

## ORIGINAL RESEARCH

# Self-protection strategies and health behaviour in patients with inflammatory rheumatic diseases during the COVID-19 pandemic: results and predictors in more than 12 000 patients with inflammatory rheumatic diseases followed in the Danish DANBIO registry

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**To cite:** Glintborg B, Jensen DV, Engel S, *et al.* Self-protection strategies and health behaviour in patients with inflammatory rheumatic diseases during the COVID-19 pandemic: results and predictors in more than 12 000 patients with inflammatory rheumatic diseases followed in the Danish DANBIO registry. *RMD Open* 2021;7:e001505. doi:10.1136/rmdopen-2020-001505

Received 2 November 2020  
Revised 14 December 2020  
Accepted 17 December 2020



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## ABSTRACT

**Aims** In Danish patients with inflammatory rheumatic diseases to explore self-protection strategies and health behaviour including adherence to disease-modifying antirheumatic treatment (DMARD) during the initial phase of the COVID-19 pandemic and again after the reopening of the society started. Furthermore, to identify characteristics of patients with high levels of anxiety and self-isolation.

**Methods** Patients in routine care followed prospectively in the nationwide DANBIO registry were invited to answer an online questionnaire regarding disease activity and COVID-19 infection, behaviour in March and June 2020. Responses were linked to patient data in DANBIO.

Characteristics potentially associated with anxiety, self-isolation and medication adherence (gender/age/diagnosis/education/work status/comorbidity/DMARD/smoking/EQ-5D/disease activity) were explored with multivariable logistic regression analyses.

**Results** We included 12 789 patients (8168 rheumatoid arthritis/2068 psoriatic arthritis/1758 axial spondyloarthritis/795 other) of whom 65% were women and 36% treated with biological DMARD. Self-reported COVID-19 prevalence was 0.3%. Patients reported that they were worried to get COVID-19 infection (March/June: 70%/45%) and self-isolated more than others of the same age (48%/38%). The fraction of patients who changed medication due to fear of COVID-19 were 4.1%/0.6%. Female gender, comorbidities, not working, lower education, biological treatment and poor European Quality of life, 5 dimensions were associated with both anxiety and self-isolation.

## Key messages

### What is already known about this subject?

- ▶ During the COVID-19 pandemic, fear of contracting SARS-CoV-2 infection impacts lives of patients with rheumatic diseases by reducing well-being, increasing self-isolation and leading to medication non-adherence.
- ▶ Patient and disease characteristics associated with anxiety, self-isolation and medication non-adherence remain unexplored as well as are changes in behaviour during the ongoing pandemic.

### What does this study add?

- ▶ In this nationwide study including >12 000 patients, we demonstrated high levels of anxiety and self-isolation in the early phase (March–April) but also when society gradually reopened in June 2020.
- ▶ Among risk factors for anxiety and self-isolation were female gender, not working, current biological treatment, having comorbidities and poor quality of life.
- ▶ Medication compliance was high, but fear of COVID-19 was the main reason for non-adherence.

### How might this impact on clinical practice?

- ▶ Attention to anxiety and self-isolation is important during the ongoing pandemic.

**Conclusion** In >12 000 patients with inflammatory arthritis, we found widespread anxiety and self-isolation, but high medication adherence, in the initial phase of the COVID-19 pandemic. This persisted during the gradual opening of society during the following months. Attention to patients' anxiety and self-isolation is important during this and potential future epidemics.

## BACKGROUND

During the corona pandemic, 36 million individuals have tested positive and global deaths associated with SARS-CoV-2 infection have exceeded 1 million.<sup>1</sup> In contrast to what was initially expected, no increased risk of SARS-CoV-2 infection in patients with rheumatic autoimmune diseases has been reported despite frequent treatment with immunosuppressive disease-modifying antirheumatic drugs (DMARDs).<sup>2-4</sup>

The pandemic has nevertheless had huge impact on the lives of patients with rheumatic diseases. Fear of infection has reduced well-being and impacted daily activities including self-isolation strategies.<sup>5,6</sup> Lock-down and lower access to counselling at the rheumatology clinics potentially cause misconceptions regarding medication risk and may induce self-protecting strategies such as non-adherence to DMARDs.<sup>5,7-9</sup> Previous studies of behavioural changes by the use of questionnaire or telephone interview have so far been fairly small (<500–900 patients), monocentric or with low response rates. Few have aimed to identify risk factors for anxiety and self-isolation (eg, diagnosis, gender, age, DMARD use, socioeconomic status),<sup>5</sup> and behavioural changes from the initial phase in March 2020 to the gradual reopening of society are unexplored.<sup>9</sup> To understand the full impact of the pandemic on rheumatologic patients, such knowledge is needed to identify risk groups that may need specific information or guidance.

In Denmark, a nationwide lock-down was introduced on 11 March 2020—the same day that the WHO declared COVID-19 disease a pandemic—including limited physical access to healthcare professionals, which was replaced by remote assistance (virtual consultations by phone/video). There was no access to physiotherapy and exercise, and for example, schools, museums, restaurants were closed. Moving freely around in the community, including shopping at supermarkets and the use of public transportation, was allowed, but a social distance of  $\geq$  (1–)2 m was encouraged. The use of facial masks and other protection aids were voluntary, whereas frequent hand washing and the use of hand sanitizer were recommended. Due to decreasing COVID-19 incidence, gradual reopening of society started on 14 April 2020 (after Easter).

In Denmark, patients with inflammatory rheumatic diseases treated in routine care (hospital and rheumatology private practice) are followed prospectively in the nationwide DANBIO registry.<sup>10</sup> The registry contains extensive information on disease characteristics, disease activity and treatment in individual patients. The aim

of the present study was to explore (1) self-protection strategies and health behaviour including adherence to DMARD treatment during the early stages of the pandemic (March 2020) and (2) changes therein by June 2020 in patients with inflammatory rheumatic diseases followed in DANBIO. Furthermore, we aimed to explore a wide range of patient and disease characteristics and their potential association with levels of anxiety and self-isolation.

## METHODS

The nationwide registry, DANBIO (danbio-online.dk), is a quality registry that covers >95% of adults with rheumatic diseases treated with biological(b-) DMARDs.<sup>10</sup> Since year 2005 newly diagnosed patients with rheumatoid arthritis (RA) and patients with established or suspected inflammatory rheumatic diseases irrespective of treatment (eg, psoriatic arthritis (PsA), axial spondyloarthritis (AxSpA)) have also been included. Registration of patients with connective tissue disorders (eg, systemic lupus erythematosus) is optional.<sup>11</sup> According to national treatment guidelines, disease activity, current antirheumatic treatment and outcomes (patient-reported and physician evaluated) should be registered prospectively at least annually and when medication is changed.<sup>10</sup>

Patients with inflammatory rheumatic disease,  $\geq$ 18 years old,  $\geq$ 1 registered DANBIO contact (=visit in hospital or rheumatology specialists in primary care) after 11 May 2019, alive and with ongoing contact to the clinic were eligible for inclusion. Invitations were sent by the use of the national electronic online system (e-boks.com/Danmark/da), a mandatory, national infrastructure for communication (electronic letters) from, for example, healthcare authorities to most (80%–90%, lower access with higher age) Danish citizens.<sup>12</sup> Patients were invited to answer the questionnaire 'You and your rheumatic disease during times with corona-virus' (in the following denoted 'COVID-19 questionnaire') from home by computer, tablet or smartphone after secure log-on with NemID (using a unique person-identifier (social security number)) at patient.danbio.dk.<sup>13</sup> Patient.danbio.dk (a Plone/Angular/Elasticsearch based IT-system with a HL7 FHIR questionnaire engine) enables patients in DANBIO to routinely enter patient-reported outcomes from home<sup>14</sup> and was implemented as part of this project.

Included participants answered the questionnaire once. The questionnaire had the following sections: current disease activity (health assessment questionnaire (HAQ)), patient acceptable symptom state (PASS), patient-reported outcomes depending on rheumatic diagnosis), consent to the present study, background information (number of persons in household, education and occupational status), self-reported comorbidities (eight conditions, see table 1), self-reported COVID-19 infection, impact of COVID-19 in the *first period* from 11 March to Easter (14 April 2020) (mental impact and behaviour including anxiety, self-isolation strategies and medication adherence), impact of

**Table 1** Baseline characteristics of included patients, stratified by diagnosis

	Rheumatoid arthritis* n=8168	Psoriatic arthritis* n=2068	Axial spondyloarthritis* n=1758	Other* n=795	Total n=12789
Gender, n (%)	Female	1194 (58)	811 (46)	547 (69)	8366 (65)
Age, years, n (%)	≤39	349 (4)	143 (7)	361 (21)	996 (8)
	40–59	2307 (28)	896 (43)	903 (51)	4436 (35)
	60–79	5022 (61)	987 (48)	483 (27)	6799 (53)
	≥80	490 (6)	42 (2)	11 (1)	558 (4)
From the questionnaire: self-reported characteristics					
Lives alone, n (%)	Yes	1652 (20)	356 (17)	281 (16)	2422 (19)
Highest education†, n (%)	Lower education	4415 (54)	1116 (54)	829 (47)	6715 (53)
	Medium/long	3696 (45)	942 (46)	920 (52)	5996 (47)
Occupational status†, n (%)	Working	3281 (40)	1104 (53)	1229 (70)	6076 (48)
Self-reported comorbidities, >1 answer allowed, n (%)	Lung disease, asthma	1019 (12)	213 (10)	165 (9)	1485 (12)
	Diabetes	603 (7)	204 (10)	84 (5)	935 (7)
	Heart disease	921 (11)	225 (11)	119 (7)	1341 (10)
	Cancer	208 (3)	33 (2)	23 (1)	276 (2)
	Hypertension	2778 (34)	751 (36)	398 (23)	4165 (33)
	Obesity	703 (9)	297 (14)	154 (9)	1218 (10)
	Psychiatric/depression	467 (6)	181 (9)	131 (7)	847 (7)
	Other	2167 (27)	585 (28)	495 (28)	3424 (27)
Number of self-reported comorbidities	0	2699 (33)	581 (28)	679 (39)	4204 (33)
	1	2860 (35)	708 (34)	584 (33)	4409 (34)
	≥2	2123 (26)	640 (31)	362 (21)	3351 (26)
Pregnancy, n	Yes	17 (0)	1 (0)	12 (1)	37 (0)
PASS, n (%)	Yes	6119 (75)	1414 (68)	1217 (69)	9295 (73)
Current disease activity, median (IQR)	HAQ, median (IQR)	0.50 (0.13–0.63)	0.63 (0.13–0.75)	0.50 (0.13–0.88)	0.50 (0.13–1.00)
	Patient global, VAS, mm, median (IQR)	28 (9–34)	35 (13–40)	31 (12–62)	29 (10–57)
	EQ-5D	0.80 (0.72–0.86)	0.77 (0.66–0.83)	0.77 (0.69–0.83)	0.80 (0.71–0.86)
Information captured from DANBIO: patient and disease characteristics‡					
Smoking status, n (%)	Current	1447 (18)	353 (17)	354 (20)	2266 (18)
	Previous	2364 (29)	621 (30)	447 (25)	3605 (28)
	Never	4279 (52)	1073 (52)	943 (54)	6769 (53)

Continued

Table 1 Continued

	Rheumatoid arthritis* n=8168	Psoriatic arthritis* n=2068	Axial		Total n=12 789
			spondyloarthritis* n=1758	Other* n=795	
Year of diagnosis, n (%)	Before 2005 2587 (34)	524 (25)	450 (26)	180 (23)	3741 (29)
Current medication§, n (%)	bDMARD (±csDMARD) 2572 (32)	790 (38)	1088 (62)	202 (25)	4652 (36)
	csDMARD (no bDMARD) 5014 (61)	1052 (51)	131 (7)	377 (47)	6574 (51)

Total n=12 789. Percentages are calculated among patients with available data (questionnaire: 93%–100% complete, previous information in DANBIO: 70%–100%, details in online supplemental table S2).

\*Diagnoses in DANBIO include rheumatoid arthritis (sero-positive, sero-negative, unspecified, juvenile arthritis) (47% erosive disease, 65% anti-CCP positive, 58% IgM-RF positive)/axial spondyloarthritis (ankylosing spondylitis, undifferentiated spondyloarthritis, non-radiographic axial spondyloarthritis)/psoriatic arthritis (psoriatic arthritis/arthritis)/other (systemic lupus erythematosus, Sjogren's disease, chorioretinitis, reactive arthritis, 'other', missing).

†Status before corona lockdown. The categories include education: lower (Blue collar, short courses, no education), medium/long (2–3 years+3–4 years+>4 years, other). Occupational status: working (student, full-time employee, part-time employee, flex-job, self-employed, other), not working (unemployed, retired, sick-leave).

‡According to latest registration in DANBIO before 11 March 2020.

§bDMARD irrespective of concomitant csDMARD, csDMARD group exclude patients on concomitant bDMARD.

¶bDMARD, biological disease-modifying antirheumatic drug; csDMARD, conventional synthetic disease-modifying antirheumatic drug; EQ-5D, European Quality of life, 5 Dimensions; HAQ, health assessment questionnaire; PASS, patient acceptable symptom state; VAS, visual analogue scale.

COVID-19 during the gradual reopening of society from Easter to the date of replying (mental and behaviour) and quality of life (EQ-5D, European Quality of life, 5 dimensions). It was beyond the scope to further explore symptoms and direct impact of any COVID-19 infection. Detailed patient information was available at [www.danbio.dk](http://www.danbio.dk). In the following, the first period is denoted *March* and the later period *June* 2020. Although SARS-CoV-2 is the infectious agent causing the COVID-19 disease, the term 'COVID-19' was used in the questionnaire in alignment with the terminology used in the media.

The questionnaire was developed in collaboration with four patient representatives. The full Danish version is available on request. The invitations were sent during week 21 (May 2020), and reminders to non-respondents during week 24 (June). Response was allowed until 1 July 2020. For patient flow, see online supplemental figure S1. Future questionnaires are planned.

For the current study, we obtained information from DANBIO regarding rheumatic diagnosis (ICD-10), disease characteristics (year of diagnosis, for RA: serological status and erosive status), current use of DMARDs and smoking status (current/previous/never) at the latest visit before 11 March 2020.

### Statistics

All data were analysed in the statistical software package R, V.3.6.1 (5 July 2019).

Patient characteristics are reported as numbers/percentages and medians (interquartile ranges) as appropriate. Tests were two-tailed with  $p < 0.05$  considered statistically significant. All data are reported as observed.

All questions and the corresponding answers are provided as reported by the patients. For a subgroup of questions, the answers were converted into binary outcomes, for example, 'I am very worried to get COVID-19 infection', yes (completely agree/mostly agree), no (neither nor/mostly disagree/completely disagree/do not know). These binary outcomes were explored with univariable and multivariable logistic regression analyses including covariables identified a priori as clinically relevant: gender, age ( $\leq 39/40-59/60-79/\geq 80$  years), diagnosis (RA/PsA/AxSpA/other rheumatic disease), number of comorbidities (0/1/>1), occupational status (working/non-working), education (none/lower, short/longer), cohabiting (yes/no), smoking status (current/previous/never), current use of biological DMARDs (including targeted synthetic DMARDs) (yes/no), current use of conventional synthetic (cs-)DMARDs (yes/no), PASS (yes/no), health-related quality of life (EQ-5D, continuous variable, 1=best score).

Current use of DMARD was categorised as the use of any biologic (b-)DMARD (irrespective of concomitant use of cs-DMARDs) or the use of any csDMARD (without concomitant bDMARD).

## Ethics

The project was approved by the regional data protection agency (P-2020-543, 14 May 2020). Patients gave electronic consent to participation.

## RESULTS

### Patient characteristics

A total of 36 152 patients in DANBIO were potentially eligible for inclusion, whereof 32 766 (91%) had access to E-boks and were invited to participate. Overall, 35% (12 789/36 152) patients answered the questionnaire and were included in the study (online supplemental figure S1). In patients aged 80+years, 55% (1419/2585) had access to E-boks. Included patients tended more frequently to be women, have RA and to be aged 60–79 years, whereas fewer patients ≤39 years of age completed the questionnaire (online supplemental table S1). Most patients answered the questionnaire between end of May and the first half of June (online supplemental figure S2).

Table 1 shows the baseline characteristics of the included patients. Of the 12 789 included patients 8168 had RA, 2068 PsA and 1758 had AxSpA, whereas few had connective tissue disorders, reflecting the cohorts in DANBIO. Most patients were women (8366/12789=65%) and few lived alone (2422/12789=19%). The cohort included 37 patients who were currently pregnant, 558 patients ≥80 years old and 67% (8585/12787) reported having at least one comorbidity. Most patients had HAQ <1, 73% (9295/12789) of patients reported to have acceptable symptom state (PASS), and 36% (4652/12789) were treated with a bDMARD (table 1; available data are listed in online supplemental table S2).

### SARS-CoV-2 infected

A total of 40/12 789 (0.3%) reported to have tested positive, seven of those had been hospitalised. Among infected, 50% (20/40) were male, median age was 54 years and 38% (15/40) were treated with a bDMARD at the time of infection (table 2). Characteristics of the SARS-CoV-2-infected patients appeared similar to that of included patients overall.

### Contact to rheumatology clinics and treatment

In total, 64% (8143/12789) of patients replied that they had been in contact with their rheumatology clinic during the first 2 months after lock-down, often by phone, and 31% (3932/12789) of patients had experienced cancellation of contacts due to the pandemic, mainly with the physician (67% (2618/3932) of patients with cancellations) and physiotherapist (17% (687/3932)) (online supplemental table S3). Due to COVID-19, 7% (857/12 789) of patients had experienced poorer access to their rheumatologist and 7% (905/12 789) reported poorer treatment options for their rheumatic disease, whereas most patients reported unchanged access, or that these questions were irrelevant (online supplemental table S3). Among the 38% (4856/12 789) of patients who had needed more information regarding their arthritis during

**Table 2** Impact of the COVID-19 pandemic

Question	Answering options	N (%)
Have you been tested for COVID-19?	Yes	1809 (14)
	No	10949 (86)
	Do not know	31 (0)
	Missing/no reply	0 (-)
If yes, was the test positive?*	Yes	40 (2)
	No	1668 (92)
	Do not know	94 (5)
	Missing	7 (-)
Characteristics of patients with positive COVID-19 test, n=40	<b>Characteristics</b>	<b>N (%)</b>
	Gender, female, n (%)	20 (50)
	Age, years, median (IQR)	54 (47–67)
	HAQ, median (IQR)	0.38 (0.09–0.88)
	Diagnosis	
	RA	23 (58)
	PsA	<5 patients
	AxSpA	9 (23)
	Other	<5 patients
	bDMARD treatment, yes	15 (38)
	Comorbidities, yes	20 (50)
	Smoking	
	Current	<5
Previous	13	
Never	24	

Testing for SARS-CoV-2 by June 2020. N=12 789.

\*If positive, what was the consequence (>1 answer allowed): self-isolation at home (n=33), hospitalisation (7), other (2), do not know (3).

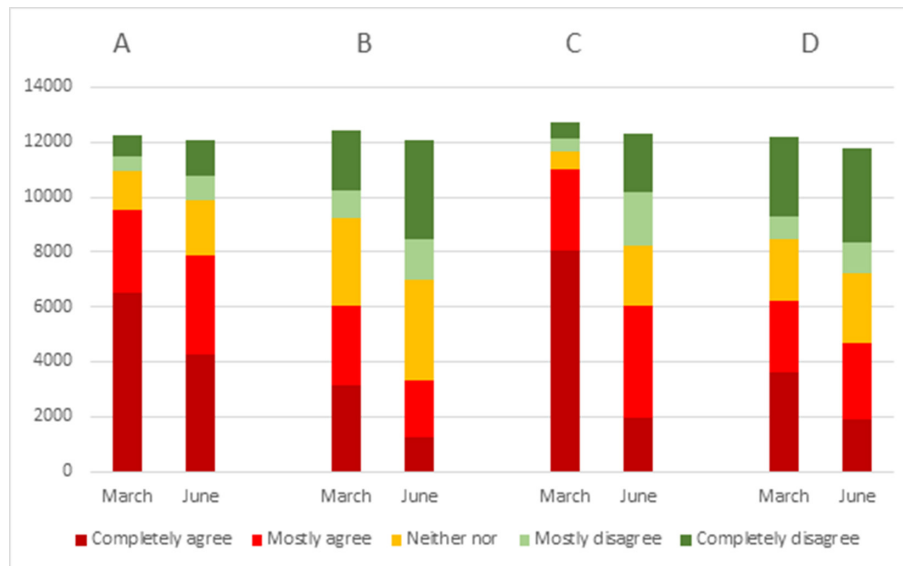
AxSpA, axial spondyloarthritis; bDMARD, biological disease modifying antirheumatic agent; HAQ, health assessment questionnaire; PsA, psoriatic arthritis; RA, rheumatoid arthritis.

the pandemic, 50% (2408/4856) had approached their rheumatology clinic and 33% (1588/4856) the Danish Rheumatism Association (online supplemental table S3, footnote).

### Anxiety and self-isolation in March and in June 2020

In March 2020, 26% (3365/12 789) of patients reported not seeing other people face-to-face at close distance (<2 m) and 14% (1807/12 789) were not seeing any people on >2 m distance (10% (1330/12 706) reported none to both questions), 29% (3688/12 789) did not leave the home for shopping and 96% (12 255/12 789) of respondents did not use public transportation (online supplemental table S4).

Figures 1 and 2 and table 2 show changes in anxiety and self-isolation strategies in March versus June 2020 with levels generally being higher in March than in June.



**Figure 1** Changes in self-isolation strategies and anxiety during the COVID-19 pandemic (March and June 2020). (A) 'I consider myself at high risk of COVID-19 infection'. (B) 'I worry more about COVID-19 than about my rheumatic disease'. (C) 'I stay at home and avoid others as much as possible'. (D) 'My arthritis causes me to self-isolate more than others my age'.

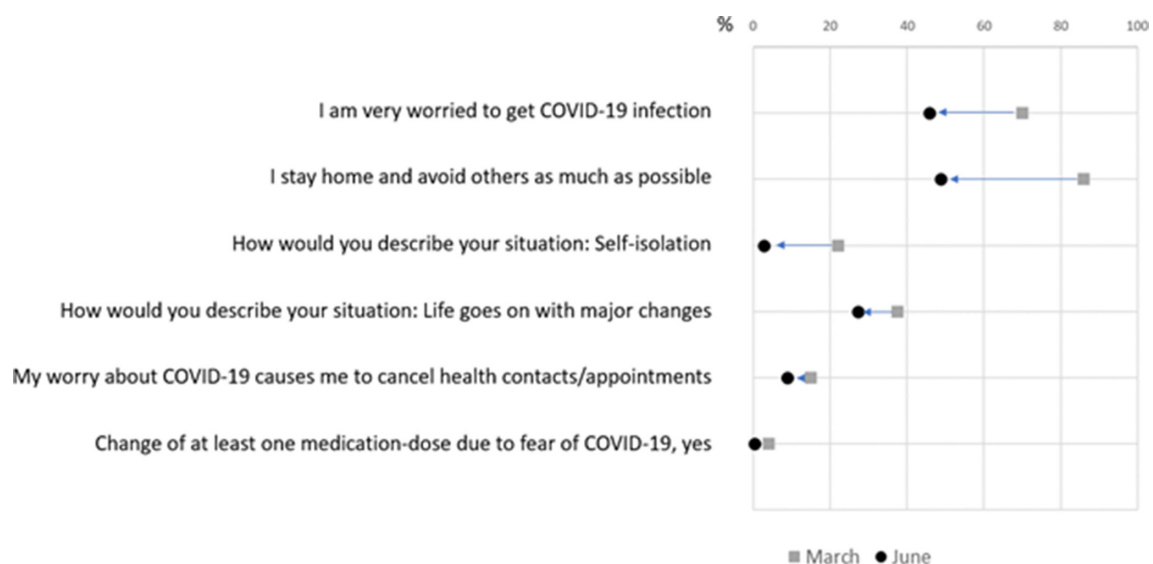
For example, the proportion of patients who considered themselves at high risk (completely agree/mostly agree) of COVID-19 infection decreased from 75% (9559/12754) to 63% (7858/12431), respectively (figure 1, online supplemental table S5). Similarly, the proportion of patients who worried getting COVID-19 changed from 70% (8899/12754) to 45% (5644/12433) (figure 2). Overall, 27% (3319/12414) of patients were worried in March but not in June, whereas 43% (5361/12414) were worried at both time-points. In March and June, the proportions of patients who described their current situation as 'self-isolation' were 22% (2765/12789) and 3% (395/12429), respectively (figure 2), and the proportions of patients who due to their arthritis self-isolated themselves more than others their age (completely/mostly agree) were 48% (6208/12752) and 38% (4685/12367),

respectively (figure 1). In June, 39% (4821/12420) worried about the reopening of the society (completely/mostly agree) (online supplemental table S5).

#### Changes in medication use

Most of the included patients (10 089/12 789=79%) reported current use of DMARDs (table 3). In March, the proportion of patients who reported to have changed the dosage of csDMARD and/or bDMARD were 4% (417/10 089) and 6% (583/10 089), respectively, whereas proportions in June were 2% (160/9685) and 4% (419/9685), respectively.

Overall, 415/10 089 (4.1%) DMARD users had changed dose of at least one drug in March due to fear of COVID-19, whereas the corresponding numbers in June were 54/9685 (0.6%). In March, fear of COVID-19 was the main



**Figure 2** Changes in self-isolation strategies, anxiety and medication use during the pandemic (March and June 2020).

**Table 3** Use of immunosuppressive antirheumatic medication and medication adherence

March 2020			June 2020	
Question	Answer, n (%)	Answering options	Answer, n (%)	Question
Did you on start of the COVID-19 lock-down use immunosuppressing antirheumatic medication?	10089 (79)	Yes	9685 (76)	Do you currently use immunosuppressing antirheumatic medication?
	2226 (17)	No	2184 (17)	
	427 (3)	Do not know	519 (4)	
	47 (-)	Missing	401 (-)	
If yes, did you change the dose*	1029 (10)	Yes	657 (7)	If yes, do you currently use another dose than prior to the COVID-10 pandemic*
	8997 (89)	No	8953 (92)	
	60 (1)	Do not know	67 (1)	
	3 (-)	Missing	9 (-)	
If yes to change, which medication(s) was affected? >1 medication per patient allowed †	546 (54)	csDMARD	374 (63)	If yes to change, which medication(s) are affected?>1 medication per patient allowed †
	45 (4)	Prednisolone	57 (10)	
	417 (41)	bDMARD	160 (27)	
	21 (-)	Missing/other	66 (-)	
Change of bDMARD n=417 patients (4%)*			Change of bDMARD n=160 patients (2%)*	
If yes to change, how did you change the dose§?	18 (4)	Dose increase	47 (29)	If yes to change, how did you change the dose§?
	39 (9)	Dose reduction	27 (17)	
	262 (63)	Paused medication	17 (11)	
	70 (17)	Stopped medication	13 (8)	
	38 (-)	Missing	64 (-)	
If yes to change, who recommended the change?§	258 (62)	Own initiative	28 (18)	If yes to change, who recommended the change?§
	11 (3)	General practitioner	0 (0)	
	102 (24)	Rheumatology clinic	88 (55)	
	20 (5)	Other	5 (3)	
	2 (0)	Do not know	1 (1)	
If yes to change, what was the reason(s)?	34 (-)	Missing	46 (-)	If yes to change, what was the reason(s)?
	28 (7)	My disease changed	57 (36)	
	4 (1)	No assess to medication	2 (1)	
	211 (51)	<b>Fear of COVID-19‡</b>	20 (13)	
	38 (9)	Worry about side-effects	8 (5)	
	10 (2)	No need to take medication	5 (3)	
	2 (0)	Avoid blood sampling	0 (0)	
	95 (23)	Other	23 (14)	
	2 (0)	Do not know	2 (1)	
37 (-)	Missing	51 (-)		
Change of csDMARD including prednisolone, n=583 patients (6%)			Change of csDMARD including prednisolone, n=419 patients (4%)	
If yes to change, how did you change the dose§?	92 (16)	Dose increase	166 (40)	If yes to change, how did you change the dose§?
	143 (25)	Dose reduction	153 (37)	
	228 (39)	Paused medication	19 (5)	
	108 (19)	Stopped medication	30 (7)	
	43 (-)	Missing	84 (-)	
If yes to change, who recommended the change§?	294 (50)	Own initiative	91 (22)	If yes to change, who recommended the change§?
	20 (3)	General practitioner	6 (1)	
	230 (39)	Rheumatology clinic	261 (62)	
	23 (4)	Other	19 (5)	
	2 (0)	Do not know	1 (0)	
45 (-)	Missing	74 (-)		

Continued

Table 3 Continued

March 2020			June 2020	
Question	Answer, n (%)	Answering options	Answer, n (%)	Question
If yes to change, what was the reason(s)§?	97 (17)	My disease changed	168 (40)	If yes to dose-change, what is the reason(s)?
	8 (1)	No assess to medication	15 (4)	
	231 (40)	<b>Fear of COVID-19</b> ‡	36 (9)	
	68 (12)	Worry about side-effects	52 (12)	
	21 (4)	No need to take medication	16 (4)	
	6 (1)	Avoid blood sampling	2 (0)	
	129 (22)	Other	75 (18)	
	6 (1)	Do not know	5 (1)	
	48 (-)	Missing	83 (-)	

N=12 789.

\*Percentage of medication users.

†Percentage of medication changes.

‡Number of patients changing at least one medication due to fear of COVID-19: March: 415/10 089 (4.1%), June: 54/9685 (0.6%).

§More than 1 medication/answer allowed per patient.

bDMARD, biological disease-modifying antirheumatic agent; csDMARD, conventional synthetic disease-modifying antirheumatic drug.

reason for change (51% (211/417) of bDMARD changes and 41% (231/583) of csDMARD changes), whereas in June, the main reason was ‘my disease changed’ (36% (57/160) of bDMARD changes and 40% (168/419) of csDMARD changes) and only 13% (20/160) of bDMARD changes and 9% (36/419) of csDMARD changes, respectively, were due to fear of COVID-19 (table 3). In March, most changes were initiated by the patient, whereas in June it was by the rheumatology clinic.

### Multivariable analyses

Patients who were worried about contracting COVID-19 disease in March (70% of patients) were more frequently women, had lower education, were not working, were cohabiting, had comorbidities, were treated with a bDMARD, were current smokers and had poorer EQ-5D (multivariable logistic regression analyses, table 4). Similar factors were associated with being very worried about COVID-19 disease in June (46% of patients), in addition to age 60–80 years (compared with being ≤39 years) (online supplemental table S6).

Factors associated with change from being very worried in March to not being worried in June (27% of patients) were being ≤39 years of age (compared with being 40–59 and 60–79 years), not having ≥2 comorbidities, being a previous smoker and scoring high on EQ-5D (ie, high health-related quality of life) (table 4).

Patients who self-isolated more than others the same age in March (48% of patients) and in June (38% of patients) were more frequently women, ≤39 years of age, not working, had comorbidities, were treated with a bDMARD or csDMARD and had poorer EQ-5D (table 4). In June, being a smoker and having PASS=yes were also associated with more self-isolation (online supplemental table S6).

Patients who changed dose of at least one immunosuppressant agent due to fear of COVID-19 in March were

more frequently male, treated with bDMARDs, ≤39 years of age (compared with being ≥80 years), higher educated and working (table 4).

### DISCUSSION

This study represents, to the best of our knowledge, the largest study of patients with inflammatory rheumatic diseases exploring the impact of the COVID-19 pandemic on changes in behaviour, anxiety and self-isolation strategies including medication adherence in a period with lock-down and subsequent gradual reopening of the society. The study cohort was nationwide and included >12 000 well-described patients monitored in the prospective registry DANBIO. The large number of participants enabled us to explore the impact of many patient characteristics, and data completeness among respondents was high (>90%–95%).

Very few patients (0.3%) reported to have contracted COVID-19. This suggests a risk similar to that of the general Danish population (1 July 12 831 COVID-19 infected/total population 5.8 mill=0.22%) (www.SSI.dk).<sup>15</sup> Similarly, previous studies have found no evidence of an overrepresentation of patients with inflammatory rheumatic disease among SARS-CoV-2 infected.<sup>2–4</sup>

Overall, the patients reported a high degree of self-isolation and fear of contracting COVID-19 at the start of the pandemic, but also in June 2020, when the Danish epidemic was well controlled, and society was reopening. Patients with comorbidities and to some extent smokers reported more fear and self-isolation—that is, carrying risk factors that were widely accepted as increasing COVID-19 risk early in the pandemic.<sup>16 17</sup> Women with lower educational level, not in the work force and receiving bDMARD treatment were more worried about infection and self-isolated more. Lower quality of life was associated with more anxiety and self-isolation, which reflects the impact of dimensions such as depression and physical impairment.



**Table 4** Factors associated with anxiety, self-isolation and medication adherence**Results of multivariable logistic regression analyses**

	I was very worried to get COVID-19 infection, March n=11 295		Change from being worried in March to not being worried in June, n=11 288		My arthritis caused me to self-isolate more than others my age, March n=11 302		Changed at least one medication due to fear of COVID-19, March† n=8976	
	Multivariable HR (95% CI)	P value	Multivariable HR (95% CI)	P value	Multivariable HR (95% CI)	P value	Multivariable HR (95% CI)	P value
Male gender	<b>0.54</b> (0.50 to 0.59)	<0.001	<b>0.86</b> (0.78 to 0.94)	<b>0.001</b>	<b>0.57</b> (0.52 to 0.62)	<0.001	<b>1.51</b> (1.21 to 1.89)	<0.001
Age, years			1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)
≤39								
40–59	0.91 (0.76 to 1.07)	0.2	<b>0.81</b> (0.69 to 0.96)	<b>0.01</b>	<b>0.77</b> (0.65 to 0.90)	<b>0.001</b>	1.26 (0.85 to 1.95)	0.3
60–79	1.09 (0.91 to 1.32)	0.3	<b>0.79</b> (0.66 to 0.95)	<b>0.01</b>	<b>0.71</b> (0.60 to 0.84)	<0.001	0.92 (0.59 to 1.48)	0.7
≥80	0.89 (0.68 to 1.17)	0.4	0.93 (0.71 to 1.23)	0.6	<b>0.60</b> (0.46 to 0.78)	<0.001	<b>0.11</b> (0.006 to 0.52)	<b>0.03</b>
Diagnosis			1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)
RA								
PsA	0.99 (0.88 to 1.22)	0.95	1.05 (0.93 to 1.19)	0.4	1.04 (0.93 to 1.16)	0.5	1.26 (0.95 to 1.65)	0.1
AxSpA	0.90 (0.78 to 1.04)	0.16	1.05 (0.91 to 1.21)	0.5	0.88 (0.77 to 1.01)	0.06	0.91 (0.64 to 1.27)	0.6
Other	1.56 (0.96 to 1.39)	0.12	1.11 (0.92 to 1.33)	0.3	1.03 (0.87 to 1.22)	0.7	0.84 (0.48 to 1.38)	0.5
Lower education, yes	<b>1.18</b> (1.08 to 1.29)	<0.001	0.96 (0.88 to 1.05)	0.3	0.99 (0.92 to 1.07)	0.8	<b>0.56</b> (0.45 to 0.69)	<0.001
Working, yes*	<b>0.83</b> (0.75 to 0.93)	<b>0.001</b>	0.97 (0.87 to 1.07)	0.5	<b>0.78</b> (0.71 to 0.86)	<0.001	<b>1.52</b> (1.16 to 1.99)	<b>0.003</b>
Cohabitant, yes	<b>1.16</b> (1.04 to 1.30)	<b>0.005</b>	1.10 (0.98 to 1.22)	0.1	1.04 (0.94 to 1.15)	0.5	1.33 (0.99 to 1.84)	0.07
Use of bDMARD, yes	<b>1.83</b> (1.60 to 2.11)	<0.001	1.12 (0.97 to 1.30)	0.1	<b>2.34</b> (2.04 to 2.67)	<0.001	<b>1.86</b> (1.02 to 3.81)	<b>0.05</b>
Use of cdDMARD, yes	1.06 (0.92 to 1.22)	0.4	1.08 (0.93 to 1.25)	0.3	<b>1.29</b> (1.13 to 1.47)	<0.001	1.25 (0.68 to 2.59)	0.5
PASS, yes	1.03 (0.92 to 1.15)	0.7	0.98 (0.88 to 1.10)	0.8	1.03 (0.93 to 1.14)	0.6	1.02 (0.77 to 1.36)	0.9

Continued

**Table 4** Continued

**Results of multivariable logistic regression analyses**

	I was very worried to get COVID-19 infection, March n=11 295		Change from being worried in March to not being worried in June, n=11 288		My arthritis caused me to self-isolate more than others my age, March n=11 302		Changed at least one medication due to fear of COVID-19, March n=8976	
	Multivariable HR (95% CI)	P value	Multivariable HR (95% CI)	P value	Multivariable HR (95% CI)	P value	Multivariable HR (95% CI)	P value
Number of comorbidities	1 (ref)		1 (ref)		1 (ref)		1 (ref)	
0								
1	<b>1.23</b> (1.11 to 1.36)	<0.001	0.95 (0.86 to 1.05)	0.4	<b>1.24</b> (1.13 to 1.36)	<0.001	0.96 (0.75 to 1.22)	0.7
≥2	<b>1.52</b> (1.36 to 1.71)	<0.001	<b>0.83</b> (0.74 to 0.93)	<b>0.001</b>	<b>1.36</b> (1.23 to 1.51)	<0.001	0.90 (0.70 to 1.21)	0.5
Smoking status	1 (ref)		1 (ref)		1 (ref)		1 (ref)	
Current								
Previous	<b>0.87</b> (0.76 to 0.99)	<b>0.03</b>	<b>1.17</b> (1.03 to 1.33)	<b>0.02</b>	0.89 (0.79 to 1.00)	0.06	0.91 (0.67 to 1.24)	0.6
Never	<b>0.83</b> (0.74 to 0.93)	<b>0.002</b>	1.06 (0.94 to 1.19)	0.3	0.96 (0.87 to 1.07)	0.5	0.79 (0.60 to 1.06)	0.1
EQ-5D	<b>0.21</b> (0.15 to 0.30)	<0.001	<b>2.36</b> (1.72 to 3.25)	<0.001	<b>0.009</b> (0.074 to 0.13)	<0.001	0.52 (0.25 to 1.12)	0.09

Statistically significant results are shown with bold types.

\*Status before corona lockdown.

†Only patients who used immunosuppressive medication upon lock-down eligible for analysis (N=10 089).

AxSpA, axial spondyloarthritis; bDMARD, biologic disease-modifying agent; csDMARD, conventional synthetic DMARD; EQ-5D, European Quality of life, 5 dimensions; PASS, patient acceptable symptom state; PsA, psoriatic arthritis; RA, rheumatoid arthritis.



More anxiety in women and patients with comorbidities has previously been demonstrated,<sup>5,18</sup> whereas most studies have been underpowered or have only explored few/no factors associated with healthcare behaviour.<sup>5,7</sup> Previous studies have not confirmed that self-isolation strategies in patients with inflammatory rheumatic diseases cause reduced COVID-19 disease rates.<sup>19</sup> We did not have statistical power to explore this further with only 40 patients reporting a positive test for SARS-CoV-2.

We collected information about the patients' behaviour both in the beginning of the pandemic and also 3 months later. Interestingly, although anxiety and self-isolation had declined by June (similar to the general population where fewer individuals reported feeling isolated during spring/summer 2020),<sup>20</sup> rates were still high and one in three patients worried about the reopening of society. This highlights the continuous challenge in adjusting to daily life in patients with inflammatory rheumatic diseases during the pandemic. Indeed, addressing these issues in routine care is challenging as some degree of self-isolation is appropriate and in accordance with guidelines from the health authorities, especially in patients with comorbidities. It was however beyond the scope of our study to explore interventional measures towards anxiety and other approaches related to patient-centred care.

Overall, we found the compliance to DMARD treatment to be high. Only 4.1% of patients changed medication due to fear of COVID-19 in the early phase of the pandemic, which nevertheless accounted for nearly 50% of all medication changes in that period. Adherence was even higher in June. This finding is in contrast to previous studies, which have reported non-adherence rates of up to 15% in rheumatic patients during the pandemic.<sup>5,7,9,21-23</sup> We speculate that our findings reflect that access to the rheumatologists was maintained even in the initial, hectic weeks (primarily by phone) and in addition several institutions including the patient organisations recommended patients to continue treatment with DMARDs.<sup>7,24</sup> In March, changes in medication due to fear were mainly seen in young ( $\leq 39$  years), well-educated male patients treated with biologicals, regardless of rheumatological diagnosis. Other studies have identified lower age, poorer disease control,<sup>5</sup> unemployment and biological treatment<sup>21</sup> as associated factors. Previous studies have reported shortage of medication, mainly hydroxychloroquine, as a challenge during the COVID-19 pandemic,<sup>21</sup> but this was not an issue in this Danish cohort.

Not surprisingly, the ongoing pandemic had high impact on routine care, and one in three patients reported cancelling of consultations at the rheumatology clinic. However, <10% of patients reported reduced access to rheumatological counselling and treatment, and two-thirds had been in contact with the clinic during the 2 months after lock-down. Previous papers have described high patient satisfaction with telehealth during the pandemic<sup>5</sup> and has recommended its use.<sup>24</sup> It was beyond the scope of the current paper to explore this further. Interestingly, patient organisations were often approached for advice. This underlines the importance

of collaboration between patient organisations and healthcare professionals when it comes to up-to-date information and counselling. This might especially be of importance during pandemics where scientific evidence is evolving rapidly resulting in risk of misinformation and overabundance of information ('Infodemic'),<sup>25</sup> and optimal behaviour becomes a moving target with guidelines changing almost from day to day.

The study had challenges to be addressed. Previously, patients entered their patient-reported outcomes (PROs) into DANBIO using touch screens in the rheumatology clinics. As part of the present project, an online solution for routinely reporting PROs from home was implemented, which patients were not familiar with. This may have affected response rates. We have previously reported that online reporting of PROs from home versus in the clinic is valid.<sup>14</sup> Recall bias regarding the initial phase in March–April cannot be excluded, because the questionnaire was distributed in May–June where society was gradually reopening. This could potentially cause under-reporting of medication compliance. Selection bias was a risk, since fewer eligible younger patients ( $\leq 39$  years) participated. Furthermore, elderly patients with comorbidities and lack of IT competences were underrepresented due to no access to the E-boks system. On the other hand, more than 500 patients above 80 years of age participated in the study. It could also be speculated if patients with more anxiety and self-isolation were more motivated to answer the questionnaire.

In conclusion, this large study of >12 000 patients, who were followed in the nationwide DANBIO registry, demonstrated that despite low infection rates, high levels of anxiety and self-isolation persisted also after the Danish epidemic was well controlled in June 2020. Among risk factors were female gender, not working, current bDMARD treatment, having comorbidities and poor quality of life. Medication compliance was high, but fear of COVID-19 was the main reason for non-adherence in the early phase of the pandemic. Attention to anxiety and self-isolation is important during the ongoing pandemic.

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**Acknowledgements** We acknowledge all patients and all Danish departments of rheumatology contributing to the DANBIO registry. Thanks to Anne Pape and Mikkel Abildtoft, Zitelab, for technical support and expertise during the development of online questionnaire.

**Contributors** Study conception and design: BG, DVJ, SE and MLH. Acquisition of data: BG, DVJ, SE and NSK. Statistical analysis: BG, SHR and NSK. All authors contributed to the interpretation of the data. BG and MLH wrote the manuscript. All authors critically revised the manuscript. All authors revised and approved the final manuscript to be published.

**Funding** Partly funded by an unrestricted grant from The Lundbeck Foundation (grant number R349-2020-629).

**Competing interests** Bente Glinthorg: Research grants: AbbVie, BMS, Pfizer. Oliver Hendricks: Research grants: AbbVie, Novartis, Pfizer. Lene Terslev: Speakers fee: Speakers fee from AbbVie, Janssen, Roche, Novartis, Pfizer, MSD, BMS and GE. Mikkel Østergaard: Research grants: Abbvie, BMS, Celgene, Merck, Novartis; Consultancy and/or speaker fees: Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli-Lilly, Hospira, Janssen, Merck, Novartis, Novo, Orion, Pfizer, Regeneron, Roche, Sandoz, Sanofi and UCB. Rene Østgaard: Research grants: Abbvie; Consultancy and/or speaker fees: Abbvie, BMS, Boehringer-Ingelheim, Eli-Lilly, Janssen, Merck, Novartis, Pfizer, Roche, Sanofi and UCB. Anne Gitte Loft: Consultancy and/or speakers fees: AbbVie, Eli-Lilly, Janssen, MSD, Novartis, Pfizer, and UCB. Merete Lund Hetland: AbbVie, Biogen, BMS, Celtrion, Eli Lilly Denmark A/S, Janssen Biologics B.V, Lundbeck Fonden, MSD, Pfizer, Roche, Samsung Biopis, Sandoz. MLH chairs the steering committee of the Danish Rheumatology Quality Registry (DANBIO), which receives public funding from the hospital owners and funding from pharmaceutical companies. MLH cochairs the EuroSpA research collaboration, which generates real-world evidence of treatment of psoriatic arthritis and axial spondyloarthritis based on secondary data and is partly funded by Novartis. Remaining authors: none declared.

**Patient and public involvement statement** Patients and/or the public were involved in the design, or conduct, or reporting or dissemination plans of this research. Refer to the 'Methods' section for further details.

**Patient consent for publication** Not required.

**Ethics approval** Patients gave electronic consent to participation. According to Danish legislation, questionnaire research projects do not require ethical approval.

**Provenance and peer review** Not commissioned; externally peer reviewed.

**Data availability statement** All data relevant to the study are included in the article or uploaded as supplementary information.

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