Acute mental health service use is increased in rheumatoid arthritis and ankylosing spondylitis: a population-based cohort study

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Abstract

Background: Rheumatoid arthritis (RA) and ankylosing spondylitis (AS) are associated with mental illness. Whether acute mental health (MH) service utilization (i.e., emergency visits or hospitalizations) is increased in RA or AS is not known.

Methods: Two population-based cohorts were created where individuals with RA \((n = 53,240)\) or AS \((n = 13,964)\) were each matched by age, sex, and year to unaffected comparators \((2002–2016)\). Incidence rates per 1000 person-years (PY) were calculated for a first MH emergency department (ED) presentation or MH hospitalization. Hazard ratios (HR) and 95% confidence intervals (CI) were calculated, adjusting for demographic, clinical, and health service use variables.

Results: Individuals with RA had higher rates of ED visits \(6.59/1000\) PY in comparators) and hospitalizations for MH \(3.11/1000\) versus 1.80/1000 PY in comparators) and hospitalizations \(3.03/1000\) versus 1.94/1000 PY in comparators) were also observed in AS. Overall, RA was associated with a 34% increased risk for MH hospitalization \(HR 1.34, 95\% CI 1.22–1.47\) and AS was associated with a 36% increased risk of hospitalization \(HR 1.36, 95\% CI 1.12–1.63\). The risk of ED presentation was attenuated, but remained significant, after adjustment in both RA \(HR 1.08, 95\% CI 1.01–1.15\) and AS \(HR 1.14, 95\% CI 1.02–1.28\).

Conclusions: RA and AS are both independently associated with a higher rate and risk of acute ED presentations and hospitalizations for mental health conditions. These findings underscore the need for routine evaluation of MH as part of the management of chronic inflammatory arthritis. Additional research is needed to identify the underlying individual characteristics, as well as system-level variation, which may explain these differences, and to help plan interventions to make MH service use more responsive to the needs of individuals living with RA and AS.

Keywords: ankylosing spondylitis, cohort study, health services research, mental health, rheumatoid arthritis

Introduction

Individuals with inflammatory arthritis, including rheumatoid arthritis (RA) and ankylosing spondylitis (AS), frequently experience psychological distress. The adaptation to living with a chronic illness and physical symptoms of pain and fatigue can contribute to unpleasant feelings or emotions. Systemic inflammation may have direct effects on regulating mood and emotion. Negative psychological symptoms may also arise from adverse effects of disease-modifying antirheumatic drugs and corticosteroids that are used to treat RA and AS. It follows that rates of mental illness including depression, anxiety and substance abuse are substantially higher in both RA and AS compared with the general population.
Mental health (MH) conditions are important to recognize and treat because their effects extend beyond just the mental illness itself. Comorbid mental illness is associated with poor arthritis outcomes: higher rates of disability, medication non-adherence, and lower likelihood of achieving and maintaining clinical remission. Therefore, mental illness may be a potentially modifiable determinant of arthritis prognosis and is important to identify and manage.

Similar to the disease course of RA or AS that is often punctuated by acute flares, mental illness symptoms can be episodic or fluctuate and make identification of severe mental illness challenging. However, it is important to differentiate acute and chronic mental illness as they may require different systems and approaches to care. The use of acute medical services may also provide insights into potential gaps in ambulatory rheumatology care. For example, an emergency department (ED) presentation for a mental illness may be the first time an individual is presenting with a MH concern or be an exacerbation of their existing mental illness. In addition, it may indicate inadequate recognition before a “crisis,” stemming from poor access to primary care where most mental illness is diagnosed, treated, and referred for specialty services. An acute hospitalization, that may follow an ED visit, typically reflects the severity of an individual’s mental health status and/or need for urgent therapy. Furthermore, the impact of an acute mental illness added to a physically disabling condition like RA or AS could have multiplicative health effects.

This study aimed to fill this knowledge gap. Our objective was to estimate acute mental health service use following a diagnosis of RA or AS. Understanding the extent of ED visits and hospitalizations as a point of contact for mental health care in RA and AS would be an important first step to help plan services and targeted interventions for these complex inflammatory conditions.

Patients and methods

Study design and data sources

We conducted two retrospective, population-based cohort studies of subjects with each of RA (n = 53,240) or AS (n = 13,964) matched to population comparators between April 1, 2002 and March 31, 2016.

We used the following health administrative databases for the province of Ontario, Canada: (1) The Registered Persons Database identified residents eligible for the universal Ontario Health Insurance Plan (OHIP), and information on date of birth, sex, and postal code (to determine urban versus rural residence) was obtained; (2) The Canadian Institutes of Health Information Discharge Abstract Database was used to identify hospital admissions and the most responsible diagnoses for the acute hospitalization, according to the International Classification of Diseases (ICD) 10th revision diagnosis codes, the Canadian Classification of Procedures, and the Canadian Classification of Health Interventions codes; (3) The Ontario Mental Health Reporting System provided clinical and administrative data on all mental health hospitalizations from 2005 onward; (4) The National Ambulatory Care Reporting System identified all ED visits and; (5) The OHIP Claims History Database identified diagnoses and procedures associated with physician billing claims. All datasets were de-identified and linked using unique encoded identifiers and analyzed at ICES (www.ices.on.ca). The use of data in this project was authorized under section 45 of Ontario’s Personal Health Information Protection Act, which does not require review by a Research Ethics Board.

Study population

Two parallel matched cohorts were created. In the first, we compared individuals with incident RA with a matched, non-RA comparator cohort. In the second, we compared individuals with incident AS with a separate matched non-AS comparator cohort.

All subjects (RA, AS, and comparators) were excluded if they had any mental illness or addiction encounter with a family physician or psychiatrist (by outpatient billing codes ICD-9: 290-315), hospitalization, or ED visit for a mental health diagnosis in the two years prior to RA or AS diagnosis. We identified an inception RA cohort within the Ontario Rheumatoid Arthritis Dataset (ORAD), from April 1, 2002 to March 31, 2014. ORAD is a validated population-based research database of all Ontarians with RA. Patients were excluded if they had missing age or sex, AS diagnosis, or
other systemic autoimmune rheumatic disorder (SARD) in the 2 years before RA diagnosis. The comparison cohort comprised Ontarians without RA, matched 4:1 on age (±365 days), sex, and calendar year. Comparators were randomly assigned an index date of the corresponding RA cases by calendar year and quarter.

For the second matched cohort, we used a published algorithm to identify an incident AS cohort. Patients were excluded if missing age or sex, RA, or any SARD in the 2 years before AS diagnosis. The comparison cohort included Ontarians without AS, matched 4:1 to AS patients on age (±365 days), sex, and calendar year. Index date for comparators was randomly assigned to match AS cases by calendar year and quarter.

Patients were followed from cohort entry date until migration, death, end of study period (31 March 2016), or outcome occurrence, whichever came first.

Acute mental health care outcomes
We had two primary outcomes of interest subsequent to an RA or AS diagnosis: (1) A first ED presentation for mental illness but not requiring admission to hospital or (2) a first hospitalization attributable to mental illness. These were considered independent events and outcomes were identified by validated diagnostic codes, following the approach of the Mental Health and Addictions Scorecard Evaluation Framework research team at ICES. The most responsible mental illness diagnosis from the ED or hospital discharge record was summarized according to psychiatric diagnostic categories (Supplementary Table 1).

Exposure and covariates
Our main exposures of interest were arthritis diagnosis (RA or AS). In addition to age and sex, we ascertained patient residence (urban versus rural), socioeconomic status, and ethnicity (Chinese, South Asian, and Other) with a validated surname algorithm. Baseline comorbidities were determined using a 24-month look back window from time of cohort entry. Validated algorithms were used to identify hypertension, diabetes, inflammatory bowel disease (IBD), coronary artery disease and acute myocardial infarction, cerebrovascular accident, chronic obstructive pulmonary disease (COPD)/asthma, renal failure, cancer, upper gastrointestinal bleed, osteoarthritis, osteoporosis, infection, or psoriasis. We measured overall comorbidity severity using the Charlson Comorbidity Index, which reflects relevant diagnoses during an episode of care as an inpatient. We also examined non-mental health care use (number of outpatient visits, rheumatology visits, hospitalizations, ED visits) in the 2 years prior to index date.

Statistical analysis
We used standardized differences to compare baseline characteristics of individuals with RA, AS, and matched comparators. For each outcome, we calculated overall sex- and age-stratified incidence rates (IR) per 1000 person-years (PY) with four age categories (<20, 21–44, 45–64, 65+ years).

We conducted separate Cox proportional hazards models to estimate hazard ratios (HRs) and 95% confidence intervals (CI) for RA and AS for each outcome of ED visit or hospitalization. Age and sex were a priori selected as clinically important confounders, and were used as matching criteria, so were not further entered into Cox models. We generated unadjusted HRs for the association between RA or AS and each acute mental illness outcome, separately. Then, we constructed univariate models including all baseline variables. The full multivariable models adjusted for previous non-mental health care use regardless of p-value, as well as any variables with p < 0.05 in the univariate models. All analyses were conducted using SAS statistical software (version 9.3; SAS Institute, Cary, NC).

Results
A total of 53,240 individuals with RA (matched to 212,960 unaffected comparators) and 13,964 individuals with AS (matched to 55,856 unaffected comparators) with no previous history of MH care use were included in the analyses (Supplementary Figures 1 and 2). Baseline characteristics of the cohorts are shown in Table 1. The mean age of RA patients was 56.5 years (SD, 17.1) and 67% were female. Patients with AS were younger, with a mean age of 46.4 years (SD, 16.6) and 43% were female. The average duration of follow up in both cohorts was 7 years. Compared with their matched comparators, a greater number of comorbid conditions was observed in both RA patients (osteoarthritis,
Table 1. Baseline characteristics of individuals with RA, AS, or matched unaffected comparators with no prior history of mental illness.

| Variable                   | RA  | Non-RA comparator | Standardized difference | AS  | Non-AS comparator | Standardized difference |
|----------------------------|-----|-------------------|-------------------------|-----|-------------------|-------------------------|
| Age at index date, mean ± SD | 56.5 ± 17.1 | 56.5 ± 17.1       | 0                       | 46.4 ± 16.6 | 46.4 ± 16.6       | 0                       |
| Female sex, n (%)           | 35,702 (67.1) | 142,808 (67.1)   | 0                       | 6064 (43.4) | 24,256 (43.4)   | 0                       |
| Rural residence, n (%)      | 7743 (14.5)  | 25,771 (12.1)    | 0.07                    | 1608 (11.5) | 6216 (11.1)     | 0.01                    |
| Income quintile, n (%)      |     |                   |                         |     |                   |                         |
| 1 (lowest)                 | 9878 (18.6)  | 41,582 (19.5)    | 0.02                    | 2359 (16.9) | 11,275 (20.2)  | 0.08                    |
| 2                          | 10,777 (20.2) | 42,800 (20.1)   | 0                       | 2595 (18.6) | 11,237 (20.1)  | 0.04                    |
| 3                          | 10,930 (20.5) | 41,616 (19.5)   | 0.02                    | 2715 (19.4) | 11,038 (19.8)  | 0.01                    |
| 4                          | 10,907 (20.5) | 42,697 (20.0)   | 0.01                    | 3056 (21.9) | 11,163 (20.0)  | 0.05                    |
| 5                          | 10,748 (20.2) | 44,265 (20.8)   | 0.01                    | 3239 (23.2) | 11,143 (19.9)  | 0.08                    |
| Ethnicity, n (%)           |     |                   |                         |     |                   |                         |
| Chinese                    | 1279 (2.4)   | 12,943 (6.1)     | 0.18                    | 709 (5.1)   | 3.677 (6.6)     | 0.06                    |
| South Asian                | 1980 (3.7)   | 6820 (3.2)       | 0.03                    | 434 (3.1)   | 2070 (3.7)      | 0.03                    |
| Other                      | 49,981 (93.9)| 193,197 (90.7)   | 0.12                    | 12,821 (91.8)| 50,109 (89.7) | 0.07                    |
| Comorbidities, n (%)       |     |                   |                         |     |                   |                         |
| Charlson Comorbidity Index |     |                   |                         |     |                   |                         |
| 0                          | 48,895 (91.8)| 202,214 (95.0)  | 0.13                    | 13,211 (94.6)| 54,237 (97.1) | 0.13                    |
| 1                          | 2131 (4.0)   | 4569 (2.1)       | 0.11                    | 426 (3.1)   | 725 (1.3)       | 0.12                    |
| 2                          | 1260 (2.4)   | 3440 (1.6)       | 0.05                    | 207 (1.5)   | 517 (0.9)       | 0.05                    |
| 3+                         | 954 (1.8)    | 2737 (1.3)       | 0.04                    | 120 (0.9)   | 377 (0.7)       | 0.02                    |
| Osteoarthritis             | 15,200 (28.5)| 11,602 (5.4)    | 0.65                    | 2164 (15.5)| 1658 (3.0)     | 0.44                    |
| Osteoporosis               | 1153 (2.2)   | 3286 (1.5)       | 0.05                    | 237 (1.7)   | 370 (0.7)       | 0.10                    |
| Chronic Obstructive Pulmonary Disease | 6970 (13.1)| 18,334 (8.6)    | 0.14                    | 984 (7.0)   | 2791 (5.0)     | 0.09                    |
| Coronary Artery Disease    | 2807 (5.3)   | 7912 (3.7)       | 0.08                    | 434 (3.1)   | 1190 (2.1)      | 0.06                    |
| Myocardial Infarction      | 502 (0.9)    | 1351 (0.6)       | 0.03                    | 68 (0.5)    | 203 (0.4)       | 0.02                    |
| Cardiovascular Disease     | 114 (0.2)    | 447 (0.2)        | 0                       | 17 (0.1)    | 51 (0.1)        | 0.01                    |
| Hypertension               | 21,674 (40.7)| 70,533 (33.1)   | 0.16                    | 3663 (26.2)| 11,082 (19.8)  | 0.15                    |
| Acute Renal Failure        | 594 (1.1)    | 1170 (0.5)       | 0.06                    | 107 (0.8)   | 195 (0.3)       | 0.06                    |
| Chronic Renal Failure      | 1284 (2.4)   | 2757 (1.3)       | 0.08                    | 224 (1.6)   | 433 (0.8)       | 0.08                    |
| Diabetes Mellitus          | 8161 (15.3)  | 27,304 (12.8)    | 0.07                    | 1473 (10.5)| 4622 (8.3)      | 0.08                    |

Continued
AS, ankylosing spondylitis; RA, rheumatoid arthritis.

COPD, hypertension, IBD, psoriasis) and AS patients (osteoarthritis, osteoporosis, hypertension, infections, IBD, psoriasis). RA and AS patients had greater non-mental health care use, including outpatient physician visits, hospitalizations, and non-mental health related ED visits compared with matched subjects (Table 1).

The overall crude incidence rate of an ED visit for mental illness following RA diagnosis was 6.59/1000 PY compared with 4.39/1000 PY in non-RA comparators. Median time-to-first ED visit was 6.4 years among RA subjects and 7.4 years for comparators. AS subjects also had higher rates of an ED visit (7.92/1000 PY) compared with non-AS comparators (5.62/1000 PY) and this occurred a median of 6.9 years following AS diagnosis and 7.2 years for comparators. The incidence of an ED visit was higher in RA and AS versus comparators in all analyses stratified by age, and sex (Table 2).

In the RA, AS, and comparator groups, risk for an ED visit was higher in men and in subjects less than 20 years of age (data not shown). ED visits were most common for anxiety and adjustment disorders, followed by substance-related disorders, mood, and affective disorders, and lastly due to psychotic disorders (Figure 1a and b).

The incidence rates for a first MH hospitalization were also higher in subjects with RA (3.11/1000 PY versus 1.80/1000 PY in comparators) and AS (3.03/1000 PY versus 1.94/1000 PY) (Table 2). Median time to hospitalization was 6.5 years after RA diagnosis and 7 years after AS diagnosis. Hospitalization was most common in men and younger subjects (Table 2). Mood and affective...
disorders, followed by substance-related disorders, were the most responsible diagnoses leading to an acute hospitalization (Figure 1b and c).

In final multivariable analyses, the risk of an acute ED presentation for mental illness was attenuated but remained statistically significant after adjustment for income, ethnicity, comorbidities, and previous non-mental health care use in both RA (adjusted HR 1.08, 95% CI 1.01–1.15) and AS (adjusted HR 1.14, 95% CI 1.02–1.28, Table 3). RA was also independently associated with a 34% increased risk of acute mental illness hospitalization (multivariate adjusted HR 1.34, 95% CI 1.22–1.47). Similarly, AS was associated with a 36% increased risk of hospitalization compared with non-AS subjects (multivariate adjusted HR 1.36, 95% CI 1.12–1.643, Table 3).

**Discussion**

To the best of the authors’ knowledge, this is the first population-based study to examine acute MH care utilization among individuals with RA or AS. RA and AS were both independently associated with higher rates and risk of emergency department presentations for mental illness. A key finding was a significantly increased risk of acute hospitalization associated with RA and AS, particularly for mood disorders, anxiety, and substance-related disorders. Our findings indicate that emergency service use is a more frequent point of contact with the mental health system for individuals with inflammatory arthritis, compared with those without RA or AS. While this may suggest a higher acuity or severity of mental illness, this may also represent system or individual level barriers in access to outpatient care. While we cannot answer this with our data alone, future work is needed to explore if inequities in outpatient mental health, lower quality, or effectiveness of care when it is accessed are possible contributors to the high rates of emergency mental health care we observed.

The finding that acute mental health care service use differed by age and sex is of interest. Younger age and men with RA or AS had higher rates of ED visits and hospitalizations compared with women. Studies of the general population, and...
those with chronic illness, have identified a similar trend of ED presentations for psychiatric disorders to be more common in adolescent and young adult men, but this has not been verified in
an inflammatory arthritis population to our knowledge.\textsuperscript{28–30} Interestingly, a study specific to general health care use in RA demonstrated that women had higher ambulatory physician use, but ER visits and hospitalizations were more common in men, as our data support.\textsuperscript{31} Our findings suggest that men with RA and AS may be particularly vulnerable to crisis situations prompting emergency care, or it may relate to the acuity and manner of the presentation (e.g. substance-related disorder, overdose), which is best managed in an acute care setting.\textsuperscript{29} Future work might explore whether there are also age and sex differences in receipt of outpatient MH visits, which may account for these imbalances observed in acute care settings.

On average, the first ED visit or hospitalization occurred approximately 7 years following RA or AS diagnosis. While this is limited by the duration of follow-up available in the study, the observed timing of a first acute MH presentation contrasts non-mental health care use that has been reported to be highest in the first year following arthritis diagnosis and declines steadily thereafter.\textsuperscript{31} The reasons for this difference in health care use may be postulated. At the system level, the initial focus after RA or AS diagnosis may be on the “window of opportunity” where early and aggressive disease-modifying anti-rheumatic disease (DMARD) therapy can significantly improve arthritis outcomes. In this setting, mental symptoms, even if severe, may be prioritized as lower than physical concerns of pain and disability.\textsuperscript{7,32} There may also be little or no time devoted to MH screening, either due to lack of training or expertise by the rheumatologist or the belief that other health care providers would better address MH concerns.\textsuperscript{32,33} At the patient level, mental illness may appear clinically very similar to symptoms of RA or AS, and can be misattributed to active arthritis rather than comorbid mental illness.\textsuperscript{32} Importantly, many patients face stigma associated with disclosing feelings of depression, anxiety, or admission of substance misuse or dependency.\textsuperscript{32} These barriers may prevent timely diagnosis and treatment of mental illness that eventually reaches a “crisis” threshold, or there may be inadequacies in how outpatient medical and MH services are integrated.\textsuperscript{34} Multiple system and patient-level barriers are likely responsible for the higher acute mental health care encounters observed in RA and AS, but the implication of our findings is that surveillance for mental illness should be regular and frequent because mental illness sequelae may occur at any point along the disease continuum.

The strengths of our study include the large sample sizes and inclusion of a population with universal health care coverage for emergency and hospital services. This population is reflective of real-world clinical practice and enhances generalizability of our findings to similar health care settings. We also used validated algorithms to reduce misclassification of our exposure and outcome definitions.

Our study was limited by the clinical detail available in health administrative data. Information on RA or AS disease severity could not be ascertained, although inconsistent results have been reported about the association between arthritis disease activity and mental illness symptom severity.\textsuperscript{35,36} We were not able to assess the quality or appropriateness of care received and did not assess repeat admissions. Our findings may be an underestimate of the true rate of mental illness as we restricted our population to those with no prior history of mental illness health care encounters. We did not have information on personality traits or perceived impact of illness that could influence the decision to seek out emergency care. Underestimates of acute mental illness may have occurred if the underlying rheumatic disease was listed as the most responsible diagnosis instead. We did not explore time-varying factors such as mental health diagnoses, new comorbidities, or health care visits in the interval after RA or AS diagnosis that may have influenced emergency care.

Finally, details on disease modifying anti-rheumatic drugs, psychiatric medications, or medications that may be misused (e.g. opioids) were lacking as a minority of patients were over the age of 66 for whom prescription data are universally available. Our findings indicate that substance abuse disorders were the second most common reason for ED visits and hospital admission. We cannot determine whether this was related to an abuse of medications intended for medical use, driven by alcohol, illicit drug use, or a combination of all. Further evaluation is necessary to help inform strategies for diversion of substance abuse in this population.

In conclusion, RA and AS are both associated with an increased acute mental health care utilization. These findings suggest that screening for mental illness should be considered in the management of chronic inflammatory arthritis. Additional research is needed to identify the types
and extent of barriers facing individuals with RA
and AS that may contribute to acute mental ill-
ness presentations. This knowledge can help plan
interventions aimed at prevention but more
importantly, make existing mental health services
more responsive to the needs of our patients.

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The authors declare that there is no conflict of
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