

Supplementary materials

Table S1: Data sources included in the study	
Swedish Rheumatology Quality Register (SRQ)	A nationwide longitudinal clinically integrated register operated by The Swedish Society for Rheumatology, started in 1996. Patients with RA and other rheumatologic diseases are registered in the SRQ by the treating rheumatologist. SRQ contains information about disease activity and additional information such as treatment and smoking status. SRQ covers 95% of all patients with RA treated with b/tsDMARD s in Sweden.
Swedish Patient Register (NPR)	A national register maintained by The National Board of Health and Welfare. Hospital discharges from inpatient care and patients visits in non-primary outpatient care, have been registered, since 1964 and 2001 respectively. Diagnoses are coded according to the Swedish version of the International Classification of Disease (ICD). The coverage of the inpatient part is close to 100%, for the outpatient part, the overall coverage is around 80% (higher for public than for private care-providers).
Prescribed Drug Register (PDR)	A national register maintained by The National Board of Health and Welfare. It contains information about all drugs dispensed on prescription in Sweden and is linked to the personal identification number since 2005. The coverage is close to 100%.
Swedish Population Register	A national register maintained by Swedish Tax agency. Contains information such as home district, civil status and migration data.
Longitudinal database for insurance and labor market-studies (LISA)	A national register maintained by Statistics Sweden. It contains information about sick leave, parental leave and employment status in Sweden from 1990.
Cause of Death Register	The Cause of Death Register is a national register containing information on date and cause of death (underlying and contributory) for all deceased residents, including deaths among Swedish residents who died abroad. The register was started in 1952, and the data is considered complete since 1961. From that year and onward, cause of death is missing for less than 0.5% of deceased individuals, and in 2002, a validation study estimated that only 3.3% had any errors at the three-digit level of the ICD-coded underlying cause of death

Table S2: International Classification of Disease version 10 (ICD10) and Anatomical Therapeutic Chemical (ATC) codes used to define cohorts			
Inflammatory joint disease cohort definitions		DMARD treatment cohort definitions*	
Disease	ICD10 code	DMARD	ATC code
Rheumatoid arthritis	M05, M06	csDMARD	L04AX01, A07EC01, L04AD01, P01BA01, M01CB01, L04AA06, L04AX03, L01AA01, P01BA02, J01AA08, L04AA13, M01CC01
Psoriatic arthritis	M070, M071, M073, L405	TNFi	L04AB04, L04AB05, L04AB01, L04AB06, L04AB02
Ankylosing spondylitis	M45	Abatacept	L04AA24
Other spondyloarthropathies	M460, M461, M468, M469	Tocilizumab	L04AC07
Juvenile idiopathic arthritis	M08, M09	Rituximab	L01XC02
		JAKi	L04AA29, L04AA37, L04AA44

*As recorded in the Prescribed Drug Register

Table S3: Description of variables included in analyses	
Variable	Description
Comorbidity	
History of cancer	History of cancer recorded within 5 years prior to cohort entry. Data retrieved from the Cancer Register. Indicator variable (Y/N). Note that information on cancer diagnoses recorded in the Swedish Cancer Register was only available until December 31 st 2018.
History of diabetes	History of diabetes recorded in the 10 years recorded prior to cohort entry. Defined as a record in the National Patient Register (inpatient and outpatient components, ICD10: E10-E11) or dispensation of treatment (ATC: A10) in the Prescribed Drug Register. Indicator variable (Y/N).
History of heart failure	History of heart failure recorded in the 5 years recorded prior to cohort entry. Defined as record in National Patient Register (inpatient component, ICD10: I50). Indicator variable (Y/N).
History of ischemic heart disease	History of ischemic heart disease recorded in the 5 years recorded prior to cohort entry. Defined as record in National Patient Register (inpatient component, ICD10: I20-I25). Indicator variable (Y/N).
History of hospitalised infections	History of infections recorded in the 2 years prior to cohort entry. Defined as recorded in National Patient Register (inpatient component, ICD10: A00-B99, D73.3, E06.0, E32.1, G00-G02, G04.2, G05-G07, H00.0, H44.0, H60.0-H60.3, H66-H67, H70, I30.1, I40.0, J00-J22, J32, J34.0, J36, J38.3, J39.0-J39.1, J44.0, J85, J86, K04.4, K04.6, K04.7, K10.2, K11.3, K12.2, K14.0, K57.0, K57.2, K57.4, K57.8, K61, K63.0, K65.0, K65.1, K65.2, K65.9, L00-L08, L30.3, M00-M01, M46.2-M46.5, M60.0, M65.0, M71.0, M71.1, M72.6, M86, N10, N11, N12, N13.6, N15.1, N15.9, N30.0 N30.8, N34.0, N41.2, N43.1, N45.2, N45.3, N45.4, N48.2, N61, N70, N73, N75.1). Indicator variable (Y/N).
History of lung disease	History of lung disease other than infectious pneumonia recorded in the 5 years recorded prior to cohort entry. Defined as record in National Patient Register (inpatient and outpatient components, ICD10: J40-J94). Indicator variable (Y/N).
History of kidney failure	History of kidney failure recorded in the 5 years recorded prior to cohort entry. Defined as record in National Patient Register (inpatient and outpatient components, ICD10:N17-N19). Indicator variable (Y/N).
History of stroke	History of stroke recorded in the 5 years recorded prior to cohort entry. Defined as record in National Patient Register (inpatient and outpatient components, ICD10:I50-I69). Indicator variable (Y/N).
History of joint surgery	History of joint surgery recorded in the 10 years prior to cohort entry. Defined as record in National Patient Register (inpatient and outpatient components, operational codes: NGB, NFB, NBB, NHB, NHC, NHE, NHF, NHG, 8423, 8424, 8426, 8419, 8437, 8436, 8420, 8421, 8422, 8400-8415). Indicator variable (Y/N).
History of venous thrombotic event	History of VTE recorded in the 5 years recorded prior to cohort entry. Defined as record in National Patient Register (inpatient component, ICD10:I82, I26). Indicator variable (Y/N).
Influenza hospitalisation in the previous year	Hospitalisation in the year prior to cohort entry recording influenza (main and secondary diagnoses, ICD10 codes J09, J10, J11) in the inpatient component of the National Patient Register. Indicator variable (Y/N).
Health-care resource utilisation	
Hospital days in the previous year	The number of days spent in hospital during the 365 days prior to cohort entry. Data obtained from the inpatient component of the National Patient Register.

	Categorised into 0, 1-3, and 4+ days.
Hospital days in the previous 10 years	The number of days spent in hospital during the period 10 years to 365 days prior to cohort entry. Data obtained from the inpatient component of the National Patient Register. Categorised into 0, 1-6, and 7+ days.
Socioeconomics	
Education	Highest education achieved as recorded in the year prior to cohort entry. Data obtained from the Longitudinal integrated database for health insurance and labour market studies (LISA). Note that education information was only available to 2018 in LISA so the value in 2018 was assumed for any subsequent years. Categorised into: 1= <9 years 2=9-12years 3=12years+
Civil status	Civil status recorded in the year prior to cohort entry. Data obtained from LISA, Note that civil status information was only available to 2017 in LISA so the value in 2017 was assumed for any subsequent years. Categorised into married/partner, or single.
Country of birth	Country of birth obtained from the Total Population Register categorised as Sweden, rest of Europe, and rest of world.
Disease-related	
DAS28	DAS28 value (ESR) from most recent rheumatology visit recorded in the SRQ within one year prior to start of follow-up. Categorised into remission (<2.6), low (2.6-3.1), moderate (3.2- 5.1), high (5.2+), and missing.
Disease duration	Disease duration in years, taken as the difference between the diagnosis date (defined using the disease selection definition and data in the National Patient register) and entry to cohort. Categorised as <2, 2-4, 5-9, 10+ years.
Treatment-related	
Number of previous b/tsDMARDs	Number of previous b/tsDMARDs prior to the treatment that caused entry to cohort. Identified by combining the PDR and SRQ. Categorised as 0, 1-2, 3+.
b/tsDMARD recorded in the previous 180 days	Identifies if a different b/tsDMARD was recorded in the previous 180 days prior to start. Indicator variable (Y/N).
Concomitant steroid use	Dispensation of steroids (ATC: H02AB06) recorded in the Prescribed Drug Register in the 90 days prior to cohort entry.

Table S4: Descriptive statistics for patients with inflammatory joint diseases and matched population comparators during influenza seasons 2015/2016 to 2018/2019 in Sweden

	Influenza season 2015-2016		Influenza season 2016-2017		Influenza season 2017-2018		Influenza season 2018-2019	
	IJD	General population	IJD	General population	IJD	General population	IJD	General population
Individuals	99 175	443 776	102 811	459 031	106 360	474 101	109 465	485 987
RA patients (%)	50 652 (51)	-	51 750 (50)	-	52 780 (49)	-	53 704 (49)	-
Age, median years (IQR)	61 (48-71)	59 (46-69)	61 (48-72)	59 (46-70)	61 (48-72)	59 (47-70)	62 (48-72)	60 (47-70)
Female, %	62%	62%	62%	62%	62%	61%	61%	61%
Disease duration, median years (IQR)	7.8 (3.9-12.3)	-	8.4 (4.1-13.0)	-	8.8 (4.4-13.7)	-	9.3 (4.7-14.5)	-
Days hospitalised in past year median (IQR)	5 (3-12)	4 (2-9)	5 (3-12)	4 (2-9)	5 (3-11)	4 (2-9)	5 (3-11)	4 (2-9)
Education 12+ years,	29%	33%	29%	34%	30%	35%	31%	35%
Education missing,	0%	1%	0%	1%	0%	1%	1%	1%
Married/partner	50%	49%	49%	48%	49%	48%	49%	48%
Married/partner missing,	0%	0%	0%	0%	0%	0%	0%	0%
Born in Sweden	89%	85%	89%	85%	89%	85%	89%	85%
Born in Sweden missing,	0%	0%	0%	0%	0%	0%	0%	0%
<i>Comorbidities,</i>								
Cancer	4%	4%	5%	4%	4%	4%	5%	4%
Diabetes	11%	8%	11%	8%	11%	9%	12%	9%
Heart failure	3%	2%	3%	2%	3%	1%	3%	2%
Ischaemic heart disease	6%	3%	6%	3%	6%	3%	6%	3%
Infections	5%	2%	5%	2%	5%	2%	5%	2%
Lung disease	9%	4%	9%	4%	9%	4%	9%	4%
Kidney failure	2%	1%	2%	1%	3%	1%	3%	1%
Stroke	4%	2%	4%	2%	3%	2%	3%	2%
Surgery	13%	5%	13%	5%	13%	5%	13%	5%
Venous thrombotic event	1.0%	0.5%	0.9%	0.5%	1.0%	0.5%	0.9%	0.5%
Influenza hospitalisation in the previous year	0.2%	0.1%	0.1%	0.1%	0.3%	0.1%	0.3%	0.1%
<i>Treatment N</i>								
csDMARD	28244	-	28691	-	29065	-	29810	-
TNFi	16252	-	17333	-	18479	-	20134	-
Abatacept	923	-	1030	-	1112	-	1245	-

Tocilizumab	974	-	1070	-	1161	-	1087	-
Rituximab	1836	-	2010	-	2137	-	2155	-
JAKi	0	-	0	-	157	-	915	-

Table S5: Descriptive statistics for patients with inflammatory joint diseases and population comparators in Sweden during influenza seasons 2015/2016-2018/2019 and March-September 2020

	Average across influenza seasons 2015/2016-2018/2019			2020		
	All inflammatory joint disease	RA (50% of all IJD)	General population	All inflammatory joint disease	RA (48% of all IJD)	General population
Individuals	104276	52149	464819	110567	53455	484277
Age, Median years (IQR)	61 (48-72)	68 (56-76)	59 (47-70)	62 (49-73)	69 (57-77)	60 (47-71)
Females	62%	72%	62%	62%	73%	62%
<i>Comorbidities</i>						
History of cancer	5%	5%	4%	3%	4%	3%
History of diabetes	11%	13%	9%	12%	14%	10%
History of heart failure	3%	4%	2%	3%	4%	2%
History of ischemic heart disease	6%	8%	3%	6%	7%	3%
History of infections	5%	7%	2%	5%	7%	2%
History of lung diseases	9%	11%	4%	9%	11%	4%
History of kidney failure	3%	3%	1%	3%	4%	1%
History of stroke	3%	4%	2%	3%	4%	2%
History of joint surgery	13%	19%	5%	12%	18%	5%
History of VTE	0.9%	1.2%	0.5%	1.0%	1.3%	0.5%
Influenza hospitalisation in the previous year	0.2%	0.3%	0.1%	-	-	-
Highest achieved education						
<9 years	13%	18%	10%	11%	16%	9%
9-12 years	58%	55%	55%	58%	56%	55%
12+ years	30%	26%	35%	31%	28%	36%
Missing	0%	1%	1%	0%	0%	0%
Civil status: Married	49%	50%	48%	49%	50%	48%
Civil status: missing	0%	0%	0%	0%	0%	0%
Born in Sweden	89%	88%	85%	89%	87%	84%
Born in Sweden missing	0%	0%	0%	0%	0%	0%
Hospitalisation days past year, median (IQR)	5 (3-11)	6 (3-13)	4 (2-9)	5 (3-11)	5 (3-12)	4 (2-8)
Number of individuals on treatment						
csDMARD	40572	27757	-	33296	22904	-
TNFi	26028	13257	-	22070	10463	-

Abatacept	2022	1881	-	1324	1221	-
Tocilizumab	1787	1624	-	1037	942	-
Rituximab	2905	2861	-	2180	2150	-
JAKi*	970	864	-	1725	1384	-

*Note JAKi available in Sweden from 2017

Table S6: Descriptive statistics for patients with inflammatory joint diseases on active cs- and b/ts DMARD treatment, and population comparators in Sweden during influenza seasons 2015/2016 to 2018/2019

	csDMARD (N=123 094)	TNFi (N=75 362)	Abatacept (N=4431)	Tocilizumab (N=4405)	Rituximab (N=8203)	JAKi (N=1081)	All b/tsDMARDs (N=93 482)	General population (N=990 467)
Individuals*, N	40572	26028	2022	1787	2905	970	31077	343200
Age, Median years (IQR)	65 (53-74)	52 (40-64)	61 (50-70)	58 (46-68)	66 (55-73)	59 (48-69)	54 (42-66)	59 (46-69)
Female,	64%	61%	79%	79%	76%	82%	63%	63%
Disease duration, median years (IQR)	5.4 (1.1-10.9)	6.8 (2.5-12.3)	9.4 (4.4-14.1)	8.5 (4.0-13.7)	10.4 (5.8-14.3)	10.2 (5.4-15.9)	7.3 (2.7-12.6)	-
DAS28, median (IQR)	2.7 (1.9-3.6)	2.6 (1.8-3.7)	3.7 (2.7-4.7)	2.6 (1.5-4.2)	3.4 (2.5-4.5)	4.2 (3.0-5.2)	2.7 (1.9-3.8)	
DAS28, % missing	66%	46%	37%	34%	30%	36%	44%	
Previous number of b/tsDMARDs, median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-1.0)	1.0 (0.0-2.0)	1.0 (0.0-2.0)	1.0 (0.0-2.0)	2.0 (1.0-3.0)	0.0 (0.0-1.0)	
Concomitant csDMARD use,	-	42%	48%	34%	45%	28%	42%	-
Concomitant steroid use,	26%	19%	42%	37%	40%	46%	22%	-
Days hospitalised in past year**, median (IQR)	5 (3-12)	4 (2-8)	5 (3-10)	5 (3-9)	5 (3-11)	5 (3-10)	4 (2-9)	4 (2-9)
Highest achieved education,								
≤9 years	17%	6%	11%	9%	14%	7%	8%	11%
10-12 years	58%	60%	60%	60%	59%	60%	60%	55%
≥12 years	26%	34%	29%	31%	27%	33%	33%	34%
Missing	1%	1%	1%	1%	1%	0%	1%	1%
Married/partner	51%	48%	52%	47%	51%	52%	49%	48%
Married/partner missing,	0%	0%	0%	0%	0%	0%	0%	0%
Born in Sweden	89%	88%	87%	88%	85%	88%	88%	85%
Born in Sweden missing,	0%	0%	0%	0%	0%	0%	0%	0%
Comorbidities,								
Cancer	5%	2%	3%	2%	7%	2%	2%	4%
Diabetes	12%	8%	13%	10%	13%	10%	8%	8%
Heart failure	3%	1%	3%	2%	3%	2%	1%	1%
Ischaemic heart disease	7%	3%	7%	3%	8%	5%	4%	3%
Infections	5%	4%	10%	5%	9%	8%	4%	2%
Lung disease	9%	6%	16%	10%	17%	11%	7%	4%
Kidney failure	2%	1%	2%	2%	3%	2%	2%	1%
Stroke	4%	1%	3%	2%	4%	1%	2%	2%
Surgery	13%	13%	24%	24%	29%	25%	15%	5%

Venous thrombotic event	1.1%	0.5%	1.1%	0.8%	1.8%	1.3%	0.6%	0.5%
Influenza hospitalisation in the previous year,	0.1%	0.1%	0.2%	0.2%	0.2%	0.5%	0.1%	0.1%

** Note characteristics presented limiting to one individual per cohort (can be more than one observation per individual due to year cohorts)*

***of those hospitalized*

Table S7: Number of events, absolute risk, excess risk and hazard ratios (HR) estimated from Cox proportional hazards models comparing 1) patients with inflammatory joint diseases to matched comparators for hospitalisation listing any cause, or death from any cause during influenza seasons 2015-2019.

Outcome	N events (average risk, %) in IJD cohort	N events (average risk, %) in general population	Crude excess risk per 100 patients	HR 1*	HR 2**
All IJD					
All hospitalisations	56 703 (13.6)	152 124 (8.2)	5.4	1.72 (1.70, 1.73)	1.22 (1.21, 1.24)
All death	6751 (1.61)	15 650 (0.84)	0.8	1.92 (1.87, 1.98)	1.13 (1.10, 1.17)
RA					
All hospitalisations	34 802 (16.7)	85 451 (9.7)	5.0	1.80 (1.77, 1.82)	1.26 (1.24, 1.28)
All death	5058 (2.42)	10 595 (1.20)	1.2	2.03 (1.96, 2.10)	1.21 (1.16, 1.25)

*HR1 accounts for age, sex and region (and influenza season for influenza analyses) via the matching.

**HR2 additionally adjusts for socioeconomic factors (education, civil status, country of birth), influenza hospitalisation in the previous year and comorbidities (history of the following diseases: cancer, diabetes, heart failure, ischemic heart disease, lung disease, stroke, surgery, venous thrombotic event, and kidney failure).

Table S8: Hazard ratios (HR) estimated from Cox proportional hazards models comparing 1) patients with inflammatory joint diseases (IJD) to matched comparators for outcomes death listing influenza (influenza seasons 2015-2019), with alternative death due to influenza definition

Outcome	HR 2*
All IJD	
Death listing influenza, original definition	1.46 (1.06, 2.01)
Death due to influenza, 30 days after hospitalisation	1.51 (1.10, 2.07)
RA	
Death listing influenza	1.56 (1.07, 2.27)
Death due to influenza, 30 days after hospitalisation	1.56 (1.07, 2.26)

*HR2 accounts for age, sex and region and influenza season via matching and additionally adjusts for socioeconomic factors (education, civil status, country of birth), influenza hospitalisation in the previous year and comorbidities (history of the following diseases: cancer, diabetes, heart failure, ischemic heart disease, lung disease, stroke, surgery, venous thrombotic event, and kidney failure).

Table S9: Hazard ratios (HR) comparing the rates of deaths and hospitalisation (all-cause) in patients with inflammatory joint diseases receiving csDMARDs to patients receiving b/tsDMARDs in Sweden. Previously published corresponding HRs for COVID-19 in the right-most column.

Outcome	Cohort	N events	Absolute risk, %	HR1 (95% CI)**	HR2 (95% CI)#	HR2 COVID (95% CI)***
Hospitalisation	csDMARD	15952	13.8	1 (ref)	1 (ref)	1 (ref)
	TNFi	7480	10.3	0.73 (0.71, 0.76)	1.06 (1.03, 1.10)	0.99 (0.89-1.10)
	Abatacept	777	18.0	1.33 (1.23, 1.45)	1.12 (1.04, 1.22)	0.94 (0.69-1.26)
	Tocilizumab	596	13.9	1.00 (0.92, 1.10)	1.09 (1.00, 1.19)	0.92 (0.64-1.33)
	Rituximab	1610	19.8	1.49 (1.40, 1.58)	1.16 (1.10, 1.23)	1.25 (1.02-1.53)
	All b/tsDMARDs combined*	10671	11.8	0.85 (0.82, 0.87)	1.08 (1.05, 1.12)	0.99 (0.90-1.10)
Death	csDMARD	1880	1.6	1 (ref)	1 (ref)	1 (ref)
	TNFi	319	0.4	0.27 (0.24, 0.30)	0.77 (0.57, 1.06)	0.71 (0.49-1.03)
	Abatacept	44	1.0	0.63 (0.47, 0.85)	0.97 (0.51, 1.85)	1.12 (0.50-2.48)
	Tocilizumab	39	0.9	0.56 (0.41, 0.77)	0.84 (0.34, 2.08)	1.11 (0.41-3.02)
	Rituximab	137	1.7	1.04 (0.87, 1.23)	1.16 (0.76, 1.78)	2.52 (1.56-4.07)
	All b/tsDMARDs combined*	551	0.6	0.38 (0.34, 0.41)	0.90 (0.70, 1.16)	0.91 (0.67-1.24)

Note results only presented where treatment cohorts have 5 or more events.

*Includes Janus kinases inhibitors (JAKi).

**Adjusted for influenza season; age, sex and region accounted for via matching.

#Additionally adjusted for disease duration, disease activity score on 28 joints (DAS28), number of previous b/tsDMARDs and concomitant steroid use, socioeconomic factors (education, civil status, country of birth), influenza hospitalisation in the previous year and comorbidities (history of the following diseases: cancer, diabetes, heart failure, ischemic heart disease, lung disease, stroke, surgery, venous thrombotic event, and kidney failure)

***Taken from the COVID analyses presented in Bower et al.¹¹, adjusted for the same factors as #, but via inverse probability treatment weighting via propensity score estimation.

Table S10: Hazard ratios (HR) comparing the rates hospitalisation listing influenza in patients with inflammatory joint diseases receiving csDMARDs to patients receiving b/tsDMARDs in Sweden. A comparison of approaches for dealing with missing DAS28 information in adjusted Cox proportional hazards models

Outcome	Cohort	Original analysis (as displayed in Table 2)*		Complete case	
		N events	HR2** (95% CI)	N events	HR2** (95% CI)
Hospitalisation	csDMARD	327	1 (ref)	72	1 (ref)
	All b/tsDMARDs combined	191	1.32 (1.06, 1.64)	93	1.56 (1.07, 2.27)

*Original analysis assumes one category for missing DAS28 information, the proportion missing is displayed in Supplementary Table S6

**Influenza season; age, sex and region accounted for via matching. Further adjusted for disease duration, disease activity score on 28 joints (DAS28), number of previous b/tsDMARDs and concomitant steroid use, socioeconomic factors (education, civil status, country of birth), influenza hospitalisation in the previous year and comorbidities (history of the following diseases: cancer, diabetes, heart failure, ischemic heart disease, lung disease, stroke, surgery, venous thrombotic event, and kidney failure)

Figure S1: Crude rates for influenza deaths and hospitalisations listing influenza in inflammatory joint disease patients (solid lines) and matched comparators (dashed lines) over four influenza seasons in Sweden.

