Health care utilisation before and after intensive care unit admission in rheumatoid arthritis

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Abstract

Objective

We evaluated the incidence of intensive care unit (ICU) admission in a rheumatoid arthritis (RA) population according to health care utilisation and use of immune therapies in the year preceding admission. Also, we compared health care utilisation after ICU admission in persons with and without RA.

Methods

We identified all persons with RA in Manitoba, Canada using population-based administrative data, and controls matched by age, sex, and region of residence. ICU admissions were identified using special care unit codes included in hospital discharge abstracts. We estimated the annual incidence rate of ICU admission in the RA population according to health care utilisation using generalised linear models, adjusting for age, sex, comorbidity, region and socioeconomic status. We compared health care utilisation post-ICU admission in persons with and without RA.

Results

From 2000/01 through 2009/10, the average annual incidence of ICU admission was 1.26% in the RA population. Corticosteroid use was associated with an increased incidence of ICU admission (IRR 1.07; 95%CI: 1.05, 1.09). Use of disease-modifying anti-rheumatic drugs and biologics was not associated with an increased incidence of ICU admission. In the year following ICU admission, 45.3% of the RA population was re-hospitalised, and 8.9% were readmitted to the ICU.

Conclusion

Persons with RA who are admitted to the ICU have higher rates of health care utilisation in the year before ICU admission than those who are not admitted. Corticosteroid use is associated with an increased risk of ICU admission even after accounting for other health care utilisation.

Key words

rheumatoid arthritis, critical illness, administrative data, hospitalisations, disease-modifying anti-rheumatic drugs

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Introduction

Rheumatoid arthritis (RA) is a chronic immune-mediated arthropathy that affects 0.5–1.0% of Canadians (1) Inflammation of multiple small and large joints leads to permanent joint damage, and disability rates reach 50% after several years of disease (2-4). Health care utilisation by persons with RA is high (5, 6), and increases with greater pain and disability-accumulated comorbidities (7, 8). As compared to the general population, the RA population also has an increased incidence of critical illness, as measured by intensive care unit (ICU) admission, even after accounting for age, sex, socioeconomic status and burden of comorbidity (9). Mortality after ICU admission is 40% higher in RA than among persons without RA (9).

Since ICU care is costly, and persons with RA are at increased risk for ICU admission, and at increased risk of death after ICU admission, it is important to understand what characteristics of persons with RA and their treatments are associated with the risk of critical illness. The role of treatment is of particular interest because of the increasingly early use of combination immune therapies and biologic immunomodulators (10, 11), all of which increase risks of infection (12, 13). However, relatively little is known about the effects of such therapies on the risk of ICU admission in RA, as most prior studies of critical illness have lumped various rheumatic diseases together despite differences in their clinical characteristics and management (14). Further, little is known about the consequences of critical illness, such as subsequent health resource use, other than mortality. These issues are relevant to clinicians aiming to prevent critical illness and to mitigate the effects of critical illness after it occurs, and to policymakers assessing health service needs.

We evaluated the incidence of ICU admission in the RA population according to the burden of chronic disease, as measured by health care utilisation and use of immune therapies in the year preceding admission. We hypothesised that among persons with RA, the risk of ICU admission would increase with increasing health care utilisation in the year preceding admission, and that persons using immune therapies would be at particularly high risk of ICU admission. Also, we compared health care utilisation after ICU admission among persons with and without RA.

Materials and methods

Data source

This study was conducted in the central Canadian province of Manitoba, using population-based administrative data located in the Population Health Research Data Repository at the Manitoba Centre for Health Policy. Universal health care services are provided to the region's approximately 1.2 million residents (15) by Manitoba Health, the provincial health authority, which maintains electronic records of health services claims including a unique personal health identification number. We accessed anonymised hospital, physician and prescription claims data and the population registry for the period from April 1, 1984 to March 31, 2010. Hospital claims include dates of admission and discharge and diagnostic codes recorded using International Classification of Disease (ICD)-9 or 10 codes, depending on the year. Physician claims include the date of service and ICD-9-CM code for one physician-assigned diagnosis. Prescription claims are captured through the Drug Program Information Network and include all outpatient prescription drug dispensations including the date, drug name, and drug identification number. The population registry captures sex, dates of birth, death and health care coverage.

Study population

We identified Manitobans with RA using a previously validated administrative case definition (9). Specifically, Manitobans who resided in the province for ≥2 years were identified as having RA if they had ≥5 physician visits or hospitalisations with ICD-9-CM/ICD-10 codes 714/M05, M06 recorded. Persons resident for <2 years were identified as having RA if they had ≥3 such claims. Our prevalent cohorts included all cases of RA identified using this definition; in the period 1984

to 2010, we identified 10078 prevalent cases of RA. Our incident cohort required a five-year run-in period with no RA-related claims before the first health claim for RA, thus the first year in which we could identify an incident case was 1989. The first claim was used as the date of diagnosis (index date).

After we identified the RA cohorts, we identified a cohort from the general population, matched on sex, birth year, and region of residence based on 6 digit postal code (or the first 3 digits if a full match was not possible). We excluded individuals with any claims for RA from this cohort. We also excluded persons with multiple sclerosis or inflammatory bowel disease claims as this analysis was conducted as part of a larger study. We identified up to five controls for each case, and controls were assigned the same index date as their matched cases.

Intensive care unit admission

We identified ICU admissions using hospital discharge abstracts, as described elsewhere (16). Briefly, these abstracts contain codes that identify admissions to special care units such as ICUs, and these codes are highly sensitive and specific for identifying ICU admissions (16). Then we estimated the annual incidence of ICU admission for fiscal years 2000/01 to 2009/10 in the prevalent RA and matched populations. We chose these years as they represent the modern period of ICU care, and for consistency with prior work (17). We age- and sex-standardised the results to the 2007 Canadian population, to aid comparisons to other studies.

Prior health care utilisation

For subsequent analyses, we focused on persons with RA who were admitted to the ICU so that we could explore the relationship of prior health care utilisation to ICU admission. First, we compared health care utilisation in the year before ICU admission to that for persons with RA who were not admitted to the ICU using chi-square tests, student's *t*-tests and Wilcoxon tests as appropriate. For persons who were not admitted to the ICU we randomly assigned a pseudo-ICU date corresponding to the date of an actual ICU admission in the RA population. The health care utilisation variables considered were hospitalisations (any *vs*. none), number of physician visits (tertiles), total cost of prescription drugs (in 2011 Canadian dollars) excluding immunomodulatory and immunosuppressive therapy (quartiles). We also considered any use of disease-modifying anti-rheumatic drugs (DMARD), any use of biologics, and cumulative corticosteroid use in prednisone equivalents (18) in the year before ICU admission (Suppl. Table I). We compared health care utilisation between the groups using chi-square tests, Fisher's exact tests, *t*-tests and Wilcoxon tests as appropriate.

Second, we estimated the annual incidence rate of ICU admission in the entire RA population according to the amount of health care utilisation using a series of generalised linear models (19). These models used generalised estimating equations with an exchangeable correlation to account for repeated ICU admissions by individuals. The duration of Manitoba Health coverage was included as an offset. Independent variables of interest were the measures of health care utilisation described above. The first model included measures of hospitalisation, physician visits and prescription costs, for comparability to prior work in other immune-mediated inflammatory diseases (19, 20).

The second model added joint surgery, and added use of DMARD, biologics, and cumulative corticosteroid use in the year before ICU admission. As administrative data do not capture clinical measures of disease severity, a potentially important confounder, we identified joint-related surgical procedures (Suppl. Table II) as a measure of disease severity, and included these as two variables: (i) surgery in year before ICU admission, or (ii) surgery more than one year before ICU admission. For models that included joint surgery we excluded joint-related surgeries from the hospitalisations variable (to avoid double counting those admissions).

The final model evaluated the association of immune therapies with ICU admission in more depth. Because the immune therapies for RA may be used in combination, and we wished to understand if they conferred a differential risk of ICU admission, we aimed to create indicator variables to represent the following mutually exclusive treatment groups: corticosteroids only, DMARD (one or more) only, DMARD and corticosteroids, biologics only, biologics and corticosteroids, biologics with DMARD, biologics and DMARD and corticosteroids, none (reference group). Because the number of individuals receiving biologics only or biologics and DMARD were small, these groups were collapsed. Total prescription costs were removed as the quartiles of costs were too closely related to the immunotherapies used.

Covariates for all models were age (continuous), sex, region of residence (urban *vs*. rural), comorbidity and socioeconomic status. Comorbidity status was classified a modified version of the Charlson Comorbidity Index (CCI) (21). Briefly, we collapsed the categories of diabetes with and without chronic complications, because this distinction was inaccurate in Manitoba before 2006 (22), and the HIV/AIDS category was not included due to small numbers; this created a Charlson score that was no longer an integer. Socioeconomic status (SES) was divided into quintiles based on average household income in the postal code of residence by linkage to census data; a sixth category included those residing in locations where household incomes are not calculated, mainly institutions such as nursing homes and prisons (23). We categorised region of residence as urban (population ≥50,000) or rural.

Subsequent health care utilisation

Among survivors of ICU admission we assessed subsequent health care utilisation. For comparison with our prior work regarding mortality after ICU admission, these analyses used an incident RA cohort compared to a cohort of matched controls who were admitted to the ICU for the first time. We used health care utilisation measures in the year after ICU admission that focused on the frequency and intensity of use including: (i) proportion with any hospitalisations; (ii) proportion with any

ICU-containing hospitalisations; (iii) number of hospital days; (iv) number of outpatient physician visits; and (v) total costs of prescription drugs using 2011 Canadian dollars. We compared health care utilisation post-ICU admission for the RA population and the matched population using chi-square tests, Fisher's exact tests, *t*-tests and Wilcoxon tests as appropriate. For each health care utilisation measure we also age- and sex-standardised the results to the 2007 Canadian population to facilitate comparisons to other studies.

For multivariable analysis we created general linear models where the independent variable of interest was population (RA *vs*. general population matches). We included an offset which was the fraction of the year following incident ICU care that the patient survived and was resident in Manitoba to adjust for differing follow-up time between individuals. Covariates were age, sex, SES, region of residence, comorbidity, and health care utilisation in the year before ICU admission (any prior hospitalisation, number of physician visits). The model was logistic for binary outcomes (proportion hospitalised), and zero-inflated negative binomial for the number of hospital days, and Poisson for the number of physician visits.

The University of Manitoba Health Research Ethics Board (H2010:200) and the Manitoba Health Information Privacy Committee approved the study. Statistical analyses were conducted using SAS v.9.3 (SAS Institute Inc., Cary NC).

Results

Characteristics associated with ICU admission

During the period 2000–2010, 7797 prevalent cases of RA were identified. Compared to the matched cohort, RA cases were more frequently in the lowest income quintiles and had higher CCI scores; their characteristics and those of the matched population are shown in Table I. From 2000/01 through 2009/10, the average annual incidence of ICU admission was 1.26% in the RA population and 0.70% in the matched population (RR 1.79; 95% CI: 1.64–1.95) (9). Of 7797 prevalent RA cases, 620 (7.9%) were admitted to the ICU. As

Table I. Demographic characteristics of prevalent RA cases and matched controls.

Characteristic	Matches (n=33084)	RA (n=7797)	*p*-value
Female, n (%)	23847 (72.1)	5722 (73.4)	0.025
Age at first year included in prevalent cohort, mean (SD)	56.5 (19.3)	56.7 (18.5)	0.6959
Urban region of residence, n (%)	18903 (57.1)	4486 (57.5)	0.56
Socioeconomic status, n (%)			
Quintile 1 (lowest)	7157 (21.6)	1804 (23.1)	0.034
Quintile 2	7218 (21.1)	1656 (21.2)	
Quintile 3	6626 (21.8)	1548 (19.8)	
Quintile 4	6325 (19.1)	1403 (18.0)	
Quintile 5 (highest)	5131 (15.5)	1181 (15.1)	
Not calculated*	866 (2.6)	205 (2.6)	
Modified Charlson Index, n (%)			
0	28875 (87.3)	5827 (74.7)	<0.0001
0.01-1.9	1823 (5.5)	1057 (13.5)	
≥2	2386 (7.2)	913 (11.7)	

*Could not be calculated for some individuals who lack a postal code, such as those living in personal care homes.

Table II. Characteristics of the rheumatoid arthritis (RA) population who were and were not admitted to the intensive care unit (ICU).

Characteristic	RA – ICU (n=620)	RA – non ICU (n=7177)	*p*-value
Female, n (%)	396 (63.9)	5326 (74.2)	<0.0001
Age at diagnosis, mean (SD)	56.4 (13.9)	52.3 (16.8)	<0.0001
Age at ICU admission, mean (SD)	67.9 (12.8)	-	
Duration of follow-up,* mean (SD)	14.3 (6.9)	12.0 (7.7)	0.32
Urban region of residence, n (%)	405 (65.3)	4081 (56.9)	<0.0001
Socioeconomic status, n (%)			
Quintile 1 (lowest)	175 (28.2)	1629 (22.7)	0.0029
Quintile 2	133 (21.4)	1523 (21.2)	
Quintile 3	121 (19.5)	1427 (19.9)	
Quintile 4	93 (15.0)	1310 (18.2)	
Quintile 5 (highest)	92 (14.8)	1089 (15.2)	
Not calculated¥	6 (0.97)	199 (2.8)	
Modified Charlson Index, n (%)			
0	298 (48.1)	5529 (77.0)	<0.0001
0.01-1.9	164 (26.4)	893 (12.4)	
≥2	158 (25.5)	755 (10.5)	
Health care utilisation			
Any acute care hospitalisation in year before ICU admission, n (%)	236 (38.1)	893 (12.4)	<0.0001
No. physician visits (median, p25, p75)	19 (11-29)	9 (4-16)	<0.0001
Tertiles of physician visits (as coded for models), n (%)			
Tertile1	29 (1.7)	1684 (23.5)	<0.0001
Tertile2	82 (13.2)	1986 (27.7)	
Tertile3	509 (82.1)	3507 (48.9)	
Prescription costs,[1] median, p25, p75	1669.7 (900.8, 2877.0)	501.9 (67.7, 1342.2)	<0.0001
Any DMARD use in year before ICU admission, n (%)	295 (47.6)	2383 (33.2)	<0.0001
Any Biologic use in year before ICU admission, n (%)	37 (6.0)	225 (3.1)	0.0002
Cumulative prednisone dose equivalents, (median, p25, p75)	1110.1 (2441.0)	298.5 (992.1)	<0.0001

*Refers to duration of follow-up from index date (date of diagnosis) to the end of the study not to the date of ICU admission; ¥Could not be calculated for some individuals who lack a postal code, such as those living in personal care homes; [1]Total prescription costs minus the costs of disease-specific immune therapies.

Table III. Multivariable analysis of the incidence of intensive care unit admission in the RA population.

Variable	IRR	95% CI
Health care utilisation in the prior year		
Any acute care hospitalisation	1.70	1.42, 2.03
Number of physician visits		
Tertile1	1.00	
Tertile2	1.46	1.12, 1.91
Tertile3	2.41	1.84, 3.15
Prescription costs*		
Quartile1	1.00	
Quartile2	0.96	0.54, 1.72
Quartile3	1.45	0.83, 2.53
Quartile4	2.07	1.19, 3.60
Covariates		
Sex		
Females	1.00	
Male	1.78	1.52, 2.08
Age	1.11	1.05, 1.17
Modified Charlson Index		
0	1.00	
0.01-1.9	1.58	1.28, 1.95
≥2	1.86	1.50, 2.31
Socioeconomic status		
Not calculated	0.79	0.50, 1.24
Quintile1 (lowest)	1.04	0.82, 1.32
Quintile2	0.88	0.68, 1.14
Quintile3	0.92	0.72, 1.19
Quintile4	0.71	0.54, 0.95
Quintile5 (highest)	1.00	
Region		
Rural	1.00	
Urban	1.59	1.35, 1.87

IRR: incidence rate ratio.
*Total prescription costs.

Table IV. Multivariable analysis of the incidence of intensive care unit admission in the RA population.

Variable	IRR	95% CI
Health care utilisation in the prior year		
Any acute care hospitalisation	1.83	1.53, 2.19
Number of physician visits		
Tertile1	1.00	
Tertile2	1.44	1.11, 1.89
Tertile3	2.30	1.76, 3.02
Prescription costs		
Quartile1	1.00	
Quartile2	0.93	0.52, 1.67
Quartile3	1.29	0.79, 2.44
Quartile4	1.92	1.10, 3.35
DMARD	1.04	0.89, 1.22
Biologic	1.06	0.77, 1.45
Corticosteroids/1000 mg	1.07	1.05, 1.09
Covariates		
Sex		
Females	1.00	
Male	1.77	1.51, 2.07
Age	1.11	1.05, 1.17
Modified Charlson Index		
0	1.00	
0.01-1.9	1.49	1.20, 1.85
≥2	1.72	1.38, 2.14
Socioeconomic status		
Not calculated	0.78	0.49, 1.24
Quintile1 (lowest)	1.05	0.83, 1.33
Quintile2	1.05	0.69, 1.15
Quintile3	0.93	0.73, 1.20
Quintile4	0.92	0.54, 0.95
Quintile5 (highest)	1.00	
Region		
Rural	1.00	
Urban	1.59	1.35, 1.87
Surgery		
Last year	0.76	0.54, 1.09
More than a year ago	1.29	1.07, 1.54

IRR: incidence rate ratio, DMARD: disease-modifying anti-rheumatic drug.

Table V. Multivariable analysis of the incidence of intensive care unit admission in the RA population.

Variable	IRR	95% CI
Health care utilisation in the prior year		
Any acute care hospitalisation	1.82	1.52, 2.19
Number of physician visits		
Tertile1	1.00	
Tertile2	1.57	1.20, 2.05
Tertile3	2.66	2.03, 3.50
Treatment		
None	1.00	
Corticosteroids only	1.63	1.29, 2.04
DMARD only	1.02	0.81, 1.27
DMARD and corticosteroids	1.63	1.31, 2.02
Biologics and corticosteroids	1.28	0.77, 1.45
Biologics with/without DMARD	1.20	0.89, 1.22
Biologics and DMARD and corticosteroids	1.99	1.05, 1.09
Covariates		
Sex		
Females	1.00	
Male	1.76	1.50, 2.06
Age	1.13	1.07, 1.19
Modified Charlson Index		
0	1.00	
0.01-1.9	1.58	1.27, 1.96
≥2	1.90	1.53, 2.36
Socioeconomic status		
Not calculated	0.81	0.51, 1.28
Quintile1 (lowest)	1.06	0.84, 1.34
Quintile2	1.06	0.69, 1.16
Quintile3	0.90	0.72, 1.19
Quintile4	0.92	0.53, 1.16
Quintile5 (highest)	1.00	
Region		
Rural	1.00	
Urban	1.57	1.34, 1.86
Surgery		
Last year	0.77	0.54, 1.10
More than a year ago	1.32	1.10, 1.58

IRR: incidence rate ratio.

compared to persons with RA who were not admitted to the ICU, those admitted to the ICU were more likely to be men, of lower SES, with a greater burden of comorbidity (Table II). Prior health care utilisation also differed between groups. Persons with RA who were admitted to the ICU were three times more likely to have been hospitalised in the prior year, had twice as many physician visits, and had higher prescription costs. They were more likely to have used DMARDs or biologics, and had been exposed to higher mean doses of corticosteroids.

On multivariable analysis, hospitalisations, number of physician visits, prescription costs (excluding those for immune therapies) remained independently associated with the risk of ICU admission even after accounting for age, sex, socioeconomic status and comorbidity (Table III). Subsequently, we included a history of surgery in the model, and substituted use of specific classes of therapies for RA instead of prescription drug costs. Remote surgery was associated with an increased incidence of ICU admission (IRR 1.29; 95%CI: 1.07, 1.54), as was the use of corticosteroids (IRR 1.07/1000 mg of corticosteroids; 95%CI: 1.05, 1.09). The use of DMARDs and biologics were not associated with an increased incidence of ICU admission (Table IV).

In the more complex model that assessed the association of combinations of immune therapies and ICU incidence, use of corticosteroids alone or in any combination conferred an increased risk of ICU admission except in combination with biologics. Specifically the increased risks of ICU admission were: use of corticosteroids alone (IRR 1.63; 95%CI: 1.29, 2.04), use of DMARD in combination with corticosteroids (IRR 1.63; 95%CI: 1.31, 2.02), and use of biologics in combination with DMARD and corticosteroids (IRR 1.99; 95%CI: 1.05, 1.09; Table V). In contrast, use

Table VI. Health care utilisation in the year after ICU admission in the RA population *versus* the matched general population.

Outcome	GP Crude Rate (SD)	Std Rate (95% CI)	RA Crude Rate (SD)	Std Rate (95% CI)	Rate Ratio (95% CI)
Any ICU hospitalisations	102 (8.7)	5.5 (4.2, 6.8)	37 (8.9)	5.8 (3.5, 8.0)	1.06 (0.61, 1.77)
Any hospitalisations after ICU	497 (42.6)	32.5 (29.8, 35.1)	197 (47.4)	45.3 (40.5, 50.0)	1.39 (0.85, 2.10)
No. hospital days after ICU	11.5 (28.4)	7.3 (7.2, 7.4)	15.9 (38.7)	12.3 (12.0, 12.6)	1.68 (1.16, 2.37)
No. physician visits	25.9 (23.3)	22.2 (21.9, 22.4)	31.1 (28.1)	33.2 (32.6, 33.8)	1.50 (1.21, 1.75)
No. specialist physician visits	4.76 (0.06)	4.26 (4.14, 4.38)	6.07 (0.12)	7.19 (6.90, 7.48)	1.69 (1.07, 2.38)
Prescription drug costs[a], mean (SD)	1913.3 (2425.2)	2593.0 (2589.2, 2596.8)	3275.7 (5526.5)	3143.7 (3137.7, 3149.6)	1.21 (0.57, 2.53)

GP: matched general population; RA: rheumatoid arthritis; Crude rate: Number of utilisations per person-year; SD: standard deviation; Std rate: direct age and sex-standardised rate per 100 persons; Excluding immunomodulatory and immunosuppressive therapy.

of DMARD alone did not confer an increased risk (IRR 1.02; 95%CI: 0.81, 1.27), nor did use of biologics with or without DMARD (IRR 1.20; 95%CI: 0.89, 1.22), or use of biologics in combination with corticosteroids (IRR 1.28; 95%CI: 0.77, 1.45).

Health care utilisation after ICU admission

We identified 5560 incident cases of RA, of whom 507 (9.1%) were admitted to the ICU (9). Of these, 416 survived their admission, a similar survival rate to those without RA. Of 1477 members of the matched population admitted to the ICU, 1168 survived their admission. Individuals with RA who were admitted to the ICU were younger at the time of ICU admission, and had a higher burden of comorbidity than those without RA, but had a relatively short mean (SD) disease duration of 5.81 (4.7) years (Suppl. Table III). Hospitalisations and physicians visits were also more frequent in the RA cohort compared to controls in the year before ICU admission.

In the year following ICU admission, nearly half of the RA population was re-hospitalised, and 8.9% were readmitted to the ICU. However, this did not differ from persons without RA who survived ICU admission (Table VI). After age and sex-standardisation, the number of physician visits after ICU admission was higher in the RA population. This was true for any physician visits which were 50% higher in the RA population, and for visits to specialists specifically, which were 69% higher. The RA population averaged 2.72 visits/month for physician-coded diagnoses of RA. On multivariable analysis, the RA population did not have higher health care utilisation post-ICU admission than the non-RA population with respect to hospitalisations or physician visits (Suppl. Table IV).

Discussion

Although the rates of hospitalisation appear to be declining in the RA population over time in both Canada and the United States (24, 25), health care utilisation and costs remain higher in the RA population than in the general population (26, 27). Intensive care unit admissions are a particularly serious and costly form of health care utilisation which has an increased incidence in the RA population (9). In this large, population-based study, we found that older age, male sex, living in an urban centre, and greater comorbidity were also associated with an increased incidence of ICU admission among persons with RA. These findings are consistent with the known associations of age, comorbidity, disability and socioeconomic status with increased health services use and cost in RA (7, 28). Even after accounting for these factors, and prior surgery as a proxy for disability, the incidence of ICU admission was associated with higher medical resource use in the prior one year, specifically, hospitalisation, physician visits, and outpatient prescription costs. These findings were consistent with our hypotheses. Of greatest clinical relevance was the observation that the use of corticosteroids but not biologics was particularly associated with an increased risk of ICU admission. This finding persisted even after we accounted for sociodemographic factors, and multiple measures of medical resource use.

The care of RA has changed substantially over time with increasing, and earlier use of immunologic therapies. The use of these therapies is aimed at improving disease control in those with active disease, and may delay or reduce the need for hospitalisations and joint surgeries (29, 30). However, these therapies are also associated with increased risks of serious infections. Notably, infection was the second most common reason for ICU admission in our earlier study, leading to 19.8% of admissions (9). In the present study, the use of corticosteroids was associated with an increased incidence of ICU admission after adjusting for prior surgery, as well as the use of DMARD and biologics (Table IV). When we explicitly evaluated the effects of combination immunotherapy, only the combinations that included corticosteroids were associated with an increased incidence of ICU admission. Our data echo findings from multiple other studies showing that corticosteroids increase the risk of infection in RA (31-35). Each of these large studies showed corticosteroids to be a more important risk factor for infections than DMARDs or biologics alone. This included a recent study of 838 biologic naïve individuals with RA treated with infliximab found that concomitant use of corticosteroids, regardless of dose, was associated with an increased risk of infection, but was not associated with sustainability of remission (36). In a prior observational study of individuals with other systemic autoimmune diseases, including systemic lupus erythematosus and

systemic vasculitis, an increase in the dose of corticosteroid therapy during ICU admission was associated with a substantially increased risk of poor long-term survival (HR 22.9; 95%CI: 4.31-121.3) (37). Collectively, these findings suggest that substantial efforts should be made to avoid the chronic use of corticosteroids in RA. Caution may also be warranted with their use during ICU admission but this requires further evaluation.

The RA population had a high rate of health care utilisation in the year following ICU admission, although utilisation was similar to that observed in the matched population, after adjusting for age, sex, socioeconomic status and comorbidity. Nearly 50% of the RA cohort required re-hospitalisation, and the mean number of physician visits was more than 2 per month. We were unable to identify comparable studies that assessed health care utilisation after ICU admission. One American study of 496 persons with RA and 33,815 persons with osteoarthritis reported following total hip or total knee arthroplasty, persons with RA are more likely to be readmitted than persons with OA (38). However, this effect was observed only in the last year of the three-year study period. For clinicians our findings indicate that individuals with RA who have been admitted to the ICU have high health care needs, and that close attention may be warranted thereafter.

Study limitations should be considered. Due to the small number of individuals taking biologics we could not evaluate the effects of sole use of these agents on the risk of ICU admission. Administrative data lack clinical information regarding disease severity and phenotype. We used joint surgery to partially capture disease severity, but other relevant clinical features were not available. However, as expected, the RA population requiring ICU admission had several indicators of more severe disease overall, including more overall medication use, greater comorbidity, and older age and longer follow-up duration, suggesting longer disease duration. Thus, it may be that the finding of corticosteroids as an added risk for infection, in part reflects disease severity in this group. Conversely, the effect of corticosteroids may be underestimated, since corticosteroids prescribed during hospitalisations, or administered at clinic visits, are not included in the analysis.

Persons with RA are more likely to be admitted to an ICU than their age, sex and geographically matched counterparts from the general population. Persons with RA who are admitted to the ICU have higher rates of health care utilisation in the year before ICU admission than those who are not admitted. The use of corticosteroids but not synthetic or biologic DMARDs, are associated with an increased risk of ICU admission even after accounting for other predisposing factors for health care utilisation. This reinforces other reports of the risk of corticosteroids in RA, and should inform patient-physician risk-benefit discussions, as well as funding of biologic therapies. Our findings also provide some reassurance regarding the safety of biologic therapies. Although the use of health care resources after ICU admission is not higher in persons with RA than in other persons without RA who survive an ICU admission, health care needs are high, warranting attention from clinicians.

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