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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 prednisolone-equivalent 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 anti-rheumatic 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-19-related 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.^{1–3}

Whether people with rheumatic diseases belong to a vulnerable, higher risk population for SARS-CoV-2 infection and have poorer outcomes is unclear.^{1–8} In general, this population seems to have similar or only slightly poorer outcomes compared with those without rheumatic disease.^{7–9} 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,¹⁰ 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.^{11–12} Analysis of the first 600 patients revealed that older age and comorbidities were associated with hospitalisation,¹³ similar to results in the general population.^{8–14} 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.^{11–13} 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 anti-rheumatic 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 Burmester¹⁵; 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 diseases¹⁶ 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.

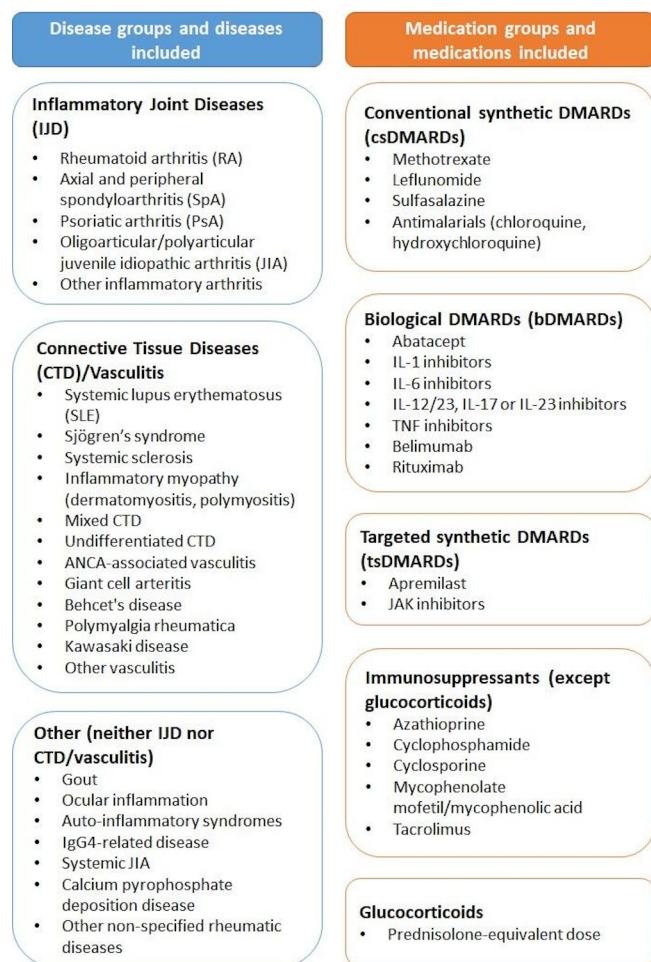


Figure 1 Disease and medication groups. ANCA, anti-neutrophil cytoplasm antibodies; DMARD, disease-modifying antirheumatic drugs; IgG, immunoglobulin; IL, interleukin; JAK, Janus kinase; TNF, tumour necrosis factor.

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.¹⁷ 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.¹⁸

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 ≤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 ≤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. One-quarter 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.

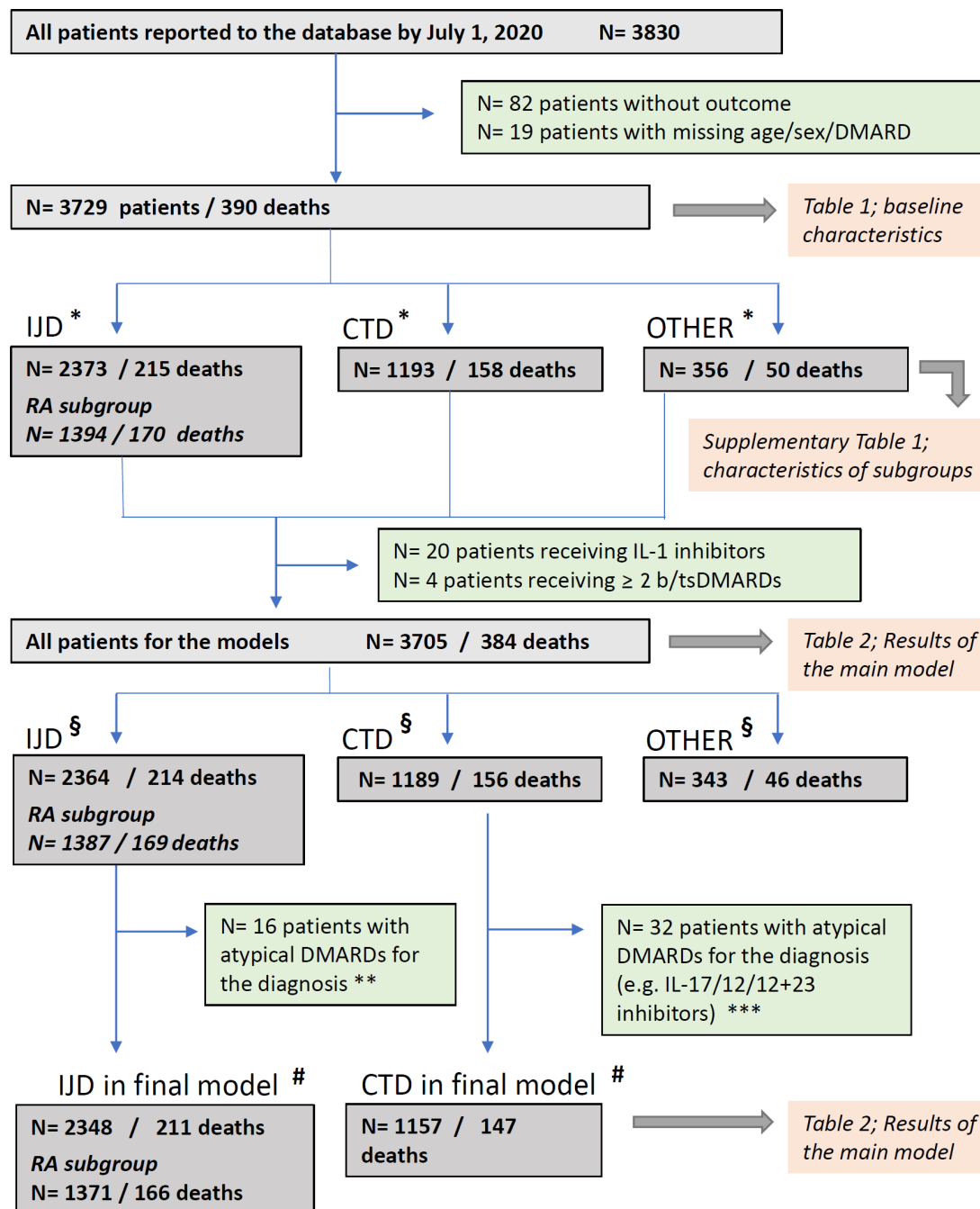


Figure 2 Patient flowchart. Some patients had diagnoses in multiple groups; as a result, the sum of patients in each group is greater than the total number of patients. (*) Patients belonging to more than one diagnostic group: IJD and CTD: N=78 (10 deaths); IJD and other: N=70 (12 deaths); CTD and other: N=50 (13 deaths); IJD and CTD and other: N=5 (2 deaths). (§) Patients belonging to more than one diagnostic 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 diagnostic 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 ≥ 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 ≥ 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

Table 1 Patient demographic and clinical characteristics

Parameter	Not deceased	Deceased	Total
N	3339	390	3729
General			
Age (years)	55.5 (15.2)	69.7 (14.6)	57.0 (15.7)
≤30	197 (5.9)	9 (2.3)	206 (5.5)
31–50	1012 (30.3)	31 (7.9)	1043 (28)
51–65	1255 (37.6)	82 (21)	1337 (35.9)
66–75	536 (16.1)	109 (27.9)	645 (17.3)
>75	339 (10.2)	159 (40.8)	498 (13.4)
Male sex	1031 (30.9)	164 (42.1)	1195 (32)
Ever smoker	664 (23.3) (N=2854) (Missing=485)	112 (36.1) (N=310) (Missing=80)	776 (24.5) (N=3164) (Missing=565)
Regions			
African region	14 (0.4)	2 (0.5)	16 (0.4)
Eastern Mediterranean region	83 (2.5)	11 (2.8)	94 (2.5)
European region	2040 (61.1)	275 (70.5)	2315 (62.1)
North American region	1024 (30.7)	81 (20.8)	1105 (29.6)
South American region	112 (3.4)	10 (2.6)	122 (3.3)
South-East Asian region	11 (0.3)	0	11 (0.3)
Western Pacific region	55 (1.6)	11 (2.8)	66 (1.8)
Inflammatory joint diseases			
Rheumatoid arthritis	1224 (36.7)	170 (43.6)	1394 (37.4)
Spondyloarthritis	416 (12.5)	15 (3.8)	431 (11.6)
Psoriatic arthritis	420 (12.6)	20 (5.1)	440 (11.8)
Juvenile idiopathic arthritis (poly, oligo, not systemic)	21 (0.6)	4 (1)	25 (0.7)
Other inflammatory arthritis	90 (2.7)	8 (2.1)	98 (2.6)
Total Inflammatory joint diseases	2158 (64.6)	215 (55.1)	2373 (63.6)
Connective tissue diseases/Vasculitis			
Systemic lupus erythematosus	355 (10.6)	36 (9.2)	391 (10.5)
Connective tissue diseases (other than SLE)	473 (14.2)	60 (15.4)	533 (14.3)
Vasculitis	258 (7.7)	68 (17.4)	326 (8.7)
Total CTD	1035 (31)	158 (40.5)	1193 (32.0)
Other RMDs			
Total	306 (9.2)	50 (12.8)	356 (9.5)
Disease activity			
	N=2464 (Missing=875)	N=294 (Missing=96)	N=2758 (Missing=971)
Remission	799 (32.4)	94 (32)	893 (32.4)
Minimal/low disease activity	1202 (48.8)	107 (36.4)	1309 (47.5)
Moderate disease activity	388 (15.7)	60 (20.4)	448 (16.2)
Severe/high disease activity	75 (3)	33 (11.2)	108 (3.9)
Other outcomes			
Hospitalised	1368 (43.3) (N=3162) (Missing=177)	371 (96.6) (N=384) (Missing=6)	1739 (49) (N=3546) (Missing=183)
Invasive ventilation	67 (2.5) (N=2701) (Missing=638)	120 (40.8) (N=294) (Missing=96)	187 (6.2) (N=2995) (Missing=734)
Comorbidities			
	N=3314 (Missing=25)	N=386 (Missing=4)	N=3700 (Missing=29)
Hypertension	1095 (33)	212 (54.9)	1307 (35.3)
Cardiovascular disease	318 (9.6)	124 (32.1)	442 (11.9)
Cerebrovascular disease	89 (2.7)	20 (5.2)	109 (2.9)
Chronic lung disease	581 (17.5)	138 (35.8)	719 (19.4)
Chronic kidney disease	181 (5.5)	77 (19.9)	258 (7)
Obesity (BMI ≥30)	539 (16.3)	58 (15)	597 (16.1)
Morbid obesity (BMI ≥40)	106 (3.2)	16 (4.1)	122 (3.3)
Diabetes	410 (12.4)	95 (24.6)	505 (13.6)
Cancer	165 (5)	49 (12.7)	214 (5.8)

Continued

Table 1 Continued

Parameter	Not deceased	Deceased	Total
Other comorbidities	771 (23.3)	126 (32.6)	897 (24.2)
Number of comorbidities	1.3 (1.3)	2.5 (1.6)	1.4 (1.3)
No comorbidity	1090 (32.9)	28 (7.3)	1118 (30.2)
One comorbidity	1032 (31.1)	83 (21.5)	1115 (30.1)
Two comorbidities	597 (18)	110 (28.5)	707 (19.1)
≥3 comorbidities	595 (18)	165 (42.7)	760 (20.5)
DMARD therapies			
csDMARDs monotherapy	592 (17.7)	59 (15.1)	651 (17.5)
csDMARDs combination therapy	692 (20.7)	61 (15.6)	753 (20.2)
Methotrexate monotherapy	531 (15.9)	47 (12.1)	578 (15.5)
Methotrexate combination therapy	607 (18.2)	52 (13.3)	659 (17.7)
Leflunomide monotherapy	61 (1.8)	12 (3.1)	73 (2)
Leflunomide combination therapy	120 (3.6)	10 (2.6)	130 (3.5)
Sulfasalazine monotherapy	51 (1.5)	16 (4.1)	67 (1.8)
Sulfasalazine combination therapy	129 (3.9)	26 (6.7)	155 (4.2)
Antimalarial monotherapy	287 (8.6)	17 (4.4)	304 (8.2)
Antimalarial combination therapy	322 (9.6)	39 (10)	361 (9.7)
Immunosuppressants monotherapy	149 (4.5)	26 (6.7)	175 (4.7)
Immunosuppressants combination therapy	147 (4.4)	21 (5.4)	168 (4.5)
Mycophenolate mofetil monotherapy	68 (2)	14 (3.6)	82 (2.2)
Mycophenolate mofetil combination therapy	81 (2.4)	15 (3.8)	96 (2.6)
Azathioprine monotherapy	63 (1.9)	7 (1.8)	70 (1.9)
Azathioprine combination therapy	51 (1.5)	3 (0.8)	54 (1.4)
Cyclophosphamide monotherapy	10 (0.3)	3 (0.8)	13 (0.3)
Cyclophosphamide combination therapy	5 (0.1)	5 (1.3)	10 (0.3)
Tacrolimus monotherapy	5 (0.1)	2 (0.5)	7 (0.2)
Tacrolimus combination therapy	11 (0.3)	0	11 (0.3)
Ciclosporin monotherapy	3 (0.1)	0	3 (0.1)
Ciclosporin combination therapy	11 (0.3)	1 (0.3)	12 (0.3)
bDMARDs monotherapy	675 (20.2)	48 (12.3)	723 (19.4)
bDMARDs combination therapy	562 (16.8)	46 (11.8)	608 (16.3)
TNF inhibitors monotherapy	434 (13)	13 (3.3)	447 (12)
TNF inhibitors combination therapy	340 (10.2)	17 (4.4)	357 (9.6)
Abatacept monotherapy	28 (0.8)	4 (1)	32 (0.9)
Abatacept combination therapy	46 (1.4)	5 (1.3)	51 (1.4)
B-cell-targeted bDMARDs monotherapy	71 (2.1)	25 (6.4)	96 (2.6)
B-cell-targeted bDMARDs combination therapy	106 (3.2)	18 (4.6)	124 (3.3)
Rituximab monotherapy	66 (2)	25 (6.4)	91 (2.4)
Rituximab combination therapy	85 (2.5)	17 (4.4)	102 (2.7)
Belimumab monotherapy	5 (0.1)	0	5 (0.1)
Belimumab combination therapy	22 (0.7)	1 (0.3)	23 (0.6)
IL-6 inhibitors monotherapy	51 (1.5)	3 (0.8)	54 (1.4)
IL-6 inhibitors combination therapy	34 (1)	2 (0.5)	36 (1)

Continued

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. One-fifth (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 ≤65 years. The association was even more pronounced in patients over 75 years (6.18, 4.47 to 8.53; vs ≤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

Table 2 Multivariable logistic regression analysis of factors associated with COVID-19-related death in patients with rheumatic diseases (all patients)

N deaths/patients (%)	All				Patients with inflammatory joint diseases (IJDs)				Only patients with rheumatoid arthritis				Patients with connective tissue diseases (CTDs) or vasculitis			
	384/3705 (10.4%)				211/2348 (9.0%)				166/1371 (12.1%)				147/1157 (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	N deaths/patients	OR	95% CI	
Age, years																
Ages<65	118/2565	1	Reference	55/1657	1	Reference	40/840	1	Reference	56/779	1	Reference				
65 years<=Ages<75	109/644	3	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				
Ages>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	1	Reference	166/1373	1	Reference	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.				
Systemic lupus erythematosus	36/391	1.2	0.70 to 2.04	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	32/378	1	Reference				
Vasculitis	67/325	0.8	0.60 to 1.08	n.a.	n.a.	n.a.	n.a.	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.	n.a.	n.a.	n.a.	n.a.	51/461	0.78	0.39 to 1.54				
Psooriasis arthritis	19/429	0.75	0.53 to 1.07	19/437	0.82	0.55 to 1.22	n.a.	n.a.	n.a.	n.a.	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.	n.a.	n.a.	n.a.	n.a.				
Other inflammatory arthritis or non-systemic IIA	10/109	0.79	0.46 to 1.34	11/114	0.76	0.43 to 1.36	n.a.	n.a.	n.a.	n.a.	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.	n.a.	n.a.	n.a.	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	1	Reference	34/354	1	Reference	6/94	1	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.	n.a.	n.a.				
Antimalarials	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				
Sulfasalazine	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.	n.a.	n.a.				
Immunosuppressants	38/276	2.22	1.43 to 3.46	n.a.	n.a.	n.a.	n.a.	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				
Abatacept	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.	n.a.	n.a.				
Rituximab	42/192	4.04	2.32 to 7.03	22/90	5.42	2.77 to 10.61	12/86	4.99	2.43 to 10.26	22/104	3.72	1.21 to 11.48				
Belimumab	1/27	0.71	0.19 to 2.68	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	1/27	1.07	0.21 to 5.37				
IL-6 inhibitors	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.	n.a.	n.a.	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.	n.a.	n.a.				
Glucocorticoids (GCs)																
No GCs	165/2417	1	Reference	109/1721	1	Reference	78/863	1	Reference	38/551	1	Reference				
GCs 1-10 mg/day	170/1062	1.43	0.98 to 2.09	89/567	1.36	0.76 to 2.45	78/464	1.34	0.66 to 2.74	75/469	1.69	1.11 to 2.57				

Continued

Table 2 Continued

	Patients with inflammatory joint diseases (JDs)			Only patients with rheumatoid arthritis			Patients with connective tissue diseases (CTDs) or vasculitis		
All	211/2348 (9.0%)			166/1371 (12.1%)			147/1157 (12.7%)		
	N deaths/patients	OR	95% CI	N deaths/patients	OR	95% CI	N deaths/patients	OR	95% CI
GCs > 10mg/day	49/226	1.69	1.18 to 2.41	12/60	1.55	0.67 to 3.57	10/44	1.59	0.6 to 4.18
							34/137	1.93	1.11 to 3.36

Missing values were 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 ≤ 20 patients for that analysis or if there were no deaths reported for that specific medication. TNF, tumour necrosis factor; CTD, connective tissue diseases; CVD, cardiovascular disease; DMARD, disease-modifying antirheumatic drugs; GC, glucocorticoids; IL, interleukin; JIA, juvenile idiopathic arthritis; N, number; n.a., not applicable; sDMARD, targeted synthetic disease-modifying antirheumatic drugs.

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.¹ Other factors associated with death were older age, male sex and the presence of comorbidities, which is consistent with reports from the general population.⁸ 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.¹⁹ 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)).²⁰ 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.²¹⁻²⁴ 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

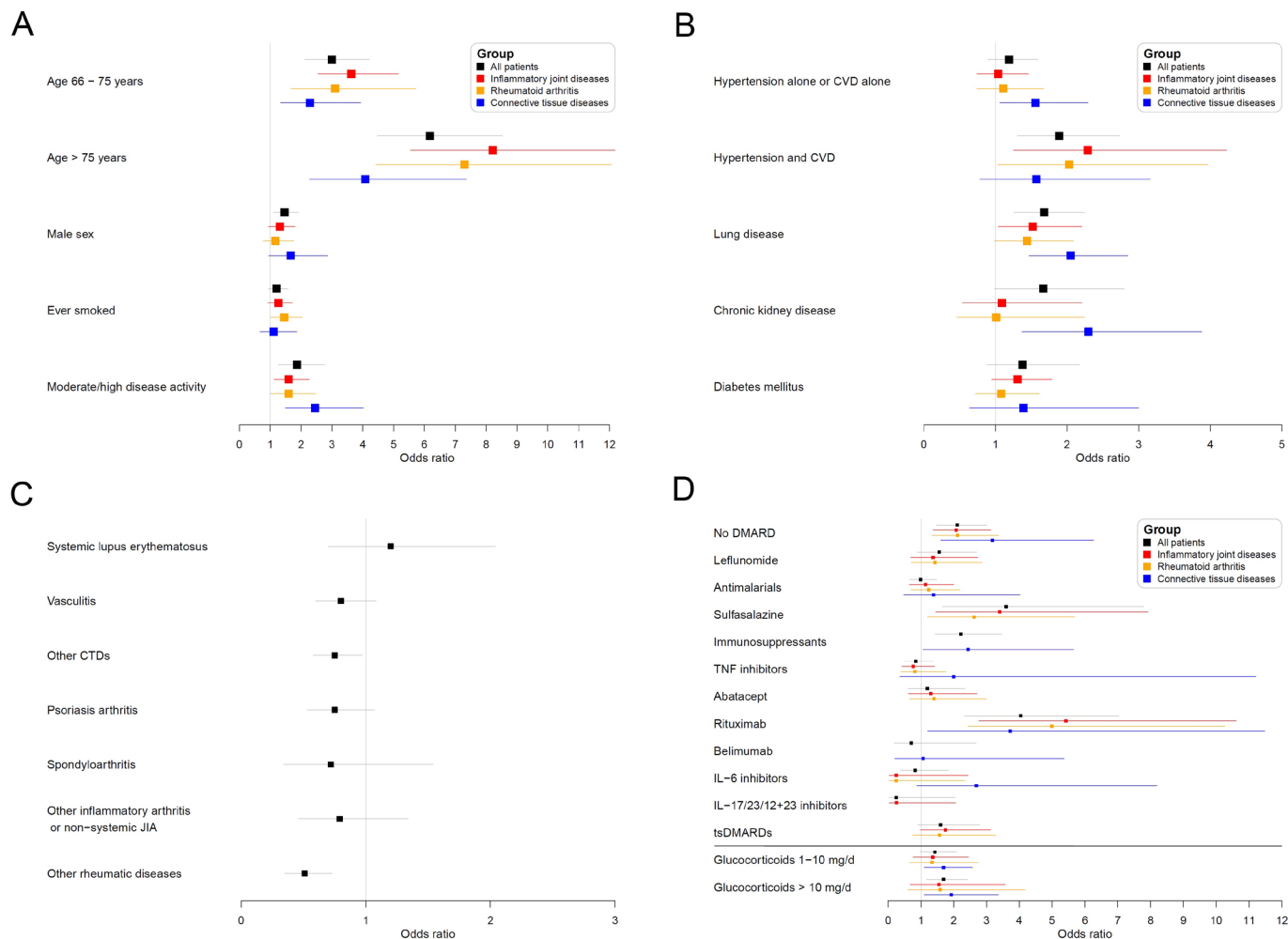


Figure 3 Results of the main logistic regression analysis. Shown are multivariable-adjusted ORs for the outcome COVID-19-related death with 95% CIs, assessing the association with (A) general patient characteristics, (B) comorbidities, (C) rheumatic disease diagnoses (RMD) and (D) rheumatic disease medications. 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) ≤ 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 antirheumatic 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 hyperinflammatory state produced by COVID-19, with mostly disappointing randomised trial results.^{25 26} 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.^{27 28} 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, case-reporting registry, it may be subject to selection bias if more

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.^{29 30} 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

Supplementary table 1. Patient demographic and clinical characteristics stratified by rheumatic disease diagnostic subgroup									
	Inflammatory joint diseases			Rheumatoid arthritis			Connective tissue diseases and vasculitis		
Parameter	Not deceased	Deceased	Total	Not deceased	Deceased	Total	Not deceased	Deceased	Total
N	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) (N=162)	508 (25.4) (N=2001)	260 (25.4) (N=1025)	56 (43.1) (N=130)	316 (27.4) (N=1155)	185 (20.6) (N=897)	36 (27.5) (N=131)	221 (21.5) (N=1028)
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)

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)	8 (3.7)	98 (4.1)	3 (0.2)	0	3 (0.2)	7 (0.7)	1 (0.6)	8 (0.7)
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	<i>N=1563</i>	<i>N=168</i>	<i>N=1731</i>	<i>N=943</i>	<i>N=131</i>	<i>N=1074</i>	<i>N=822</i>	<i>N=118</i>	<i>N=940</i>
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) (<i>N=1148</i>)	158 (95.2) (<i>N=166</i>)	655 (49.8) (<i>N=1314</i>)	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) (<i>N=1771</i>)	75 (43.9) (<i>N=171</i>)	112 (5.8) (<i>N=1942</i>)	22 (2.2) (<i>N=993</i>)	61 (44.5) (<i>N=137</i>)	83 (7.3) (<i>N=1130</i>)	28 (3.4) (<i>N=815</i>)	44 (38.3) (<i>N=115</i>)	72 (7.7) (<i>N=930</i>)
Comorbidities	<i>N=2143</i>	<i>N=214</i>	<i>N=2357</i>	<i>N=1215</i>	<i>N=169</i>	<i>N=1384</i>	<i>N=1026</i>	<i>N=155</i>	<i>N=1181</i>
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 comorbidities	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 comorbidityes	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)

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, IL-23, IL-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) (N=2130)	101 (48.6) (N=208)	622 (26.6) (N=2338)	417 (34.6) (N=1205)	90 (54.2) (N=166)	507 (37) (N=1371)	501 (48.8) (N=1027)	115 (74.2) (N=155)	616 (52.1) (N=1182)

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

Supplementary table 2. Patient demographic and clinical characteristics stratified by country (six countries with the highest number of reported cases)							
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) (N=793)	132 (45.2) (N=292)	86 (29.5) (N=292)	60 (27.5) (N=218)	14 (7.8) (N=18)	633 (24.6) (N=2569)
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)							
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)	275 (65.8) (N=418)	201 (64.2) (N=313)	133 (55.6) (N=239)	60 (30.6) (N=196)	1360 (47.3) (N=2873)
Invasive ventilation	64 (7.9) (N=807)	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	<i>N=1000</i>	<i>N=791</i>	<i>N=434</i>	<i>N=300</i>	<i>N=247</i>	<i>N=192</i>	<i>N=2964</i>
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 ≥ 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 comorbidities	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 comorbidities	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) (N=793)	128 (30) (N=427)	165 (52.4) (N=315)	98 (40.3) (N=243)	82 (41.6) (N=197)	1009 (34) (N=2965)
0 mg/d < GC <= 10mg/d	226 (22.9) (N=985)	205 (25.9) (N=791)	87 (20.5) (N=425)	135 (43.7) (N=309)	64 (30.2) (N=212)	74 (37.8) (N=196)	791 (27.1) (N=2918)
GC > 10 mg/d	52 (5.3) (N=985)	45 (5.7) (N=791)	37 (8.7) (N=425)	24 (7.8) (N=309)	3 (1.4) (N=212)	6 (3.1) (N=196)	167 (5.7) (N=2918)
NSAID	209 (22.9) (N=914)	85 (10.7) (N=793)	51 (13.3) (N=385)	53 (18.6) (N=285)	52 (21.9) (N=21.9)	36 (19.7) (N=19.7)	486 (17.4) (N=2798)
<p>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.</p> <p>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 anti-inflammatory drugs; SLE, systemic lupus erythematosus; TNF, tumour necrosis factor; tsDMARD, targeted synthetic disease modifying antirheumatic drugs.</p>							

Supplementary table 3. Patient demographic and clinical characteristics stratified by main medication of interest

Parameter	MTX	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) (N=290)	167 (23.6) (N=709)	20 (27.8) (N=72)	38 (23.3) (N=163)	10 (12.5) (N=80)	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)
Spondyloarthritis	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) (N=77)	127 (71.3) (N=178)	26 (29.9) (N=87)	37 (34.3) (N=108)	55 (43.7) (N=126)	442 (61.7) (N=716)	1739 (49) (N=3546)
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/Leflunomide	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) (N=90)	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)

Supplementary table 4. Multivariable logistic regression analysis of factors associated with COVID-19-related death in patients with rheumatic diseases (excluding patients reported from France)																
	All				Patients with inflammatory joint diseases (IJDs)				Only patients with rheumatoid arthritis				Patients with connective tissue diseases (CTDs) or vasculitis			
N deaths/patients (%)	324 / 2921 (11.1%)				186 / 1818 (10.2%)				146 / 1124 (13.0 %)				113 / 932 (12.1%)			
	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	108 / 2018	1	[Reference]		52 / 1259	1	[Reference]		38 / 692	1	[Reference]		49 / 657	1	[Reference]	
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	[Reference]		146 / 1126	1	[Reference]							n.a.		
Systemic lupus erythematosus	34 / 341	1.28	0.71	2.29									30 / 328	1	[Reference]	
Vasculitis	49 / 254	0.75	0.54	1.05									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	[Reference]		33 / 366	1	[Reference]		27 / 273	1	[Reference]		5 / 69	1	[Reference]			
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						n.a.
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.								
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.
Glucocorticoids (GCs)																		

No GCs	148 / 1885	1	[Reference]		103 / 1301	1	[Reference]		76 / 700	1	[Reference]		31 / 465	1	[Reference]	
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 ≤ 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 5. Multivariable logistic regression analysis of factors associated with COVID-19-related death in patients with rheumatic diseases in patients with no missing values (complete case analysis)																
	All				Patients with inflammatory joint diseases (IJDs)				Only patients with rheumatoid arthritis				Patients with connective tissue diseases (CTDs) or vasculitis			
N deaths/patients (%)	207 / 2081 (9.9%)				113 / 1232 (9.1%)				87 / 770 (11.3%)				74 / 699 (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	[Reference]		33 / 868	1	[Reference]		24 / 493	1	[Reference]		33 / 518	1	[Reference]	
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																
Rheumatoid arthritis	84 / 772	1	[Reference]		87 / 770	1	[Reference]								n.a.	
Systemic lupus erythematosus	19 / 265	0.99	0.409	2.37			n.a.				n.a.		16 / 256	1	[Reference]	

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						n.a.		
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								
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	[Reference]		22 / 252	1	[Reference]		17 / 182	1	[Reference]		2 / 46	1	[Reference]	
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		n.a.				n.a.			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	[Reference]			59 / 917	1	[Reference]			41 / 511	1	[Reference]			22 / 373	1	[Reference]
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 ≤ 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. Multivariable logistic regression analysis of factors associated with COVID-19-related death in patients with rheumatic diseases with a confirmed or highly likely COVID-19 diagnosis																
	All				Patients with inflammatory joint diseases (IJDs)				Only patients with rheumatoid arthritis				Patients with connective tissue diseases (CTDs) or vasculitis			
N deaths/patients (%)	345 / 2968 (11.6%)				184 / 1619 (10.2%)				143 / 946 (13.1%)				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	[Reference]		48 / 1204	1	[Reference]		35 / 627	1	[Reference]		53 / 666	1	[Reference]	
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	[Reference]		143 / 1091	1	[Reference]								n.a.	
Systemic lupus erythematosus	35 / 336	1.31	0.77	2.23		n.a.				n.a.			31 / 326	1	[Reference]	

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						n.a.		
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								
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	[Reference]		39 / 387	1	[Reference]		32 / 279	1	[Reference]		6 / 80	1	[Reference]	
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	[Reference]		97 / 1298	1	[Reference]		67 / 681	1	[Reference]		36 / 467	1	[Reference]	
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 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 ≤ 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 7. Multivariable logistic regression analysis of factors associated with COVID-19-related death or invasive ventilation in patients with rheumatic diseases													
	All			Patients with inflammatory joint diseases (IJDs)			Only patients with rheumatoid arthritis			Patients with connective tissue diseases (CTDs) or vasculitis			
N deaths or invasive ventilations (IV) /patients (%)	451 / 3075 (14.7%)			248 / 1970 (12.6%)			188 / 1148 (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	[Reference]	81 / 1425	1	[Reference]	51 / 721	1	[Reference]	80 / 638	1	[Reference]	
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	[Reference]	188 / 1150	1	[Reference]			n.a.			n.a.	

Systemic lupus erythematosus	46 / 322	1.26	0.83	1.91		n.a.							42 / 310	1	[Reference]	
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		n.a.							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								
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	[Reference]		48 / 390	1	[Reference]		39 / 289	1	[Reference]		8 / 70	1	[Reference]	
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.				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		n.a.		
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.						
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				
Glucocorticoids (GCs)																
No GCs	202 / 2032	1	[Reference]		136 / 1450	1	[Reference]		90 / 722	1	[Reference]		45 / 452	1	[Reference]	
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
<p>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 ≤ 20 patients for that analysis or if there were no deaths reported for that specific medication.</p> <p>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.</p>																

Supplementary table 8. Multivariable logistic regression analysis of factors associated with COVID-19-related death in all patients with a reduced number of regressor variables																
	All				Patients with inflammatory joint diseases (IJDs)				Only patients with rheumatoid arthritis				Patients with connective tissue diseases (CTDs) or vasculitis			
N deaths/patients (%)	384/3705 (10.4%)				211/2348 (9.0%)				166/1371 (12.1%)				147/1157 (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	[Reference]		55 / 1657	1	[Reference]		40 / 840	1	[Reference]		56 / 779	1	[Reference]	
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																
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	[Reference]		166 / 1373	1	[Reference]							n.a.		
Systemic lupus erythematosus	36 / 391	1.10	0.67	1.81									32 / 378	1	[Reference]	
Vasculitis	67 / 325	0.85	0.64	1.11		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	[Reference]		41 / 487	1	[Reference]		34 / 354	1	[Reference]		6 / 94	1	[Reference]	
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	9 / 89	2.04	0.60	6.92
Belimumab						n.a.				n.a.						
IL-6 inhibitors																
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	[Reference]		109 / 1721	1	[Reference]		78 / 863	1	[Reference]		38 / 551	1	[Reference]	

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
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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 ≤ 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 9. Multivariable logistic regression analysis of factors associated with COVID-19 death in patients from the six countries providing the largest number of patients, considering country effects, with an otherwise reduced number of regressor variables																
	All				Patients with inflammatory joint diseases (IJDs)				Only patients with rheumatoid arthritis				Patients with connective tissue diseases (CTDs) or vasculitis			
N deaths/patients (%)	306 / 2974 (10.3%)				170 / 1903 (8.9%)				134 / 1102 (12.2%)				117 / 927 (12.6%)			
	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	76 / 2015	1	[Reference]		36 / 1321	1	[Reference]		25 / 658	1	[Reference]		36 / 597	1	[Reference]	
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	[Reference]		134 / 1103	1	[Reference]							n.a.		
Systemic lupus erythematosus	18 / 299	0.78	0.39	1.55									15 / 288	1	[Reference]	
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	[Reference]		28 / 387	1	[Reference]		23 / 278	1	[Reference]		6 / 77	1	[Reference]	
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																
Abatacept	14 / 268	1.25	0.62	2.51	10 / 216	1.05	0.46	2.40	9 / 109	1.38	0.56	3.41		n.a.		
IL-17/IL-23/IL-12+23 inhibitors										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	[Reference]		80 / 1406	1	[Reference]		55 / 701	1	[Reference]		30 / 454	1	[Reference]	

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	[Reference]		36 / 568	1	[Reference]		31 / 380	1	[Reference]		27 / 380	1	[Reference]	
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
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 ≤ 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 10. Multivariable logistic regression analysis of factors associated with COVID-19-related death stratified by age (> 65 years vs. ≤ 65 years)								
	> 65 years				≤ 65 years			
N deaths/patients (%)	266 / 1140 (23.3%)				118 / 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

Medication								
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
<p>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 ≤ 20 patients for that analysis or if there were no deaths reported for that specific medication.</p> <p>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.</p>								

Supplementary table 11. Multivariable logistic regression analysis of factors associated with COVID-19-related death stratified by sex								
	Male sex				Female sex			
N deaths/patients (%)	161 / 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

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)								
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
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 ≤ 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 12. Multivariable logistic regression analysis of factors associated with COVID-19-related death stratified by smoking habits								
	Ever smoked				Never smoked			
N deaths/patients (%)	140 / 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

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								
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)								
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
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 ≤ 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 13. Multivariable logistic regression analysis of factors associated with COVID-19-related death stratified by heart disease (hypertension and/or cardiovascular disease)								
	Heart disease				No heart disease			
N deaths/patients (%)	242 / 1439 (16.8%)				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

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]	[Reference]	33 / 238	1	[Reference]	[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]	[Reference]	69 / 1584	1	[Reference]	[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
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 ≤ 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 14. Multivariable logistic regression analysis of factors associated with COVID-19-related death stratified by chronic lung disease								
	Chronic lung disease				No chronic lung disease			
N deaths/patients (%)	136 / 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

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		[Reference]
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)								
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
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 ≤ 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 15. Multivariable logistic regression analysis of factors associated with COVID-19-related death stratified by disease activity								
	Moderate / severe disease activity				Low disease activity / remission			
N deaths/patients (%)	109 / 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								
Rheumatoid arthritis	46 / 283	1	[Reference]		123 / 1104	1	[Reference]	
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		[Reference]
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
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 ≤ 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 16. Multivariable logistic regression analysis of factors associated with COVID-19-related death stratified by glucocorticoid use								
	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	57 / 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	[Reference]	
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]	[Reference]	29 / 383	1	[Reference]	[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

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 ≤ 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.

COVID-19-related death in rheumatic diseases

This is the lay version of a paper published on behalf of the COVID-19 Global Rheumatology Alliance Consortium. It examines COVID-19-related death in people with rheumatic diseases. The original publication can be downloaded from the EULAR website: www.eular.org.

[Strangfeld A, et al. Factors Associated with COVID-19-related Death in People with Rheumatic Diseases: Results from the COVID-19 Global Rheumatology Alliance physician-reported registry. Ann Rheum Dis Published Online First: 27 January 2021. doi: 10.1136/annrheumdis-2020-219498](#)

Introduction

EULAR gives advice to doctors, nurses and patients about the best way to treat and manage rheumatic diseases. As part of the current global effort to understand and combat COVID-19, EULAR gave financial support to this registry project.

What do we already know?

There are more than 200 rheumatic diseases, including rheumatoid arthritis, spondyloarthritis, and systemic lupus erythematosus. Many of these diseases are autoimmune conditions that cause inflammation in the body. Rheumatic diseases typically affect joints, muscle, or connective tissue. They can also affect a person's internal organs.

People with rheumatic diseases are more prone to infection. This can be because of the disease itself and the way it affects the immune system, but also affected by some of the medicines used to treat the rheumatic disease. COVID-19 is the disease caused by a new type of coronavirus called severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). Clinical information for people with COVID-19 who have a rheumatic disease is limited, especially about factors that might make them more likely to die from the infection.

What does the paper say?

The registry collected information on 3729 people with rheumatic disease who had either a confirmed or highly likely case of COVID-19, or had symptoms of this infection. In total, 390 people died – just over 10%. The authors looked to see if there were any common factors in the people who died compared to those who recovered from the COVID-19 infection.

- **Older age and male sex are associated with COVID-19-related death.**
Of those who died, over two-thirds were over the age of 65. The risk of dying was even higher in people in over the age of 75, and for men compared to women. This is similar to what has been found in the general population.
- **Comorbidities are more common in people who die from COVID-19.**
Across all 3729 people included, most people had at least one other disease (comorbidity). The most common were hypertension (high blood pressure), chronic lung disease, and obesity. In the whole group, 21% of people had three or more comorbidities. When the authors looked only at the people who had died, 43% had three or more comorbidities. This is similar to what has been found in the general population.
- **Cardiovascular and chronic lung disease are more common in people dying from COVID-19.**
Other factors associated with dying from COVID-19 included chronic lung disease, or having

cardiovascular disease combined with hypertension. Chronic kidney disease was also a risk for people with connective tissue disease or vasculitis, but did not increase the risk of death for people with other types of rheumatic disease.

- **Disease-specific factors are associated with COVID-19-related death.**
People with moderate or high disease activity were more likely to die from COVID-19 than those with low disease activity or people who were in remission (no current signs and symptoms of their rheumatic disease).
- **Certain medications are associated with COVID-19-related death.**
People taking rituximab or sulfasalazine were more likely to die from COVID-19. A similar association was seen for a mixed group of immunosuppressants (azathioprine, cyclophosphamide, ciclosporin, mycophenolate and tacrolimus) compared to those using immunomodulators such as disease-modifying anti-rheumatic drugs (often shortened to DMARDs). However, the numbers were too low to allow individual analysis by immunosuppressive drug, making it difficult to interpret these results. Moderate to high doses of glucocorticoids (steroids) – more than 10 mg per day – were also associated with a higher risk of dying across all rheumatic diseases.

What does this mean for me?

These findings will help patients and doctors reach a shared understanding of risk of COVID-19 severe outcomes in patients with RMDs. If you have been in contact with a COVID-19 patient or have symptoms of COVID-19, you should contact your local health authorities and your rheumatologist. Generally, patients with RMD should continue to comply with all preventive and control measures and vaccination efforts prescribed by the health authorities in their countries, such as hand hygiene, wearing masks (ideally FFP2 masks) and holding distance of at least 2 meters from others.

Summary

Overall, the papers highlight that the risk of dying from COVID-19 varies according to people's underlying disease activity and what medicine they are taking. It is important for people with a rheumatic disease to continue to control their disease activity with DMARDs, but preferably without increasing the dose of any glucocorticoids, if possible. Withdrawal of effective treatments should be based on sound evidence, even during a pandemic.

If you have any questions or concerns about your disease or your medication, you should speak to a health professional involved in your care.

Disclaimer

The EULAR COVID-19 Database is based on rheumatologists and other clinicians voluntarily reporting cases, meaning that patients included do not necessarily represent the majority of patients with RMDs and COVID-19, but those who their doctors reported data to the database. Additionally, this database does not account for non-COVID-19 patients. Therefore, results cannot be directly extrapolated to the entire population of patients with RMDs and COVID-19, and should be interpreted cautiously.