rheumatoid arthritis (RA) relative to the general population.

Methods: We identified individuals meeting a validated case definition for RA based on ICD-9-CM and ICD-10-CA codes in years 2002-2023. Four general population controls were matched to each RA case by age and sex. We identified hospitalizations for ambulatory care sensitive conditions (ACSCs) including grand mal seizures, chronic lower respiratory diseases, asthma, diabetes, heart failure and pulmonary edema, hypertension, and angina from 2007-2023 by established diagnostic codes. Incidence rate ratios 3 and 5 years from date of diagnosis were calculated using a multivariable regression model adjusting for age, sex, and location of residence. A Cox proportional hazards model was used to identify predictors of avoidable hospitalizations among RA patients.

Results: Cases (n=83,811) had 1.12 times the risk of hospitalization for heart failure and pulmonary edema compared to those without RA (n=190,304) (IRR 1.12, 95% 1.01, 1.25). Significant predictors of ACSC hospitalizations for RA cases were increasing age, prolonged exposure to corticosteroids, being from a rural location, and having comorbid conditions, especially if the comorbid condition is an ACSC (HR 7.33, 95% CI 6.25, 8.62).

Conclusion: Persons with RA are at a higher risk of potentially avoidable hospitalizations 3 and 5 years after diagnosis compared to those without RA. Improved ambulatory care access and quality, inclusive of primary care and contributing role of subspecialty care, is proposed to prevent unnecessary hospitalizations and reduce burden on the acute care system.

3.2 Significance and Innovations

- This study estimates rates of hospitalizations for ambulatory care sensitive conditions (also known as “avoidable” or “preventable” hospitalizations) among persons with rheumatoid arthritis to identify how often these events occur and to see how care providers can intervene to reduce the burden on the acute care system.
- The study was conducted in Alberta, Canada, a province of ~4.6 million people with universal health care coverage We used population-level administrative health data to identify persons meeting a validated case definition for RA, and had a 5-year washout period to establish an incident cohort.
- Our results showed that persons with RA had a higher incidence of avoidable hospitalizations 3 and 5 years from their index date compared to those without RA. People with RA are at an especially higher risk of being hospitalized for heart failure and pulmonary edema, which are known comorbid conditions of RA. We also identified that elderly patients, those living in rural locations, prolonged exposure to corticosteroids, and having a comorbid condition that is condition an ambulatory care sensitive condition are at a higher risk for potentially avoidable hospitalizations.
- We highlight the need for better quality of care for persons with RA, specifically better coordination of care among primary and specialty care, to address the burden of comorbidities and reduce the risk of hospitalizations.

3.3 Introduction

Despite improved management of rheumatoid arthritis (RA), persons affected by this condition continue to have an increased risk of morbidity and mortality compared to the general population in part due to comorbidities such as cardiovascular disease(1, 2), depression(3, 4), and osteoporosis(5). The presence of these comorbidities also leads to increased healthcare utilization, including hospitalizations(6), which is a major driver of health system costs.

Health system performance indicators are useful in assessing the effectiveness of the health care system. One indicator of a well-performing healthcare system is a low frequency of hospitalizations related to avoidable acute care use. This indirectly measures access to primary care and the capacity of the healthcare system to manage these "avoidable" conditions in the outpatient setting(7). Ambulatory Care Sensitive Conditions (ACSCs) were thus derived as a list of conditions where appropriate ambulatory care would prevent or reduce the need for hospital admission. The Canadian Institute for Health Information (CIHI) has developed a list of ACSCs used for surveillance in Canada, which are: grand mal status and other epileptic convulsions, chronic lower respiratory diseases, asthma, diabetes, heart failure and pulmonary edema, hypertension, and angina(8). As of 2023, the province of Alberta, where this study was conducted, is currently performing below the national average for hospitalizations for ACSCs at 287 admissions per 100,000 population, compared to the national average of 275 per 100,000(9).

Relatively few studies have characterized ACSC hospitalization rates in inflammatory arthritis conditions(10-12). The single study conducted in RA was in Taiwan, where RA patients had 61% higher odds of avoidable hospitalizations compared to those without RA, in both the year preceding and following RA diagnosis(10). Among those with spondyloarthritis in that same

country, there was a five-fold increase in the odds of an ACSC hospitalization associated with corticosteroid use(11). In Sweden, persons with gout had a 41% increased risk of ACSC hospitalizations compared to those without gout 3 years preceding and following diagnosis(12).

The frequency of ACSC hospitalizations in persons with RA in the Canadian context, which has a universal health care system, has not been described. Canada has one of the richest collections of health data, including administrative health databases that record each patient interaction with the healthcare system, including hospitalizations, outpatient physician visits, and pharmacy dispensations. We conducted this project to estimate and describe the frequency of ACSC hospitalizations by persons with RA, relative to the general population, to inform if ambulatory care service delivery should be enhanced to mitigate avoidable acute care use.

3.4 Methods

3.4.1 Study Design

This was a retrospective cohort study using population-level administrative data. In Alberta, a province of 4.6 million people, all health administrative data are maintained by Alberta Health for the Alberta Health Care Insurance Plan (AHCIP) and Alberta Health Services, as a single-payer health system. The administrative datasets represent patient interactions with the healthcare system at all sources (ambulatory care with primary care physicians and specialists; emergency department and urgent care use; hospital admissions; pharmacy dispensations). Linkage for cohort creation and outcome ascertainment is made possible through a Unique Lifetime Identifier (ULI) assigned to each patient.

3.4.2 Datasets

For this project, four datasets were accessed: the Discharge Abstract Database (hospitalizations, April 2007-March 2023), Practitioner Claims (outpatient physician visits, April 2002-March 2023), Provincial Registry (demographic information, April 2002-March 2023), and Pharmaceutical Information Network (pharmacy dispensations, April 2007-March 2023). See Supplementary Material Appendix Table 3 for data elements and sources, and Supplementary Material Appendix Figure 1 for datasets and timeframes used for cohort identification and outcomes.

3.4.3 Participants

All individuals registered with the AHCIP beginning in fiscal year 2002/2003 up until the study end date of March 31, 2023 were considered for inclusion. A five year washout period from study start date or registration date with the AHCIP was applied to exclude prevalent RA cases. The case cohort was determined using a validated case definition for RA(13, 14) using an algorithm with diagnostic codes from the International Classification of Diseases Ninth Revision (ICD-9-CM 714.X) for Practitioner Claims, or Tenth Revision (ICD-10-CA M05.X-M06.X) for Discharge Abstract Database. Those included in the cohort must have had 1 hospitalization discharge or at least 2 practitioner claims for RA in 2 years, but at least 8 weeks apart (97% sensitivity, 77% specificity, 67% PPV, 98% NPV)(13). This case definition has been validated and used in many studies, including RA surveillance by the Canadian Chronic Health Disease Surveillance System(14). We excluded individuals younger than 18 years of age, and those

meeting case definitions of other inflammatory arthritis conditions of psoriatic arthritis (696.X, 720.X, L40.X, M07.0, M07.1, M07.2, M07.3 and M45.X), ankylosing spondylitis (720.X, M45.X), and gout (274.X, 712.X, M10.X, M11.X). The general population controls were randomly selected among all eligible persons in Alberta enrolled under the AHCIP. We employed control matching based on age (±5 years) and sex in a 1 case to 4 control ratio. The index date for RA cases to determine the beginning of the follow-up period was the date of first RA diagnosis code, and this same calendar date was applied as the index date for their matched controls.

3.4.4 Outcomes

The primary outcome of this study was hospitalization rates for any ACSC, and individual ACSCs, calculated as incidence rate ratios (IRR) (95% CI)) for cases relative to controls. Cases and controls were followed three and five years from their index dates, with the follow-up period being between 2007 to 2023. We applied the defining ICD-10-CA codes for each ACSC following Canadian Institute for Health Information (CIHI) methodology (See Appendix Table 1 in Supplementary material). We adjusted for age, sex, and location of residence using Poisson regression. The secondary outcome was to identify potential predictors for an ACSC hospitalization amongst RA cases, reported using hazard ratios (HR) (95% CI) estimated from a Cox proportional hazards model.

3.4.5 Covariates

Potential predictors for ACSC hospitalizations were sex (binary characterization of male or female), age at admission (continuous), geographic location of residence (binary characterization of urban or rural, using the second character of the forward sortation area)(15), attachment to an ambulatory care physician (defined as a visit to a family physician or rheumatologist at least once a year after diagnosis), continuous exposure to disease-modifying anti-rheumatic drugs (DMARDs) (defined as having a disease-appropriate drug (See Appendix Table 2 in Supplementary material) dispensed for ≥70% eligible days in a fiscal year), continuous corticosteroid exposure (categorized as a binary of yes/no, if dispensed for ≥30 days in a fiscal year), and the burden of comorbidities from index date to hospitalization as defined by the Charlson comorbidity index scores(16) excluding RA in the score calculation, and whether the comorbid conditions are themselves ACSCs.

3.4.6 Statistical analyses

Descriptive statistics were used to report the characteristics of ACSC hospitalizations from 2007 to 2023 for cases and controls. The IR for any ACSC, and individual ACSCs, was calculated for cases and controls. IRRs (95% CI) for each ACSC were calculated using a zero-inflated Poisson regression model to account for the excess zeros. Poisson regression is a generalized linear model used to model count variables (e.g., number of ACSC hospitalizations three and five years from index date). The counts of ACSC hospitalizations follow a Poisson distribution, with an excess of zeros (i.e., most had no hospitalization for any ACSC). A Cox proportional hazards model was used to identify predictors of avoidable hospitalizations in the RA cohort, considering

the covariates listed above. The follow-up time was from index date until 2023. The proportional hazards assumptions were tested and validated based on the Schoenfeld residuals. Cases were censored if no events occurred during the follow-up time, or if the case died while admitted to hospital. Predictors were assessed to be statistically significant at a level of $p < 0.05$. Statistical analyses were performed using R version 4.4.0 using packages *pscl*(17) for zero-inflated Poisson regression, *survival* for Cox proportional hazards model(18, 19), and *car* for model validation(20).

3.4.7 Ethics

Ethics approval for this study was provided by the University of Calgary Conjoint Health Research Board (Ethics ID REB22-1316).

3.5 Results

3.5.1 Cohort Characteristics

From an incident RA cohort composed of 52,596 individuals and 210,384 age- and sex-matched controls, there were a total of 25,281 cases and 70,313 controls with hospital encounters during the study period (Table 3—1). The number of unique hospitalizations studied was 83,811 in cases and 190,304 in controls. Over 65% of the study population were female. The average age at admission for RA patients was 64.3 (SD 16.8) years and 69.4 (SD 16.1) years for non-RA patients. Over 80% of the patients were from an urban setting. Among individuals with RA, the median follow-up time available was 10.8 years (IQR 6.9, 13.8).

3.5.2 ACSC Hospitalizations

Any ACSC accounted for 8.3% of hospitalizations in RA cases, compared to 9.1% for controls (Figure 3—1). The frequency and proportion of hospitalizations for each ACSC as a proportion of all ACSC hospitalizations are reported in Table 3—1, with the highest number of hospitalizations for RA cases being for chronic lower respiratory diseases (except asthma) at 45.7% (3202/7005) of all ACSC hospitalizations, followed by heart failure and pulmonary edema at 32.5% (2280/7005), and diabetes at 8.2% (576/7005). For controls, the conditions that contributed to the highest frequency of hospitalizations out of all ACSC hospitalizations were similar with chronic lower respiratory diseases at 42.7% (7434/17391), heart failure and pulmonary edema at 37.0% (6440/17391), but with the third most common admission being for grand mal seizures at 6.7% (1160/17391).

3.5.3 Incidence of ACSCs

For all ACSCs combined, RA cases had an 11% higher risk of being hospitalized compared to the general population (IRR 1.11, 95% CI 1.03, 1.19) within three years after the index date (Table 3—2). This difference persisted at five years after adjusting for sex, age, and location of residence (IRR 1.14, 95% CI 1.08, 1.20).

This difference was driven by particular individual ACSC conditions. The risk of being hospitalized for heart failure and pulmonary edema was significantly higher among RA cases compared to those without RA (IRR 1.22, 95% CI 1.06, 1.41) three years from date of diagnosis. Five years after diagnosis, the risk of hospitalization for heart failure and pulmonary edema was

1.12 times higher among those with RA compared to those without RA (IRR 1.12, 95% 1.01, 1.25).

3.5.4 ACSC hospitalizations over time

We examined the temporal trends in ACSC hospitalizations over the study period as a proportion of all hospitalizations (Figure 3—1). There was a 48% increase in ACSC hospitalizations among RA cases, from 6.1% of all hospitalizations in 2007 to 9.1% in 2023, and a 92% increase among controls (5.0% in 2007 to 9.6% in 2023). Notably, there were decreases in ACSC admissions during 2012, and again in 2020 and 2021, particularly for chronic lower respiratory diseases. The latter is assumed to represent the consequences of the COVID-19 pandemic. There was a 33% decrease in hospitalizations for chronic lower respiratory diseases from 4.2% in 2019 to 2.8% in 2021 and a 62% increase from 2.8% in 2021 to 4.5% in 2023. Hospitalizations for heart failure and pulmonary edema also increased among cases, by 66% from 1.8% in 2007 to 3.1% in 2023.

3.5.5 Predictors of avoidable hospitalizations amongst RA cases

As expected, having a comorbid condition that was one of the ACSCs was associated with an increased risk for an ACSC admission (HR 7.34, 95% CI 6.25, 8.62) compared to those without the comorbid condition (Table 3—3). The risk for an ACSC admission increases by 2% for every additional year in age (HR 1.02, 95% CI 1.02, 1.02) (Table 3—4). Individuals who were exposed to corticosteroids had their risk of being hospitalized for any ACSC increased by 44% (HR 1.44, 95% CI 1.28, 1.63). Residing in a rural location (HR 1.41 95% CI 1.29, 1.53) was also a

significant predictor for an ACSC admission. Sex, exposure to DMARDs, and attachment to a physician were not significant predictors of avoidable hospitalizations.

3.6 Discussion

ACSC admissions account for nearly 10% of all hospitalizations in the Canadian universal health care system model, and persons meeting the administrative data case definition for RA have a persistently higher risk (11% at 3 years and 14% at 5 years after diagnosis) for these admissions. The most frequent ACSCs were chronic lower respiratory diseases (which include bronchitis, emphysema, and chronic obstructive pulmonary disease) and heart failure and pulmonary edema for both RA cases and controls. There is an increasing rate over time for hospitalizations for chronic lower respiratory diseases, which resulted in 4.5% of all hospitalizations in persons with RA in 2023, following a notable decrease in the incidence of avoidable hospitalizations for this ACSC during the COVID-19 pandemic. The decrease observed was likely due to the efforts to redirect hospital capacity for COVID-19 hospitalizations, while also reflecting the benefits of reduced exposure to triggers for respiratory infections in persons upholding pandemic distancing restrictions(21, 22), which persons with RA were likely to do(23).

The predictors for an ACSC admission among patients with RA reflect personal characteristics, such as age, location of residence, and medical conditions, while also reflecting prolonged steroid use that may be indicative of poor disease control. It is important to consider how personal characteristics could influence a patient's recognition that they should seek care, uptake in preventative services, or result in delayed care such as when people only see healthcare providers for serious conditions that may require intensive treatment(24). We were surprised to

see that in this study that male sex was not associated with an increased risk of an ACSC hospitalization specifically, as in a prior study also conducted in Alberta, Canada we found that males were more likely to present to emergency departments and with higher acuity, and they were also more likely to be admitted to the hospital, for any condition(25). Our findings are in line with studies in Canada that have examined predictors of hospitalizations in the general population, where they did not find male sex as a significant predictor(26, 27). In the general population, while it has been shown that males have higher rates of ACSC hospitalizations compared to females(28), it does not necessarily predict the first event. Another study in Canada also highlighted that for males in the general population, severe disability was an important factor associated with ACSC hospitalization. At the same time, for females, it was the presence of comorbid conditions(7), and this is likely reflected in the RA population. Another reason for this may be differences in health-seeking behaviour among males and females. Finally, females in general reported disparities in the amount and quality of care received in primary care settings: specifically, females with ACSCs were less likely than males to receive tests for chronic diseases such as blood pressure, blood cholesterol, body weight and blood sugar measurements(29). We believe sex alone may not accurately predict ACSC hospitalization, but a cumulative factor of sex, age, lifestyle behaviours, socioeconomic status, and presence of comorbidities that lead to ACSC hospitalization.

We did however identify that people living in rural areas showed a higher magnitude of risk for ACSC hospitalization. This is consistent with the literature that people with RA from rural and remote communities face additional challenges with access to medical care. Thus, increased ACSC hospitalizations could reflect both difficulties with access to primary care for medical condition management, and also delays in diagnosis and treatment initiation specific to their

rheumatic disease(30) and thus with worse disease outcomes contributing to more systemic disease complications. Arguing against this hypothesis in our study results however was that attachment to an ambulatory care provider was not protective against an ACSC hospitalization. This may be due to how this covariate was defined. Due to the nature of administrative data, we could only use a proxy definition, which was a visit to a general practitioner or a rheumatologist at least once a year following RA diagnosis, which may not be highly indicative of whether someone is attached to an ambulatory care physician nor receiving high quality care. Another study on ACSCs in the general population also did not find access to primary care a significant factor(7), while also highlighting that access may matter less than the appropriateness and quality of services being provided. Co-occurring medical conditions were predictors of the outcome. Cumulatively, unaddressed inflammation could result in an increased risk for complications of inflammation such as another chronic medical condition. Several studies have examined the link between chronic inflammation from rheumatoid arthritis and heart failure: in one study in the United States, higher C-reactive protein levels indicative of inflammation were associated with a higher risk of developing heart failure; in Denmark using population-level health registries, the risk of incident heart failure was 2.06 and 1.23 times higher among those with and without ischaemic heart disease, respectively(31).

Exposure to DMARDs was not found to protect against ACSC hospitalizations, although it was hypothesized that individuals with RA with continuous exposure to DMARDs would have better disease control and lower disease activity, and thus perhaps some effect on admissions. Consistent with the literature and the study in ankylosing spondylitis, we found that exposure to corticosteroids increases the risk of ACSC admissions, possibly indicating uncontrolled inflammation and poorer disease control and those effects on comorbid disease. We were

surprised by the finding that attachment to an ambulatory care provider was not protective for ACSC presentations. Primary health care (PHC) is a critical factor in achieving an "acceptable level of health throughout the world"(32), emphasizing the need to be universally available to everyone in the community(33). PHC has been seriously eroded in healthcare contexts. An international survey in 2023 looked at healthcare experiences, including access to PHC, in 10 high-income countries, including Canada, and found that Canadians had the lowest proportion who reported having access to an ambulatory care provider (83% vs an average of 93% across 10 countries)(34). Appropriate access to primary and specialty healthcare providers could help RA patients reduce complications and inflammation through treatment and follow-up. Consequently, lack of access can lead to worse health outcomes and an increase in acute care use.

Our study contributes knowledge of ACSC hospitalization among those with RA from a health system with universal access to care. Studies examining ACSC hospitalizations for other IA conditions do not necessarily apply to the Canadian population, due to differences in the healthcare system and how "avoidable conditions" or ACSCs are defined. For example, in the ankylosing spondylitis study in Taiwan, the list of ACSCs was defined by the Agency for Healthcare Research and Quality, which includes some conditions not listed in CIHI's list of ACSCs such as dehydration, urinary tract infection, perforated appendix, and low birth weight(35).

This study has some limitations. Data in administrative health databases are collected in the operation of health services, not specifically designed for research and surveillance purposes. The diagnostic criteria applied to identify RA cases, while validated, may not fully capture all patients with RA. There are also additional confounders, disease severity for example, that were not accounted for as we did not have laboratory and diagnostic imaging data to estimate disease

activity. Due to the nature of administrative data, we also were not able to adjust for socioeconomic status, ethnicity, and other factors such as adherence to medications and smoking behaviours.

Persons with RA are at a higher risk of avoidable hospitalizations 3 and 5 years after getting diagnosed. They are especially at a higher risk of avoidable hospitalizations for conditions that are known to be comorbid with RA, specifically congestive heart failure. There is a need for better collaborative, team-driven care that may consist of the patient's general practitioner, rheumatologist, and specialist for whatever comorbid condition they have. Having better access and quality of ambulatory care, inclusive of primary and specialty care, as well as collaborative care among specialists, is necessary in order to reduce the burden on the acute care system and improve the quality of care for people with RA.

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3.8 Chapter 3 Tables and Figures

Figures.

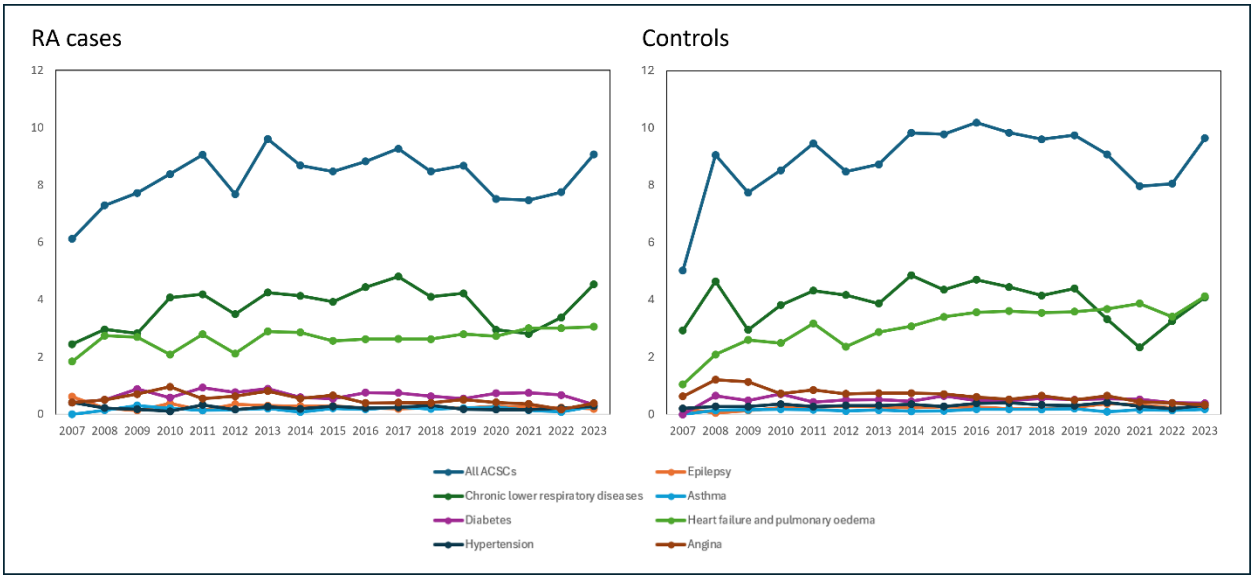

Figure 3—1. Hospitalizations for specific ACSCs and all ACSCs combined as a proportion of all hospitalizations, among RA cases and controls.

Tables.

Table 3—1. Characteristics of the study cohort.

Characteristic	**N (%) unless otherwise indicated**	
	RA Cases	Controls
Individuals	25281	70313
Hospitalizations	83811	190304
Sex		
Female	16652 (66%)	46551 (66%)

Male	8629 (34%)	23759 (34%)
Age at admission		
Mean (SD)	64.3 (16.8)	69.4 (16.1)
Median (IQR)	66 (54, 77)	72 (60, 81)
Location of Primary Residence[1]		
Rural	4843 (19%)	12469 (18%)
Urban	20349 (81%)	57630 (82%)
Comorbidities[2]		
Mean CCI score (SD)	3.78 (2.67)	3.21 (2.61)
Congestive heart failure	6343 (25%)	17311 (25%)
Cerebrovascular disease	5396 (21%)	16168 (23%)
Dementia	4347 (17%)	14840 (21%)
Chronic pulmonary disease	11909 (47%)	27844 (40%)
Cancer (any malignancy)	7594 (30%)	22619 (32%)
Metastatic solid tumour	1510 (6.0%)	4678 (6.7%)
Mild liver disease	2183 (8.6%)	4067 (5.8%)
Moderate/severe liver disease	329 (1.3%)	708 (1.0%)
All ACSC Hospitalizations	**7005**	**17391**
Grand Mal status and other epileptic convulsions	207 (3.0%)	486 (2.8%)

Chronic lower respiratory diseases	3202 (45.7%)	7434 (42.7%)
Asthma	152 (2.2%)	292 (1.7%)
Diabetes	576 (8.2%)	970 (5.6%)
Heart failure	2280 (32.5%)	6440 (37.0%)
Hypertension	183 (2.6%)	609 (3.5%)
Angina	405 (5.8%)	1160 (6.7%)

[1] Frequency missing N = 89 for RA, N = 214 for Non-RA

[2] CCI: Charlson Comorbidity Index Score, Frequency missing N=1 Non-RA

Table 3—2. Crude and adjusted incidence rate ratios (95% Confidence Interval) of Ambulatory Care Sensitive Condition (ACSC) hospitalizations.

	3 years		5 years	
Ambulatory Care Sensitive Condition	Unadjusted	Adjusted[1]	Unadjusted	Adjusted[1]
Overall	1.12 (1.04, 1.20)*	1.11 (1.03, 1.19)*	1.14 (1.08. 1.21)*	1.14 (1.08, 1.20)*
Grand Mal Seizures	1.05 (0.57, 1.92)	0.86 (0.45, 1.62)	0.78 (0.49, 1.23)	0.59 (0.37, 0.96)*
Chronic lower respiratory diseases	0.98 (0.88, 1.09)	0.94 (0.85, 1.05)	1.05 (0.97, 1.13)	1.01 (0.94, 1.10)
Asthma	0.59 (0.25, 1.37)	0.57 (0.20, 1.64)	0.96 (0.53, 1.72)	0.88 (0.47, 1.65)
Diabetes	1.61 (1.18, 2.18)*	0.91 (0.67, 1.24)	1.45 (1.14, 1.85)*	0.97 (0.76, 1.25)
Heart failure and pulmonary edema	1.20 (1.05, 1.38)*	1.22 (1.06, 1.41)*	1.13 (1.02, 1.25)*	1.12 (1.01, 1.25)*
Hypertension	0.45 (0.14, 1.51)	0.59 (0.18, 1.96)	0.79 (0.35, 1.78)	0.99 (0.44, 2.27)
Angina	1.05 (0.67, 1.67)	1.00 (0.67, 1.50)	1.23 (0.88, 1.73)	1.21 (0.88, 1.66)

[1] Adjusted IRR – Incidence rate ratio of RA: Non-RA patients. Adjusted by age, sex, and geographic location.

[2] ACSC – Ambulatory Care Sensitive Condition

* Indicates statistical significance ($p<0.05$)

Table 3—3. Characteristics of predictors of avoidable hospitalizations amongst individuals with RA.

Covariates	N (%) RA with ACSC Hospitalization (N=3561)	RA with no ACSC Hospitalization (N=49035)
ACSC as comorbidity	3374 (94.75%)	23147 (47.21%)
Rural resident[1]	822 (23.08%)	4021 (8.2%)
Attached to a physician	3548 (99.63%)	48748 (99.41%)
Mean CCI[2] Score (SD)	4.50 (2.72)	1.72 (2.15)
Mean age at admission (SD)	72.4 (13.5)	63.0 (16.9)
Male sex	1349 (37.88%)	16540 (33.73%)
Exposure to DMARDs	1007 (28.28%)	17806 (36.31%)
Exposure to corticosteroids	896 (25.16%)	6135 (12.51%)
Attached to a rheumatologist	1040 (29.21%)	21102 (43.03%)

[1]Missing Geographic location N = 27394

[2]CCI: Charlson Comorbidity Index

Table 3—4. Predictors of first Ambulatory Care Sensitive Condition (ACSC) hospitalizations among RA cases

Predictors	HR (95% CI)	p-value
ACSC[1] as comorbidity	7.42 (5.92, 9.30)	< 0.001 *
Prolonged exposure to corticosteroids[2]	1.44 (1.28, 1.63)	< 0.001 *
Rural resident	1.19 (1.05, 1.35)	< 0.007 *
CCI[3] Score	1.04 (1.02, 1.06)	< 0.001 *
Age at admission	1.02 (1.02, 1.03)	< 0.001 *
Male sex	1.08 (0.97, 1.20)	0.16
Exposure to DMARD[4]	0.94 (0.84, 1.06)	0.30
Attachment to a physician	0.64 (0.31, 1.35)	0.24

[1] ACSC – Ambulatory Care Sensitive Condition

[2] categorized as a binary of yes/no, if dispensed for ≥30 days in a fiscal year

[3]CCI: Charlson Comorbidity Index

[4]DMARD – Disease modifying anti-rheumatic drug

* Indicates statistical significance ($p<0.05$)

3.8 Chapter 3 – Supplementary Material

Appendix Table 1. ICD codes for ACSCs as defined by CIHI (8).

Ambulatory Care Sensitive Conditions	**Diagnostic codes**
Grand mal status and other epileptic convulsions	ICD-9/9-CM: 345 ICD-10-CA: G40, G41
Chronic lower respiratory diseases (except asthma)	ICD-9/9-CM: 491, 492, 494, 496 ICD-10-CA: J41, J42, J43, J44, J47 **OR** MRDx[1] of acute lower respiratory infection, only when a secondary diagnosis[2] of J44 in ICD-10-CA or 496 in ICD-9/9-CM is also present ICD-9/9-CM: 466, 480–486, 487.0 ICD-10-CA: J10.0, J11.0, J12–J16, J18, J20, J21, J22
Asthma	ICD-9/9-CM: 493 ICD-10-CA: J45
Diabetes	ICD-9: 250.0, 250.1, 250.2, 250.7 ICD-9-CM: 250.0, 250.1, 250.2, 250.8 ICD-10-CA: E10.0, E10.1, E10.63, E10.64, E10.9, E11.0, E11.1, E11.63, E11.64, E11.9, E13.0, E13.1, E13.63, E13.64, E13.9, E14.0, E14.1, E14.63, E14.64, E14.9

Heart failure and pulmonary edema[3]	ICD-9/9-CM: 428, 518.4 ICD-10-CA: J81 (MRDx), I50 (MRDx), I50 as diagnosis type (1) when I11 is MRDx
Hypertension[3]	ICD-9/9-CM: 401.0, 401.9, 402.0, 402.1, 402.9 ICD-10-CA: I10 (MRDx), I11 as MRDx when I50 as diagnosis type (1) is not present
Angina[3]	ICD-9: 411, 413 ICD-9-CM: 411.1, 411.8, 413 ICD-10-CA: I20, I23.82, I24.0, I24.8, I24.9
Diagnostic codes of cardiac procedure for exclusion	CCP: 47XX, 480X–483X, 489.1, 489.9, 492X–495X, 497X, 498X ICD-9-CM: 336, 35XX, 36XX, 373X, 375X, 377X, 378X, 379.4–379.8 CCI codes beginning with: 1HA58, 1HA80, 1HA87, 1HB53, 1HB54, 1HB55, 1HB87, 1HD53, 1HD54, 1HD55, 1HH59, 1HH71, 1HJ76, 1HJ82, 1HM57, 1HM78, 1HM80, 1HN71, 1HN80, 1HN87, 1HP76, 1HP78, 1HP80, 1HP82, 1HP83, 1HP87, 1HR71, 1HR80, 1HR84, 1HR87, 1HS80, 1HS90, 1HT80, 1HT89, 1HT90, 1HU80, 1HU90, 1HV80, 1HV90, 1HW78, 1HW79, 1HX71, 1HX78, 1HX79, 1HX80, 1HX83, 1HX86, 1HX87, 1HY85, 1HZ53, 1HZ54, 1HZ55, 1HZ56, 1HZ57, 1HZ59, 1HZ80, 1HZ85, 1HZ87, 1IF83, 1IJ50, 1IJ55, 1IJ57, 1IJ76, 1IJ80, 1IK57, 1IK80, 1IK87, 1IN84, 1LA84, 1LC84, 1LD84, 1IJ86 **AND** not

	equal to (1HZ53LAKP, 1HZ55LAKP) **AND** not equal to abandoned at onset

[1]MRDx = Most responsible diagnosis

[2]Secondary diagnosis = diagnosis other than MRDx

[3]Excluding cases with cardiac procedures. Exclusionary codes are listed.

Appendix Table 2. Disease Modifying Anti-Rheumatic Drugs and associated Anatomical Therapeutic Chemical codes.

Medications	**ATC Codes**
Sulfasalazine	A07EC01
Prednisone[1]	H02AB07
Methotrexate	L01BA01
Rituximab	L01XC02
Leflunomide	L04AA13
Abatacept	L04AA24
Tofacitinib	L04AA29
Baricitinib	L04AA37
Upadacitinib	L04AA44

Etanercept	L04AB01
Infliximab	L04AB02
Adalimumab	L04AB04
Certolizumab	L04AB05
Golimumab	L04AB06
Tocilizumab	L04AC07
Sarilumab	L04AC14
Hydroxychloroquine	P01BA02

[1] Corticosteroid

Appendix Table 3. Data Elements and Sources

A. Data elements, Discharge Abstract Database

Data Element Description	Source
encrypted Personal Health Care Number	derived
Fiscal year	DAD
Person Gender Code	DAD
Age at admission	DAD
Institution number	DAD
Admission date	DAD
Admission time	DAD
Discharge date	DAD
Discharge time	DAD
Transfer to	DAD
Transfer from	DAD
Disposition status	DAD
Diagnosis codes.	DAD
Diagnosis types	DAD
Procedure codes	DAD
Acute length of stay	DAD
Total length of stay	DAD
First 3 digits of postal code	DAD

B. Data elements, Practitioner Claims Database

Data Element Description	Source
encrypted Personal Health Care Number	derived
Fiscal year	Claims
Service Event Start Date	Claims
Service Event End Date	Claims
Recipient Years of age at date of service event	Claims
Recipient Gender Code	Claims
Primary diagnosis code	Claims
Secondary diagnosis code	Claims
Tertiary diagnosis code	Claims
Delivery Site Functional Centre Code	Claims
Delivery Site Functional Centre Type Code	Claims
Type of facility where the service was provided	Claims
EDW derived data element. Physician billing expense	derived

Financial Resource Event Actual Paid Amount	Claims
EDW derived data element. Combination of SECTOR and DOCTOR_CLASS	Claims

C. Data elements, Pharmaceutical Information Network

Data Element Description	**Source**
Encrypted Personal Health Number	derived
Drug Identification Number	PIN
Dispensed Amount Quantity	PIN
Dispensed Amount Unit Measure Code	PIN
Dispensed Date	PIN
Dispensed Day Supply Quantity	PIN
Dispensed Day Supply Unit Measure Code	PIN
Supply Drug Anatomical Therapeutic Chemical Code	PIN

Appendix Figure 1. Datasets and timeframes used to identify cohort and outcomes.

Chapter 4 – MANUSCRIPT: Emergency Department Visits for Ambulatory Care Sensitive Conditions by Persons with Rheumatoid Arthritis: A Population-Based Study

Emergency Department Visits for Ambulatory Care Sensitive Conditions by Persons with Rheumatoid Arthritis: A Population-Based Study

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4.1 Abstract

Purpose: We estimated emergency department (ED) visit rates for Canadian-indicator Ambulatory Care Sensitive Conditions (ACSCs) by persons with rheumatoid arthritis (RA) relative to age- and sex-matched general population controls.

Methods: Cases were identified using a validated definition based on International Classification of Diseases codes (years 2002-2023). We identified visits in the National Ambulatory Care Reporting System (NACRS) where the most responsible diagnosis was for any ACSC (grand mal seizures, chronic lower respiratory diseases, asthma, diabetes, heart failure and pulmonary edema, hypertension, angina) and extracted visit acuity. Annual incidence rates were calculated within five years from the index date. The incidence rate ratio between RA and non-RA was estimated using a multivariable regression model, adjusting for age, sex, and location of residence.

Results: RA (n=35,389 individuals) had higher ED visit rates for all ACSCs combined compared to Non-RA (n=99,262 individuals) (crude IRR 1.08, 9%% CI 1.08, 1.09), persisting after adjusting for confounders (adjusted IRR 1.06, 95% Cl 1.05, 1.07). More than two-thirds of ED visits for ACSCs were triaged as “urgent” or higher severity. Over the study period, there was a 76% increase in the proportion of ED visits for an ACSC condition among those with RA.

Conclusion: RA cases had a 6% higher rate of avoidable ED visits in the first 5 years following diagnosis compared to non-RA. Improved ambulatory care access and care quality, inclusive of primary care and subspecialty care, is proposed to reduce the burden on the acute care system.

4.2 Introduction

The consequences of systemic inflammation in Rheumatoid Arthritis (RA) are posited to lead to increased healthcare utilization, including emergency department (ED) visits, which drives healthcare system costs. In Alberta, persons with RA are overrepresented in ED utilization. In 2017, 2.1% of all the ED visits in the province were made by persons with RA (1) despite the prevalence of the condition only being 1.1% (2). Some of these ED visits may be avoidable.

Ambulatory Care Sensitive Conditions (ACSCs) are conditions where appropriate and timely access to ambulatory care could prevent complications, a more severe disease course, or the need for ED visits and hospitalizations, and are also used as indicators of primary care access (3). Accepted ACSCs used for surveillance of the Canadian health care system performance include grand mal status and other epileptic convulsions, chronic lower respiratory diseases, asthma, diabetes, heart failure and pulmonary edema, hypertension, and angina (3). People with RA remain at increased risk for some of these, including excess morbidity and mortality related to comorbid conditions such as cardiovascular (4, 5) and chronic pulmonary diseases (6) compared to the general population.

Canada has one of the richest and most comprehensive collections of health data, including administrative health databases that record patient interaction with the healthcare system, including emergency and urgent care visits, hospitalizations, outpatient physician visits, and pharmacy dispensations. We conducted this study to investigate whether ED visits by RA patients are driven by conditions that could be avoidable. Our objective was to estimate the frequency of ACSC-related ED visits by persons with RA relative to the general population, characterize acuity at presentation, and examine whether there have been temporal changes in use over a 17-year time period.

4.3 Materials and Methods

4.3.1 Study Design

This was a retrospective cohort study using population-level administrative health data. In Alberta, a province of 4.6 million people, all health administrative data are maintained by Alberta Health for the Alberta Health Care Insurance Plan (AHCIP) and Alberta Health Services, as a single-payer health system. The administrative datasets represent patient interactions with the healthcare system at all sources (ambulatory care with primary care physicians and specialists; emergency department and urgent care visits; hospital admissions; pharmacy dispensations). Linkage for cohort creation and outcome ascertainment is made possible through a Unique Lifetime Identifier (ULI) assigned to each patient.

4.3.2 Datasets

For this project, four datasets were accessed: the Discharge Abstract Database (hospitalizations, April 2007-March 2023), Practitioner Claims (inpatient/outpatient physician visits, April 2002-March 2023), National Ambulatory Care Reporting System (emergency department and urgent care visits, April 2007-March 2023), and Provincial Registry (demographic information, April 2002-March 2023).

4.3.3 Participants

A cohort of persons meeting a validated case definition for RA (7, 8) was extracted from the datasets using an algorithm with diagnostic codes from the International Classification of Diseases Ninth Revision (ICD-9) for Practitioner Claims, or Tenth Revision (ICD-10) for

Discharge Abstract Database for RA (in ICD-9-CM 714.X and ICD-10-CA M05.X-M06.X). Those included in the cohort must have had one hospitalization discharge or at least two practitioner claims for RA in two years, but at least 8 weeks apart (97% sensitivity, 77% specificity, 67% PPV, 98% NPV) (8). There was a conservative five-year washout period applied to establish an incident cohort and exclude prevalent cases. To compare estimates to the general population not meeting the criteria for RA, 1:4 age- and sex-matching (within five years) was employed. The index date for RA cases was the date of first diagnostic code for RA, and this same date was applied as the index date for each case's matched controls. We excluded individuals younger than 18 years of age, and those meeting case definitions of other inflammatory arthritis conditions of psoriatic arthritis (696.X, 720.X, L40.X, M07.0, M07.1, M07.2, M07.3 and M45.X), ankylosing spondylitis (720.X, M45.X), and gout (274.X, 712.X, M10.X, M11.X).

4.3.4 Outcomes

The primary outcome of interest was ED visit rates for any ACSC, and individual ACSCs, calculated as incidence rate ratios (IRR) (95% CI)) for RA relative to non-RA. Annual rates of visits were calculated for a 5-year period following the index date. We applied the defining ICD-10-CA/CM codes for each ACSC following the Canadian Institute for Health Information (CIHI) methodology (See Appendix Table 1). The acuity of ACSC visits as recorded at presentation using the Canadian Triage and Acuity Scale (CTAS) (1 Resuscitation, 2 Emergent, 3 Urgent, 4 Less urgent, 5 Non-urgent) (9) was a secondary outcome.

4.3.5 Statistical analyses

Descriptive statistics were used to report the characteristics of ACSC ED visits up to five years from the index date for RA and non-RA. IRRs (95% CI) for each ACSC were calculated using a zero-inflated Poisson regression model, adjusting for age at presentation (continuous), biological sex (male/female), and location of residence (urban/rural), determined using forward sortation area (10). Statistical analyses were performed using R version 4.4.0.

4.3.6 Ethics

Ethics approval for this study was provided by the University of Calgary Conjoint Health Research Board (Ethics ID REB22-1316).

4.4 Results

4.4.1 Cohort and Visit Characteristics (Table 4—1).

The incident cohort consisted of 52,596 individuals with RA, matched to 210,384 individuals who did not meet the RA case definition. From the RA cohort 67.3% (n=35,389 individuals) had at least one ED visit for any reason up to five years after their index date. This proportion is significantly higher compared to non-RA (n=99,262 individuals, 47.2%). The average age at ED visit was 58.6 (SD 17.2) years for RA and 64.4 (SD 16.4) years for non-RA, with no difference in sex proportion (approximately 66% identified as female sex for both cohorts). Those with RA had an average of 5.9 (SD 13.0) visits per person throughout the 5-year observation study period, compared to 4.2 (SD 6.6) visits per person among non-RA ($p < 0.001$).

Approximately 5.2% (32,606 out of the total 623,499 ED visits) of all ED visits by RA cases had a most responsible diagnosis of an ACSC. Among individual ACSCs, ED visits for chronic lower respiratory diseases comprised more than 30% of all ACSC ED visits: 37.2% for all ACSC ED visits for RA and 34.5% for non-RA, respectively. This was followed by heart failure and pulmonary edema (19.2% for RA and 21.1% for non-RA), hypertension (14.6% for RA and 19.6% for non-RA), diabetes (9.5% for RA and 7.6% for non-RA), asthma (8.6% for RA and 6.4% for non-RA), angina (7.2% for RA and 8.3% for non-RA), and grand mal seizures (3.7% for RA and 2.5% for non-RA).

4.4.2 Incidence rate ratios (Table 4—2).

The crude IRR for any ACSC ED visit was higher in RA cases compared to non-RA (IRR 1.08, 95% CI 1.08, 1.09). After adjusting for potential confounders, we determined that RA cases had 6% higher rates of ED visits for any ACSC compared to non-RA (IRR 1.06, 95% CI 1.05, 1.07). The ED visit incidence rates were higher in those with RA for heart failure and pulmonary edema (crude IRR 1.11, 95% CI 1.02, 1.20), persisting after adjusting for confounders (adjusted IRR 1.12, 95% CI 1.03, 1.22). The crude incidence rate for diabetes visits was higher among RA compared to non-RA (IRR 1.31, 95% CI 1.15, 1.48) but was not statistically different after adjusting for confounders (IRR 0.95, 95% CI 0.83, 1.09).

4.4.3 Acuity of ACSC Visits and Hospitalizations (Table 4—3).

Using the CTAS scores, 76.4% of all ACSC ED visits by RA cases were triaged as CTAS 1-3 (Resuscitation, Emergent, and Urgent) (1.7%, 29.2%, and 45.5%, respectively). This was

comparable to the 76.3% of all ACSC ED visits by non-RA triaged CTAS 1-3. Approximately 31.9% of ACSC ED visits by RA patients led to hospital admission (2,872 of 8,994 ED visits for an ACSC), comparable to the proportion of ACSC ED visits by non-RA (32%, 7,551 of 23,612 ACSC ED visits).

4.4.4 ACSC Visit Frequency Over Time (Figure 4—1).

There was a 76% increase in the proportion of ED visits, as a proportion of all visits, that were for an ACSC among those with RA over the 17-year study period. In 2007, 3.3% of all ED visits by RA cases were for an ACSC, increased to 5.8% in 2023. In contrast, there was an approximate 39% increase in ACSC ED visits by non-RA over the same period, from 5% of visits in 2007 to 6.9% of all visits in 2023. Notable was a lower proportion of visits in both cohorts that were for an ACSC during the years 2020, 2021 and 2022, coinciding with the COVID-19 pandemic.

4.5 Discussion

Our study contributes knowledge of ED utilization, and specifically ACSC-related healthcare utilization, by RA patients. Overall, individuals with RA more frequently attend the ED in the first five years following diagnosis as compared to their matched controls. Approximately 6% of these ED visits are potentially avoidable, and the proportion of visits for ACSCs has nearly doubled over the last decades. The risk of having an avoidable ED visit is elevated compared to those without RA. Over 75% of all ACSC visits were triaged “Urgent” or with higher severity, and approximately one-third resulted in hospital admission for both RA and non-RA. While our

results are consistent with previous studies showing higher healthcare utilization by RA patients compared to those without RA (11, 12), it demonstrates the increasing burden of avoidable health care use, and what proportion of these visits are amenable to intervention to reduce acute care use.

Close to 40% of these ACSC visits were for chronic lower respiratory diseases, which include emphysema and chronic obstructive pulmonary disease. It was not surprising that patients with RA present to the ED for cardiovascular and pulmonary conditions, as these are common complications and comorbidities of RA. A cross-sectional study across 17 countries examined the prevalence of comorbid conditions among RA patients and found a high prevalence of asthma (prevalence proportion 6.6%), cardiovascular events such as stroke and myocardial infarction (6%), and chronic obstructive pulmonary disease (3.5%) (13). Comorbid conditions that are also ACSCs may increase healthcare utilization, particularly hospitalizations among RA patients (14).

This study also highlights that avoidable health care utilization estimates are amenable to intervention. There was a noticeable decline in ED visits during the period of the COVID-19 pandemic, likely driven by the increased social distancing restrictions resulting in fewer exacerbations of chronic lung disease, public avoidance of EDs and hospitals, and the attribution of COVID-related visits and admissions to the denominator of the estimates. Different approaches to seeking healthcare were likely employed. A study in Alberta examined patients with inflammatory arthritis (IA) conditions, which include RA, and found that 35% of the patients attempted to seek care from different providers prior to their ED visits (e.g., primary care provider, walk-in clinic, rheumatology clinic, virtual telehealth, the Health Link, an Alberta-based, nurse-led service providing health advice over the phone, or another healthcare provider

such as a chiropractor, physiotherapist, or nurse practitioner) during a period coinciding with the pandemic (15).

While not all hospital admissions are avoidable, high-quality primary ambulatory care could mitigate the frequency or severity of presentations for ACSCs (3), and thereby reduce the need for ED visits and/or hospitalizations. Our results reinforce the need for collaborative care between ambulatory care physicians, inclusive of primary and specialty care, in the diagnosis, treatment, and management of RA and its comorbidities. In primary care settings, interprofessional teams have been shown to reduce avoidable hospitalizations, specifically for congestive heart failure (16). Team-based care, which provides services by an interprofessional team, can ensure that patients can access health services in a timely and efficient manner. The Canadian Medical Association (CMA) highlighted the need to include not only physicians, but also allied health professionals, including psychologists, psychotherapists, and a registered dietitian, into a "primary care team" to improve access and quality of care (17). Primary Care Networks in Alberta, Family Health Teams in Ontario, and Family Medicine Groups in Quebec all adopt a team-based primary care (17), although these structures are not available to every individual patient. Benefits of team-based care include a reduction in acute care service use; in Ontario, patients who were part of team-based care had slower increase in ED visits compared to patients in non-team-based care (18). With the recent crisis in primary care access, 5.4 million Canadians 18 and older with no regular health provider (19), led to an influx of ED use for otherwise avoidable conditions. According to CIHI, approximately 15% of all ED visits between April 2023 to March 2024 could have been managed in primary care settings (20).

We acknowledge limitations of our study. Data in administrative health databases are collected in the operation of health services, not specifically designed for research and surveillance

purposes. The diagnostic criteria applied to identify RA cases, while validated, may not fully include all persons with RA, and could include persons who do not have the condition too. We chose a widely used case definition that has been used by the Canadian Chronic Disease Surveillance System with optimal sensitivity and specificity (97% sensitivity, 77% specificity). There are also additional confounders, such as disease severity, smoking behaviour, and obesity, that were not accounted for as we did not have laboratory and diagnostic imaging data to estimate disease activity. Previous studies have noted that the definition of ACSCs only includes hospitalizations, but not ED visits. Therefore, a proportion of ED visits that do not lead to hospital admissions were not included in the estimates (21). Finally, due to the nature of administrative data and lack of data availability, we also were not able to adjust for socioeconomic status and ethnicity. Despite these limitations, our research still provides data critical to understanding acute care use needs of persons with RA, so that a response through health system innovation can be developed and implemented.

4.6 Conclusion

Persons with RA are at a higher risk of avoidable ED visits 5 years after diagnosis, with ED use for ACSC higher than the control population, and increasing over time. Better access to and quality of ambulatory care, including primary and specialty care, is necessary to reduce the burden on the acute care system and improve the quality of care for people with RA.

4.7 Chapter 4 References

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Tables and Figures.

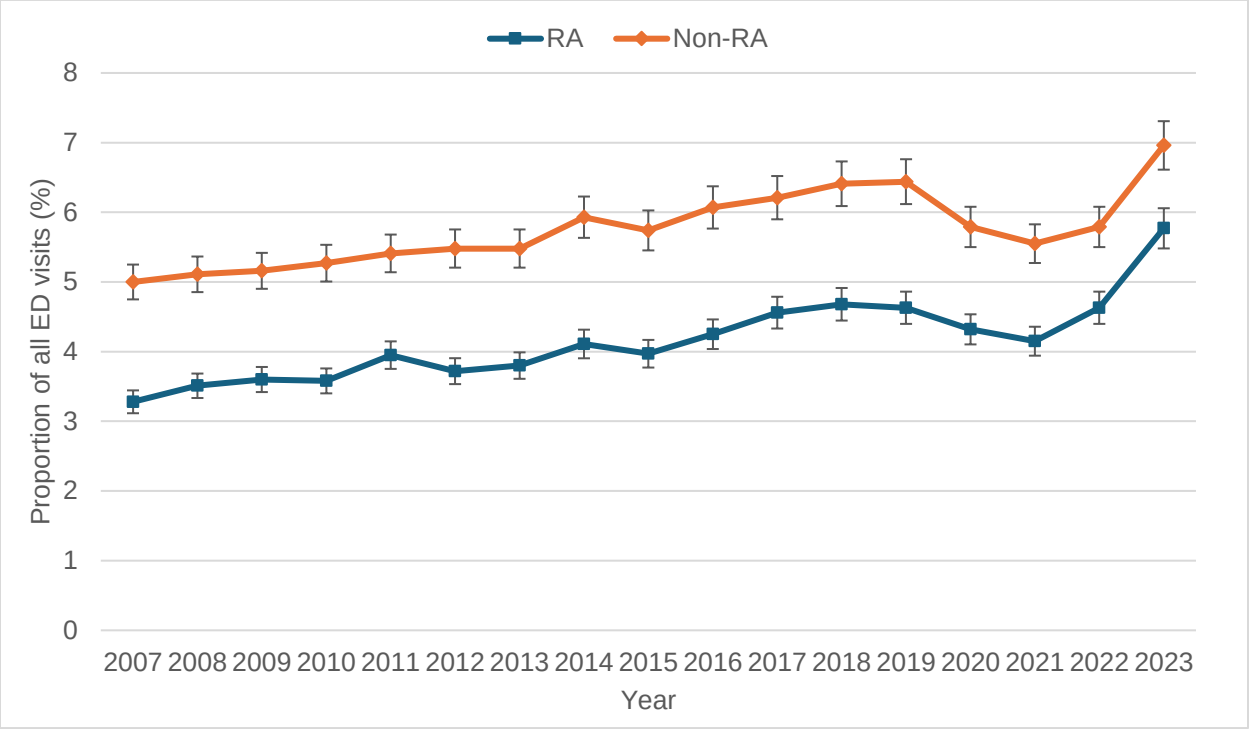

Figure 4—1. Proportion of ED visits for any Ambulatory Care Sensitive Condition (ACSC), relative to all ED visits, in RA and non-RA, by fiscal year end.

Table 4—1. Characteristics of RA and Non-RA that had an ED visit for any reason during the study period.

	RA Cases (N=35,389 individuals with an ED visit)	**Non-RA (N=99,262 individuals with an ED visit)**
ED Visits	210,191	413,308

Average ED visit frequency, over 5 years (SD)	5.9 (13.0)	4.2 (6.6)
Female sex	23,437 (66.2%)	66,290 (66.9%)
Age at ED visit, years		
Mean (SD)	58.6 (17.2)	64.4 (16.4)
Median (IQR)	59 (47, 77)	66 (53, 77)
Rural Location of residence[a]	5,569 (15.7%)	14,270 (14.4%)

[a]Missing Location of residence: RA N = 9,121, Non-RA N = 29,529

Table 4—2. Crude and adjusted incidence rate ratios (95% Confidence Interval) of ACSC ED visits.

Ambulatory Care Sensitive Condition	Unadjusted	Adjusted[b]
Overall	1.08 (1.08, 1.09)*	1.06 (1.05, 1.07)*
Grand Mal Seizures	1.17 (0.96, 1.41)	0.92 (0.75, 1.13)
Chronic lower respiratory diseases	1.04 (0.98, 1.09)	1.00 (0.95, 1.06)
Asthma	1.11 (0.97, 1.29)	1.00 (0.86, 1.17)
Diabetes	1.31 (1.15, 1.48)*	0.95 (0.83, 1.09)
Heart failure and pulmonary edema	1.11 (1.02, 1.20)*	1.12 (1.03, 1.22)*
Hypertension	0.89 (0.79, 1.00)	0.95 (0.83, 1.08)
Angina	1.06 (0.86, 1.30)	1.06 (0.85, 1.31)

[b] Adjusted IRR – Incidence rate of RA : Non-RA patients. Adjusted by age, sex, and geographic location.

*Indicates statistical significance

Table 4—3. Acuity of ACSC related ED visits (n, %)

CTAS[c]	RA (N = 8,994)	Non-RA (N = 23,612)	Difference (RA vs Non-RA)
1 Resuscitation	155 (1.7)	449 (1.9)	-0.2% (95% CI -0.5, 0.1)
2 Emergent	2623 (29.2)	6639 (28.1)	1.05% (95% CI -0.05, 2.15)
3 Urgent	4093 (45.5)	10929 (46.3)	-0.78% (95% CI -1.99, 0.43)
4 Less urgent	1465 (16.3)	3957 (16.8)	-0.47% (95% CI -1.37, 0.43)
5 Non-urgent	378 (4.2)	968 (4.1)	0.10% (95% CI -0.38, 0.59)
9 Unknown	278 (3.1)	666 (2.8)	0.27% (95% CI -0.15, 0.69)

[c]CTAS = Canadian Triage Acuity Scale

4.8 Chapter 4 – Supplementary Material

Appendix Table 1 ICD codes for ACSCs as defined by CIHI (3).

Ambulatory Care Sensitive Conditions	**Diagnostic codes**
Grand mal status and other epileptic convulsions	ICD-9/9-CM: 345 ICD-10-CA: G40, G41
Chronic lower respiratory diseases (except asthma)	ICD-9/9-CM: 491, 492, 494, 496 ICD-10-CA: J41, J42, J43, J44, J47 **OR** MRDx[1] of acute lower respiratory infection, only when a secondary diagnosis[2] of J44 in ICD-10-CA or 496 in ICD-9/9-CM is also present ICD-9/9-CM: 466, 480–486, 487.0 ICD-10-CA: J10.0, J11.0, J12–J16, J18, J20, J21, J22
Asthma	ICD-9/9-CM: 493 ICD-10-CA: J45
Diabetes	ICD-9: 250.0, 250.1, 250.2, 250.7 ICD-9-CM: 250.0, 250.1, 250.2, 250.8 ICD-10-CA: E10.0, E10.1, E10.63, E10.64, E10.9, E11.0, E11.1, E11.63, E11.64, E11.9, E13.0, E13.1, E13.63, E13.64, E13.9, E14.0, E14.1, E14.63, E14.64, E14.9
Heart failure and pulmonary edema[3]	ICD-9/9-CM: 428, 518.4

	ICD-10-CA: J81 (MRDx), I50 (MRDx), I50 as diagnosis type (1) when I11 is MRDx
Hypertension[3]	ICD-9/9-CM: 401.0, 401.9, 402.0, 402.1, 402.9 ICD-10-CA: I10 (MRDx), I11 as MRDx when I50 as diagnosis type (1) is not present
Angina[3]	ICD-9: 411, 413 ICD-9-CM: 411.1, 411.8, 413 ICD-10-CA: I20, I23.82, I24.0, I24.8, I24.9
Diagnostic codes of cardiac procedure for exclusion	CCP: 47XX, 480X–483X, 489.1, 489.9, 492X–495X, 497X, 498X ICD-9-CM: 336, 35XX, 36XX, 373X, 375X, 377X, 378X, 379.4–379.8 CCI codes beginning with: 1HA58, 1HA80, 1HA87, 1HB53, 1HB54, 1HB55, 1HB87, 1HD53, 1HD54, 1HD55, 1HH59, 1HH71, 1HJ76, 1HJ82, 1HM57, 1HM78, 1HM80, 1HN71, 1HN80, 1HN87, 1HP76, 1HP78, 1HP80, 1HP82, 1HP83, 1HP87, 1HR71, 1HR80, 1HR84, 1HR87, 1HS80, 1HS90, 1HT80, 1HT89, 1HT90, 1HU80, 1HU90, 1HV80, 1HV90, 1HW78, 1HW79, 1HX71, 1HX78, 1HX79, 1HX80, 1HX83, 1HX86, 1HX87, 1HY85, 1HZ53, 1HZ54, 1HZ55, 1HZ56, 1HZ57, 1HZ59, 1HZ80, 1HZ85, 1HZ87, 1IF83, 1IJ50, 1IJ55, 1IJ57, 1IJ76, 1IJ80, 1IK57, 1IK80, 1IK87, 1IN84, 1LA84, 1LC84, 1LD84, 1IJ86 **AND** not equal to (1HZ53LAKP, 1HZ55LAKP) **AND** not equal to abandoned at onset

[1]MRDx = Most responsible diagnosis

[2]Secondary diagnosis = diagnosis other than MRDx

[3]Excluding cases with cardiac procedures. Exclusionary codes are listed.

Chapter 5 – DISCUSSION

5.1 Results

This thesis estimated the incidence rate ratios of acute care use for ACSCs by persons with and without RA. ACSCs are used as indicators of health care quality: these are a set of conditions reflecting access and quality of ambulatory care, with higher rates signaling health care utilization that is amenable to intervention. High rates of ACSC acute care use may reflect problems in accessing appropriate and timely primary care. Population-based administrative datasets collected in the routine administration of the healthcare system in Alberta, Canada were used to derive these estimates. Persons meeting the case definition for RA had a 14% higher rate of hospitalizations and a 6% higher rate of ED visits for any ACSC compared to matched controls within the 5 years following their diagnosis. After adjusting for confounders, both hospitalizations and ED visits for heart failure and pulmonary edema remained 12% higher among those with RA as compared to their matched controls.

Approximately 10% of all hospitalizations and 6% of all emergency visits by persons with RA from 2007-2023 could be considered avoidable, primarily driven by chronic lower respiratory diseases, along with heart failure and pulmonary edema, having the highest frequencies of acute care use.

The proportion of ACSC-related acute care use among those with RA has increased over time. The main drivers of these ACSC acute care use are heart failure and pulmonary edema, accounting for 3% of all hospitalizations by RA patients in 2023.

Significant predictors of ACSC hospitalization among persons with RA include having ACSCs as comorbidities, being from a rural location, prolonged exposure to corticosteroids, an increasing number of comorbid conditions, and increasing age.

5.2 Incidence of composite ACSC and time trends and acuity of ED visits

When looking at ACSC hospitalizations by persons with RA as a proportion of all hospitalizations, the proportion increased by 49% from 6.1% in 2007 to 9.1% in 2023. ED visits for ACSCs have also increased over time. The majority of these visits were triaged “urgent” or higher. This likely implies that appropriate and quality care in primary care settings was not sought or met, leading to the worsening of disease severity and significant disruptions in health status when finally presenting to the ED.

People with RA have a higher risk of potentially avoidable acute care use. It is helpful to understand which ACSC is driving these rates and how interventions could be designed to reduce them.

5.3 Incidence for specific conditions

The main causes for hospitalizations among ACSCs were chronic lower respiratory diseases and heart failure and pulmonary edema – for both cases and controls. This is in line with data from the Canadian Institute for Health Information (CIHI), with the most common reasons for hospitalizations in 2022-2023 apart from childbirth were COPD and bronchitis, and heart failure, and pneumonia (1). Interestingly, the proportion of hospitalizations (for cases and controls) for chronic lower respiratory diseases decreased in 2019-2021, before increasing again in 2023. The

COVID-19 pandemic and enforced restrictions may have led to fewer patients going to the hospital. Additionally, hospital admissions for this new infection lead to a larger denominator of total hospitalizations. There was also a direct influence on healthseeking behaviour, differential amongst those with autoimmune conditions (2). Qualitative work on perceptions of the COVID-19 social distancing restrictions among those with autoimmune rheumatic diseases including RA, found that they were more likely to avoid public gatherings and opted to stay in their homes to adhere to social distancing regulations (3, 4). This would have reduced exposure to respiratory illnesses that are responsible for exacerbations of chronic lower respiratory disease.

CIHI has included specific conditions under "chronic lower respiratory diseases", namely simple and mucopurulent bronchitis, unspecified chronic bronchitis, other chronic obstructive pulmonary disease, and bronchiectasis. Asthma was considered its own category of ACSC. Acute care use for chronic lower respiratory diseases were not significantly higher among those with RA compared to controls. The Public Health Agency of Canada estimated over 2 million Canadians (9.5%) 35 years and older were diagnosed with chronic obstructive pulmonary disease (COPD) in 2012-2013 (5). It was also estimated that approximately 9.2% of Albertans were living with COPD in 2012 (5). Another study conducted in British Columbia found a higher incidence of COPD among persons with RA compared to the general population, especially in the first and second year following the index date (6). It was initially hypothesized that persons with RA had higher rates of hospitalizations for chronic lower respiratory diseases due to the increased prevalence of chronic obstructive pulmonary disease (COPD) among those with RA, but this was not what was observed. A plausible explanation for this could be the use of corticosteroids among those with RA, which help control inflammation. Some studies have shown a lower risk of adverse respiratory events among those with concomitant RA and COPD

using a DMARD (7, 8). Being on corticosteroids may have lowered the risk for exacerbation of chronic lower respiratory diseases, thus the rates of hospitalizations were not much different compared to the general population. There were also no differences in acute care use between cases and controls for conditions like asthma, diabetes, hypertension, and angina. These conditions were the least frequent reasons for acute care use in both populations. It is worth noting that the crude incidence rates for acute care use for diabetes were higher among those with RA, but did not persist after adjusting for confounders.

Cardiovascular comorbidities, such as congestive heart failure, are prevalent among those with RA (9, 10), so it was not surprising to see that people with RA present to the ED and are hospitalized for these conditions. A higher rate of hospitalizations among those with RA relative to controls may imply inadequate screening and monitoring for CVD. Prior studies showed suboptimal cardiovascular risk assessment among RA patients, despite being at a higher risk of CVD (11, 12). The European Alliance of Associations for Rheumatology recommends "adequate control of disease activity" to lower the risk of cardiovascular diseases, as well as annual risk assessments for all patients with RA (13). Whether this recommendation is being actively heeded in Canada has not been evaluated. Tumor necrosis factor inhibitors (TNFi) are used as treatment for RA, and have been found to reduce the risk of cardiovascular events in RA patients (14), but this was not observed, likely due to a small proportion of RA patients being on this medication.

5.4 Predictors

Predictors for an ACSC hospitalization were examined within the cohort of RA cases. Four conditions in the Charlson comorbidity index are also considered ACSCs: congestive heart

failure, chronic pulmonary disease, and diabetes with and without complications. When these conditions are present as a comorbidity among those with RA, the hazard ratio for ACSC hospitalization increased sevenfold. The association between comorbidities and avoidable hospitalizations has been studied in Portugal. The number of chronic conditions someone has increases the likelihood of being hospitalized for an avoidable condition by 35% and 55% higher risk for each additional organ system involved (15) . The same study also found that patients hospitalized for ACSCs were more likely to have multiple chronic conditions affecting several organ systems compared to those hospitalized for non-ACSCs.

This thesis considered the role of medication exposures in avoidable acute care use risk. Corticosteroids, such as prednisone, may be prescribed to RA patients to help lower inflammation and disease activity. There are associated risks with taking corticosteroids, including an increased infection risk. Prolonged exposure to corticosteroids may imply that inflammation and disease activity are not controlled, further driving risk for ACSC comorbidities. A study in Sweden among patients with gout found that corticosteroid use has a 41% increased risk of an avoidable hospitalization 3 years before and after diagnosis (16).

People with RA who live in rural and remote areas may face additional barriers to access to primary care physicians. More than 90% of physicians in Canada work in urban settings (5). With the limited number of physicians in rural areas, persons with RA who have concerns may not be able to see a physician immediately, leading to further complications and a more severe disease course that would soon require hospitalization. This was reflected in the findings in Chapter 3, with RA patients living in rural areas having a 19% higher risk for an ACSC hospitalization compared to RA patients residing in urban areas.

Increasing age was also a significant predictor of ACSC hospitalization. This was consistent with previous literature on ACSCs, where one study in the United States found that approximately 11% of all ED visits by older adults were for these avoidable conditions (17), and over half of the ACSC-related hospitalizations in Canada were by patients aged 60 and older (18). While RA can occur at any age, it has an increasing prevalence among the elderly, thus it is not surprising to see that increasing age is a predictor of avoidable hospitalizations. Elderly people with RA may also develop and manage other comorbid conditions on top of RA.

While sex was not found to be a predictor of ACSC hospitalizations after adjusting for other variables in this study, male patients with RA were more frequently admitted to hospital than females (6). Additionally, literature examining risk factors for ACSC hospitalizations noted that while there is a higher rate of events among males, it was not the most significant risk factor, stating that "high risk" patients were those with poorer health and higher healthcare utilization (18). There is also the societal expectations of masculinity and gender roles, which may play a part in the lack of engagement of male patients with the healthcare system (7,8). Another is the role of age and comorbidities in RA. Females were more likely to have worse disease activity and less likely to achieve clinical remission (19-21), and thus may develop more comorbid conditions.

Another relevant system-level predictor is exposure to medications, specifically disease-modifying anti-rheumatic drugs (DMARDs). DMARDs can only be dispensed by rheumatologists, therefore, those whom a rheumatologist cannot see in a timely manner will not have access to pharmacotherapy, possibly worsening RA progression in the meantime. Furthermore, the need to be seen by a family physician initially before initiating a rheumatology referral may also hinder access to timely and effective treatment strategies.

Surprisingly, attachment to an ambulatory care physician was not protective of ACSC hospitalizations. It was initially expected that not being attached to a physician, either a family physician or a rheumatologist, would be the most significant predictor of avoidable hospitalizations among RA patients. Among those with RA, we found that 71% of the cohort had at least one visit annually to a family physician and 63% had at least one visit with their rheumatologist each year. Due to the nature of administrative data, we were limited to the use of proxy measures to define physician attachment. The algorithm used to determine physician attachment was likely too broad and was unable to properly capture continuity or quality of care. Registries may be a more accurate way to investigate physician attachment. In Alberta, the Central Patient Attachment Registry (CPAR) captures confirmed relationships between primary care physicians and patients, but no studies have examined data linkage and feasibility alongside administrative data (22).

5.5 Implications for care

With the increased risk of potentially avoidable acute care use among patients with RA, there is a need to identify possible ways to improve access to providers. This is to properly screen and manage comorbid conditions among those with RA. It should be a combined responsibility between primary care and rheumatologists to ensure that RA patients get screened for comorbid conditions such as cardiovascular diseases, as recommended by clinical practice guidelines (23, 24). There are established benchmarks for the quality of care among patients with inflammatory arthritis (IA) that are connected to their rheumatic disease control main drivers of ACSC-related acute care use (25). Specifically, performance measures such as wait times for a rheumatology consult among those with new-onset IA, percentage of patients seen by a rheumatologist,

percentage of patients treated with a DMARD, and time to DMARD therapy are all important quality measures when looking at RA patients' access to timely diagnosis and treatment.

5.5.1 Interaction between providers

RA is a chronic disease, and patients are followed longitudinally, thus the relationship between their providers needs to be sustained. Primary care providers are usually the first point of contact for health services. They are responsible for referring a patient to a rheumatologist if they suspect that the patient needs either a second opinion or services outside the scope of their medical practice (26). It is essential for primary care providers, rheumatologists, and other specialists to interact and support each other to ensure that patient concerns are addressed on time.

5.5.2 RA control and comorbidities

The relationship between RA disease activity and comorbidities has been previously studied. Patients with more comorbidities at baseline may have higher disease activity compared to those without (27-29). The American College of Rheumatology highlight the need to investigate how early and efficient treatment initiation in RA can affect specific populations, including those with comorbid conditions (23). With the presence of comorbidities, rheumatologists will need to consider more factors when initiating or changing treatments, such as possible contraindications and side effects, as well as adherence and whether patients will be able to afford medications. Some studies have also shown that treatment of comorbidities in patients with RA can improve disease activity and lower inflammation (30, 31). Once again, this highlights the need to address

and control both RA and any other comorbid conditions to improve outcomes and reduce acute care use.

5.5.3 Funding models for providers

With the increasing demand for family physicians in Canada and patients with more complex needs, governments are considering new funding models for providers. Approximately 87% of physicians in general practice are fee-for-service (FFS) under the Alberta Health Care Insurance Plan in fiscal year 2014-2015 (32). This funding model incentivizes volume of appointments for non-complex issues. Concerns by patients with complex needs may not be addressed in a short time. The College of Family Physicians of Canada called for "Equitable and Fair Remuneration for Family Physicians", noting that FFS is not a sustainable payment model, especially in times of significant changes in practice patterns such as the COVID-19 pandemic where people did not see providers in person (33). Appropriately remunerating high-quality care that addresses multiple risk factors is a requirement for improving both primary and rheumatology care provision.

5.5.4 Other ways to improve access

There are several ways to improve access to care for patients with RA while taking into account fair remuneration for providers. A study in Ontario, Canada found that switching from a capitation-based model to an interprofessional team-based care reduces ACSC hospitalizations for heart failure (34). Team-based care ensures that patients can access health services promptly and efficiently.

There has also been an increase in nurse practitioners in Canada working in primary and acute care settings (35). Governments across Canada are looking at nurse practitioners to help with the ever-increasing burden of primary care (36, 37).

Additionally, the Advanced Clinician Practitioner in Arthritis Care (ACPAC) Program could serve as another point-of-contact for patients with suspected or diagnosed RA. ACPAC is an advanced educational program made for other healthcare professionals such as physical therapists, occupational therapists, nurses, and chiropractors to support RA patient care, including diagnosis and management of patients with RA and other musculoskeletal conditions (38). This program was shown to have a 40% lower time-from-referral-to-treatment-decision for patients with inflammatory arthritis compared to the solo-rheumatologist model (39), which is helpful for timely and accurate diagnosis and early treatment for RA patients.

Finally, patient navigators can help identify what services a patient requires at a given time. There have already been some initiatives looking at rheumatology-specific patient navigator care models (40, 41). One study did not report any differences in DMARD adherence, but recommended a larger, multicenter randomized controlled trial to ascertain adherence over time (40), while another study found barriers to adherence such as fear of adverse events and reported that the navigators most often facilitated communication between patient and provider, and provided more education on their diagnosis and treatment (41). Another study in Canada found that an “arthritis liaison” in First Nations communities fostered care continuity and helped patients receive coordinated care (42).

5.6 Future research

This project is a foundation for future research in understanding quality and access to care among patients with RA. Potential avenues for research may include qualitative research to identify root causes of hospitalizations, as well as exploring equity factors to identify possible disparities in access to care among RA patients.

5.6.1 Qualitative research

A prior study in Alberta found that for 35% of all visits, patients with IA attempted to access ambulatory care before presenting to the ED (43). Additionally, the study reported that only 40% of IA patients were able to follow up with a rheumatologist after the ED visit. A root-cause analysis using qualitative interviews can help understand how health system and health service delivery as well as social determinants of health led to otherwise avoidable acute care use among RA patients, to understand patient perspectives and factors that lead to acute care use.

5.6.2 Equity factors

Predictors of avoidable ACSC hospitalization highlight important factors and barriers to care. We found that those who reside in rural areas have a higher risk of being hospitalized for avoidable conditions. This is largely assumed to be related to people living in rural areas do not have the same access to healthcare as patients in urban areas. This needs to be confirmed in future work. First Nations (FN) patients in Alberta were found to have three times higher IA prevalence compared to non-FN patients (44), with less favourable disease outcomes. This study did not permit consideration of differential ACSC admission rates based on First Nations

identity, nor other racial and ethnic populations. We were not able to examine socioeconomic status and how it affects acute care use for ACSCs, but studies have shown that lower socioeconomic status has been linked to more severe disease activity and poorer disease outcomes (45-47). Future work should examine how differences in socioeconomic status affect avoidable acute care use by RA patients; to identify possible ways patients could be supported to reduce the burden on the acute care system and improve patient quality of life.

5.7 Conclusion

This thesis examined rates of avoidable acute care use by persons with RA relative to the general population five years after the date of diagnosis. Hospitalizations for ACSCs were consistently higher among those with RA, especially for heart failure and pulmonary edema. There is a need for physicians to work collaboratively to address patient comorbidities in a timely manner to reduce otherwise avoidable acute care use.

5.8 Chapter 5 References

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18.2) There shall be no right whatsoever for any third party to enforce the terms and conditions of this Agreement. The Parties hereby expressly wish to exclude the operation of the Contracts (Rights of Third Parties) Act 1999 and any other legislation which has this effect and is binding on this agreement.
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