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# EPIDEMIOLOGICAL SCIENCE

# Factors associated with COVID-19-related death in people with rheumatic diseases: results from the COVID-19 Global Rheumatology Alliance physician-reported registry

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# ABSTRACT

**Objectives** To determine factors associated with COVID-19-related death in people with rheumatic diseases.

**Methods** Physician-reported registry of adults with rheumatic disease and confirmed or presumptive COVID-19 (from 24 March to 1 July 2020). The primary outcome was COVID-19-related death. Age, sex, smoking status, comorbidities, rheumatic disease diagnosis, disease activity and medications were included as covariates in multivariable logistic regression models. Analyses were further stratified according to rheumatic disease category.

Results Of 3729 patients (mean age 57 years, 68% female), 390 (10.5%) died. Independent factors associated with COVID-19-related death were age (66-75 years: OR 3.00, 95% CI 2.13 to 4.22; >75 years: 6.18, 4.47 to 8.53; both vs ≤65 years), male sex (1.46, 1.11 to 1.91), hypertension combined with cardiovascular disease (1.89, 1.31 to 2.73), chronic lung disease (1.68, 1.26 to 2.25) and prednisoloneequivalent dosage >10 mg/day (1.69, 1.18 to 2.41; vs no glucocorticoid intake). Moderate/high disease activity (vs remission/low disease activity) was associated with higher odds of death (1.87, 1.27 to 2.77). Rituximab (4.04, 2.32 to 7.03), sulfasalazine (3.60, 1.66 to 7.78), immunosuppressants (azathioprine, cyclophosphamide, ciclosporin, mycophenolate or tacrolimus: 2.22, 1.43 to 3.46) and not receiving any disease-modifying antirheumatic drug (DMARD) (2.11, 1.48 to 3.01) were associated with higher odds of death, compared with methotrexate monotherapy. Other synthetic/biological DMARDs were not associated with COVID-19-related death.

**Conclusion** Among people with rheumatic disease, COVID-19-related death was associated with known general factors (older age, male sex and specific

## Key messages

# What is already known about this subject?

- To date, most available data on outcomes for people with rheumatic diseases infected with SARS-CoV-2 come from single centre or single country case series or from one large international registry; the COVID-19 Global Rheumatology Alliance (GRA) physician registry.
- ► The first GRA publication identified factors associated with higher odds of COVID-19 hospitalisation, including older age, presence of comorbidities and higher dosages of glucocorticoids (≥10 mg/day of prednisolone equivalent).
- Clinical outcome information on patients with COVID-19 who have rheumatic disease therefore remains limited, particularly with regard to factors associated with COVID-19related death.

## What does this study add?

- In this analysis of 3729 patients with rheumatic diseases, older age, male sex, and cardiovascular and chronic lung disease were associated with COVID-19-related death.
- Disease-specific factors, namely, moderate/ high disease activity and certain medications (rituximab, sulfasalazine and immunosuppressants (as opposed to immunomodulators like disease-modifying anti-rheumatic drugs (DMARDs)) were also associated with COVID-19-related death.

comorbidities) and disease-specific factors (disease activity and specific medications). The association with moderate/high disease activity highlights the importance



#### Key messages

# How might this impact on clinical practice or future developments?

There is differential risk of COVID-19-related death according to disease activity and treatments in patients with rheumatic disease, highlighting the need for adequate disease control with DMARDs, preferably without increasing the glucocorticoid dosage.

of adequate disease control with DMARDs, preferably without increasing glucocorticoid dosages. Caution may be required with rituximab, sulfasalazine and some immunosuppressants.

#### **INTRODUCTION**

There is a lack of robust data to inform our understanding of outcomes following SARS-CoV-2 infection in patients with inflammatory rheumatic diseases, leading to uncertainties regarding chronic disease management, especially for those taking immunosuppressant or immunomodulatory drugs.<sup>1–3</sup>

Whether people with rheumatic diseases belong to a vulnerable, higher risk population for SARS-CoV-2 infection and have poorer outcomes is unclear.<sup>1-8</sup> In general, this population seems to have similar or only slightly poorer outcomes compared with those without rheumatic disease.<sup>7-9</sup> However, important confounding disease-related factors, such as disease activity or treatments, have previously not been addressed.

Medications commonly used to treat rheumatic diseases have been used or are being tested for the prevention and/or treatment of COVID-19 and its complications,<sup>10</sup> raising questions about the impact of these treatments on the outcomes of SARS-CoV-2 infection. Continuation of immunomodulatory or immunosuppressive therapy is essential for controlling rheumatic disease activity, avoiding disease progression and preventing joint or organ-damage related to sustained inflammation. Withdrawal of effective treatments should be based on sound evidence, even during a pandemic.

To generate more granular data relevant to rheumatic diseases, a global network of rheumatologists, data scientists and patients developed a COVID-19 physician-reported case registry in March 2020.<sup>11 12</sup> Analysis of the first 600 patients revealed that older age and comorbidities were associated with hospitalisation,<sup>13</sup> similar to results in the general population.<sup>8 14</sup> More robust data on the risk of poor outcomes, in particular risk of death, are required.

The aim of this study was to investigate factors associated with COVID-19-related death in patients with rheumatic diseases and to analyse these associations by disease group.

#### **METHODS**

#### Data source

The COVID-19 Global Rheumatology Alliance (C19-GRA) physician-reported registry is an observational registry launched on 24 March 2020. Data are entered voluntarily by rheumatologists or under supervision of rheumatologists; patients are eligible for inclusion if they have a pre-existing rheumatic disease and a COVID-19 diagnosis. Data are entered either directly into the global or European data entry systems or transferred from national registries (France, Germany, Italy, Portugal and Sweden).

We used data collected on or before 1 July 2020. Further details of this registry have been described elsewhere.<sup>11-13</sup> Countries were assigned to the six WHO regions (www.who.int); the 'Americas' was further divided into north and south. Given the registry collects anonymous data, the UK Health Research Authority and the University of California San Francisco Institutional Review Board considered it exempt from patient consent.

#### Patient stratification into diagnostic groups

Rheumatic diseases differ regarding the disease-modifying antirheumatic drugs (DMARDs) approved for their treatment. To minimise the impact of this heterogeneity on the associations of interest, in addition to the main analysis with all patients, diagnostic categories were defined (figure 1) and stratified analyses were undertaken for patients with (1) inflammatory joint diseases (IJD), (2) rheumatoid arthritis (a subset of the IJD subgroup) and (3) connective tissue diseases (CTD)/vasculitis.

#### **COVID-19 reporting and outcome**

Both confirmed and presumptive cases of COVID-19 were reported. The method of COVID-19 diagnosis was specified: PCR, CT scan, metagenomic testing, laboratory assays or based on symptoms only.

For analysis, patients were subsequently categorised into (1) *confirmed* or high likelihood of COVID-19 (chest imaging (CT or chest X-ray) showing bilateral infiltrates and/or symptoms after close contact with a known laboratory-confirmed COVID-19 positive patient) or (2) *presumptive* cases based on symptoms alone.

The primary outcome was COVID-19-related death.

#### Treatment prior to COVID-19

Antirheumatic medications used prior to COVID-19 diagnosis were categorised into groups shown in figure 1. Immunomodulatory drugs (conventional synthetic (cs)/biological (b)/targeted synthetic (ts) DMARDs) were distinguished from immunosuppressive drugs (azathioprine, cyclophosphamide, ciclosporin, mycophenolate mofetil/mycophenolic acid, tacrolimus) as recommended by Isaacs and Burmester<sup>15</sup>; glucocorticoids are also immunosuppressive but they were examined separately and categorised by prednisolone-equivalent dosage (1–10 mg/day and >10 mg/day). Methotrexate monotherapy was adopted as the medication reference group; methotrexate is the anchor drug in multiple rheumatic diseases<sup>16</sup> and it represents the largest medication category in the registry.

#### Statistical analyses

Descriptive tables were produced for the whole cohort and then by diagnostic group, country (for the six countries with the highest number of cases: France, Germany, Italy, Spain, UK and USA) and medication. Independent associations between demographic and disease features and COVID-19-related death were estimated using multivariable logistic regression and reported as OR and 95% CI. Covariates included in the model were age, sex, key comorbidities (hypertension alone or cardiovascular disease (CVD) alone, hypertension combined with CVD, chronic lung disease, chronic kidney disease (CKD) and diabetes), smoking status (ever vs never), rheumatic disease diagnostic group, disease activity as per the physician's global assessment (severe/ high or moderate disease activity vs minimal/low disease activity or remission), rheumatic disease treatment prior to COVID-19 diagnosis and prednisolone-equivalent glucocorticoid use.

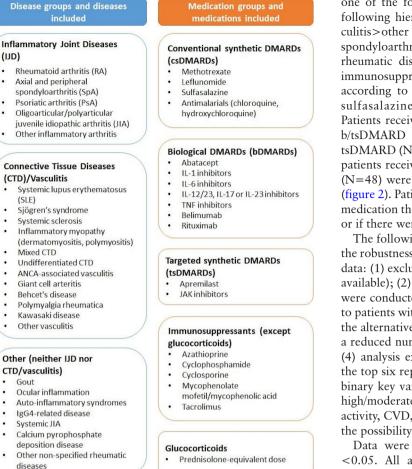


Figure 1 Disease and medication groups. ANCA, anti-neutrophil cytoplasm antibodies; DMARD, disease-modifying antirheumatic drugs; IgG, immunoglobulin; IL, interleukin; JAK, Janus kinase; TNF, tumour necrosis factor.

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All patients with confirmed or presumptive COVID-19 were included in the main analyses. Patients with missing primary outcome (N=82) or missing values for age, sex and DMARD (N=19) were excluded from analysis. Missing values for comorbidities, smoking status, glucocorticoid therapy and disease activity were derived by multiple imputation using full conditional specification.<sup>17</sup> Results of the logistic regression analyses for 10 imputed datasets were pooled by Rubin's rules. As disease activity was missing for all French patients, country-level life expectancy was used in the imputation model to explain potential structural differences in disease activity between countries not accounted for in the patient-level data (data from 2018, source: http://hdr.undp.org/).

To account for pronounced heterogeneity between participating countries regarding both healthcare systems and infection dynamics, countries were implicitly considered as data clusters in the regression analysis by assuming that the data arose from a cluster sample design; this was done by applying a Taylor series linearisation in the variance estimation.<sup>1</sup>

For patients listed as having more than one rheumatic disease or being treated with more than one of the medications of interest, we created a hierarchy based on clinical expertise to categorise patients. This process creates disjoint categories, allowing a clear reference group for interpretation of the regression models and avoiding collinearities. Patients with more than

one of the following diseases were grouped according to the following hierarchy: systemic lupus erythematosus (SLE)>vasculitis>other CTD>RA>psoriatic arthritis (PsA)>(other) spondyloarthritis (SpA)>other IJD>other non-IJD/non-CTD rheumatic disease. Patients receiving multiple csDMARDs or immunosuppressants (except glucocorticoids) were grouped according to the following hierarchy: immunosuppressants>sulfasalazine>antimalarials>leflunomide>methotrexate. Patients receiving a b/tsDMARD were considered solely in the b/tsDMARD group. Patients treated with more than one b/ tsDMARD (N=4), patients receiving IL-1 inhibitors (N=20) and patients receiving DMARDs atypical for their disease subgroup (N=48) were excluded from analysis due to very low numbers (figure 2). Patients were excluded from a particular analysis if the medication they received provided  $\leq 20$  patients for that analysis or if there were no deaths reported for that specific medication.

The following sensitivity analyses were performed to examine the robustness of our findings to procedures for handling missing data: (1) excluding patients from France (no disease activity data available); (2) complete case analysis. Further sensitivity analyses were conducted to assess the stability of the results: (1) limited to patients with confirmed or highly likely COVID-19; (2) using the alternative outcome 'death or invasive ventilation'; (3) using a reduced number of covariates to assess the risk of overfitting; (4) analysis explicitly controlling for country, using data from the top six reporting countries; (5) analysis stratified for several binary key variables (age >65 or not, sex, ever smoked vs not, high/moderate/severe disease activity vs remission/low disease activity, CVD, chronic lung disease, glucocorticoid use) to assess the possibility of interactions.

Data were considered statistically significant for p values <0.05. All analyses were conducted in SAS (V.9.4) and R (V.3.6.3).

#### RESULTS

As of 1 July 2020, 3830 patients were in the registry, of whom 3729 had no missing values for death, age, sex and DMARD therapy (table 1, results for all patients; online supplemental table 1, results stratified by diagnostic subgroup; online supplemental table 2, results stratified by country; online supplemental table 3, results stratified by medication of interest).

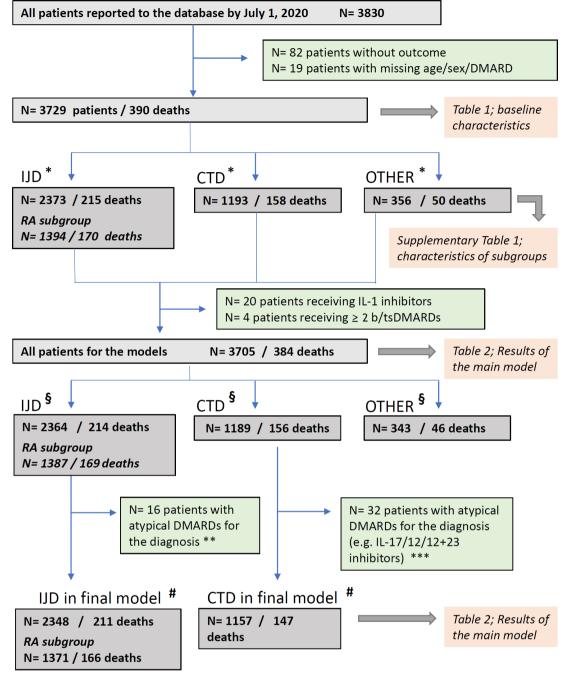
#### Patient characteristics and outcomes of COVID-19

Mean age was 57 (15.7) years and most patients were  $\leq 65$  years (2586/3729, 69.3%) and female (2534/3729, 68%). The most common disease was RA (1394/3729, 37.4%), followed by CTDs other than SLE (533/3729, 14.3%), SLE (391/3729, 10.5%), PsA (440/3729, 11.8%) and other SpA (431/3729, 11.6%).

Patients were primarily from Europe (2315/3729, 62.1%) or North America (1105/3729, 29.6%). Nearly half (1309/2758, 47.5%) had minimal or low disease activity and one-third (893/2758, 32.4%) were in remission before COVID-19. Onequarter of all patients (776/3164, 24.5%) were ever smokers.

Most patients had a laboratory-confirmed diagnosis of COVID-19 (2897/3729, 77.7%); 2.4% (91/3729) had a high likelihood of infection based on imaging or confirmed COVID-19 contacts.

Death occurred in 10.5% (390/3729) of patients; 68.7% (268/390) of those who died were >65 years. Nearly half of all patients (1739/3546; 49.0%) were hospitalised. Invasive ventilation was reported in 6.2% (187/2995) of patients, but in 40.8% (120/294) of those who died.



**Figure 2** Patient flowchart. Some patients had diagnoses in multiple groups; as a result, the sum of patients in each group is greater than the total number of patients. (\*) Patients belonging to more than one diagnosic group: IJD and CTD: N=78 (10 deaths); IJD and other: N=70 (12 deaths); CTD and other: N=50 (13 deaths); IJD and CTD and other: N=5 (2 deaths). (§) Patients belonging to more than one diagnosic group: IJD and CTD: N=77 (10 deaths); IJD and other: N=70 (12 deaths); CTD and other: N=49 (12 deaths); IJD and CTD and other: N=5 (2 deaths). (#) Patients belonging to more than one diagnosic group: IJD and CTD: N=77 (10 deaths); IJD and other: N=70 (12 deaths); CTD and other: N=49 (12 deaths); IJD and CTD and other: N=5 (2 deaths). (#) Patients belonging to more than one diagnosic group: IJD and CTD: N=59 (7 deaths). (\*\*) Non-typical DMARDs for IJD and RA: immunosuppressants and belimumab; non-typical DMARDs for RA: IL-17/IL-23/IL-12+23 inhibitors. (\*\*\*) Non-typical DMARDs for CTD: abatacept, IL-17/IL-23/IL-12+23 inhibitors, sulfasalazine, leflunomide and tsDMARDs. b/tsDMARDs, biological/targeted synthetic disease-modifying antirheumatic drugs; CTD, connective tissue disease/vasculitis; DMARDs, disease-modifying anti-rheumatic drugs; IJD, inflammatory joint disease; IL, interleukin; RA, rheumatoid arthritis.

#### Comorbidities

Most patients (2582/3700, 69.8%) had at least one comorbidity, and 20.5% (760/3700) had more than three. The most frequent were hypertension (1307/3700, 35.3%), chronic lung disease (719/3700, 19.4%), obesity (BMI  $\geq$ 30; 597/3700, 16.1%), diabetes (505/3700, 13.6%), other CVD (442/3700, 11.9%) and CKD (258/3700, 7.0%). Among deceased patients, the proportion of those with comorbidities was higher, with 42.7% (165/386) having  $\geq$ 3 comorbidities, namely, 54.9% (212/386) with hypertension, 35.8% (138/386) with chronic lung disease, 24.6% (95/386) with diabetes, 32.1% (124/386) with other CVD and 19.9% (77/386) with CKD.

#### Treatments

At the time of COVID-19 diagnosis, 40.6% (1514/3729) of patients were treated only with csDMARDs, immunosuppressants or combinations of these; 35.7% (1331/3729) received

	emio	
Enin	amia	
LUIU	GIIIU	

897 (24.2)

1118 (30.2)

1115 (30.1)

707 (19.1)

760 (20.5)

651 (17.5)

753 (20.2)

578 (15.5)

659 (17.7)

73 (2)

130 (3.5)

67 (1.8)

155 (4.2)

304 (8.2)

361 (9.7)

175 (4.7)

168 (4.5)

82 (2.2)

96 (2.6)

70 (1.9)

54 (1.4)

13 (0.3)

10 (0.3)

7 (0.2)

11 (0.3)

3 (0.1)

12 (0.3)

723 (19.4)

608 (16.3)

447 (12)

357 (9.6)

32 (0.9)

51 (1.4)

96 (2.6)

124 (3.3)

91 (2.4)

102 (2.7)

5 (0.1)

23 (0.6)

54 (1.4)

1.4 (1.3)

Total

Dationt day	mographic and	clinical characte	rictics	Table 1 Continued		
ratient dei	Not deceased	clinical characte	Total	Parameter	Not deceased	Deceased
	3339	390	3729			
	5555	350	5725	Other comorbidities	771 (23.3)	126 (32.6
	55.5 (15.2)	69.7 (14.6)	57.0 (15.7)	Number of comorbities	1.3 (1.3)	2.5 (1.
	197 (5.9)	9 (2.3)	206 (5.5)	No comorbidity One comorbidity	1090 (32.9)	28 (7.3)
	1012 (30.3)	31 (7.9)	1043 (28)	Two comorbidities	1032 (31.1) 597 (18)	83 (21.5
	1255 (37.6)	82 (21)	1337 (35.9)	≥3 comorbidites	595 (18)	165 (42.7
	536 (16.1)	109 (27.9)	645 (17.3)	DMARD therapies	555 (10)	105 (42.7
	339 (10.2)	159 (40.8)	498 (13.4)	csDMARDs monotherapy	592 (17.7)	59 (15.1
	1031 (30.9)	164 (42.1)	1195 (32)	csDMARDs combination	692 (20.7)	61 (15.6
	664 (23.3)	112 (36.1)	776 (24.5)	therapy	052 (20.7)	01 (15.0
	(N=2854)	(N=310)	(N=3164)	Methotrexate	531 (15.9)	47 (12.1
	(Missing=485)	(Missing=80)	(Missing=565)	monotherapy		
	44 (0.4)	2 (0.5)	45 (0.4)	Methotrexate combination therapy	607 (18.2)	52 (13.3
ion	14 (0.4)	2 (0.5)	16 (0.4)	Leflunomide monotherapy	61 (1.8)	12 (3.1)
editerranean	83 (2.5)	11 (2.8)	94 (2.5)	Leflunomide combination	120 (3.6)	12 (3.1)
egion	2040 (61.1)	275 (70.5)	2315 (62.1)	therapy	120 (5.0)	10 (2.0)
rican region	1024 (30.7)	81 (20.8)	1105 (29.6)	Sulfasalazine	51 (1.5)	16 (4.1)
rican region	112 (3.4)	10 (2.6)	122 (3.3)	monotherapy		
Asian region	11 (0.3)	0	11 (0.3)	Sulfasalazine combination	129 (3.9)	26 (6.7)
cific region	55 (1.6)	11 (2.8)	66 (1.8)	therapy	297 (9.6)	17 (4 4)
y joint	. ,	. ,	. ,	Antimalarial monotherapy Antimalarial combination	287 (8.6)	17 (4.4)
				therapy	322 (9.6)	39 (10)
arthritis	1224 (36.7)	170 (43.6)	1394 (37.4)	Immunosuppressants	149 (4.5)	26 (6.7)
ritis	416 (12.5)	15 (3.8)	431 (11.6)	monotherapy		
ritis	420 (12.6)	20 (5.1)	440 (11.8)	Immunosuppressants	147 (4.4)	21 (5.4)
athic arthritis	21 (0.6)	4 (1)	25 (0.7)	combination therapy	(2)	11(2,0)
ot systemic)	00 (2 7)	0 (2 4)	00 (2 C)	Mycophenolate mofetil monotherapy	68 (2)	14 (3.6)
natory arthritis	90 (2.7)	8 (2.1)	98 (2.6)	Mycophenolate mofetil	81 (2.4)	15 (3.8)
atory joint	2158 (64.6)	215 (55.1)	2373 (63.6)	combination therapy	. ,	
tissue				Azathioprine monotherapy	63 (1.9)	7 (1.8)
culitis				Azathioprine combination	51 (1.5)	3 (0.8)
S	355 (10.6)	36 (9.2)	391 (10.5)	therapy		- ()
IS	(72) (4.4.2)	60 (45 A)	522 (112)	Cyclophosphamide monotherapy	10 (0.3)	3 (0.8)
ssue diseases LE)	473 (14.2)	60 (15.4)	533 (14.3)	Cyclophosphamide	5 (0.1)	5 (1.3)
/	258 (7.7)	68 (17.4)	326 (8.7)	combination therapy	5 (0.1)	5 (1.5)
	1035 (31)	158 (40.5)	1193 (32.0)	Tacrolimus monotherapy	5 (0.1)	2 (0.5)
				Tacrolimus combination	11 (0.3)	0
	306 (9.2)	50 (12.8)	356 (9.5)	therapy		
vity	N=2464	N=294	N=2758	Ciclosporin monotherapy	3 (0.1)	0
	(Missing=875)	(Missing=96)	(Missing=971)	Ciclosporin combination therapy	11 (0.3)	1 (0.3)
	799 (32.4)	94 (32)	893 (32.4)	bDMARDs monotherapy	675 (20.2)	48 (12.3
disease activity	1202 (48.8)	107 (36.4)	1309 (47.5)	bDMARDs combination	562 (16.8)	46 (12.5
ease activity	388 (15.7)	60 (20.4)	448 (16.2)	therapy	502 (1010)	10 (1110
lisease activity	75 (3)	33 (11.2)	108 (3.9)	TNF inhibitors monotherapy	434 (13)	13 (3.3)
mes				TNF inhibitors combination	340 (10.2)	17 (4.4)
	1368 (43.3)	371 (96.6)	1739 (49)	therapy		
	(N=3162) (Missing=177)	(N=384) (Missing=6)	(N=3546) (Missing=183)	Abatacept monotherapy	28 (0.8)	4 (1)
lation	67 (2.5)	120 (40.8)	187 (6.2)	Abatacept combination therapy	46 (1.4)	5 (1.3)
	(N=2701)	(N=294)	(N=2995)	B-cell-targeted bDMARDs	71 (2.1)	25 (6.4)
	(Missing=638)	(Missing=96)	(Missing=734)	monotherapy	/1 (2.1)	25 (0.4)
es	N=3314 (Missing=25)	N=386 (Missing=4)	N=3700 (Missing=29)	B-cell-targeted bDMARDs	106 (3.2)	18 (4.6)
	( <i>wissing=23</i> ) 1095 (33)	( <i>wissing=4</i> ) 212 (54.9)	( <i>Wissing=23</i> ) 1307 (35.3)	combination therapy		
ar disease	318 (9.6)	124 (32.1)	442 (11.9)	Rituximab monotherapy	66 (2)	25 (6.4)
lar disease	89 (2.7)	20 (5.2)	109 (2.9)	Rituximab combination	85 (2.5)	17 (4.4)
disease	581 (17.5)	138 (35.8)	719 (19.4)	therapy Relimumeh monotherapy	E (0.1)	0
y disease	181 (5.5)	77 (19.9)	258 (7)	Belimumab monotherapy	5 (0.1)	0
≥30)	539 (16.3)	58 (15)	597 (16.1)	Belimumab combination therapy	22 (0.7)	1 (0.3)
	333 (10.3)	50(15)	337 (10.1)			

IL-6 inhibitors monotherapy

IL-6 inhibitors combination

therapy

Continued

51 (1.5)

34 (1)

36 (1)

3 (0.8)

2 (0.5)

tını	

Parameter Not deceased Deceased Ν 3339 390 General 55.5 (15.2) 69.7 (14.6) Age (years) ≤30 197 (5.9) 9 (2.3) 31-50 1012 (30.3) 31 (7.9) 1255 (37.6) 82 (21) 51-65 66-75 536 (16.1) 109 (27.9) 339 (10.2) 159 (40.8) >75 Male sex 1031 (30.9) 164 (42.1) Ever smoker 664 (23.3) 112 (36.1) (N=2854) (N=310) (Missing=485) (Missing=80) Regions African region 14 (0.4) 2 (0.5) Eastern Mediterranean 83 (2.5) 11 (2.8) region 275 (70.5) European region 2040 (61.1) 1024 (30.7) 81 (20.8) North American region 10 (2.6) South American region 112 (3.4) 0 South-East Asian region 11 (0.3) 55 (1.6) 11 (2.8) Western Pacific region Inflammatory joint diseases 1224 (36.7) 170 (43.6) Rheumatoid arthritis Spondyloarthritis 416 (12.5) 15 (3.8) Psoriatic arthritis 420 (12.6) 20 (5.1) Juvenile idiopathic arthritis 21 (0.6) 4 (1) (poly, oligo, not systemic) Other inflammatory arthritis 90 (2.7) 8 (2.1) 215 (55.1) Total Inflammatory joint 2158 (64.6) diseases **Connective tissue** diseases/Vasculitis Systemic lupus 355 (10.6) 36 (9.2) erythematosus 473 (14.2) 60 (15.4) Connective tissue diseases (other than SLE) 68 (17.4) Vasculitis 258 (7.7) Total CTD 1035 (31) 158 (40.5) Other RMDs Total 50 (12.8) 306 (9.2) **Disease activity** N=2464 N=294 (Missing=875) (Missing=96) Remission 799 (32.4) 94 (32) Minimal/low disease activity 1202 (48.8) 107 (36.4) Moderate disease activity 388 (15.7) 60 (20.4) Severe/high disease activity 75 (3) 33 (11.2) Other outcomes 371 (96.6) Hospitalised 1368 (43.3) (N=3162) (N=384) (Missing=177) (Missing=6) 120 (40.8) Invasive ventilation 67 (2.5) (N=294)(N=2701) (Missing=638) (Missing=96) Comorbidities N=3314 N=386 (Missing=25) (Missing=4) Hypertension 212 (54.9) 1095 (33) Cardiovascular disease 318 (9.6) 124 (32.1) Cerebrovascular disease 89 (2.7) 20 (5.2) Chronic lung disease 581 (17.5) 138 (35.8) Chronic kidney disease 181 (5.5) 77 (19.9) Obesity (BMI  $\geq$  30) 539 (16.3) 58 (15) 122 (3.3) Morbid obesity (BMI ≥40) 106 (3.2) 16 (4.1) Diabetes 410 (12.4) 95 (24.6) 505 (13.6) Cancer 165 (5) 49 (12.7) 214 (5.8)

Table 1

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Table 1         Continued			
Parameter	Not deceased	Deceased	Total
IL-1 inhibitors monotherapy	10 (0.3)	2 (0.5)	12 (0.3)
IL-1 inhibitors combination therapy	4 (0.1)	4 (1)	8 (0.2)
IL-17, IL-23, IL-12/23 inhibitors monotherapy	79 (2.4)	1 (0.3)	80 (2.1)
IL-17, IL-23, IL-12/23 inhibitors combination therapy	36 (1.1)	0	36 (1)
tsDMARDs monotherapy	61 (1.8)	5 (1.3)	66 (1.8)
tsDMARDs (*) combination therapy	71 (2.1)	10 (2.6)	81 (2.2)
JAK inhibitors monotherapy	54 (1.6)	4 (1)	58 (1.6)
JAK inhibitors combination therapy	67 (2)	9 (2.3)	76 (2)
Apremilast monotherapy	7 (0.2)	1 (0.3)	8 (0.2)
Apremilast combination therapy	3 (0.1)	1 (0.3)	4 (0.1)
No DMARD therapies	615 (18.4)	124 (31.8)	739 (19.8)
Further therapies			
Glucocorticoids (#)	1056 (32) (N=3302) (Missing=37)	217 (57.1) (N=380) (Missing=10)	1273 (34.6) (N=3682) (Missing=47)
Glucocorticoids 1–10 mg/day	833 (25.6) (N=3254) (Missing=85)	150 (41.3) (N=363) (Missing=27)	983 (27.2) (N=3617) (Missing=112)
Glucocorticoids>10 mg/day	171 (5.3) (N=3254) (Missing=85)	49 (13.5) (N=363) (Missing=27)	220 (6.1) (N=3617) (Missing=112)
NSAIDs	600 (19.3) (N=3103) (Missing=236)	38 (11.0) (N=345) (Missing=45)	638 (18.5) (N=3448) (Missing=281)

Data are N (column %) for categorical variables or mean (SD) for continuous variables. The table includes all patients with a non-missing outcome and non-missing values for age, sex and disease-modifying anti-rheumatic drugs (DMARDs) (101 patients excluded). Data refer to patients with non-missing values for the respective variable; total N for patients with non-missing values is given in parentheses for variables with missing values; the total number of missing values is also given in parenthesis, for the applicable variables. (\*) Includes one patient on a study medication (Lenabasum). (#) Includes patients with a missing glucocorticoid dosage.

bDMARD, biological disease-modifying antirheumatic drug; BMI, body mass index; csDMARD, conventional synthetic disease-modifying antirheumatic drug; CTD, connective tissue diseases; DMARD, disease-modifying antirheumatic drug; IL, interleukin; JAK, Janus kinase; JIA, juvenile idiopathic arthritis; N, number; NSAID, non-steroidal anti-inflammatory drugs; SLE, systemic lupus erythematosus; TNF, tumour necrosis factor; tsDMARD, targeted synthetic disease-modifying antirheumatic drug.

bDMARDs and 3.9% (147/3729) received tsDMARDs. Onefifth (739/3729, 19.8%) were not receiving any DMARD/ immunosuppressive treatment (except glucocorticoids), and this proportion was higher among deceased patients (124/390, 31.8%).

Among the patients not receiving any DMARD/immunosuppressive treatment, 39.8% (290/729) received glucocorticoids, 9.8% (70/712) with a prednisolone-equivalent dosage of >10 mg/day; the most frequent diagnostic categories being other non-specified rheumatic diseases (173/739, 23.4%), vasculitis (161/739, 21.8%), CTD other than SLE (156/739, 21.1%) and RA (110/739, 14.9%).

#### **Country-specific differences**

The majority of cases (2993/3729, 80.3%) were reported from six countries with considerable differences in reported percentages of death (online supplemental table 2). Overall, 10.5% (390/3729) of patients died, with highest proportions in the UK (91/435, 20.9%) and Italy (53/315, 16.8%). Death was reported in lower proportions in the USA (70/1005, 7.0%), Germany (15/198, 7.6%), France (62/793, 7.8%) and Spain (21/247, 8.5%). Other major differences between the countries were the distribution of rheumatic diseases and the distribution and frequency of comorbidities.

# Factors associated with death

In multivariable analyses (table 2, figure 3), patients between 66 and 75 years of age were more likely to have died (OR 3.00, 95% CI 2.13 to 4.22) than those  $\leq 65$  years. The association was even more pronounced in patients over 75 years (6.18, 4.47 to 8.53; vs  $\leq 65$  years). Male sex was also associated with higher odds of death (1.46, 1.11 to 1.91). Current or former smoking was only associated with death in the RA subgroup (1.45, 1.02 to 2.04).

Other factors associated with death included chronic lung disease (1.68, 1.26 to 2.25) and CVD combined with hypertension (1.89, 1.31 to 2.73), whereas hypertension or CVD alone did not show a significant association. CKD was significantly associated with death in patients with CTD or vasculitis (2.30, 1.37 to 3.88) but not in other disease subgroups.

Across all diagnostic groups, treatments with leflunomide, antimalarials, TNF inhibitors, abatacept, belimumab, IL-6 inhibitors, IL-17/IL-23/IL-12+23 inhibitors and tsDMARDs were not associated with death, as compared with methotrexate monotherapy. In the overall model, not receiving DMARD treatment was associated with death (2.11, 1.48 to 3.01) compared with methotrexate monotherapy. This was also seen in the IJD, RA and CTD subgroups.

Compared with methotrexate monotherapy, treatments associated with a higher odds of death were rituximab (4.04, 2.32 to 7.03, in the overall model; 5.42, 2.77 to 10.61, in the IJD subgroup; 4.99, 2.43 to 10.26, in the RA subgroup; 3.72, 1.21 to 11.48, in the CTD/vasculitis subgroup), sulfasalazine (3.60, 1.66 to 7.78, in the overall model and consistent across all subgroups) and immunosuppressants (azathioprine, cyclophosphamide, ciclosporin, mycophenolate or tacrolimus: 2.22, 1.43 to 3.46, in the overall model; 2.44, 1.06 to 5.65, in the CTD/ vasculitis subgroup; not applicable to other subgroups).

An additional analysis indicated that the association of sulfasalazine with an increased odds for death was mainly driven by the larger group of sulfasalazine monotherapy and persisted even when sulfasalazine combination treatment (plus either antimalarials, leflunomide or methotrexate) was considered separately (data not shown).

Treatment with higher dosages of glucocorticoids (>10 mg/ day prednisolone-equivalent dose vs no use) was also found to be associated with death (1.69, 1.18 to 2.41), particularly in the CTD/vasculitis subgroup (1.93, 1.11 to 3.36).

Higher disease activity at COVID-19 diagnosis was consistently associated with death across all disease groups. Patients with high/moderate/severe disease activity had higher odds of death (1.87, 1.27 to 2.77) than patients with low disease activity or in remission (overall model and consistent across all subgroups).

## Sensitivity analyses

Results were largely consistent in our sensitivity analyses (online supplemental tables 4–9). In the complete case analysis (online supplemental table 5), the association between sulfasalazine and death was no longer statistically significant. In stratified analyses (online supplemental tables 10–16), sulfasalazine use was not associated with death among patients that never smoked, with the OR among ever smokers being almost threefold than among non-smokers (online supplemental table 12).

## DISCUSSION

With global cooperation, the C19-GRA physician-reported registry is the largest collection to date of patients with rheumatic

		All		Patients v	vith inflammat	Patients with inflammatory joint diseases (IJDs)	Only	patients with	Only patients with rheumatoid arthritis	Patients w	vith connective vaso	Patients with connective tissue diseases (CTDs) or vasculitis
1		384/3705 (10.4%)	(10.4%)		211/2348 (9.0%)	(%0.6) {		166/13	166/1371 (12.1%)		147/115	147/1157 (12.7%)
– N deaths/patients (%)	N deaths/patients OR	OR	95% CI	N deaths/patients OR	nts OR	95% CI	N deaths/ patients	N	95% CI	N deaths/ patients	NO	95% CI
Age, years												
Age≤65	118/2565	-	Reference	55/1657	-	Reference	40/840	-	Reference	56/779	-	Reference
65years <age≤75< td=""><td>109/644</td><td>e</td><td>2.13 to 4.22</td><td>71/426</td><td>3.63</td><td>2.55 to 5.15</td><td>55/314</td><td>3.10</td><td>1.68 to 5.72</td><td>33/187</td><td>2.29</td><td>1.34 to 3.93</td></age≤75<>	109/644	e	2.13 to 4.22	71/426	3.63	2.55 to 5.15	55/314	3.10	1.68 to 5.72	33/187	2.29	1.34 to 3.93
Age>75	157/496	6.18	4.47 to 8.53	85/265	8.21	5.54 to 12.18	71/217	7.30	4.42 to 12.06	58/191	4.08	2.27 to 7.36
Male sex (vs female)	161/1188	1.46	1.11 to 1.91	82/788	1.31	0.95 to 1.8	55/345	1.17	0.78 to 1.76	63/296	1.66	0.96 to 2.86
Ever smoked (vs never)	140/922	1.21	0.94 to 1.57	84/607	1.26	0.93 to 1.72	71/385	1.45	1.02 to 2.04	42/248	1.11	0.67 to 1.86
Comorbidities												
Hypertension alone or CVD alone	155/1150	1.19	0.89 to 1.59	79/690	1.04	0.74 to 1.46	66/454	1.11	0.74 to 1.67	69/406	1.56	1.06 to 2.29
Hypertension and CVD	89/301	1.89	1.31 to 2.73	53/168	2.29	1.25 to 4.23	38/118	2.03	1.03 to 3.97	28/106	1.57	0.78 to 3.16
Chronic lung disease	136/721	1.68	1.26 to 2.25	76/406	1.52	1.04 to 2.21	63/293	1.44	0.99 to 2.09	54/285	2.05	1.47 to 2.85
Chronic kidney disease	76/259	1.67	0.99 to 2.8	27/111	1.09	0.54 to 2.21	21/83	1.01	0.46 to 2.24	41/124	2.30	1.37 to 3.88
Diabetes mellitus	96/508	1.38	0.88 to 2.17	55/313	1.31	0.95 to 1.79	39/213	1.08	0.72 to 1.61	32/154	1.39	0.64 to 3
Rheumatic disease												
Rheumatoid arthritis	160/1326	-	Reference	166/1373	-	Reference		n.a.			n.a.	
Systemic lupus erythematosus	36/391	1.2	0.70 to 2.04		n.a.			n.a.		32/378	-	Reference
	67/325	0.8	0.60 to 1.08		n.a.			n.a.		64/318	0.81	0.49 to 1.33
Other connective tissue diseases	53/473	0.75	0.58 to 0.97		n.a.			n.a.		51/461	0.78	0.39 to 1.54
Psoniasis arthritis	19/429	0.75	0.53 to 1.07	19/437	0.82	0.55 to 1.22		n.a.			n.a.	
Spondyloarthritis	15/423	0.72	0.34 to 1.54	15/424	0.82	0.4 to 1.69		n.a.			n.a.	
Other inflammatory arthritis or non-systemic JIA	10/109	0.79	0.46 to 1.34	11/114	0.76	0.43 to 1.36		n.a.			n.a.	
Other rheumatic diseases (not IJDs/CTDs/ vasculitis)	24/229	0.51	0.35 to 0.73		n.a.			n.a.			n.a.	
High/moderate/severe disease activity (DA) vs remission/low DA	109/722	1.87	1.27 to 2.77	54/453	1.6	1.13 to 2.26	44/274	1.60	1.03 to 2.47	51/230	2.45	1.49 to 4.02
Medication												
Methotrexate	47/595	1	Reference	41/487	-	Reference	34/354	-	Reference	6/94	-	Reference
No DMARD therapy	124/739	2.11	1.48 to 3.01	38/239	2.08	1.38 to 3.14	25/110	2.12	1.34 to 3.37	67/353	3.18	1.61 to 6.27
Leflunomide	12/90	1.56	0.9 to 2.7	10/83	1.37	0.69 to 2.73	9/68	1.43	0.71 to 2.86		n.a.	
	27/426	0.99	0.66 to 1.48	17/167	1.14	0.65 to 2	17/141	1.24	0.7 to 2.19	11/271	1.38	0.48 to 4.02
	33/144	3.6	1.66 to 7.78	31/137	3.40	1.46 to 7.93	21/85	2.62	1.21 to 5.68		n.a.	
essants	38/276	2.22	1.43 to 3.46		n.a.			n.a.		32/247	2.44	1.06 to 5.65
TNF inhibitors	30/803	0.85	0.52 to 1.36	26/764	0.77	0.42 to 1.41	16/292	0.82	0.39 to 1.76	4/39	2.00	0.36 to 11.2
	9/81	1.20	0.61 to 2.34	9/75	1.3	0.62 to 2.71	9/68	1.4	0.65 to 2.99		n.a.	
Rituximab	42/192	4.04	2.32 to 7.03	22/90	5.42	2.77 to 10.61	21/86	4.99	2.43 to 10.26	22/104	3.72	1.21 to 11.48
	1/27	0.71	0.19 to 2.68		n.a.			n.a.		1/27	1.07	0.21 to 5.37
	5/90	0.83	0.38 to 1.84	1/68	0.25	0.03 to 2.43	1/63	0.25	0.03 to 2.33	4/23	2.69	0.88 to 8.19
IL-17/IL-23/IL-12+23 inhibitors	1/115	0.25	0.03 to 2.04	1/112	0.26	0.03 to 2.06		n.a.			n.a.	
tsDMARDs	15/145	1.60	0.91 to 2.8	15/142	1.75	0.99 to 3.12	13/118	1.57	0.75 to 3.27		n.a.	
coids (GCs)												
No GCs	165/2417	-	Reference	1 09/1 7 2 1	-	Reference	78/863	-	Reference	38/551	-	Reference

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# Epidemiology

								Dationts wit	th connective	Batiants with connactive tissue diseases (CTDs) or
	A	NI	Patients with infle	Patients with inflammatory joint diseases (IJDs)	Only p	atients with rl	Only patients with rheumatoid arthritis		un connective tissue vasculitis	ulitis
	384/370	384/3705 (10.4%)	21	211/2348 (9.0%)		166/1371 (12.1%)	(12.1%)		147/1157	147/1157 (12.7%)
N deaths/patients (%)	N deaths/patients OR	95% CI	N deaths/patients OR	95% CI	N deaths/ patients	OR	95% CI	N deaths/ patients OR	OR	95% CI
GCs>10mg/day	49/226 1.69	1.69 1.18 to 2.41	12/60 1.55	5 0.67 to 3.57	10/44	1.59	0.6 to 4.18	34/137 1.93	1.93	1.11 to 3.36
Missing slues were imputed via multiple imputation, patient numbers may thus be rounded. Effects significant at level 0=0.05 are marked in bold. Patients were excluded from a particular analysis if the medication they received provided <20 patients for that analysis or if there were no deaths reported for that specific medication. TNF: numour necrosis factor, CID, connective tissue disease; DMARD, disease; dispathic antineunatic drugs; GC, glucocorticolds; IL, interleukin; JA, juvenile idiopathic antiniti; N, number, n.a., not applicable; tageed synthetic disease; modifying antinheumatic drugs; GC, glucocorticolds; IL, interleukin; JA, juvenile idiopathic antinit; N, number, n.a., not applicable; tageed synthetic disease; modifying antinheumatic drugs; GC, glucocorticolds; IL, interleukin; JA, juvenile idiopathic antinit; N, number, n.a., not applicable; tageed synthetic disease; modifying antinheumatic drugs; GC, glucocorticolds; IL, interleukin; JA, juvenile idiopathic antinit; N, number, n.a., not applicable; tageed synthetic disease; modifying antinheumatic drugs; GC, glucocorticolds; IL, interleukin; JA, juvenile idiopathic antinit; N, number, n.a., not applicable; tageed synthetic disease; modifying antinheumatic drugs; GC, glucocorticolds; IL, interleukin; JA, juvenile idiopathic antinit; N, number, n.a., not applicable; tageed synthetic disease; modifying antinheumatic drugs; GC, glucocorticolds; IL, interleukin; JA, juvenile idiopathic antinit; N, number, n.a., not applicable; tageed synthetic drugs; GC, glucocorticolds; IL, interleukin; JA, juvenile idiopathic antinit; SL, applicable; tageed synthetic drugs; GC, glucocorticolds; GC, glucocorticolds; GC, glucocorticolds; GC, glucocorticolds; GC, glucocor	atient numbers may thus be rounded. El ases; CVD, cardiovascular duisease; DM/	ffects significant at level $\alpha$ =0.0 ARD, disease-modifying antirhe	35 are marked in bold. Patients wer sumatic drugs; GC, glucocorticoids;	e excluded from a particular analysis if t. IL, interleukin; JIA, juvenile idiopathic an	he medication they re thritis; N, number; n.a	ceived provided ≤ ., not applicable;	20 patients for that analysis o. tsDMARD, targeted synthetic di	r if there were no de: lisease-modifying ant	aths reported for tirheumatic drugs	that specific medication.

diseases and COVID-19. We found that moderate/high disease activity was significantly associated with COVID-19-related death, confirming recent recommendations regarding the importance of disease control in rheumatic diseases in the COVID-19 era.<sup>1</sup> Other factors associated with death were older age, male sex and the presence of comorbidities, which is consistent with reports from the general population.<sup>8</sup> Overall, compared with methotrexate monotherapy, most DMARDs were not associated with higher odds of death, although rituximab and sulfasalazine were notable exceptions. Prednisolone-equivalent dosages >10 mg/day and other immunosuppressive drugs (as opposed to immunomodulatory DMARDs) were also associated with COVID-19-related death.

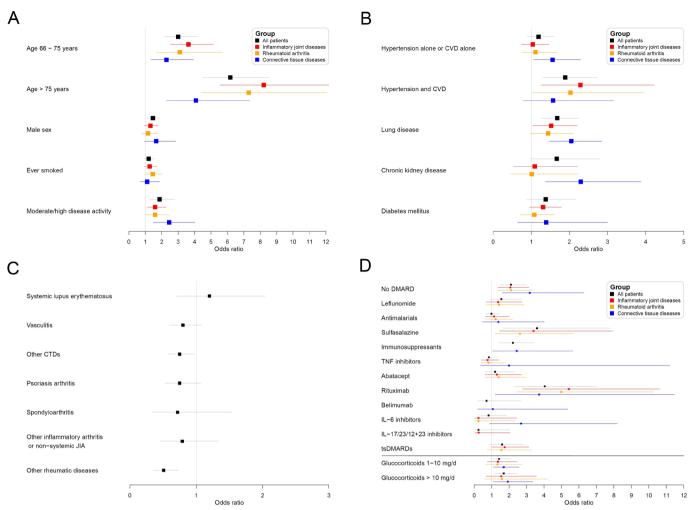
In this cohort of patients with underlying rheumatic diseases, the COVID-19-related death rate was 10.5%, clearly higher than that reported in the general population in most countries. However, this study was not designed to calculate a precise point estimate for mortality. Reporting biases and population-related factors, including COVID-19 testing rates, could explain this figure and, importantly, it should not be taken as an estimate of the overall death rate among patients with rheumatic diseases and COVID-19.

The association of rituximab with poorer COVID-19-related outcomes is a previously unreported finding outside of case reports. Rituximab binds to CD20 on the surface of B-cells, effectively depleting this cell type, and interferes with antibody development. Therefore, B-cell depletion could potentially compromise antiviral immunity, including the development of SARS-CoV-2 antibodies.<sup>19</sup> With our data, it was not possible to determine the exact timing of infection following rituximab infusion, although all patients were clinically judged by their rheumatologist to have been exposed to the immunological effects of the drug at the time of COVID-19 diagnosis. The association between rituximab and COVID-19-related death could have also been influenced by the typical coadministration of methylprednisolone with rituximab.

A finding that merits further research is the higher odds of death found with sulfasalazine treatment. This association has also been reported in results from an international registry of patients with inflammatory bowel disease and COVID-19, where sulfasalazine or 5-aminosalicylate (5-ASA) use was associated with severe COVID-19 (adjusted OR of 3.1 (1.3 to 7.7)).<sup>20</sup> This finding is surprising as sulfasalazine is usually considered to have a low immunosuppressive effect. Prior research supports an immune regulatory effect driven by sulfasalazine or its metabolite 5-ASA against other RNA viruses.<sup>21-24</sup> However, causal interpretation of the association between sulfasalazine and COVID-19-related death should not be made. The perceived low immunosuppressive effect of sulfasalazine may have led rheumatologists to prescribe preferentially sulfasalazine over methotrexate in patients who were perceived to be at higher risk, for example, patients with pulmonary disease, smoking or recurrent chest infections. In an observational study like ours, this could lead to unmeasured confounding. A salient difference in sulfasalazine users in our study was a higher proportion of current or former smokers, compared with non-users. In the stratified analyses for chronic lung disease, the association between death and sulfasalazine was significant in both subgroups with and without chronic lung disease, while in the stratified analyses for smoking, the association between death and sulfasalazine was limited to ever smokers, so the factor 'smoking' could potentially be an effect modifier. Another potential explanation for this finding could be the

Table 2 Continued

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**Figure 3** Results of the main logistic regression analysis. Shown are multivariable-adjusted ORs for the outcome COVID-19-related death with 95% Cls, assessing the association with (A) general patient characteristics, (B) comorbidities, (C) rheumatic disease diagnoses (RMD) and (D) rheumatic disease medications. ORs are shown for four groups: all patients (black), patients with inflammatory joint disease (red), patients with rheumatoid arthritis (orange), and patients with a connective tissue disease or vasculitis (blue). For (C), only ORs for all patients are shown. The reference categories are as follows: (A)  $\leq$ 65 years, females, never smoked, remission or low disease activity; (B) the non-presence of the specific comorbidities (for all effects); (C) rheumatoid arthritis (for all effects); (D) methotrexate monotherapy (for all effects except for glucocorticoids), no glucocorticoids (for glucocorticoid dosage groups). Patients receiving multiple csDMARDs or immunosuppressants (except glucocorticoids) were grouped according to the following hierarchy: immunosuppressants>sulfasalazine>antimalarials>leflunomide>methotrexate; patients receiving a b/tsDMARD were considered solely in the b/tsDMARD group; glucocorticoids were examined separately and categorised by prednisolone-equivalent dosage (1–10 mg/ day and >10 mg/day). bDMARD, biological disease-modifying anti-rheumatic drug; csDMARD, conventional synthetic disease-modifying anti-rheumatic drug; CTD, connective tissue diseases; CVD, cardiovascular disease; JIA, juvenile idiopathic arthritis; tsDMARD, targeted synthetic disease-modifying anti-rheumatic drug.

merging of sulfasalazine combination therapy (with other csDMARDs) with sulfasalazine monotherapy; however, the increased odds for death persisted in the sulfasalazine monotherapy group and was not driven by the combination treatment (data not shown).

Despite the large overall sample size, for some therapies (eg, IL-6 and IL-17/IL-23/IL-12+23 inhibitors) the number of users was low and no firm conclusions could be made. IL-6 inhibitors have been used to counteract the hyperin-flammatory state produced by COVID-19, with mostly disappointing randomised trial results.<sup>25 26</sup> Their efficacy is still being investigated in ongoing trials, but it is reassuring that they were not associated with COVID-19-related death in our analyses. Previous studies had shown an association between TNF inhibitors and a decreased risk of sepsis and mortality in patients with RA after serious infection

compared with csDMARDs.<sup>27 28</sup> We could not confirm such an association after stratification by disease and adjustment for disease activity. However, the data indicate that some associations may exist among patients diagnosed with IJD other than RA (a subgroup comprising predominantly patients with axial SpA and PsA), in whom male sex and diabetes mellitus were associated with a higher odds of death, and TNF inhibitor use was associated with a lower odds of death (univariable analysis, data not shown). Due to a small number of deceased patients in this subgroup with non-RA subtypes of IJD (n=37 deaths), these effects could not be assessed in a multivariable model and this should be investigated in the future when higher case numbers allow a more stable assessment.

This study has limitations. As a cross-sectional, casereporting registry, it may be subject to selection bias if more

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severe cases are more likely to come to the rheumatologists' attention and therefore to be reported. There is an absence of a population-based comparator, and we are unable to make comparisons between those with and without COVID-19. Moreover, we caution against interpreting our estimates causally. There is likely unmeasured confounding dependent on the particularities of health systems and case reporting differences. We tried to address this by limiting the research questions to those that could be answered with this dataset and by accounting for potential confounders in our analyses. The high number of variables compared with outcome events in the subgroup models may result in biased estimates.<sup>29 30</sup> However, the consistency between the main model and the sensitivity analyses (including using a lower number of variables) do not indicate an issue with overfitting.

In conclusion, people with rheumatic diseases with higher disease activity have higher odds of COVID-19-related death, highlighting the importance of disease control, preferably by managing DMARDs effectively without increasing glucocorticoids. Future studies should address the observed association of rituximab and sulfasalazine with poor outcomes. Finally, as in the general population, older age, male sex and/or the presence of comorbidities increase the odds of COVID-19-related death.

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# SUPPLEMENTARY TABLES

	Inflammatory j	oint diseases		Rheumatoid ar	thritis		Connective tiss	ue diseases ar	nd vasculitis
Parameter	Not deceased	Deceased	Total	Not deceased	Deceased	Total	Not deceased	Deceased	Total
Ν	2158	215	2373	1224	170	1394	1035	158	1193
General									
Age [years]	55.7 (14.3)	71.6 (11.7)	57.1 (14.8)	59.2 (13.9)	72.5 (11.1)	60.8 (14.3)	55.1 (16.3)	66.7 (17.4)	56.7 (16.9)
≤ 30 years	103 (4.8)	1 (0.5)	104 (4.4)	37 (3)	1 (0.6)	38 (2.7)	73 (7.1)	8 (5.1)	81 (6.8)
31 – 50 years	637 (29.5)	9 (4.2)	646 (27.2)	264 (21.6)	5 (2.9)	269 (19.3)	337 (32.6)	20 (12.7)	357 (29.9)
51 – 65 years	878 (40.7)	45 (20.9)	923 (38.9)	514 (42)	34 (20)	548 (39.3)	334 (32.3)	35 (22.2)	369 (30.9)
66 – 75 years	359 (16.6)	72 (33.5)	431 (18.2)	262 (21.4)	56 (32.9)	318 (22.8)	155 (15)	35 (22.2)	190 (15.9)
> 75 years	181 (8.4)	88 (40.9)	269 (11.3)	147 (12)	74 (43.5)	221 (15.9)	136 (13.1)	60 (38)	196 (16.4)
Male sex	709 (32.9)	82 (38.1)	791 (33.3)	292 (23.9)	55 (32.4)	347 (24.9)	240 (23.2)	67 (42.4)	307 (25.7)
Ever smoker	443 (24.1) (N=1839)	65 (40.1) <i>(N=162)</i>	508 (25.4) <i>(N=2001)</i>	260 (25.4) <i>(N=1025)</i>	56 (43.1) <i>(N=130)</i>	316 (27.4) (N=1155)	185 (20.6) <i>(N=897)</i>	36 (27.5) <i>(N=131)</i>	221 (21.5) <i>(N=1028)</i>
Regions									
African Region	10 (0.5)	1 (0.5)	11 (0.5)	7 (0.6)	1 (0.6)	8 (0.6)	2 (0.2)	1 (0.6)	3 (0.3)
Eastern Mediterranean Region	46 (2.1)	4 (1.9)	50 (2.1)	33 (2.7)	4 (2.4)	37 (2.7)	37 (3.6)	8 (5.1)	45 (3.8)
European Region	1405 (65.1)	157 (73)	1562	725 (59.2)	121 (71.2)	846 (60.7)	533 (51.5)	103 (65.2)	636 (53.3)
North American Region	595 (27.6)	44 (20.5)	639 (26.9)	392 (32)	38 (22.4)	430 (30.8)	397 (38.4)	35 (22.2)	432 (36.2)
South American Region	68 (3.2)	4 (1.9)	72 (3)	48 (3.9)	1 (0.6)	49 (3.5)	42 (4.1)	5 (3.2)	47 (3.9)
South-East Asian Region	8 (0.4)	0	8 (0.3)	3 (0.2)	0	3 (0.2)	2 (0.2)	0	2 (0.2)
Western Pacific Region	26 (1.2)	5 (2.3)	31 (1.3)	16 (1.3)	5 (2.9)	21 (1.5)	22 (2.1)	6 (3.8)	28 (2.3)
Inflammatory joint diseases									
Rheumatoid arthritis	1224 (56.7)	170 (79.1)	1394	1224 (100)	170 (100)	1394 (100)	53 (5.1)	9 (5.7)	62 (5.2)
Spondyloarthritis	416 (19.3)	15 (7)	431 (18.2)	1 (0.1)	0	1 (0.1)	2 (0.2)	0	2 (0.2)
Psoriatic arthritis	420 (19.5)	20 (9.3)	440 (18.5)	1 (0.1)	1 (0.6)	2 (0.1)	8 (0.8)	0	8 (0.7)

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JIA (poly, oligo, not systemic)	21 (1)	4 (1.9)	25 (1.1)	2 (0.2)	0	2 (0.1)	0	0	0
Other inflammatory arthritis	90 (4.2)	. ,			0	3 (0.2)	7 (0.7)	1 (0.6)	8 (0.7)
		8 (3.7)	98 (4.1)	3 (0.2)	-				
Total Inflammatory joint diseases	2158 (100)	215 (100)	2373 (100)	1224 (100)	170 (100)	1394 (100)	68 (6.6)	10 (6.3)	78 (6.5)
Connective tissue diseases / Vasculitis					- ()			/	
SLE	20 (0.9)	3 (1.4)	23 (1)	18 (1.5)	3 (1.8)	21 (1.5)	355 (34.3)	36 (22.8)	391 (32.8)
CTDs (other than SLE)	38 (1.8)	7 (3.3)	45 (1.9)	33 (2.7)	6 (3.5)	39 (2.8)	473 (45.7)	60 (38)	533 (44.7)
Vasculitis	14 (0.6)	1 (0.5)	15 (0.6)	6 (0.5)	1 (0.6)	7 (0.5)	258 (24.9)	68 (43)	326 (27.3)
Total CTD	68 (3.2)	10 (4.7)	78 (3.3)	53 (4.3)	9 (5.3)	62 (4.4)	1035 (100)	158 (100)	1193 (100)
Other RMDs									
Total	58 (2.7)	12 (5.6)	70 (2.9)	30 (2.5)	6 (3.5)	36 (2.6)	37 (3.6)	13 (8.2)	50 (4.2)
Disease activity	N=1563	N=168	N=1731	N=943	N=131	N=1074	N=822	N=118	N=940
Remission	488 (31.2)	54 (32.1)	542 (31.3)	291 (30.9)	40 (30.5)	331 (30.8)	256 (31.1)	32 (27.1)	288 (30.6)
Minimal/low disease activity	771 (49.3)	65 (38.7)	836 (48.3)	464 (49.2)	51 (38.9)	515 (48)	421 (51.2)	38 (32.2)	459 (48.8)
Moderate disease activity	264 (16.9)	38 (22.6)	302 (17.4)	161 (17.1)	30 (22.9)	191 (17.8)	115 (14)	25 (21.2)	140 (14.9)
Severe/high disease activity	40 (2.6)	11 (6.5)	51 (2.9)	27 (2.9)	10 (7.6)	37 (3.4)	30 (3.6)	23 (19.5)	53 (5.6)
Other outcomes									
Hospitalised	774 (38.1) <i>(N=2030)</i>	201 (95.3) ( <i>N=211</i> )	975 (43.5) <i>(N=2241)</i>	497 (43.3) (N=1148)	158 (95.2) <i>(N=166)</i>	655 (49.8) (N=1314)	522 (52.8) <i>(N=989)</i>	153 (98.1) <i>(N=156)</i>	675 (59) <i>(N=1145)</i>
Invasive ventilation	37 (2.1) (N=1771)	75 (43.9) (N=171)	112 (5.8) (N=1942)	22 (2.2) (N=993)	61 (44.5) <i>(N=137)</i>	83 (7.3) (N=1130)	28 (3.4) (N=815)	44 (38.3) (N=115)	72 (7.7) (N=930)
Comorbidities	N=2143	N=214	N=2357	N=1215	N=169	N=1384	N=1026	N=155	N=1181
Hypertension	658 (30.7)	116 (54.2)	774 (32.8)	423 (34.8)	90 (53.3)	513 (37.1)	385 (37.5)	87 (56.1)	472 (40)
Cardiovascular disease	183 (8.5)	71 (33.2)	254 (10.8)	126 (10.4)	54 (32)	180 (13)	121 (11.8)	43 (27.7)	164 (13.9)
Cerebrovascular disease	49 (2.3)	10 (4.7)	59 (2.5)	38 (3.1)	8 (4.7)	46 (3.3)	34 (3.3)	8 (5.2)	42 (3.6)
Chronic lung disease	332 (15.5)	78 (36.4)	410 (17.4)	231 (19)	65 (38.5)	296 (21.4)	234 (22.8)	58 (37.4)	292 (24.7)
Chronic kidney disease	83 (3.9)	27 (12.6)	110 (4.7)	61 (5)	21 (12.4)	82 (5.9)	85 (8.3)	42 (27.1)	127 (10.8)
Obesity (BMI ≥ 30)	370 (17.3)	38 (17.8)	408 (17.3)	205 (16.9)	27 (16)	232 (16.8)	155 (15.1)	19 (12.3)	174 (14.7)
Morbid obesity (BMI ≥ 40)	51 (2.4)	8 (3.7)	59 (2.5)	28 (2.3)	8 (4.7)	36 (2.6)	50 (4.9)	8 (5.2)	58 (4.9)
Diabetes	260 (12.1)	55 (25.7)	315 (13.4)	176 (14.5)	39 (23.1)	215 (15.5)	126 (12.3)	36 (23.2)	162 (13.7)

Cancer	98 (4.6)	23 (10.7)	121 (5.1)	68 (5.6)	18 (10.7)	86 (6.2)	61 (5.9)	20 (12.9)	81 (6.9)
Other comorbidities	509 (23.8)	73 (34.1)	582 (24.7)	216 (17.8)	48 (28.4)	264 (19.1)	230 (22.4)	45 (29.0)	275 (23.3)
Number of comorbities	1.2 (1.3)	2.5 (1.7)	1.4 (1.4)	1.3 (1.3)	2.3 (1.6)	1.4 (1.4)	1.5 (1.4)	2.5 (1.5)	1.6 (1.4)
No comorbidity	770 (35.9)	18 (8.4)	788 (33.4)	397 (32.7)	16 (9.5)	413 (29.8)	267 (26)	10 (6.5)	277 (23.5)
One comorbidity	639 (29.8)	50 (23.4)	689 (29.2)	374 (30.8)	39 (23.1)	413 (29.8)	357 (34.8)	31 (20)	388 (32.9)
Two comorbidities	390 (18.2)	63 (29.4)	453 (19.2)	238 (19.6)	52 (30.8)	290 (21)	182 (17.7)	43 (27.7)	225 (19.1)
≥ 3 comorbidites	344 (16.1)	83 (38.8)	427 (18.1)	206 (17)	62 (36.7)	268 (19.4)	220 (21.4)	71 (45.8)	291 (24.6)
DMARD therapies									
csDMARDs monotherapy	487 (22.6)	51 (23.7)	538 (22.7)	351 (28.7)	43 (25.3)	394 (28.3)	91 (8.8)	10 (6.3)	101 (8.5)
csDMARDs combination therapy	611 (28.3)	53 (24.7)	664 (28)	440 (35.9)	51 (30)	491 (35.2)	92 (8.9)	12 (7.6)	104 (8.7)
Methotrexate monotherapy	430 (19.9)	41 (19.1)	471 (19.8)	306 (25)	34 (20)	340 (24.4)	88 (8.5)	6 (3.8)	94 (7.9)
Methotrexate combination therapy	531 (24.6)	45 (20.9)	576 (24.3)	372 (30.4)	44 (25.9)	416 (29.8)	87 (8.4)	9 (5.7)	96 (8)
Leflunomide monotherapy	57 (2.6)	10 (4.7)	67 (2.8)	45 (3.7)	9 (5.3)	54 (3.9)	3 (0.3)	4 (2.5)	7 (0.6)
Leflunomide combination therapy	114 (5.3)	9 (4.2)	123 (5.2)	98 (8)	8 (4.7)	106 (7.6)	7 (0.7)	3 (1.9)	10 (0.8)
Sulfasalazine monotherapy	48 (2.2)	16 (7.4)	64 (2.7)	22 (1.8)	8 (4.7)	30 (2.2)	3 (0.3)	1 (0.6)	4 (0.3)
Sulfasalazine combination therapy	124 (5.7)	24 (11.2)	148 (6.2)	76 (6.2)	20 (11.8)	96 (6.9)	7 (0.7)	2 (1.3)	9 (0.8)
Antimalarial monotherapy	74 (3.4)	8 (3.7)	82 (3.5)	56 (4.6)	8 (4.7)	64 (4.6)	212 (20.5)	9 (5.7)	221 (18.5)
Antimalarial combination therapy	175 (8.1)	23 (10.7)	198 (8.3)	156 (12.7)	23 (13.5)	179 (12.8)	169 (16.3)	17 (10.8)	186 (15.6)
Immunosuppressants monotherapy	9 (0.4)	3 (1.4)	12 (0.5)	7 (0.6)	3 (1.8)	10 (0.7)	132 (12.8)	21 (13.3)	153 (12.8)
Immunosuppressants combination therapy	20 (0.9)	1 (0.5)	21 (0.9)	16 (1.3)		16 (1.1)	127 (12.3)	18 (11.4)	145 (12.2)
Mycophenolate mofetil monotherapy	3 (0.1)	1 (0.5)	4 (0.2)	2 (0.2)	1 (0.6)	3 (0.2)	64 (6.2)	13 (8.2)	77 (6.5)
Mycophenolate mofetil combination therapy	3 (0.1)	0	3 (0.1)	3 (0.2)	0	3 (0.2)	77 (7.4)	14 (8.9)	91 (7.6)
Azathioprine monotherapy	4 (0.2)	1 (0.5)	5 (0.2)	3 (0.2)	1 (0.6)	4 (0.3)	54 (5.2)	4 (2.5)	58 (4.9)
Azathioprine combi	12 (0.6)	1 (0.5)	13 (0.5)	9 (0.7)	0	9 (0.6)	39 (3.8)	2 (1.3)	41 (3.4)
Cyclophosphamide monotherapy	0	0	0	0	0	0	9 (0.9)	3 (1.9)	12 (1)
Cyclophosphamide combination	0	0	0	0	0	0	5 (0.5)	4 (2.5)	9 (0.8)
Tacrolimus monotherapy	0	1 (0.5)	1 (0)	0	1 (0.6)	1 (0.1)	4 (0.4)	1 (0.6)	5 (0.4)
Tacrolimus combination therapy	2 (0.1)	0	2 (0.1)	1 (0.1)	0	1 (0.1)	8 (0.8)	0	8 (0.7)
Cyclosporin monotherapy	2 (0.1)	0	2 (0.1)	2 (0.2)	0	2 (0.1)	1 (0.1)	0	1 (0.1)

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Cyclosporin combination therapy	4 (0.2)	0	4 (0.2)	4 (0.3)	0	4 (0.3)	8 (0.8)	1 (0.6)	9 (0.8)
bDMARDs monotherapy	581 (26.9)	29 (13.5)	610 (25.7)	163 (13.3)	19 (11.2)	182 (13.1)	81 ( 7.8)	18 (11.4)	99 (8.3)
bDMARD combination therapy	478 (22.2)	31 (14.4)	509 (21.5)	308 (25.2)	29 (17.1)	337 (24.2)	91 (8.8)	15 (9.5)	106 (8.9)
TNF inhibitors monotherapy	417 (19.3)	12 (5.6)	429 (18.1)	88 (7.2)	4 (2.4)	92 (6.6)	15 (1.4)	1 (0.6)	16 (1.3)
TNF inhibitors combination therapy	322 (14.9)	14 (6.5)	336 (14.2)	189 (15.4)	12 (7.1)	201 (14.4)	20 (1.9)	3 (1.9)	23 (1.9)
Abatacept monotherapy	25 (1.2)	4 (1.9)	29 (1.2)	20 (1.6)	4 (2.4)	24 (1.7)	2 (0.2)	0	2 (0.2)
Abatacept combination therapy	43 (2)	5 (2.3)	48 (2)	41 (3.3)	5 (2.9)	46 (3.3)	6 (0.6)	0	6 (0.5)
B-cell-targeted bDMARDs monotherapy	22 (1)	11 (5.1)	33 (1.4)	20 (1.6)	10 (5.9)	30 (2.2)	45 (4.3)	15 (9.5)	60 (5)
B-cell-targeted bDMARDs combination therapy	49 (2.3)	11 (5.1)	60 (2.5)	48 (3.9)	11 (6.5)	59 (4.2)	62 (6)	8 (5.1)	70 (5.9)
Rituximab monotherapy	22 (1)	11 (5.1)	33 (1.4)	20 (1.6)	10 (5.9)	30 (2.2)	40 (3.9)	15 (9.5)	55 (4.6)
Rituximab combi	47 (2.2)	11 (5.1)	58 (2.4)	46 (3.8)	11 (6.5)	57 (4.1)	42 (4.1)	7 (4.4)	49 (4.1)
Belimumab monotherapy	0	0	0	0	0	0	5 (0.5)	0	5 (0.4)
Belimumab combination therapy	2 (0.1)	0	2 (0.1)	2 (0.2)	0	2 (0.1)	21 (2)	1 (0.6)	22 (1.8)
IL-6 inhibitors monotherapy	36 (1.7)	1 (0.5)	37 (1.6)	33 (2.7)	1 (0.6)	34 (2.4)	18 (1.7)	2 (1.3)	20 (1.7)
IL-6 inhibitors combination therapy	31 (1.4)	0	31 (1.3)	29 (2.4)	0	29 (2.1)	1 (0.1)	2 (1.3)	3 (0.3)
IL-1 inhibitors monotherapy	1 (0)	0	1 (0)	0	0	0	1 (0.1)	0	1 (0.1)
IL-1 inhibitors combination therapy	3 (0.1)	1 (0.5)	4 (0.2)	3 (0.2)	1 (0.6)	4 (0.3)	1 (0.1)	2 (1.3)	3 (0.3)
IL-17, Il-23, Il-12/23 inhibitors monotherapy	78 (3.6)	1 (0.5)	79 (3.3)	1 (0.1)	0	1 (0.1)	0	0	0
IL-17, II-23, II-12/23 inhibitors combination therapy	34 (1.6)	0	34 (1.4)	1 (0.1)	0	1 (0.1)	1 (0.1)	0	1 (0.1)
tsDMARDs monotherapy	61 (2.8)	5 (2.3)	66 (2.8)	47 (3.8)	4 (2.4)	51 (3.7)	0	0	0
tsDMARDs (*) combination therapy	68 (3.2)	10 (4.7)	78 (3.3)	59 (4.8)	9 (5.3)	68 (4.9)	6 (0.6)	2 (1.3)	8 (0.7)
JAK inhibitors monotherapy	54 (2.5)	4 (1.9)	58 (2.4)	47 (3.8)	4 (2.4)	51 (3.7)	0	0	0
JAK inhibitors combination therapy	65 (3)	9 (4.2)	74 (3.1)	59 (4.8)	9 (5.3)	68 (4.9)	5 (0.5)	2 (1.3)	7 (0.6)
Apremilast monotherapy	7 (0.3)	1 (0.5)	8 (0.3)	0	0	0	0	0	0
Apremilast combination therapy	3 (0.1)	1 (0.5)	4 (0.2)	0	0	0	0	0	0
No DMARD therapies	201 (9.3)	38 (17.7)	239 (10.1)	85 (6.9)	25 (14.7)	110 (7.9)	286 (27.6)	67 (42.4)	353 (29.6)
Further therapies									
Glucocorticoids (#)	521 (24.5) <i>(N=2130)</i>	101 (48.6) <i>(N=208)</i>	622 (26.6) <i>(N=2338)</i>	417 (34.6) <i>(N=1205)</i>	90 (54.2) <i>(N=166)</i>	507 (37) <i>(N=1371)</i>	501 (48.8) <i>(N=1027)</i>	115 (74.2) <i>(N=155)</i>	616 (52.1) <i>(N=1182)</i>

0 mg/d < Clussesstissids <= 10mg/d	448 (21.3)	83 (40.9)	531 (23)	366 (30.8)	74 (46)	440 (32.6)	373 (37.3)	68 (47.6)	441 (38.6)
0 mg/d < Glucocorticoids <= 10mg/d	(N=2108)	(N=203)	(N=2311)	(N=1190)	(N=161)	(N=1351)	(N=999)	(N=143)	(N=1142)
Glucocorticoids > 10 mg/d	48 (2.3)	12 (5.9)	60 (2.6)	34 (2.9)	10 (6.2)	44 (3.3)	100 (10)	35 (24.5)	135 (11.8)
Glucocol ticolus > 10 llig/u	(N=2108)	(N=203)	(N=2311)	(N=1190)	(N=161)	(N=1351)	(N=999)	(N=143)	(N=1142)
NSAID	484 (24.2)	26 (13.8)	510 (23.3)	240 (21.3)	22 (14.8)	262 (20.5)	112 (11.6)	12 (8.6)	124 (11.2)
NSAID	(N=2002)	(N=188)	(N=2190)	(N=1129)	(N=149)	(N=1278)	(N=966)	(N=140)	(N=1106)

Data are N (column %) for categorical variables or mean (SD) for continuous variables. Table includes all patients with a non-missing outcome and non-missing values for age, sex and disease modifying anti-rheumatic drugs (DMARDs) (101 patients excluded). Data refers to patients with non-missing values for the respective variable, total N for patients with non-missing values is given in parentheses for variables with missing values. (\*) Includes one patient on a study medication (Lenabasum). (#) Includes patients with a missing glucocorticoid dose.

bDMARD, biologic disease modifying antirheumatic drugs; BMI, body mass index; csDMARD, conventional synthetic disease modifying antirheumatic drugs; CTD, connective tissue diseases; DMARD, disease modifying antirheumatic drugs; IL, interleukin; JAK, Janus kinase; JIA, juvenile idiopathic arthritis; N, number; NSAID, non-steroidal anti-inflammatory drugs; SLE, systemic lupus erythematosus; TNF; tumour necrosis factor; tsDMARD, targeted synthetic disease modifying antirheumatic drugs.

Parameter	USA	France	UK	Italy	Spain	Germany	Total
N	1005	793	435	315	247	198	2993
General							
Age [years]	55.2 (15.1)	56.2 (16.3)	61.2 (16.4)	61.9 (13.7)	59.7 (15.7)	58.2 (13.8)	57.6 (15.6)
< 30 years	66 (6.6)	39 (4.9)	16 (3.7)	6 (1.9)	10 (4)	6 (3)	143 (4.8)
30 – 49 years	300 (29.9)	268 (33.8)	97 (22.3)	58 (18.4)	56 (22.7)	48 (24.2)	268 (33.8)
50 – 65 years	390 (38.8)	248 (31.3)	131 (30.1)	107 (34)	92 (37.2)	93 (47)	248 (31.3)
66 - 75 years	146 (14.5)	128 (16.1)	92 (21.1)	93 (29.5)	43 (17.4)	26 (13.1)	528 (17.6)
> 75 years	103 (10.2)	110 (13.9)	99 (22.8)	51 (16.2)	46 (18.6)	25 (12.6)	434 (14.5)
Male sex	241 (24)	272 (34.3)	169 (38.9)	107 (34)	95 (38.5)	74 (37.4)	958 (32)
Ever smoker	261 (27.3) (N=956)	80 (10.1) <i>(N=793)</i>	132 (45.2) <i>(N=292)</i>	86 (29.5) <i>(N=292)</i>	60 (27.5) <i>(N=218)</i>	14 (77.8) <i>(N=18)</i>	633 (24.6) <i>(N=2569)</i>
Inflammatory joint diseases							
Rheumatoid arthritis	388 (38.6)	247 (31.2)	187 (43.0)	105 (33.3)	88 (35.6)	99 (50.0)	1114 (37.2)
Spondyloarthritis	47 (4.7)	193 (24.3)	29 (6.7)	24 (7.6)	32 (13)	19 (9.6)	344 (11.5)
Psoriatic arthritis	101 (10)	74 (9.3)	61 (14)	64 (20.3)	31 (12.6)	32 (16.2)	363 (12.1)
JIA (poly, oligo, not systemic)	7 (0.7)	2 (0.3)	2 (0.5)	2 (0.6)	3 (1.2)	0	16 (0.5)
Other inflammatory arthritis	41 (4.1)	15 (1.9)	28 (6.4)	3 (1)	3 (1.2)	0	90 (3)
Total IJD	577 (57.4)	531 (67)	305 (70.1)	198 (62.9)	157 (63.6)	150 (75.8)	1918 (64.1)
Connective tissue diseases / Vasculitis							
Systemic lupus erythematosus	167 (16.6)	50 (6.3)	28 (6.4)	18 (5.7)	27 (10.9)	9 (4.5)	299 (10)
CTDs (other than SLE)	186 (18.5)	90 (11.3)	38 (8.7)	53 (16.8)	44 (17.8)	19 (9.6)	430 (14.4)
Vasculitis	67 (6.7)	71 (9)	51 (11.7)	44 (14)	22 (8.9)	18 (9.1)	273 (9.1)
Total CTD	394 (39.2)	211 (26.6)	111 (25.5)	114 (36.2)	85 (34.4)	43 (21.7)	958 (32)
Other rheumatic diseases							
Total	132 (13.1)	52 (6.6)	53 (12.2)	8 (2.5)	20 (8.1)	13 (6.6)	278 (9.3)
Disease activity (DA)	N=950		N=364	N=315	242	N=181	N=2052
Remission	211 (22.2)	N/A	109 (29.9)	93 (29.5)	113 (46.7)	102 (56.4)	628 (30.6)
Minimal/low DA	521 (54.8)	N/A	172 (47.3)	160 (50.8)	108 (44.6)	53 (29.3)	1014 (49.4)
Moderate DA	185 (19.5)	N/A	69 (19)	53 (16.8)	17 (7)	19 (10.5)	343 (16.7)
Severe/high DA	33 (3.5)	N/A	14 (3.8)	9 (2.9)	4 (1.7)	7 (3.9)	67 (3.3)
Other outcomes							
Death	70 (7.0)	62 (7.8)	91 (20.9)	53 (16.8)	21 (8 5)	15 (7.6)	312 (10.4)
Hospitalised	357 (39.1) (N=914)	334 (42.1) (N=793)	91 (20.9) 275 (65.8) (N=418)	201 (64.2) (N=313)	21 (8.5) 133 (55.6) (N=239)	60 (30.6) (N=196)	1360 (47.3) (N=2873)
Invasive ventilation	64 (7.9) ( <i>N=807</i> )	N/A	28 (7.5) (N=371)	23 (7.5) (N=308)	7 (3) (N=231)	15 (7.7) (N=196)	137 (5.8) (N=1913)

Comorbidities	N=1000	N=791	N=434	N=300	N=247	N=192	N=2964
Hypertension	399 (39.9)	220 (27.8)	140 (32.3)	147 (49)	103 (41.7)	72 (36.4)	1081 (36.4)
Cardiovascular disease	112 (11.2)	76 (9.6)	72 (16.6)	72 (24)	18 (7.3)	27 (13.6)	377 (12.7)
Cerebrovascular disease	27 (2.7)	28 (3.5)	17 (3.9)	14 (4.7)	6 (2.4)	0	92 (3.1)
Chronic lung disease	231 (23.1)	113 (14.3)	108 (24.9)	75 (25)	54 (21.9)	32 (16.2)	613 (20.6)
Chronic kidney disease	85 (8.5)	46 (5.8)	28 (6.5)	27 (9)	11 (4.5)	15 (7.6)	212 (7.1)
Obesity (BMI ≥ 30)	244 (24.4)	138 (17.4)	39 (9)	47 (15.7)	31 (12.6)	30 (15.2)	529 (17.8)
Morbid obesity (BMI $\ge$ 40)	87 (8.7)	0	11 (2.5)	7 (2.3)	2 (0.8)	7 (3.5)	114 (3.8)
Diabetes	171 (17.1)	74 (9.4)	73 (16.8)	42 (14)	31 (12.6)	17 (8.6)	408 (13.7)
Cancer	68 (6.8)	36 (4.6)	19 (4.4)	34 (11.3)	23 (9.3)	7 (3.5)	187 (6.3)
Other comorbidities	213 (21.3)	159 (20.1)	151 (34.8)	145 (48.3)	67 (27.1)	53 (27.6)	788 (36.2)
Number of comorbities	1.7 (1.5)	1.1 (1.1)	1.6 (1.4)	2.3 (1.8)	1.5 (1.4)	1.3 (1.3)	1.5 (1.5)
No comorbidity	250 (25)	277 (35)	105 (24.2)	44 (14.7)	70 (28.3)	67 (33.8)	813 (27.4)
One comorbidity	275 (27.5)	276 (34.9)	136 (31.3)	79 (26.3)	77 (31.2)	58 (29.3)	901 (30.3)
Two comorbidities	211 (21.1)	143 (18.1)	98 (22.6)	57 (19)	51 (20.6)	39 (19.7)	599 (20.2)
≥ 3 comorbidites	264 (26.4)	95 (12)	95 (21.9)	120 (40)	49 (19.8)	34 (17.2)	657 (22.1)
							····)
DMARD therapies							
csDMARDs mono	106 (10.5)	159 (20.1)	91 (20.9)	66 (21)	51 (20.6)	52 (26.3)	525 (17.5)
csDMARDs combi	208 (20.7)	164 (20.7)	84 (19.3)	58 (18.4)	40 (16.2)	33 (16.7)	587 (19.6)
Methotrexate mono	88 (8.8)	151 (19)	83 (19.1)	55 (17.5)	45 (18.2)	47 (23.7)	469 (15.7)
Methotrexate combi	174 (17.3)	142 (17.9)	78 (17.9)	52 (16.5)	36 (14.6)	33 (16.7)	515 (17.2)
Leflunomide mono	18 (1.8)	8 (1)	8 (1.8)	11 (3.5)	6 (2.4)	5 (2.5)	56 (1.9)
Leflunomide combi	40 (4)	22 (2.8)	11 (2.5)	6 (1.9)	7 (2.8)	3 (1.5)	89 (3)
Sulfasalazine mono	7 (0.7)	3 (0.4)	21 (4.8)	4 (1.3)	6 (2.4)	7 (3.5)	48 (1.6)
Sulfasalazine combi	33 (3.3)	6 (0.8)	47 (10.8)	10 (3.2)	10 (4)	2 (1)	108 (3.6)
Antimalarial mono	120 (11.9)	32 (4)	20 (4.6)	28 (8.9)	15 (6.1)	8 (4)	223 (7.5)
Antimalarial combi	132 (13.1)	34 (4.3)	48 (11)	31 (9.8)	18 (7.3)	10 (5.1)	273 (9.1)
Immunosuppressants mono	66 (6.6)	14 (1.8)	23 (5.3)	17 (5.4)	9 (3.6)	10 (5.1)	139 (4.6)
Immunosuppressants combi	75 (7.5)	14 (1.8)	17 (3.9)	13 (4.1)	6 (2.4)	2 (1)	127 (4.2)
Mycophenolate mofetil mono	42 (4.2)	8 (1)	11 (2.5)	6 (1.9)	3 (1.2)	2 (1)	72 (2.4)
Mycophenolate mofetil combi	44 (4.4)	9 (1.1)	13 (3)	6 (1.9)	3 (1.2)	2 (1)	77 (2.6)
Azathioprine mono	17 (1.7)	6 (0.8)	9 (2.1)	8 (2.5)	5 (2)	7 (3.5)	52 (1.7)
Azathioprine combi	24 (2.4)	5 (0.6)	3 (0.7)	4 (1.3)	3 (1.2)	0	39 (1.3)
Cyclophosph. mono	2 (0.2)	0	3 (0.7)	2 (0.6)	1 (0.4)	1 (0.5)	9 (0.3)
Cyclophosph. combi	6 (0.6)	0	1 (0.2)	1 (0.3)	0	0	8 (0.3)
Tacrolimus mono	5 (0.5)	0	0	0	0	0	5 (0.2)
Tacrolimus combi	9 (0.9)	0	0	0	1 (0.4)	0	10 (0.3)
Cyclosporin mono	0	0	0	1 (0.3)	0	0	1 (0)
Cyclosporin combi	1 (0.1)	0	1 (0.2)	4 (1.3)	0	0	6 (0.2)
bDMARDs monotherapy	174 (17.3)	228 (28.8)	53 (12.2)	63 (20)	44 ( 17.8)	43 ( 21.7)	605 ( 20.2)
bDMARDs combination therapy	178 (17.7)	144 (18.2)	67 (15.4)	48 (15.2)	34 (13.8)	29 (14.7)	500 (16.7)
TNF inhibitors mono	100 (10)	145 (18.3)	29 (6.7)	45 (14.3)	27 (10.9)	26 (13.1)	372 (12.4)
TNF inhibitors combi	106 (10.5)	84 (10.6)	39 (9)	28 (8.9)	19 (7.7)	13 (6.6)	289 (9.7)
Abatacept mono	14 (1.4)	6 (0.8)	1 (0.2)	5 (1.6)	0	0	26 (0.9)
Abatacept combi	20 (2)	13 (1.6)	3 (0.7)	2 (0.6)	3 (1.2)	3 (1.5)	44 (1.5)
B-cell affecting bDMARDs mono	29 (2.9)	26 (3.3)	10 (2.3)	1 (0.3)	8 (3.2)	3 (1.5)	77 (2.6)

B-cell affecting bDMARDs combi	37 (3.7)	22 (2.8)	20 (4.6)	9 (2.9)	8 (3.2)	10 (5.1)	106 (3.5)
Rituximab mono	26 (2.6)	26 (3.3)	10 (2.3)	1 (0.3)	7 (2.8)	3 (1.5)	73 (2.4)
Rituximab combi	24 (2.4)	20 (2.5)	19 (4.4)	7 (2.2)	8 (3.2)	8 (4)	86 (2.9)
Belimumab mono	3 (0.3)	0	0	0	1 (0.4)	0	4 (0.1)
Belimumab combi	13 (1.3)	2 (0.3)	1 (0.2)	2 (0.6)	1 (0.4)	2 (1)	21 (0.7)
IL-6 inhibitors mono	11 (1.1)	18 (2.3)	3 (0.7)	4 (1.3)	3 (1.2)	6 (3)	45 (1.5)
IL-6 inhibitors combi	12 (1.2)	11 (1.4)	2 (0.5)	3 (1)	3 (1.2)	0	31 (1)
IL-1 inhibitors mono	0	9 (1.1)	1 (0.2)	0	1 (0.4)	0	11 (0.4)
IL-1 inhibitors combi	2 (0.2)	0	1 (0.2)	2 (0.6)	0	0	5 (0.2)
Other IL inhibitors ( IL-17, Il-23, Il-12/23 inh.) mono	19 (1.9)	24 (3)	9 (2.1)	7 (2.2)	5 (2)	8 (4)	72 (2.4)
Other IL inhibitors ( IL-17, Il-23, Il-12/23 inh.) combi	3 (0.3)	14 (1.8)	2 (0.5)	6 (1.9)	1 (0.4)	3 (1.5)	29 (1)
tsDMARDs mono	32 (3.2)	10 (1.3)	7 (1.6)	4 (1.3)	3 (1.2)	4 (2)	60 (2)
tsDMARDs (*) combi	43 (4.3)	15 (1.9)	4 (0.9)	9 (2.9)	3 (1.2)	3 (1.5)	77 (2.6)
JAK inhibitors mono	26 (2.6)	10 (1.3)	7 (1.6)	4 (1.3)	2 (0.8)	4 (2)	53 (1.8)
JAK inhibitors combi	40 (4)	15 (1.9)	3 (0.7)	8 (2.5)	3 (1.2)	3 (1.5)	72 (2.4)
Apremilast mono	6 (0.6)	0	0	0	1 (0.4)	0	7 (0.2)
Apremilast combi	2 (0.2)	0	1 (0.2)	1 (0.3)	0	0	4 (0.1)
No DMARD therapies	192 (19.1)	161 (20.3)	98 (22.5)	52 (16.5)	64 (25.9)	35 (17.7)	602 (20.1)
Further therapies							
Glucocorticoids (#)	283 (28.6) (N=990)	253 (31.9) <i>(N=793)</i>	128 (30) (N=427)	165 (52.4) <i>(N=315)</i>	98 (40.3) (N=243)	82 (41.6) (N=197)	1009 (34) <i>(N=2965)</i>
0 mg/d < GC <= 10mg/d	226 (22.9) (N=985)	205 (25.9) <i>(N=791)</i>	87 (20.5) (N=425)	135 (43.7) <i>(N=309)</i>	64 (30.2) (N=212)	74 (37.8) <i>(N=196)</i>	791 (27.1) <i>(N=2918)</i>
GC > 10 mg/d	52 (5.3) <i>(N=985)</i>	45 (5.7) <i>(N=791)</i>	37 (8.7) (N=425)	24 (7.8) (N=309)	3 (1.4) (N=212)	6 (3.1) (N=196)	167 (5.7) <i>(N=2918)</i>
NSAID	209 (22.9) (N=914)	85 (10.7) <i>(N=793)</i>	51 (13.3) <i>(N=385)</i>	53 (18.6) <i>(N=285)</i>	52 (21.9) <i>(N=21.9)</i>	36 (19.7) <i>(N=19.7)</i>	486 (17.4) <i>(N=2798)</i>

Data are N (column %) for categorical variables or mean (SD) for continuous variables. Table includes all patients with a non-missing outcome and nonmissing values for age, sex and disease modifying anti-rheumatic drugs (DMARDs) (101 patients excluded). Data refers to patients with non-missing values for the respective variable, total N for patients with non-missing values is given in parentheses for variables with missing values. (\*) Includes one patient on a study medication (Lenabasum). (#) Includes patients with a missing glucocorticoid dose.

bDMARD, biologic disease modifying antirheumatic drugs; BMI, body mass index; csDMARD, conventional synthetic disease modifying antirheumatic drugs; combi, combination therapy; CTD, connective tissue diseases; DA, disease activity; DMARD, disease modifying antirheumatic drugs; GC, glucocorticoids; IL, interleukin; JAK, Janus kinase; JIA, juvenile idiopathic arthritis; mono, monotherapy; N, number; NSAID, non-steroidal antiinflammatory drugs; SLE, systemic lupus erythematosus; TNF; tumour necrosis factor; tsDMARD, targeted synthetic disease modifying antirheumatic drugs.

Parameter	мтх	LEF	ANTI- MALARIALS	SSZ	IMMUNO SUPPR.	TNFi	ABA	RTX	IL-6i	IL-17/23/ 12+23i	JAKi	No DMARDs	TOTAL
N	1237	203	665	222	338	804	83	193	90	116	134	739	3729
General													
Age [years]	58.3 (14.5)	59.5 (12.3)	53.3 (15.2)	59.0 (14.8)	50.1 (15.8)	51.1 (13.7)	59.0 (15.0)	56.2 (15.1)	57.7 (16.4)	50.1 (11.3)	58.3 (13.3)	62.8 (16.6)	57.0 (15.7)
Male sex	390 (31.5)	44 (21.7)	117 (17.6)	82 (36.9)	93 (27.5)	312 (38.8)	24 (28.9)	60 (31.1)	21 (23.3)	45 (38.8)	18 (13.4)	280 (37.9)	1195 (32)
Ever smoker	244 (23.4) (N=1044)	40 (24.7) (N=162)	129 (22.2) (N=582)	66 (37.3) (N=177)	54 (18.6) <i>(N=290)</i>	167 (23.6) <i>(N=709)</i>	20 (27.8) (N=72)	38 (23.3) (N=163)	10 (12.5) <i>(N=80)</i>	21 (20.8) (N=101)	28 (22.6) (N=124)	181 (29.8) (N=607)	776 (24.5) (N=3164)
Inflammatory joint diseases													
Rheumatoid arthritis	756 (61.1)	160 (78.8)	243 (36.5)	126 (56.8)	26 (7.7)	293 (36.4)	70 (84.3)	87 (45.1)	63 (70)	2 (1.7)	119 (88.8)	110 (14.9)	1394 (37.4)
Spondyloartrhitis	74 (6)	4 (2)	6 (0.9)	35 (15.8)	6 (1.8)	271 (33.7)	2 (2.4)	0	2 (2.2)	43 (37.1)	4 (3)	59 (8)	431 (11.6)
Psoriatic arthritis	177 (14.3)	23 (11.3)	8 (1.2)	38 (17.1)	1 (0.3)	182 (22.6)	4 (4.8)	1 (0.5)	0	70 (60.3)	9 (6.7)	38 (5.1)	440 (11.8)
Total IJD	1047 (84.6)	190 (93.6)	280 (42.1)	212 (95.5)	33 (9.8)	765 (95.1)	77 (92.8)	91 (47.2)	68 (75.6)	113 (97.4)	132 (98.5)	239 (32.3)	2373 (63.6)
Connective tissue diseases/ Vasculitis													
SLE	49 (4)	7 (3.4)	257 (38.6)	3 (1.4)	127 (37.6)	6 (0.7)	2 (2.4)	15 (7.8)	1 (1.1)	1 (0.9)	5 (3.7)	48 (6.5)	391 (10.5)
CTDs (other than SLE)	104 (8.4)	4 (2)	171 (25.7)	5 (2.3)	134 (39.6)	19 (2.4)	6 (7.2)	52 (26.9)	1 (1.1)	0	3 (2.2)	156 (21.1)	533 (14.3)
Vasculitis	44 (3.6)	7 (3.4)	7 (1.1)	5 (2.3)	53 (15.7)	14 (1.7)	0	39 (20.2)	21 (23.3)	0	0	161 (21.8)	326 (8.7)
Total CTD	190 (15.4)	17 (8.4)	407 (61.2)	13 (5.9)	294 (87)	39 (4.9)	8 (9.6)	104 (53.9)	23 (25.6)	1 (0.9)	7 (5.2)	353 (47.8)	1193 (32)
Other RMDs													
Total	60 (4.9)	7 (3.4)	33 (5)	17 (7.7)	49 (14.5)	33 (4.1)	3 (3.6)	20 (10.4)	3 (3.3)	3 (2.6)	6 (4.5)	173 (23.4)	356 (9.5)
Disease activity	N=894	N=162	N=574	N=196	N=300	N=547	N=62	N=142	N=61	N=73	N=105	N=517	N=2758
Remission	307 (34.3)	40 (24.7)	146 (25.4)	50 (25.5)	66 (22)	184 (33.6)	14 (22.6)	36 (25.4)	16 (26.2)	20 (27.4)	19 (18.1)	215 (41.6)	893 (32.4)
Minimal/low	413 (46.2)	84 (51.9)	310 (54)	100 (51)	138 (46)	265 (48.4)	32 (51.6)	64 (45.1)	25 (41)	33 (45.2)	56 (53.3)	211 (40.8)	1309 (47.5)
Moderate DA	157 (17.6)	31 (19.1)	91 (15.9)	38 (19.4)	71 (23.7)	89 (16.3)	10 (16.1)	26 (18.3)	16 (26.2)	19 (26)	26 (24.8)	56 (10.8)	448 (16.2)
Severe/high DA	17 (1.9)	7 (4.3)	27 (4.7)	8 (4.1)	25 (8.3)	9 (1.6)	6 (9.7)	16 (11.3)	4 (6.6)	1 (1.4)	4 (3.8)	35 (6.8)	108 (3.9)

Other outcomes													
Hospitalised	541 (46.2) (N=1170)	103 (52.8) (N=195)	298 (47.1) (N=633)	126 (62.4) (N=202)	197 (60.4) (N=326)	207 (27.3) (N=758)	33 (42.9) <i>(N=77)</i>	127 (71.3) (N=178)	26 (29.9) <i>(N=87)</i>	37 (34.3) (N=108)	55 (43.7) (N=126)	442 (61.7) (N=716)	1739 (49) <i>(N=3546)</i>
Death	99 (8)	22 (10.8)	56 (8.4)	42 (18.9)	46 (13.6)	30 (3.7)	9 (10.8)	42 (21.8)	5 (5.6)	1 (0.9)	13 (9.7)	124 (16.8)	390 (10.5)
Comorbidities	N=1224	N=202	N=661	N=219	N=337	N=800	N=83	N=190	N=90	N=115	N=133	N=733	N=3700
Hypertension	422 (34.5)	71 (35.1)	239 (36.2)	85 (38.8)	127 (37.7)	196 (24.5)	28 (33.7)	58 (30.5)	24 (26.7)	29 (25.2)	55 (41.4)	332 (45.3)	1307 (35.3)
Cardiovascular disease	121 (9.9)	23 (11.4)	63 (9.5)	36 (16.4)	38 (11.3)	53 (6.6)	12 (14.5)	25 (13.2)	13 (14.4)	9 (7.8)	12 (9)	146 (19.9)	442 (11.9)
Cerebrovascular disease	31 (2.5)	7 (3.5)	19 (2.9)	9 (4.1)	11 (3.3)	13 (1.6)	1 (1.2)	5 (2.6)	3 (3.3)	2 (1.7)	4 (3)	31 (4.2)	109 (2.9)
Chronic lung disease	216 (17.6)	48 (23.8)	136 (20.6)	45 (20.5)	113 (33.5)	108 (13.5)	17 (20.5)	64 (33.7)	7 (7.8)	13 (11.3)	34 (25.6)	137 (18.7)	719 (19.4)
Chronic kidney disease	42 (3.4)	12 (5.9)	58 (8.8)	11 (5)	54 (16)	24 (3)	6 (7.2)	22 (11.6)	3 (3.3)	3 (2.6)	6 (4.5)	83 (11.3)	258 (7)
Obesity (BMI ≥ 30)	187 (15.3)	30 (14.9)	108 (16.3)	38 (17.4)	55 (16.3)	148 (18.5)	15 (18.1)	22 (11.6)	18 (20)	27 (23.5)	36 (27.1)	102 (13.9)	597 (16.1)
Morbid obesity (BMI ≥ 40)	33 (2.7)	6 (3)	34 (5.1)	6 (2.7)	26 (7.7)	24 (3)	4 (4.8)	13 (6.8)	2 (2.2)	2 (1.7)	12 (9)	20 (2.7)	122 (3.3)
Diabetes	170 (13.9)	39 (19.3)	80 (12.1)	38 (17.4)	46 (13.6)	75 (9.4)	14 (16.9)	26 (13.7)	13 (14.4)	12 (10.4)	19 (14.3)	121 (16.5)	505 (13.6)
Cancer	64 (5.2)	7 (3.5)	32 (4.8)	12 (5.5)	13 (3.9)	17 (2.1)	5 (6)	18 (9.5)	3 (3.3)	5 (4.3)	2 (1.5)	76 (10.4)	214 (5.8)
Other comorbidities	267 (21.8)	43 (21.3)	138 (20.9)	63 (28.8)	98 (29.1)	209 (26.1)	19 (22.9)	50 (26.3)	22 (24.4)	44 (38.3)	33 (24.8)	178 (24.3)	897 (24.2)
DMARD therapies													
Methotrexate/Leflunomi de	1237 (100)	203 (100)	199 (29.9)	96 (43.2)	10 (3)	306 (38.1)	41 (49.4)	61 (31.6)	32 (35.6)	30 (25.9)	61 (45.5)	0	1404 (37.7)
Sulfasalazine	75 (6.1)	24 (11.8)	39 (5.9)	222 (100)	5 (1.5)	48 (6)	1 (1.2)	6 (3.1)	5 (5.6)	3 (2.6)	11 (8.2)	0	222 (6)
Antimalarials	177 (14.3)	33 (16.3)	665 (100)	39 (17.6)	108 (32)	41 (5.1)	10 (12)	29 (15)	7 (7.8)	2 (1.7)	14 (10.4)	0	665 (17.8)
Immunosuppressants	9 (0.7)	1 (0.5)	108 (16.2)	5 (2.3)	338 (100)	17 (2.1)	2 (2.4)	27 (14)	0	1 (0.9)	2 (1.5)	0	338 (9.1)
bDMARDs	424 (34.3)	63 (31)	109 (16.4)	64 (28.8)	59 (17.5)	804 (100)	83 (100)	193 (100)	90 (100)	116 (100)	1 (0.7)	0	1331 (35.7)
tsDMARDs	52 (4.2)	12 (5.9)	14 (2.1)	12 (5.4)	3 (0.9)	0	0	1 (0.5)	0	1 (0.9)	134 (100)	0	147 (3.9)
Further therapies													
Glucocorticoids (#)	410 (33.5) (N=1223)	83 (42.3) (N=196)	252 (38.3) (N=658)	66 (30.6) (N=216)	66 (30.6) (N=335)	130 (16.3) (N=796)	34 (41) (N=83)	100 (52.6) (N=190)	35 (38.9) <i>(N=90)</i>	16 (13.8) (N=116)	48 (36.9) (N=130)	290 (39.8) (N=729)	1273 (34.6) (N=3682)
0 mg/d < GC <= 10mg/d	351 (29.2) (N=1203)	75 (38.9) (N=193)	192 (30) (N=640)	52 (24.4) (N=213)	52 (24.4) (N=323)	102 (12.9) (N=789)	30 (36.6) (N=82)	67 (37) (N=181)	30 (33.7) (N=89)	14 (12.1) (N=116)	44 (33.8) (N=130)	202 (28.4) (N=712)	983 (27.2) (N=3617)
GC > 10 mg/d	38 (3.2) (N=1203)	5 (2.6) (N=193)	42 (6.6) (N=640)	11 (5.2) (N=213)	11 (5.2) (N=323)	20 (2.5) (N=789)	3 (3.7) (N=82)	22 (12.2) (N=181)	4 (4.5) (N=89)	2 (1.7) (N=116)	4 (3.1) (N=130)	70 (9.8) (N=712)	220 (6.1) (N=3617)

Data are N (column %) for	categorical var	iables or mean	(SD) for continu	uous variables.	Fable includes a	II patients with	a non-missing	outcome and r	non-missing valu	ues for age, sex	and disease mo	odifying anti-rhe	eumatic drugs

(DMARDs) (101 patients excluded). Data refers to patients with non-missing values for the respective variable, total N for patients with non-missing values is given in parentheses for variables with missing values. (\*) Includes one patient on a study medication (Lenabasum). (#) Includes patients with a missing glucocorticoid dose.

ABA, Abatacept; bDMARD, biologic disease modifying antirheumatic drugs; BMI, body mass index; csDMARD, conventional synthetic disease modifying antirheumatic drugs; CTD, connective tissue diseases; DA, disease activity; DMARD, disease modifying antirheumatic drugs; GC, glucocorticoids; IL-6i, interleukin-6 inhibitors; IL-17/23/12+23i, interleukin-17/23/12+23 inhibitors; IMMMUNOSUPPR, immunosuppressants; .JAKi, Janus kinase inhibitors; JIA, juvenile idiopathic arthritis; LEF, leflunomide; MTX, methotrexate; mono, monotherapy; N, number; NSAID, non-steroidal anti-inflammatory drugs; RTX, rituximab; SLE, systemic lupus erythematosus; SSZ, sulfasalazine; TNFi; tumour necrosis factor inhibitors.

				All	Patients w	vith infla		ory joint es (IJDs)	Only patients wit	h rheun	natoid a	arthritis	Patients with con		tissue d Ds) or va	
N deaths/patients (%)		324 /	/ 2921 (	11.1%)		186	6 / 1818	(10.2%)		146	/ 1124 (	13.0 %)		11	3 / 932 (	(12.1%)
	N deaths/patients	OR		95% CI	N deaths/patients	OR	OR 95% CI		N deaths/patients	OR	95% CI		N deaths/patients	OR		95% CI
Age, years																
Age ≤ 65	108 / 2018	1	[Refe	erence]	52 / 1259	1	[Ref	erence]	38 / 692	1	[Ref	erence]	49 / 657	1	[Refe	erence]
65 years < Age ≤ 75	97 / 516	3.18	2.26	4.47	67 / 351	3.58	2.41	5.33	53 / 259	3.33	1.80	6.18	24 / 139	2.43	1.43	4.13
Age > 75	119 / 387	5.77	4.03	8.28	67 / 208	7.22	4.89	10.66	55 / 173	6.31	3.77	10.54	40 / 136	4.34	2.11	8.91
Male sex (vs. female)	131 / 919	1.39	1.00	1.95	74 / 603	1.39	1.01	1.91	50 / 279	1.27	0.85	1.89	44 / 232	1.38	0.91	2.08
Ever smoked (vs. never)	135 / 873	1.12	0.85	1.49	85 / 576	1.15	0.79	1.67	71 / 373	1.27	0.87	1.86	39 / 234	1.13	0.70	1.82
Comorbidities					•											
Hypertension alone or CVD alone	125 / 954	1.08	0.85	1.38	67 / 568	1.03	0.69	1.54	54 / 375	1.05	0.70	1.59	53 / 337	1.40	0.95	2.08
Hypertension and CVD	72 / 253	1.77	1.20	2.62	48 / 146	2.45	1.22	4.92	34 / 102	2.09	0.99	4.42	18 / 82	1.15	0.61	2.18
Chronic lung disease	122 / 610	1.74	1.26	2.40	73 / 342	1.67	1.15	2.41	61 / 258	1.62	1.13	2.32	44 / 241	2.17	1.41	3.35
Chronic kidney disease	58 / 214	1.40	0.81	2.43	21/97	0.83	0.45	1.56	16 / 75	0.76	0.36	1.59	30 / 97	2.34	1.16	4.73
Diabetes mellitus	79 / 433	1.26	0.76	2.08	47 / 267	1.23	0.86	1.77	32 / 182	1.00	0.63	1.58	21 / 126	1.01	0.52	1.96
Rheumatic disease					•											
Rheumatoid arthritis	140 / 1079	1	[Refe	erence]	146 / 1126	1	[Ref	erence]							n.a.	
Systemic lupus erythematosus	34 / 341	1.28	0.71	2.29									30 / 328	1	[Refe	erence]
Vasculitis	49 / 254	0.75	0.54	1.05		]	n.a.				n.a.		43 / 233	0.65	0.40	1.08
Other connective tissue diseases	42 / 384	0.73	0.54	0.98									40 / 371	0.77	0.36	1.64

Psoriasis arthritis	16 / 355	0.72	0.49	1.05	16 / 363	0.75	0.50	1.13								
Spondyloarthritis	14 / 231	0.96	0.50	1.87	14 / 232	1.02	0.52	2.00								
Other inflammatory arthritis or non- systemic JIA	9 / 92	0.75	0.45	1.26	10 / 97	0.71	0.41	1.23							n.a.	
Other rheumatic diseases (not IJDs / CTDs / vasculitis)	20 / 185	0.53	0.36	0.80			n.a.									
High/moderate/severe disease activity (DA) vs. remission/low DA	96 / 585	1.91	1.24	2.95	50 / 365	1.65	1.11	2.45	40 / 233	1.67	1.00	2.81	43 / 189	2.59	1.46	4.58
Medication																
Methotrexate	38 / 444	1	[Refe	erence]	33 / 366	1	[Ref	erence]	27 / 273	1	[Refe	erence]	5 / 69	1	[Ref	erence]
No DMARD therapy	94 / 578	1.91	1.29	2.84	30 / 188	1.99	1.18	3.36	19 / 90	2.01	1.16	3.49	49 / 266	2.76	1.32	5.78
Leflunomide	12/82	1.53	0.83	2.81	10/75	1.40	0.65	3.01	9 / 62	1.46	0.68	3.15			n.a.	
Antimalarials	26 / 380	0.92	0.58	1.46	17 / 158	1.15	0.61	2.14	17 / 133	1.28	0.68	2.41	10 / 234	1.16	0.33	4.03
Sulfasalazine	33 / 138	3.19	1.39	7.32	31 / 132	3.10	1.25	7.70	21/84	2.41	1.07	5.39			n.a.	
Immunosuppressants	36 / 252	1.98	1.20	3.24			n.a.				n.a.		30 / 227	1.87	0.75	4.65
TNF inhibitors	26 / 574	0.76	0.45	1.28	23 / 544	0.73	0.36	1.46	15 / 235	0.85	0.37	1.96	3 / 34	1.22	0.19	7.68
Abatacept	8 / 62	1.22	0.55	2.68	8 / 57	1.43	0.60	3.45	8/51	1.57	0.64	3.85			n.a.	
Rituximab	32 / 146	3.56	1.94	6.53	19/73	4.75	2.21	10.20	18/69	4.35	1.91	9.91	15 / 78	2.60	0.80	8.44
Belimumab	1/25	0.62	0.15	2.53			n.a.				n.a.		1 / 25	0.80	0.15	4.33
IL-6 inhibitors	4/61	0.94	0.36	2.43	1/49	0.33	0.03	3.39	1/44	0.33	0.03	3.25				L
IL-17/IL-23/IL-12+23 inhibitors	1/77	0.29	0.03	2.41	1/75	0.31	0.04	2.43			n.a.				n.a.	
tsDMARDs	13 / 120	1.50	0.81	2.77	13 / 117	1.77	0.97	3.23	11/97	1.54	0.71	3.32			n.a.	

No GCs	148 / 1885	1	[Refe	rence]	103 / 1301	1	[Ref	erence]	76 / 700	1	[Refe	erence]	31 / 465	1	[Ref	erence]
GCs 1-10mg/d	137 / 856	1.33	0.85	2.07	75 / 467	1.18	0.61	2.28	63 / 390	1.10	0.51	2.38	57 / 372	1.92	1.21	3.03
GCs > 10 mg/d	40 / 180	1.73	1.10	2.71	9 / 50	1.07	0.48	2.36	7 / 34	0.97	0.42	2.22	28 / 111	2.40	1.32	4.38

Missing values imputed via multiple imputation, patient numbers may thus be rounded. Effects significant at level  $\alpha$ =0.05 are marked in bold. Patients were excluded from a particular analysis if the medication they received provided  $\leq$  20 patients for that analysis or if there were no deaths reported for that specific medication.

CI, confidence interval; CTD, connective tissue diseases; CVD, cardiovascular disease; DA, disease activity; DMARD, disease modifying antirheumatic drugs; GC, glucocorticoids; IJD, inflammatory joint diseases; IL, interleukin; JIA, juvenile idiopathic arthritis; N, number; OR, odds ratio; SLE, systemic lupus erythematosus; TNF; tumour necrosis factor; tsDMARD, targeted synthetic disease modifying antirheumatic drugs.

				All	Patient	s with in	flammat	ory joint	Only patients	with rhe	eumatoid	l arthritis	Patients with	connecti	ve tissue	diseases
							diseas	es (IJDs)						(0	CTDs) or v	vasculitis
N deaths/patients (%)		2	207 / 208	1 (9.9%)		:	113 / 123	82 (9.1%)			87 / 77	0 (11.3%)			74 / 699	9 (10.6%)
	N deaths/ patients	OR		95% CI	N deaths/ patients	OR		95% CI	N deaths/ patients	OR		95% CI	N deaths/ patients	OR		95% CI
Age, years																
Age ≤ 65	69 / 1476	1	[Re	ference]	33 / 868	1	[Re	ference]	24 / 493	1	[Re	eference]	33 / 518	1	[Re	eference]
65 years < Age ≤ 75	58 / 357	3.03	1.99	4.62	37 / 236	2.81	1.78	4.44	28 / 172	2.52	1.31	4.85	15 / 100	2.12	1.06	4.26
Age > 75	80 / 248	6.71	4.91	9.17	43 / 128	7.17	3.65	14.09	35 / 105	5.93	2.47	14.22	26 / 81	5.60	2.89	10.86
Male sex (vs. female)	81/614	1.30	0.96	1.76	45 / 385	1.57	1.05	2.35	29 / 175	1.35	0.79	2.32	26 / 163	1.07	0.65	1.75
Ever smoked (vs. never)	85 / 597	1.16	0.84	1.60	50 / 377	1.20	0.80	1.80	42 / 247	1.44	1.02	2.03	27 / 172	1.35	0.69	2.63
Comorbidities																
Hypertension alone or CVD alone	82 / 687	1.14	0.93	1.41	41 / 387	1.11	0.74	1.66	33 / 258	1.17	0.76	1.82	37 / 260	1.67	1.09	2.55
Hypertension and CVD	48 / 168	2.04	1.58	2.63	34 / 97	3.24	1.73	6.08	24 / 67	3.05	1.33	6.96	10 / 53	1.06	0.61	1.84
Chronic lung disease	83 / 453	1.76	1.37	2.27	42 / 232	1.39	1.02	1.90	34 / 175	1.32	0.95	1.83	37 / 194	2.80	1.88	4.16
Chronic kidney disease	38 / 135	1.59	0.94	2.69	17 / 55	1.49	0.97	2.31	13 / 42	1.53	1.03	2.29	16 / 61	2.04	0.77	5.41
Diabetes mellitus	48 / 302	1.13	0.73	1.73	32 / 185	1.24	0.91	1.69	21 / 125	0.88	0.59	1.30	10 / 89	0.69	0.28	1.70
Rheumatic disease	1															
Rheumatoid arthritis	84 / 772	1	[Re	ference]	87 / 770	1	[Re	ference]							n.a.	
Systemic lupus erythematosus	19 / 265	0.99	0.409	2.37		n.a.			n.a.			16 / 256	1	[Re	eference]	

Vasculitis	31/163	1.02	0.59	1.77									26 / 146	1.03	0.49	2.20
Other connective tissue diseases	33 / 307	0.88	0.55	1.43									32 / 297	1.14	0.55	2.39
Psoriasis arthritis	11 / 230	0.80	0.53	1.20	11 / 236	0.69	0.45	1.06								
Spondyloarthritis	9 / 157	1.11	0.56	2.18	9 / 156	1.06	0.52	2.13								
Other inflammatory arthritis or non- systemic JIA	5 / 68	0.87	0.42	1.81	6 / 70	0.79	0.41	1.55							n.a.	
Other rheumatic diseases (not IJDs / CTDs / vasculitis)	15 / 119	0.70	0.39	1.26			n.a.									
High/moderate/severe disease activity (DA) vs. remission/low DA	65 / 422	2.03	1.33	3.10	34 / 240	1.96	1.24	3.09	27 / 159	1.98	1.13	3.48	28 / 145	2.73	1.93	3.86
Medication																
Methotrexate	24 / 302	1	[Ref	erence]	22 / 252	1	[Re	ference]	17 / 182	1	[Re	eference]	2 / 46	1	[Re	eference]
No DMARD therapy	58 / 385	1.56	1.09	2.23	17 / 122	1.54	0.90	2.62	11 / 54	1.64	0.81	3.32	30 / 184	4.23	1.55	11.53
Leflunomide	7 / 51	1.35	0.76	2.41	5 / 47	0.87	0.48	1.60	4 / 41	0.76	0.41	1.40			n.a.	
Antimalarials	19 / 296	1.02	0.67	1.54	12 / 117	1.00	0.56	1.79	12 / 96	1.09	0.59	2.05	8 / 190	2.40	0.73	7.93
Sulfasalazine	16 / 90	2.77	0.88	8.69	15/87	2.43	0.78	7.53	11/51	2.16	0.72	6.46			n.a.	
Immunosuppressants	26 / 193	1.99	1.08	3.68			n.a.				n.a.		21/173	3.25	1.18	9.00
TNF inhibitors	19/ 447	0.75	0.43	1.31	17 / 425	0.65	0.33	1.29	10 / 188	0.68	0.24	1.94	2 / 24	2.26	0.12	42.16
Abatacept	6 / 49	1.17	0.43	3.19	6 / 46	1.12	0.35	3.61	6 / 40	1.21	0.35	4.20			n.a.	
Rituximab	17 / 104	2.43	1.64	3.58	8 / 45	2.99	1.36	6.55	7 / 42	2.60	1.16	5.81	10 / 62	3.48	1.23	9.88
Belimumab	1/21	0.95	0.26	3.52									1/21	2.11	0.32	13.96
IL-6 inhibitors	3 / 50	0.78	0.338	1.81			n.a.				n.a.				n.a.	
tsDMARDs	11 / 101	1.58	0.86	2.90	11/98	1.76	1.01	3.05	9 / 83	1.41	0.74	2.70				

Glucocorticoids (GCs)																
No GCs	93 / 1394	1	[Ref	ference]	59 / 917	1	[Re	eference]	41 / 511	1	[R	eference]	22 / 373	1	[Re	eference]
GCs 1-10mg/d	90 / 561	1.63	1.14	2.33	47 / 282	1.44	0.66	3.15	41 / 237	1.54	0.63	3.77	37 / 248	2.32	1.30	4.11
GCs > 10 mg/d	24 / 126	1.58	0.91	2.74	7 / 33	1.54	0.48	4.98	5 / 22	1.35	0.48	3.80	15 / 78	2.06	1.04	4.09

Effects significant at level  $\alpha$ =0.05 are marked in bold. Patients were excluded from a particular analysis if the medication they received provided  $\leq$  20 patients for that analysis or if there were no deaths reported for that specific medication.

CI, confidence interval; CTD, connective tissue diseases; CVD, cardiovascular disease; DA, disease activity; DMARD, disease modifying antirheumatic drugs; GC, glucocorticoids; IJD, inflammatory joint diseases; IL, interleukin; JIA, juvenile idiopathic arthritis; N, number; OR, odds ratio; SLE, systemic lupus erythematosus; TNF; tumour necrosis factor; tsDMARD, targeted synthetic disease modifying antirheumatic drugs.

Supplementary table 6. 19 diagnosis	Multivariable logist	ic regre	ession ar	nalysis o	f factors associated	l with C	OVID-19	-related	death in patients w	vith rhe	umatic	diseases	with a confirmed o	r highly	likely C	OVID-
				All	Patients v	vith infl		ory joint es (IJDs)	Only patients wit	h rheur	natoid a	arthritis	Patients disea		nnectivo Ds) or va	
N deaths/patients (%)		345	/ 2968 (	11.6%)		184	/ 1619	(10.2%)		14	3 / 946	(13.1%)		13	139 / 999 (13.9%)	
	N deaths/patients	OR		95% CI	N deaths/patients	OR		95% CI	N deaths/patients	OR		95% CI	N deaths/patients	OR		95% CI
Age, years																
Age ≤ 65	107 / 1971	1	[Refe	erence]	48 / 1204	1	[Ref	erence]	35 / 627	1	[Ref	erence]	53 / 666	1	[Ref	erence]
65 years < Age ≤ 75	98 / 545	2.87	1.92	4.29	62 / 358	3.43	2.43	4.84	48 / 267	2.90	1.61	5.23	32 / 161	2.37	1.27	4.43
Age > 75	140 / 452	5.40	3.58	8.14	74 / 241	7.16	4.81	10.66	60 / 195	5.91	3.76	9.29	54 / 172	3.82	1.80	8.12
Male sex (vs. female)	146 / 962	1.47	1.12	1.94	71 / 607	1.27	0.90	1.81	47 / 282	1.16	0.76	1.75	60 / 261	1.70	0.99	2.93
Ever smoked (vs. never)	119 / 740	1.13	0.85	1.50	69 / 468	1.20	0.85	1.70	58 / 310	1.33	0.98	1.79	39 / 213	0.99	0.64	1.52
Comorbidities								•			•					
Hypertension alone or CVD alone	138 / 962	1.16	0.87	1.54	67 / 553	1.00	0.72	1.37	55 / 369	1.09	0.74	1.62	63 / 357	1.45	0.96	2.19
Hypertension and CVD	80 / 271	1.83	1.34	2.51	47 / 151	2.16	1.17	3.98	34 / 108	2.05	1.00	4.19	27 / 96	1.46	0.75	2.83
Chronic lung disease	122 / 602	1.68	1.23	2.29	66 / 334	1.47	0.95	2.27	55 / 246	1.43	0.92	2.23	51 / 243	2.08	1.48	2.93
Chronic kidney disease	69 / 233	1.57	0.97	2.57	24 / 95	1.18	0.61	2.29	18 / 71	1.08	0.51	2.28	38 / 116	2.07	1.18	3.62
Diabetes mellitus	90 / 461	1.36	0.89	2.08	50 / 274	1.29	0.92	1.81	35 / 188	1.07	0.70	1.63	31 / 147	1.28	0.61	2.69
Rheumatic disease								•			•					
Rheumatoid arthritis	137 / 1055	1	[Refe	erence]	143 / 1091	1	[Ref	erence]							n.a.	
Systemic lupus erythematosus	35 / 336	1.31	0.77	2.23			n.a.				n.a.		31 / 326	1	[Ref	erence]

Vasculitis	63 / 284	0.92	0.67	1.26									60 / 277	0.81	0.49	1.35
Other connective tissue diseases	50 / 407	0.83	0.62	1.12									48 / 396	0.80	0.40	1.61
Psoriasis arthritis	17 / 324	0.76	0.60	0.97	17 / 331	0.85	0.61	1.17								
Spondyloarthritis	14 / 291	0.77	0.38	1.58	14 / 292	0.92	0.46	1.83								
Other inflammatory arthritis or non- systemic JIA	9 / 84	0.86	0.57	1.31	10 / 89	0.90	0.57	1.44							n.a.	
Other rheumatic diseases (not IJDs / CTDs / vasculitis)	20 / 187	0.49	0.35	0.70			n.a.									
High/moderate/severe disease activity (DA) vs. remission/low DA	97 / 575	1.77	1.15	2.73	47 / 337	1.63	1.06	2.50	37 / 206	1.63	0.98	2.71	47 / 204	2.11	1.28	3.46
Medication																•
Methotrexate	45 / 476	1	[Refe	erence]	39 / 387	1	[Ref	erence]	32 / 279	1	[Ref	erence]	6 / 80	1	[Ref	erence]
No DMARD therapy	109 / 620	1.88	1.31	2.68	28 / 187	1.58	1.01	2.46	17 / 88	1.55	0.92	2.61	64 / 309	3.22	1.58	6.56
Leflunomide	10/75	1.38	0.79	2.40	8 / 68	1.15	0.60	2.20	7 / 56	1.12	0.56	2.26			n.a.	
Antimalarials	24 / 360	0.86	0.52	1.43	15 / 138	1.02	0.51	2.03	15 / 116	1.09	0.54	2.18	10 / 231	1.30	0.43	3.88
Sulfasalazine	28 / 119	3.16	1.36	7.37	26 / 113	2.91	1.14	7.43	18 / 75	2.25	0.98	5.17			n.a.	
Immunosuppressants	36 / 238	1.99	1.27	3.13			n.a.				n.a.		31 / 213	2.46	1.11	5.42
TNF inhibitors	29 / 575	0.92	0.57	1.49	25 / 544	0.83	0.45	1.54	15 / 229	0.87	0.37	2.05	4 / 34	2.09	0.33	13.30
Abatacept	8 / 68	1.06	0.57	1.96	8 / 62	1.14	0.57	2.29	8 / 56	1.21	0.57	2.58			n.a.	
Rituximab	35 / 160	3.28	1.89	5.69	19 / 72	5.32	2.54	11.13	18 / 68	4.80	2.24	10.29	19/89	3.29	1.04	10.43
Belimumab	1/23	0.66	0.19	2.31			n.a.				n.a.		1/23	1.09	0.22	5.39
IL-6 inhibitors	5 / 66	0.91	0.43	1.90	1/47	0.29	0.03	2.80	1 / 42	0.29	0.03	2.79	4/21	2.72	0.91	8.09

IL-17/IL-23/IL-12+23 inhibitors	1/89	0.30	0.04	2.36	1/87	0.31	0.04	2.29			n.a.				n.a.	
tsDMARDs	14 / 114	1.66	0.85	3.21	14 / 111	1.80	0.96	3.34	12 / 91	1.54	0.66	3.60			n.a.	
Glucocorticoids (GCs)																
No GCs	148 / 1884	1	[Refe	rence]	97 / 1298	1	[Ref	erence]	67 / 681	1	[Refe	erence]	36 / 467	1	[Refe	erence]
GCs 1-10mg/d	151 / 883	1.39	0.93	2.06	76 / 454	1.32	0.71	2.46	67 / 371	1.38	0.64	3.00	70 / 406	1.74	1.14	2.67
GCs > 10 mg/d	46 / 200	1.68	1.11	2.56	11 / 51	1.41	0.68	2.90	9 / 38	1.38	0.59	3.22	33 / 126	2.16	1.21	3.88
Missing values imputed v	ia multiple imputat	ion, pat	ient nur	nbers m	ay thus be rounded	. Effects	s signific	ant at lev	el α=0.05 are mark	ed in bo	old. Pati	ents wer	e excluded from a p	articula	ar analys	is if the

Missing values imputed via multiple imputation, patient numbers may thus be rounded. Effects significant at level  $\alpha$ =0.05 are marked in bold. Patients were excluded from a particular analysis if the medication they received provided  $\leq$  20 patients for that analysis or if there were no deaths reported for that specific medication.

Cl, confidence interval; CTD, connective tissue diseases; CVD, cardiovascular disease; DA, disease activity; DMARD, disease modifying antirheumatic drugs; GC, glucocorticoids; IJD, inflammatory joint diseases; IL, interleukin; JIA, juvenile idiopathic arthritis; N, number; OR, odds ratio; SLE, systemic lupus erythematosus; TNF; tumour necrosis factor; tsDMARD, targeted synthetic disease modifying antirheumatic drugs.

Supplementary table 7. I	Multivariable log	istic reg	ression a									-					
				All	Patient	s with ir	nflammat diseas	ory joint ses (IJDs)	Only	oatients		umatoid arthritis			connectiv CTDs) or va		
N deaths or invasive ventilations (IV) /patients (%)		451	L / 3075 (	(14.7%)		2	48 / 1970	) (12.6%)		1	88 / 1148	3 (16.4%)			170 / 925	(18.4%)	
	N deaths or IVs / patients	OR		95% CI	N deaths or IVs / patients	OR		95% CI	N deaths or IVs/patients	OR		95% CI	N deaths or IVs / patients	OR		95% CI	
Age, years																	
Age ≤ 65	168 / 2173	1	[Ref	erence]	81 / 1425 1		[Reference]		51 / 721	1	[Re	eference]	80 / 638	1	[Ref	erence]	
65 years < Age ≤ 75	120 / 507	2.55	2.00	3.26	78 / 339	2.95	2.14	4.06	62 / 253	3.09	1.96	4.88	90 / 287	1.54	1.14	2.09	
Age > 75	163 / 395	5.19	3.35	8.03	89 / 206	7.22	3.90	13.35	75 / 174	7.11	3.65	13.85	58 / 146	3.21	2.08	4.96	
Male sex (vs. female)	184 / 977	1.50	1.12	2.00	92 / 652	1.29	0.91	1.83	61 / 287	1.20	0.74	1.96	72 / 242	1.76	1.18	2.60	
Ever smoked (vs. never)	161 / 821	0.98	0.74	1.30	96 / 541	0.99	0.70	1.39	78 / 344	1.10	0.74	1.63	51 / 222	1.01	0.65	1.58	
Comorbidities						•									·		
Hypertension alone or CVD alone	184 / 927	1.33	1.02	1.74	94 / 560	1.22	0.86	1.72	74 / 371	1.15	0.80	1.66	79 / 323	1.53	1.13	2.06	
Hypertension and CVD	95 / 252	1.90	1.25	2.88	57 / 144	2.33	1.20	4.53	41 / 101	1.96	0.93	4.15	30 / 82	1.55	0.74	3.22	
Chronic lung disease	158 / 590	1.80	1.38	2.35	91 / 328	1.87	1.26	2.78	74 / 234	1.76	1.21	2.56	62 / 233	2.11	1.52	2.93	
Chronic kidney disease	86 / 211	2.00	1.24	3.22	30 / 93	1.13	0.61	2.11	23 / 69	1.01	0.48	2.11	46 / 98	3.16	1.69	5.90	
Diabetes mellitus	108 / 393	1.44	0.97	2.14	62 / 246	1.30	1.02	1.67	44 / 171	1.17	0.80	1.71	35 / 114	1.42	0.61	3.31	
Rheumatic disease	•				•				•								
Rheumatoid arthritis	180 / 1107	1	[Ref	erence]	188 / 1150	1	[Re	eference]			n.a.				n.a.		

Systemic lupus erythematosus	46 / 322	1.26	0.83	1.91									42 / 310	1	[Re	ference]
Vasculitis	72 / 267	0.77	0.59	1.02			n.a.						65 / 246	0.74	0.50	1.09
Other connective tissue diseases	66 / 381	0.89	0.62	1.28									63 / 369	0.95	0.54	1.65
Psoriasis arthritis	27 / 362	0.74	0.51	1.07	27 / 369	0.78	0.51	1.18								
Spondyloarthritis	18 / 357	0.67	0.35	1.27	18 / 358	0.72	0.37	1.41								
Other inflammatory arthritis or non- systemic JIA	13 / 88	1.04	0.72	1.49	15 / 93	1.13	0.83	1.54							n.a.	
Other rheumatic diseases (not IJDs / CTDs / vasculitis)	29 / 191	0.55	0.36	0.83			n.a.									
High/moderate/severe disease activity (DA) vs. remission/low DA	119 / 592	1.57	1.13	2.19	60 / 380	1.35	0.96	1.89	48 / 235	1.32	0.88	1.98	53 / 182	1.98	1.21	3.24
Medication																
Methotrexate	56 / 468	1	[Ref	erence]	48 / 390	1	[Re	ference]	39 / 289	1	[Re	ference]	8 / 70	1	[Re	ference]
No DMARD therapy	139 / 622	1.96	1.26	3.06	41 / 208	1.93	1.15	3.23	25 / 92	2.00	1.18	3.40	75 / 287	2.77	1.48	5.19
Leflunomide	15 / 71	1.83	0.96	3.48	13 / 66	1.72	0.81	3.69	12 / 56	1.86	0.92	3.78			n.a.	
Antimalarials	35 / 357	1.02	0.67	1.56	20 / 142	1.13	0.61	2.10	19 / 117	1.25	0.67	2.31	17 / 225	1.53	0.67	3.48
Sulfasalazine	37 / 120	3.67	1.85	7.26	35 / 113	3.67	1.75	7.70	24 / 70	3.04	1.43	6.45			n.a.	
Immunosuppressants	45 / 231	1.80	1.19	2.72			n.a.				n.a.		38 / 209	1.70	0.91	3.18
TNF inhibitors	39 / 692	0.86	0.53	1.37	34 / 657	0.83	0.48	1.43	22 / 254	0.98	0.52	1.86	6/37	1.73	0.33	9.04
Abatacept	11/65	1.28	0.61	2.71	11/62	1.40	0.63	3.12	11/58	1.55	0.71	3.42			n.a.	
Rituximab	46 / 144	4.31	2.48	7.49	25 / 72	5.99	3.00	11.96	24 / 69	6.04	3.01	12.09	23 / 75	3.15	1.12	8.90
Belimumab	3 / 22	1.84	0.58	5.87			n.a.			1	n.a.		3 / 22	2.25	0.73	6.98

IL-6 inhibitors	5 / 77	0.75	0.34	1.63	1/60	0.22	0.02	2.09	1/55	0.22	0.02	2.14				
IL-17/IL-23/IL-12+23 inhibitors	6 / 92	1.42	0.59	3.43	6 / 89	1.58	0.63	3.96			n.a.				n.a.	
tsDMARDs	17 / 125	1.45	0.81	2.59	17 / 122	1.67	0.94	2.97	14 / 99	1.51	0.76	3.02			n.a.	
Glucocorticoids (GCs)																
No GCs	202 / 2032	1	[Ref	erence]	136 / 1450	1	[Re	eference]	90 / 722	1	[Re	ference]	45 / 452	1	[Re	ference]
GCs 1-10mg/d	191 / 860	1.45	1.03	2.04	99 / 468	1.31	0.72	2.38	87 / 389	1.37	0.68	2.73	86 / 362	2.02	1.44	2.84
GCs > 10 mg/d	58 / 183	2.11	1.44	3.11	13 / 53	1.47	0.58	3.74	11/37	1.74	0.56	5.40	39 / 111	2.51	1.47	4.27

Living patients with missing values for invasive ventilation excluded from the model (dependent variable unknown). Missing values in other variables imputed via multiple imputation, patient numbers may thus be rounded. Effects significant at level  $\alpha$ =0.05 are marked in bold. Patients were excluded from a particular analysis if the medication they received provided  $\leq$  20 patients for that analysis or if there were no deaths reported for that specific medication.

				All	Patients wi		nmator diseases		Only patients with	n rheum	atoid a	rthritis	Patients disea			e tissue asculitis
N deaths/patients (%)		384	/3705 (1	LO.4%)		21	1/2348	(9.0%)		166	/1371 (	12.1%)		14	7/1157 (	(12.7%)
	N deaths/patients	OR		95% CI	N deaths/patients	OR		95% CI	N deaths/patients	OR		95% CI	N deaths/patients	OR		95% CI
Age, years																
Age ≤ 65	118 / 2565	1	[Refe	rence]	55 / 1657	1	[Refe	rence]	40 / 840	1	[Refe	erence]	56 / 779	1	[Ref	erence]
Age > 65	266 / 1140	4.10	3.06	5.49	156 / 691	5.00	3.63	6.88	126 / 531	4.40	2.74	7.08	91 / 378	3.15	1.91	5.18
Male sex (vs. female)	161 / 1188	1.41	1.08	1.86	82 / 788	1.27	0.94	1.72	55 / 345	1.14	0.77	1.70	63 / 296	1.64	0.97	2.77
Ever smoked (vs. never)	140 / 922	1.18	0.89	1.56	84 / 607	1.21	0.88	1.66	71 / 385	1.38	1.00	1.92	42 / 248	1.07	0.63	1.81
Comorbidities															I	
Hypertension alone or CVD alone	155 / 1150	1.23	0.91	1.66	79 / 690	1.08	0.77	1.51	66 / 454	1.16	0.78	1.74	69 / 406	1.58	1.06	2.35
Hypertension and CVD	89 / 301	2.13	1.42	3.18	53 / 168	2.66	1.54	4.60	38 / 118	2.48	1.34	4.56	28 / 106	1.65	0.80	3.43
Chronic lung disease	136 / 721	1.63	1.21	2.20	76 / 406	1.51	1.01	2.26	63 / 293	1.45	0.96	2.20	54 / 285	1.92	1.37	2.69
Chronic kidney disease	76 / 259	1.84	1.07	3.19	27 / 111	1.25	0.59	2.64	21/83	1.17	0.50	2.75	41 / 124	2.46	1.41	4.30
Diabetes mellitus	96 / 508	1.35	0.87	2.10	55 / 313	1.27	0.93	1.73	39 / 213	1.06	0.71	1.57	32 / 154	1.37	0.65	2.89
Rheumatic disease	·		•													
Rheumatoid arthritis	160 / 1326	1	[Refe	rence]	166 / 1373	1	[Refe	rence]							n.a.	
Systemic lupus erythematosus	36 / 391	1.10	0.67	1.81									32 / 378	1	[Ref	erence]
Vasculitis	67 / 325	0.85	0.64	1.11			n.a.				n.a.					
Other connective tissue diseases	53 / 473	0.75	0.57	0.97									115 / 479	0.89	0.53	1.49
Psoriasis arthritis	19 / 429	0.66	0.49	0.90	19 / 437	0.73	0.52	1.04							n.a.	

Spondyloarthritis	15 / 423	0.66	0.32	1.35	15 / 424	0.76	0.39	1.48								
Other inflammatory arthritis or non- systemic JIA	10 / 109	0.73	0.44	1.22	11 / 114	0.70	0.40	1.23								
Other rheumatic diseases (not IJDs / CTDs / vasculitis)	24 / 229	0.52	0.36	0.74			n.a.									
High/moderate/severe disease activity (DA) vs. remission/low DA	109 / 722	1.84	1.31	2.59	54 / 453	1.49	1.09	2.02	44 / 274	1.49	0.99	2.23	51 / 230	2.54	1.63	3.95
Medication																
Methotrexate	47 / 595	1	[Refe	rence]	41 / 487	1	[Refe	rence]	34 / 354	1	[Refe	rence]	6 / 94	1	[Refe	erence]
No DMARD therapy	124 / 739	2.20	1.55	3.12	38 / 239	2.14	1.44	3.17	25 / 110	2.12	1.36	3.29	67 / 353	3.43	1.72	6.85
Leflunomide	12 / 90	1.47	0.81	2.66	10/83	1.27	0.62	2.61	9 / 68	1.32	0.63	2.73			n.a.	
Antimalarials	27 /426	0.96	0.64	1.43	17 / 167	1.07	0.59	1.93	17 / 141	1.15	0.63	2.10	11 / 271	1.46	0.50	4.23
Sulfasalazine	33 / 144	3.49	1.64	7.45	31 / 137	3.22	1.44	7.23	21/85	2.43	1.17	5.04			n.a.	
Immunosuppressants	38 / 276	2.18	1.44	3.32			n.a.				n.a.		32 / 247	2.54	1.15	5.63
Rituximab	42 / 192	3.77	2.23	6.36	22 / 90	4.91	2.60	9.25	21/86	4.57	2.35	8.92	22 / 104	3.68	1.24	10.92
TNF inhibitors	30 / 803	0.82	0.52	1.29	26 / 764	0.73	0.41	1.29	16 / 292	0.77	0.37	1.60				
Belimumab							n.a.				n.a.		9 / 89	2.04	0.60	6.92
IL-6 inhibitors									10/121	0.89	0.40	1.00				
Abatacept	16 / 313	0.82	0.47	1.42	11 / 255	0.69	0.35	1.36	10 / 131	0.89	0.40	1.98				
IL-17/IL-23/IL-12+23 inhibitors					,			,			n.a.				n.a.	
tsDMARDs	15 / 145	1.38	0.80	2.36	15 / 142	1.45	0.85	2.47	13 / 118	1.28	0.66	2.49				
Glucocorticoids (GCs)		•		•	•	•										
No GCs	165 / 2417	1	[Refe	rence]	109 / 1721	1	[Refe	rence]	78 / 863	1	[Refe	rence]	38 / 551	1	[Refe	erence]

Glucorticoids	219 / 1288	1.50	1.07	2.10	102 / 627	1.46	0.86	2.47	88 / 508	1.44	0.74	2.80	109 / 606	1.77	1.28	2.46
Missing values imputed v the medication they recei											bold. P	atients v	were excluded from	n a parti	cular an	alysis if
CI, confidence interval; C joint diseases; IL, interle modifying antirheumatic	ukin; JIA, juvenile i					,			•	, 0				,		,

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				All	Patients	with infl		ory joint es (IJDs)	Only patients wit	h rheur	natoid a	arthritis	Patients with co			diseases vasculitis
N deaths/patients (%)		306 /	<b>/ 2974 (</b> :	LO.3%)		17	70 / 1903	8 (8.9%)		134	/ 1102	(12.2%)		1	17 / 92	7 (12.6%)
	N deaths/patients	OR	9	95% CI	N deaths/patients	OR		95% CI	N deaths/patients	OR		95% CI	N deaths/patients	OR		95% CI
Age, years																
Age ≤ 65	76 / 2015	1	[Refe	rence]	36 / 1321	1	[Ref	erence]	25 / 658	1	[Ref	erence]	36 / 597	1	[R	eference]
Age > 65	230 / 959	4.57	3.24	6.45	134 / 582	5.83	3.63	9.37	109 / 444	5.15	3.03	8.75	28 / 160	2.76	1.59	4.80
Male sex (vs. female)	141 / 951	1.68	1.26	2.24	71/640	1.41	0.95	2.08	47 / 283	1.24	0.77	1.98	56 / 239	2.03	1.28	3.21
Ever smoked (vs. never)	118 / 745	1.15	0.82	1.60	73 / 500	1.10	0.71	1.70	61/323	1.22	0.73	2.03	36 / 207	1.09	0.59	2.03
Comorbidities		•														
Hypertension alone or CVD alone	130 / 941	1.41	1.01	1.96	68 / 572	1.25	0.79	1.98	56 / 369	1.41	0.85	2.35	56 / 326	1.94	1.13	3.33
Hypertension and CVD	73 / 259	2.16	1.41	3.31	43 / 141	2.58	1.43	4.68	32 / 100	2.60	1.34	5.04	26 / 100	2.09	1.07	4.11
Lung disease	115 / 614	1.58	1.16	2.16	63 / 344	1.46	0.94	2.25	53 / 245	1.43	0.89	2.30	47 / 250	1.83	1.12	2.99
Chronic kidney disease	59 / 212	1.73	1.12	2.67	24 / 97	1.32	0.68	2.57	19 / 72	1.28	0.63	2.62	30 / 96	2.08	1.09	3.96
Diabetes mellitus	78 / 410	1.26	0.89	1.79	46 / 258	1.31	0.84	2.06	35 / 181	1.23	0.74	2.04	25 / 122	1.09	0.57	2.07
Rheumatic disease																
Rheumatoid arthritis	128 / 1058	1	[Refe	rence]	134 / 1103	1	[Ref	erence]							n.a.	
Systemic lupus erythematosus	18 / 299	0.78	0.39	1.55									15 / 288	1	[R	eference]
Vasculitis	60 / 272	0.81	0.50	1.30			n.a.				n.a.					
Other connective tissue diseases	47 / 384	0.93	0.58	1.47									102 / 639	1.33	0.65	2.73
Psoriasis arthritis	17 / 353	0.70	0.38	1.30	17 / 360	0.81	0.43	1.54							n.a.	

Spondyloarthritis	10 / 340	0.57	0.27	1.20	10/340	0.70	0.33	1.50								
Other inflammatory arthritis or non- systemic JIA	8 / 95	0.68	0.30	1.58	9 / 100	0.66	0.28	1.57								
Other rheumatic diseases (not IJDs / CTDs / vasculitis)	18 / 173	0.60	0.30	1.17			n.a.									
High/moderate/severe disease activity (DA) vs. remission/low DA	87 / 569	1.84	1.26	2.69	48 / 370	1.64	1.04	2.60	39 / 220	1.62	0.98	2.69	36 / 170	2.21	1.18	4.13
Medication																
Methotrexate	34 / 477	1	[Refe	rence]	28 / 387	1	[Ref	erence]	23 / 278	1	[Refe	erence]	6 / 77	1	[Re	ference]
No DMARD therapy	101 / 602	2.61	1.61	4.26	32 / 198	2.75	1.46	5.16	21/94	2.40	1.14	5.06	56 / 302	2.82	1.22	6.49
Leflunomide	10 / 64	2.32	0.98	5.50	8 / 59	1.78	0.71	4.45	8 / 48	2.16	0.81	5.76			n.a.	
Antimalarials	18/312	1.15	0.59	2.22	14 / 125	1.32	0.61	2.85	14 / 105	1.33	0.59	3.02	4 / 197	0.90	0.24	3.37
Sulfasalazine	27 / 93	5.07	2.64	9.74	26 / 88	5.10	2.55	10.20	18 / 51	3.96	1.72	9.12			n.a.	
Immunosuppressants	28 / 212	2.94	1.53	5.63			n.a.				n.a.		23 / 192	2.59	1.02	6.58
Rituximab	35 / 159	4.38	2.37	8.10	16 / 74	4.65	2.02	10.71	15 / 70	4.45	1.84	10.77	21/89	4.17	1.56	11.09
TNF inhibitors	24 / 660	1.10	0.61	2.00	21/631	0.99	0.52	1.91	13 / 244	1.04	0.49	2.20				
Belimumab							n.a.				n.a.		7 / 71	2.13	0.65	6.93
IL-6 inhibitors									9 / 109	1.38	0.56	3.41				
Abatacept	14 / 268	1.25	0.62	2.51	10/216	1.05	0.46	2.40	9/109	1.30	0.50	3.41				
IL-17/IL-23/IL-12+23 inhibitors											n.a.				n.a.	
tsDMARDs	15 / 136	2.32	1.08	4.99	15 / 133	2.32	1.05	5.12	13/110	1.97	0.87	4.51				
Glucocorticoids (GCs)																
No GCs	120 / 1959	1	[Refe	rence]	80 / 1406	1	[Ref	erence]	55 / 701	1	[Refe	erence]	30 / 454	1	[Re	ference]

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Glucorticoids	186 / 1015	1.92	1.40	2.63	90 / 497	1.99	1.33	2.98	79 / 401	2.16	1.38	3.36	87 / 473	1.74	1.02	2.94
Countries																
USA	68 / 1001	1	[Refe	rence]	36 / 568	1	[Ref	erence]	31/380	1	[Ref	erence]	27 / 380	1	[R	eference]
France	60 / 784	1.24	0.82	1.89	25 / 530	0.95	0.52	1.72	20 / 247	0.95	0.49	1.83	31 / 209	1.80	0.91	3.56
UK	90 / 433	2.71	1.79	4.10	57 / 303	2.38	1.39	4.07	45 / 185	2.34	1.27	4.31	24 / 103	3.08	1.48	6.40
Italy	52 / 312	1.87	1.15	3.02	29 / 196	1.65	0.84	3.24	21 / 103	1.67	0.75	3.71	22 / 110	2.11	0.97	4.61
Spain	21 / 246	1.02	0.55	1.86	10 / 156	0.68	0.29	1.62	7 / 88	0.50	0.19	1.31	10 / 84	1.53	0.62	3.76
Germany	15 / 198	1.02	0.54	1.94	13 / 150	1.30	0.60	2.79	10 / 99	0.99	0.43	2.28	3 / 41	0.76	0.22	2.59

				> 65 years				≤ 65 years
N deaths/patients (%)			266	5 / 1140 (23.3%)			1	18 / 2565 (4.6%)
	N deaths/patients	OR		95% CI	N deaths/patients	OR		95% CI
Male sex (vs. female)	121 / 437	1.43	1.09	1.87	40 / 751	1.32	0.74	2.33
Ever smoked (vs. never)	105 / 388	1.04	0.75	1.44	35 / 534	1.63	1.02	2.60
Comorbidities		·						
Hypertension alone or CVD alone	103 / 544	0.85	0.53	1.36	52 / 627	2.04	1.38	3.01
Hypertension and CVD	77 / 210	1.81	0.99	3.31	12 / 91	2.16	1.09	4.31
Chronic lung disease	102 / 320	1.62	1.09	2.40	35 / 401	1.79	1.31	2.45
Chronic kidney disease	53 / 158	1.43	0.75	2.75	23 / 100	3.78	2.24	6.37
Diabetes mellitus	75 / 251	1.39	0.91	2.12	21 / 257	1.21	0.66	2.21
Rheumatic disease								
Rheumatoid arthritis	129 / 537	1		[Reference]	40 / 850	1		[Reference]
Systemic lupus erythematosus	8 / 47	0.54	0.26	1.11	28 / 344	1.24	0.66	2.34
Vasculitis	55 / 192	0.77	0.55	1.09	12 / 133	0.91	0.46	1.78
Other connective tissue diseases	32 / 147	0.66	0.51	0.85	21 / 326	0.75	0.37	1.54
Psoriasis arthritis	12 / 85	0.73	0.52	1.03	7 / 344	0.58	0.24	1.37
Spondyloarthritis	9 / 38	0.81	0.37	1.76	6 / 385	0.59	0.21	1.71
Other inflammatory arthritis or non-systemic JIA	8 / 33	0.71	0.36	1.39	2 / 76	0.67	0.31	1.44
Other rheumatic diseases (not IJDs / CTDs / vasculitis)	17 / 83	0.45	0.29	0.69	7 / 146	0.58	0.25	1.33
High/moderate/severe disease activity (DA) vs. remission/low DA	59 / 191	1.53	0.98	2.41	50 / 531	2.20	1.38	3.50

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Medication	1	1						
Methotrexate	41 / 242	1		[Reference]	6 / 353	1		[Reference]
No DMARD therapy	96 / 352	2.07	1.45	2.96	28 / 387	3.82	1.42	10.27
Leflunomide	7 / 38	0.98	0.38	2.55	5 / 52	3.90	1.12	13.61
Antimalarials	13 / 113	0.68	0.38	1.21	14 / 313	2.13	0.71	6.39
Sulfasalazine	28 / 61	3.89	1.60	9.48	5 / 83	3.22	1.14	9.06
Immunosuppressants	18 / 55	2.74	1.51	4.97	20 / 221	1.90	0.70	5.20
Rituximab	24 / 52	3.84	1.93	7.66	18 / 140	5.29	1.34	20.85
Other b/tsDMARDs	39 / 234	0.92	0.61	1.38	22 / 1026	1.27	0.46	3.48
Glucocorticoids (GCs)	· · ·				·			
No GCs	118 / 606	1		[Reference]	47 / 1811	1		[Reference]
GCs 1-10mg/d	117 / 443	1.19	0.84	1.70	54 / 619	2.10	1.19	3.71
GCs > 10 mg/d	32 / 91	1.35	0.79	2.31	17 / 135	2.24	1.32	3.79

				Male sex				Female sex
N deaths/patients (%)			16	1 / 1188 (13.6%)				223 / 2517 (8.9%)
	N deaths/patients	OR		95% CI	N deaths/patients	OR		95% CI
Age, years								
Age ≤ 65	40 / 751	1		[Reference]	78 / 1814	1		[Reference]
65 years < Age ≤ 75	55 / 252	3.81	1.96	7.41	54 / 392	2.65	1.62	4.32
Age > 75	66 / 185	6.80	2.88	16.07	91/311	6.21	4.50	8.56
Ever smoked (vs. never)	72 / 399	1.08	0.62	1.91	67 / 523	1.34	0.93	1.94
Comorbidities								
Hypertension alone or CVD alone	66 / 385	1.16	0.89	1.50	89 / 765	1.24	0.83	1.85
Hypertension and CVD	43 / 145	1.87	1.19	2.95	46 / 156	2.06	1.36	3.13
Chronic lung disease	53 / 232	1.41	0.74	2.68	84 / 489	1.95	1.47	2.60
Chronic kidney disease	30 / 104	1.26	0.59	2.71	46 / 155	2.03	1.13	3.64
Diabetes mellitus	46 / 193	1.80	1.14	2.86	50 / 315	1.12	0.66	1.90
Rheumatic disease								
Rheumatoid arthritis	55 / 347	1		[Reference]	114 / 1040	1		[Reference]
Systemic lupus erythematosus	10 / 47	1.91	0.81	4.50	26 / 344	0.99	0.51	1.92
Vasculitis	35 / 138	0.95	0.33	2.69	32 / 187	0.69	0.39	1.24
Other connective tissue diseases	21/121	0.96	0.55	1.68	32 / 352	0.66	0.44	1.01
Psoriasis arthritis	13 / 200	0.95	0.50	1.83	6 / 229	0.43	0.27	0.70
Spondyloarthritis	10 / 202	0.82	0.29	2.31	5 / 221	0.53	0.17	1.64
Other inflammatory arthritis or non-systemic JIA	3 / 35	0.41	0.07	2.31	7 / 74	1.19	0.55	2.58

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Other rheumatic diseases (not IJDs / CTDs / vasculitis)	16/112	0.49	0.30	0.79	8 / 117	0.50	0.29	0.89
High/moderate/severe disease activity (DA) vs. remission/low DA	34 / 204	1.69	1.18	2.42	75 / 518	1.99	1.16	3.41
Medication							•	
Methotrexate	23 / 206	1		[Reference]	24 / 389	1		[Reference]
No DMARD therapy	61/280	2.25	1.16	4.37	63 / 459	2.19	1.13	4.24
Leflunomide	5 / 28	1.57	0.82	3.02	7 / 62	1.79	0.82	3.89
Antimalarials	61/280	0.86	0.36	2.04	63 / 459	1.19	0.66	2.15
Sulfasalazine	16 / 52	4.71	1.92	11.54	17 / 92	3.26	0.93	11.40
Immunosuppressants	14 / 79	2.02	1.15	3.54	24 / 197	2.41	1.20	4.82
Rituximab	16 / 60	3.09	1.03	9.30	26 / 132	5.40	3.06	9.52
Other b/tsDMARDs	19 / 425	0.64	0.37	1.10	42 / 835	1.34	0.75	2.39
Glucocorticoids (GCs)	L.						ŀ	
No GCs	76 / 781	1		[Reference]	89 / 1636	1		[Reference]
GCs 1-10mg/d	65 / 319	1.07	0.61	1.87	105 / 744	1.71	1.17	2.52
GCs > 10 mg/d	20 / 88	1.20	0.67	2.17	29 / 138	2.23	1.34	3.73

analysis if the medication they received provided  $\leq$  20 patients for that analysis or if there were no deaths reported for that specific medication.

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				Ever smoked				Never smoked
N deaths/patients (%)			14	40 / 922 (15.2%)				244 / 2783 (8.8%)
	N deaths/patients	OR		95% CI	N deaths/patients	OR		95% CI
Age, years								
Age ≤ 65	35 / 534	1		[Reference]	83 / 2031	1		[Reference]
65 years < Age ≤ 75	47 / 226	2.79	1.70	4.58	62 / 418	3.18	2.06	4.91
Age > 75	58 / 162	6.43	3.33	12.42	99 / 334	6.33	4.32	9.27
Male sex (vs. female)	72 / 399	1.30	0.72	2.35	89 / 789	1.46	1.14	1.88
Comorbidities								
Hypertension alone or CVD alone	57 / 338	1.01	0.67	1.50	98 / 812	1.32	0.94	1.86
Hypertension and CVD	36 / 124	1.53	0.84	2.79	52 / 177	2.08	1.32	3.27
Chronic lung disease	62 / 271	1.49	0.78	2.84	74 / 450	1.93	1.45	2.58
Chronic kidney disease	21/87	0.74	0.38	1.42	55 / 172	2.72	1.56	4.73
Diabetes mellitus	39 / 158	1.48	0.80	2.74	57 / 350	1.33	0.79	2.22
Rheumatic disease								
Rheumatoid arthritis	71/388	1		[Reference]	98 / 999	1		[Reference]
Systemic lupus erythematosus	11 / 62	1.30	0.60	2.84	26 / 329	1.12	0.64	1.94
Vasculitis	18 / 90	0.42	0.19	0.92	49 / 235	0.96	0.67	1.37
Other connective tissue diseases	16/103	0.71	0.34	1.48	37 / 370	0.68	0.42	1.10
Psoriasis arthritis	6/111	0.60	0.24	1.54	13 / 318	0.70	0.44	1.12
Spondyloarthritis	3 / 80	0.32	0.08	1.29	12 / 343	0.82	0.37	1.85
Other inflammatory arthritis or non-systemic JIA	5 / 27	0.65	0.21	2.02	5 / 82	0.84	0.44	1.58

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Other rheumatic diseases (not IJDs / CTDs / vasculitis)	12 / 73	0.59	0.26	1.31	12 / 156	0.40	0.25	0.66
High/moderate/severe disease activity (DA) vs. remission/low DA	32 / 171	1.45	0.85	2.45	77 / 551	2.11	1.31	3.40
Medication	L. C.						1	
Methotrexate	15 / 145	1		[Reference]	33 / 450	1		[Reference]
No DMARD therapy	43 / 221	2.35	1.15	4.83	82 / 518	2.18	1.43	3.30
Leflunomide	5/21	1.41	0.39	5.12	8 / 69	1.52	0.68	3.39
Antimalarials	13 / 93	1.52	0.68	3.38	14 / 334	0.75	0.46	1.21
Sulfasalazine	21/56	6.15	2.23	16.94	12 / 89	2.16	0.81	5.73
Immunosuppressants	12 / 55	3.89	1.53	9.85	26 / 221	1.76	0.96	3.23
Rituximab	12 / 46	3.95	1.29	12.10	30 / 146	4.14	2.16	7.93
Other b/tsDMARDs	20 / 289	1.04	0.48	2.26	41/971	0.90	0.59	1.35
Glucocorticoids (GCs)			•				L	
No GCs	67 / 604	1		[Reference]	98 / 1813	1		[Reference]
GCs 1-10mg/d	57 / 260	1.52	0.91	2.53	114 / 802	1.35	0.88	2.05
GCs > 10 mg/d	16 / 57	2.53	1.33	4.80	33 / 168	1.48	0.93	2.35

analysis if the medication they received provided < 20 patients for that analysis or if there were no deaths reported for that specific medication.

				Heart disease				No heart disease
N deaths/patients (%)			24	2 / 1439 (16.8%)			3	384 / 3705 (10.4%)
	N deaths/patients	OR		95% CI	N deaths/patients	OR		95% CI
Age, years								
Age ≤ 65	63 / 711	1		[Reference]	53 / 1833	1		[Reference]
65 years < Age ≤ 75	58 / 367	1.68	1.12	2.52	49 / 270	5.98	3.72	9.63
Age > 75	121 / 361	4.77	3.08	7.40	36 / 134	7.65	5.24	11.16
Male sex (vs. female)	108 / 525	1.59	1.23	2.06	51 / 655	1.25	0.76	2.05
Ever smoked (vs. never)	93 / 458	1.13	0.82	1.56	46 / 457	1.48	0.94	2.34
Comorbidities	·							
Chronic lung disease	84 / 352	1.56	1.15	2.12	51 / 362	2.39	1.77	3.24
Chronic kidney disease	58 / 190	1.58	0.94	2.67	18 / 67	2.83	1.04	7.71
Diabetes mellitus	75 / 358	1.33	0.84	2.12	20 / 145	1.85	1.38	2.48
Rheumatic disease	·							
Rheumatoid arthritis	105 / 572	1		[Reference]	63 / 805	1		[Reference]
Systemic lupus erythematosus	24 / 154	1.16	0.55	2.46	11 / 235	1.04	0.54	2.02
Vasculitis	39 / 168	0.61	0.36	1.01	27 / 155	1.12	0.69	1.81
Other connective tissue diseases	36 / 201	0.79	0.60	1.02	16 / 264	0.59	0.31	1.12
Psoriasis arthritis	13 / 152	0.70	0.45	1.10	6 / 273	0.60	0.30	1.19
Spondyloarthritis	6 / 87	0.51	0.17	1.51	9 / 336	0.87	0.43	1.74
Other inflammatory arthritis or non-systemic JIA	8 / 34	1.30	0.66	2.55	2 / 73	0.48	0.14	1.70

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Other rheumatic diseases (not IJDs / CTDs / vasculitis)	16 / 100	0.45	0.30	0.68	8 / 128	0.54	0.19	1.51
High/moderate/severe disease activity (DA) vs. remission/low DA	66 / 283	1.92	1.01	3.63	42 / 432	1.92	1.31	2.83
Medication								
Methotrexate	14 / 352	1		[Reference]	33 / 238	1		[Reference]
No DMARD therapy	91 / 372	2.14	1.37	3.35	32 / 361	2.09	1.10	3.97
Leflunomide	5 / 40	0.79	0.24	2.61	7 / 49	3.49	1.23	9.89
Antimalarials	20 / 168	1.10	0.62	1.96	6 / 254	0.64	0.25	1.69
Sulfasalazine	18 / 64	2.78	1.08	7.15	14 / 77	4.82	1.92	12.08
Immunosuppressants	21/117	1.82	1.02	3.23	17 / 158	2.25	0.79	6.38
Rituximab	19 / 68	2.49	1.25	4.96	22 / 121	5.86	2.34	14.68
Other b/tsDMARDs	35 / 377	0.96	0.59	1.54	26 / 877	1.08	0.53	2.20
Glucocorticoids (GCs)								
No GCs	96 / 816	1	[Reference]		69 / 1584	69 / 1584 1		[Reference]
GCs 1-10mg/d	114 / 510	1.62	1.02	2.56	53 / 541	1.16	0.65	2.07
GCs > 10 mg/d	32 / 112	1.84	1.20	2.82	17 / 112	1.62	0.91	2.87

		nic lung disease	No chronic lung disease					
N deaths/patients (%)			13	36 / 721 (18.9%)				248 / 2984 (8.3%)
	N deaths/patients	OR		95% CI	N deaths/patients	OR		95% CI
Age, years								
Age ≤ 65	35 / 401	1		[Reference]	84 / 2164	1		[Reference]
65 years < Age ≤ 75	48 / 189	3.58	2.40	5.33	61 / 456	3.08	2.18	4.36
Age > 75	54 / 131	8.34	6.29	11.05	103 / 365	5.82	3.43	9.90
Male sex (vs. female)	53 / 232	1.02	0.47	2.22	108 / 956	1.60	1.24	2.07
Ever smoked (vs. never)	62 / 271	1.23	0.68	2.24	77 / 651	1.24	0.93	1.66
Comorbidities								
Hypertension alone or CVD alone	51 / 260	0.92	0.67	1.27	104 / 890	1.43	1.05	1.94
Hypertension and CVD	34 / 97	1.51	0.84	2.73	55 / 204	2.21	1.50	3.27
Chronic kidney disease	21 / 64	0.96	0.32	2.82	55 / 194	2.04	1.22	3.43
Diabetes mellitus	38 / 140	1.40	0.61	3.21	58 / 368	1.44	1.05	1.96
Rheumatic disease								
Rheumatoid arthritis	65 / 298	1		[Reference]	104 / 1089	1		[Reference]
Systemic lupus erythematosus	5 / 58	0.55	0.18	1.66	31 / 333	1.42	0.81	2.50
Vasculitis	18 / 66	0.87	0.44	1.72	49 / 259	0.75	0.57	1.00
Other connective tissue diseases	35 / 169	1.21	0.66	2.19	19 / 304	0.46	0.30	0.71
Psoriasis arthritis	4 / 44	1.19	0.45	3.14	15 / 385	0.54	0.40	0.75
Spondyloarthritis	4 / 49	0.81	0.43	1.55	11 / 374	0.60	0.26	1.35
Other inflammatory arthritis or non-systemic JIA	4 / 16	1.61	0.53	4.85	6 / 94	0.55	0.26	1.19

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Other rheumatic diseases (not IJDs / CTDs / vasculitis)	6 / 40	0.73	0.24	2.21	18 / 189	0.40	0.24	0.69
High/moderate/severe disease activity (DA) vs. remission/low DA	43 / 173	1.70	1.01	2.87	66 / 549	1.97	1.27	3.04
Medication								
Methotrexate	16/110	1		[Reference]	31 / 485	1	[Refere	
No DMARD therapy	35 / 138	2.28	1.31	3.95	89 / 601	2.17	1.39	3.39
Leflunomide	5 / 23	2.21	1.21	4.03	7 / 67	1.44	0.68	3.07
Antimalarials	12 / 78	2.03	0.68	6.06	15 / 348	0.73	0.38	1.41
Sulfasalazine	10 / 33	2.97	1.19	7.39	23 / 111	4.20	1.83	9.65
Immunosuppressants	17 / 93	2.74	1.99	3.78	21 / 183	1.68	0.86	3.28
Rituximab	20 / 65	4.95	1.59	15.39	23 / 127	4.08	1.99	8.39
Other b/tsDMARDs	21/183	1.22	0.69	2.16	40 / 1077	0.90	0.52	1.54
Glucocorticoids (GCs)		I	1			1	I	
No GCs	52 / 406	1	[Reference]		113 / 2012	1		[Reference]
GCs 1-10mg/d	68 / 258	1.95	1.30	2.91	103 / 804	1.23	0.77	1.95
GCs > 10 mg/d	17 / 58	1.70	0.96	3.00	32 / 168	1.65	0.93	2.92

Supplementary table 15. Multivariable	eu death strathleu by u	-						
		disease activity		l	ow disease a	ctivity / remission		
N deaths/patients (%)			10	09 / 722 (15.1%)				275 / 2983 (9.2%)
	N deaths/patients	OR		95% CI	N deaths/patients	OR		95% CI
Age, years								
Age ≤ 65	50 / 531	1		[Reference]	69 / 2035	1		[Reference]
65 years < Age ≤ 75	30 / 120	2.52	1.22	5.23	80 / 524	3.47	2.40	5.01
Age > 75	30 / 72	3.92	1.99	7.74	127 / 424	7.50	4.65	12.08
Male sex (vs. female)	34 / 204	1.18	0.62	2.22	127 / 984	1.50	1.15	1.97
Ever smoked (vs. never)	32 / 171	1.09	0.64	1.86	108 / 751	1.25	0.92	1.70
Comorbidities								
Hypertension alone or CVD alone	43 / 227	1.32	0.70	2.49	112 / 923	1.17	0.88	1.55
Hypertension and CVD	24 / 59	3.26	1.33	8.03	65 / 242	1.71	1.08	2.73
Chronic lung disease	43 / 173	1.78	1.20	2.64	93 / 548	1.69	1.16	2.46
Chronic kidney disease	30 / 61	3.62	1.81	7.25	47 / 197	1.18	0.58	2.39
Diabetes mellitus	25 / 115	0.85	0.39	1.84	71 / 393	1.57	1.03	2.39
Rheumatic disease							1	
Rheumatoid arthritis	46 / 283	1		[Reference]	123 / 1104	1	[Referenc	
Systemic lupus erythematosus	17 / 77	1.42	0.59	3.41	19 / 315	0.96	0.57	1.59
Vasculitis	18 / 52	1.32	0.59	2.92	49 / 273	0.68	0.44	1.04
Other connective tissue diseases	21/108	1.17	0.59	2.29	32 / 365	0.63	0.45	0.88
Psoriasis arthritis	5 / 79	0.53	0.16	1.77	15 / 350	0.72	0.41	1.27
Spondyloarthritis	3 / 79	0.45	0.15	1.34	12 / 344	0.77	0.30	1.97
Other inflammatory arthritis or non-systemic JIA	1 / 19	0.68	0.10	4.50	9 / 90	0.77	0.40	1.49

Other rheumatic diseases (not IJDs / CTDs / vasculitis)	1 / 45	0.01	0.00	1834.66	23 / 184	0.64	0.46	0.88
Medication								
Methotrexate	5 / 92	1		[Reference]	42 / 503	1		[Reference]
No DMARD therapy	27 / 134	4.64	1.64	13.15	97 / 605	1.93	1.33	2.78
Leflunomide	6 / 19	6.96	2.64	18.39	6 / 71	0.96	0.41	2.25
Antimalarials	8 / 60	2.28	0.88	5.92	19 / 366	0.96	0.57	1.60
Sulfasalazine	6 / 25	7.44	1.35	40.89	27 / 119	3.27	1.59	6.72
Immunosuppressants	19 / 83	3.95	1.24	12.59	19 / 193	1.98	1.09	3.58
Rituximab	12 / 52	3.50	1.11	11.07	30 / 140	5.16	3.00	8.89
Other b/tsDMARDs	25 / 261	2.76	1.14	6.70	36 / 999	0.76	0.49	1.20
Glucocorticoids (GCs)								
No GCs	28 / 336	1	[Reference]		136 / 2081	1	1 [Referen	
GCs 1-10mg/d	51 / 266	1.61	0.86	3.02	119 / 797	1.44	0.94	2.19
GCs > 10 mg/d	30 / 120	1.71	0.94	3.10	19 / 105	1.69	0.80	3.59

		Glucocorticoids	No glucocorticoids					
N deaths/patients (%)			219	) / 1288 (17.0%)				165 / 2417 (6.8%)
	N deaths/patients	OR		95% CI	N deaths/patients	OR		95% CI
Age, years								
Age ≤ 65	71 / 754	1		[Reference]	47 / 1811	1		[Reference]
65 years < Age ≤ 75	52 / 265	1.80	1.21	2.68	<b>5</b> 7 / 379	5.54	3.17	9.70
Age > 75	97 / 269	4.67	3.25	6.71	61 / 227	8.75	4.48	17.10
Male sex (vs. female)	85 / 407	1.16	0.86	1.57	76 / 781	1.71	1.16	2.51
Ever smoked (vs. never)	73 / 318	1.25	0.94	1.65	67 / 604	1.12	0.74	1.69
Comorbidities	·	·			·			
Hypertension alone or CVD alone	94 / 474	1.43	0.92	2.23	61 / 676	0.95	0.67	1.36
Hypertension and CVD	54 / 154	1.87	1.09	3.22	35 / 147	1.86	1.28	2.71
Chronic lung disease	84 / 316	2.03	1.43	2.89	52 / 406	1.47	0.89	2.44
Chronic kidney disease	51/151	1.79	0.99	3.22	25 / 108	1.58	0.71	3.49
Diabetes mellitus	55 / 215	1.32	0.76	2.31	41 / 293	1.51	0.97	2.35
Rheumatic disease								
Rheumatoid arthritis	91 / 516	1		[Reference]	78 / 871	1	[Refer	
Systemic lupus erythematosus	26 / 198	1.20	0.63	2.31	10/193	1.11	0.40	3.07
Vasculitis	58 / 240	0.95	0.51	1.76	9 / 85	0.57	0.11	3.11
Other connective tissue diseases	31 / 181	0.84	0.56	1.25	22 / 292	0.59	0.37	0.95
Psoriasis arthritis	4 / 53	0.52	0.11	2.50	15 / 376	0.68	0.41	1.15
Spondyloarthritis	3 / 38	0.69	0.27	1.76	12 / 385	0.68	0.28	1.68
Other inflammatory arthritis or non-systemic JIA	5 / 24	1.04	0.27	3.96	5 / 85	0.58	0.26	1.30

Other rheumatic diseases (not IJDs / CTDs / vasculitis)	7 / 69	0.48	0.17	1.33	17 / 160	0.51	0.28	0.91
High/moderate/severe disease activity (DA) vs. remission/low DA	80 / 386	1.95	1.30	2.92	28 / 336	1.74	0.98	3.08
Medication								
Methotrexate	18 / 212	1		[Reference]	29 / 383	1		[Reference]
No DMARD therapy	74 / 296	3.11	2.12	4.57	50 / 444	1.72	0.94	3.17
Leflunomide	9 / 43	3.40	1.83	6.34	3 / 47	0.52	0.17	1.63
Antimalarials	18 / 137	1.81	1.19	2.77	9 / 289	0.59	0.26	1.33
Sulfasalazine	11 / 48	3.17	1.22	8.27	22 / 96	4.00	1.72	9.28
Immunosuppressants	24 / 176	2.27	1.61	3.19	14 / 100	3.26	1.45	7.31
Rituximab	30 / 99	5.52	2.13	14.33	12 / 94	3.41	1.57	7.41
Other b/tsDMARDs	35 / 289	1.78	1.13	2.81	26 / 971	0.62	0.35	1.08