



# Functional and psychosocial impact of COVID-19 pandemic on rheumatic patients' quality of life in Saudi Arabia

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## Abstract

**Purpose** The COVID-19 pandemic might add to the stressors experienced by people living with rheumatic diseases. This study aimed to examine rheumatic patients' functional and psychosocial states during the pandemic and assess its impact on their quality of life.

**Methods** Our time-series study included a patient-centered electronic survey, sampling adult rheumatic patients living in Saudi Arabia at different time points from March to August 2020. Patient-reported outcomes included physical function, anxiety, depression, fatigue, sleep disturbance, ability to participate in social roles, and pain interference domains were measured using the Patient-Reported Outcomes Measurement Information System (PROMIS-29 Profile v2.1).

**Results** A total of 1278 respondents were enrolled. Results showed significant variation in patients' experiences. Our analyses revealed that the physical well-being of rheumatic patients was significantly impacted, and such effect was persistent over time irrespective of public health measures to control the COVID-19 outbreak.

**Conclusion** Our findings consistently demonstrated the need for psychological and social consideration to improve rheumatic patients' quality of life. Nevertheless, there is still a lot to be learned about the extent of COVID-19 impact on rheumatic patients and the implications it has on long-term disease outcomes.

**Keywords** COVID-19 · Mental health · Patient-reported outcome · Quality of life · Rheumatic disease

## Introduction

The burden of rheumatic disease generally extends beyond the effects of the disease on various organs [1]. The diagnosis of many rheumatic diseases is associated with physical, mental, and financial implications for the patient. Impairment in any of these aspects can have a negative impact on the perception of their condition, quality of life, and

therapeutic success [2]. Such understanding of the relationship between rheumatic diseases and factors that can affect a patient's quality of life has grown and improved over the past decade, with particular emphasis on patient-reported outcomes [3]. These results usually reflect factors that matter to patients and are likely to influence their quality of life.

A patient's quality of life tends to be altered by many internal and external factors. For example, concomitant mood disorders, social circumstances, and surrounding environment can affect a patient's quality of life and, consequently, patient-reported outcome [4]. Recognizing these factors is critical to improving a patient's health and overall well-being.

In the past two years, the world has been severely impacted by the COVID-19 pandemic. We recently reported in a cross-sectional study on the burden of the COVID-19 pandemic on rheumatic patients' perception and behavior [5]. The toll of this pandemic on individuals with rheumatic

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diseases ranged from disease perception, healthcare utilization, to medication adherence.

In this study, utilizing a longitudinal survey, we sought to assess changes in social, mental, and physical impairments in rheumatic patients living in Saudi Arabia (SA) at different time points during the COVID-19 pandemic. We also examined the demographic, conditional, and situational factors associated with changing quality of life.

## Methods

### Study design and setting

This study was an observational, longitudinal time-series investigation at three time points during the COVID-19 pandemic. The selected time points reflect major public health measures to contain the spread of the virus, starting with full lockdown or total curfew (Time 1 = March–April, 2020), partial relaxation of the curfew (Time 2 = May–June, 2020), and complete or full resolution of the curfew and resumption of normal clinical services in all hospitals in SA (Time 3 = July–August, 2020). These time points were chosen because of the potential impact of related factors on patients' well-being, such as healthcare accessibility. The study report was guided by the Strengthen the Reporting of Observational Studies in Epidemiology (STROBE) guidelines [6].

### Participants

The participants were recruited from the following registries: Charitable Association of Rheumatic Diseases, Saudi Inflammatory Disease Patients Support Group, and the Specialized Rheumatology Clinic at King Khalid University Hospital (KKUH) in King Saud University (KSU). Database managers accessed contact numbers to send text message invitations containing an electronic link to our study survey, while ensuring the concealment of respondent identifiers. The survey included study-related information and terms of informed consent. Individuals who understood and agreed to participate provided electronic informed consent per the guidelines of the Institutional Review Board of KSU, Riyadh, SA (Approval No. E-20–4787). Informed consent was obtained from all participants included in the study.

All individuals diagnosed with rheumatic disease, who were over 18 years of age and residing in SA at the time of the survey were included in our study. Also, individuals with concomitant conditions, including overlap syndrome, comorbidities, and psychiatric disorders, were considered eligible regardless of their diagnosis date or treatment plan.

### Variables

The administered survey was set to collect time-series data on the impact of COVID-related mandates on the functional and psychosocial states of rheumatic patients over three time points during the early months of the pandemic. Other covariates considered were: demographics (age, gender, nationality, marital status, educational level, and employment), health condition (smoking habits, diseases [rheumatic, comorbidity, and psychological disorders], and COVID-19 infection). Confounding factors related to rheumatic patients' health behaviors and perceptions in COVID-19 context were also considered, including utilizing healthcare services, obtaining medications, and fear of COVID infection. The construct of the questionnaire and scoring system have been previously delineated [5].

### Outcomes

The outcome parameters included physical and mental health domains measured using Patient-Reported Outcomes Measurement Information System 29-item (PROMIS-29) profile version 2.1 [7]. The PROMIS® domains included physical function (PF), ability to participate in social roles and activities (social participation [SP]), anxiety (ANX), depression (DEP), fatigue (FTG), sleep disturbance (SD), pain interference (PI), and pain intensity (pain level [PL]). Each domain consisted of four items, and each item was weighed on a 5-point Likert scale, except for pain intensity which consisted of one item that was weighed on a 1–10 scale. The raw scores for each domain were summed separately (score could range from a minimum of 4 to a maximum of 20 points), then converted using the *T*-score metric system for each participant. The *T*-score scaled the raw score into a standardized *T*-score with a mean of 50 and a standard deviation (SD) of 10 based on the US reference population. The *T*-scores thresholds/cut-offs were also implemented to generate four categories (within normal limits, mild, moderate, and severe) according to PROMIS-29 guidelines [7].

### Data collection and management

The electronic survey was constructed using Google Forms consisting of a series of questionnaires (in Arabic and English) focused on capturing the aforementioned variables. The captured data were collected onto Google Sheets and securely maintained in Google Drive by database governors at KKUH in KSU until further analysis.

### Statistical analysis

All observed data were included for statistical analysis. Our dataset included missing values due to participants' dropout.

The loss of data was treated as missing completely at random. Thus, multiple imputation was used to minimize biased results.

Descriptive statistics were expressed as mean ( $\pm$  SD) for continuous variables, whereas prevalence (frequency and percentage) for categorical variables. Kolmogorov–Smirnov test was used to assess the normality of continuous variables, and Levene's test was used to assess the homogeneity of equal variance. Multiple response dichotomies analysis was applied to describe questions measured with multiple simultaneous selections.

The chi-square test of independence was utilized to assess statistical associations between categorical study variables across the three time points. Also, a one-way ANOVA test was used to compare the continuous variables across the three time points of the study. Bonferroni adjusted post-hoc pairwise comparison was applied for the statistically significant mean differences between participant responses at the three time points. However, when a violation of the statistical equal variance assumption was noticed, an adjusted Welch's one-way ANOVA was used, followed by a Games-Howell adjustment.

Additionally, the multivariate linear regression analysis was used to assess the combined and individual associations between relevant key predictors and risk factors and the measured PROMIS® outcomes across the three time points accounting for the period of quarantine as a factor in the analysis. All statistical analyses were expressed with a 95% confidence level. A *P*-value of less than 0.05 was considered statistically significant. All statistical data analysis was performed using SPSS IBM version 21.

## Results

### Patients' characteristics

A total of 1278 participants completed the surveys. The response rate was about 20% for the first time point. However, it decreased by almost a half for the second, and it remained as such for the third time point, despite our attempts to improve participation (Table 1).

The overall average age was 36 ( $\pm$ 9.75) years, with the majority being females (86%), married (53.3%), Saudi (85.8%), educated (65%), and unemployed (65.1%). No significant difference was found in participants' demographics across all three surveys (Table 1).

As for their health conditions, most participants had never smoked cigarettes (94.6%). Moreover, patients with rheumatoid arthritis (RA) represented 43.1% of the participants, followed by systemic lupus erythematosus (31.2%), among other inflammatory diseases (25.7%). Their disease status at the last follow-up visit with a rheumatologist was reported

**Table 1** Descriptive analysis of rheumatic patients' characteristics

Variable	Total (N = 1278)
<b>Demographic</b>	
Age (years), mean (S.D.)	36.31 (9.75)
Gender (male), <i>n</i> (%)	179 (14)
Nationality (Saudi), <i>n</i> (%)	1097 (85.8)
<b>Marital status, <i>n</i> (%)</b>	
Never married	473 (37.7)
Currently married	681 (53.3)
Previously married	124 (9.7)
<b>Educational level, <i>n</i> (%)</b>	
Elementary education	49 (3.8)
Intermediate education	392 (30.7)
Higher education	837 (65.5)
Employment (yes), <i>n</i> (%)	446 (34.9)
<b>Health condition</b>	
Smoking (yes), <i>n</i> (%)	69 (5.4)
Psychological disorder (yes), <i>n</i> (%)	138 (10.8)
Comorbidity (yes), <i>n</i> (%)	506 (39.6)
<b>Rheumatic disease diagnosis (type), <i>n</i> (%)</b>	
Rheumatoid arthritis	551 (43.1)
Systemic lupus erythematosus	399 (31.2)
Behçet syndrome	40 (3.1)
Sjögren syndrome	27 (2.1)
Rheumatoid spondylarthritis	18 (1.4)
Other inflammatory disease	131 (10.3)
Overlap syndrome	112 (8.8)
Disease status (active), <i>n</i> (%)	417 (32.6)

mainly as inactive (67.4%); However, (20.6%) perceived that their disease activity had worsened (20.6%) during the COVID-19 pandemic.

Out of the 1278 participants, only 496 rheumatic patients were diagnosed with comorbidities (38.8%), many of whom had multiple comorbidities (63.3%). The three most prevalent conditions included hypertension, endocrine dysfunction, and diabetes. Moreover, 138 patients were diagnosed with psychological disorders (10.8%), many of whom had multiple disorders (42%). The three most common conditions included depression, stress/anxiety, and sleeping disorder. No significant difference was found in participants' health conditions across all three surveys (Table 2).

### Patients' health behaviors and perceptions

As a result of the pandemic, the prevalence of COVID-19 infection among all patients was approximately 3% in times 1 and 2 but significantly increased to 14% in time 3 ( $P < 0.001$ ). Some rheumatic patients reported experiencing difficulty accessing healthcare services (33.7%) or obtaining their prescribed medications (48.3%). Emergency visits

**Table 2** Descriptive analysis of patient-reported outcomes during COVID-19 and comparison between the three time points

Variable	Overall ( <i>N</i> = 1278)	Time 1 ( <i>N</i> = 600)	Time 2 ( <i>N</i> = 351)	Time 3 ( <i>N</i> = 327)	<i>P</i> -value
COVID-19 infection					
COVID-19 infection (confirmed), <i>n</i> (%)	75 (5.9)	19 (3.2)	10 (2.8)	46 (14.1)	< 0.001**
Healthcare access					
Hospital or clinic visit (no), <i>n</i> (%)	429 (33.7)	201 (33.5)	143 (40.7)	85 (26)	< 0.001**
Obtaining medication (no), <i>n</i> (%)	617 (48.3)	313 (52.2)	152 (43.3)	152 (46.5)	0.023*
Patient perception (worry)					
Worsening disease activity, <i>n</i> (%)	263 (20.6)	109 (18.2)	82 (23.4)	72 (22)	0.122
Contracting COVID infection, <i>n</i> (%)	703 (55)	331 (55.2)	203 (57.8)	169 (51.7)	< 0.001**
Deteriorating disease if COVID infected, <i>n</i> (%)	864 (67.6)	399 (66.5)	245 (69.8)	220 (67.3)	0.394
Losing a job, <i>n</i> (%)	230 (18)	100 (16.7)	70 (19.9)	60 (18.3)	0.742
Patient-reported outcome					
Physical function, mean (S.D.)	15.84 (3.71)	16.16 (3.64)	15.61 (3.79)	15.50 (3.70)	0.014*
Social participation, mean (S.D.)	13.51 (4.25)	13.85 (4.30)	13.27 (4.27)	13.16 (4.09)	0.028*
Anxiety, mean (S.D.)	9.57 (4.02)	9.42 (3.89)	9.63 (4.02)	9.78 (4.25)	0.403
Depression, mean (S.D.)	8.75 (4.15)	8.52 (4.10)	8.74 (4.04)	9.14 (4.39)	0.094
Fatigue, mean (S.D.)	11.82 (4.38)	11.54 (4.33)	11.83 (4.23)	12.30 (4.52)	0.042*
Sleep disturbance, mean (S.D.)	12.30 (1.76)	12.35 (1.82)	13.34 (1.64)	12.17 (1.76)	0.301
Pain interference, mean (S.D.)	10.88 (4.59)	10.48 (4.47)	11.15 (4.68)	11.34 (4.67)	0.011*
Pain intensity (levels), mean (S.D.)	4.63 (2.51)	4.37 (2.48)	4.78 (2.53)	4.94 (2.50)	0.002**

\*\**P*-value is significant at the 0.01 level (2-tailed); \**P*-value is significant at the 0.05 level (2-tailed)

and medication self-alteration were significantly increased by time 3 to almost 16% and 32%, respectively ( $P < 0.001$ ). Moreover, we found an increase in patients' fears/worries between times 1 and 2 then a decrease between times 2 and 3, particularly with fear of getting COVID-19 infection ( $P < 0.001$ ) (Table 2).

### Patient-reported outcomes

During the pandemic, rheumatic patients reported mildly impaired PF ( $T$ -score mean = 43.58 [ $\pm$  3.18]). The mean PF score significantly decreased over time,  $F(2,1275) = 4.32$ ,  $P = 0.014$  (Table 2). The Bonferroni adjusted post-hoc pairwise comparison test showed that there was a significant difference between times 1 and 3 ( $P = 0.028$ ) compared to other time periods. On the other hand, mild FTG symptoms were reported by the patients ( $T$ -score mean = 56.44 [ $\pm$  2.65]). The mean FTG score was significantly increased over time,  $F(2,1275) = 3.20$ ,  $P < 0.042$  (Table 2). The Bonferroni adjusted post-hoc pairwise comparison test showed that there was a significant difference between times 1 and 3 ( $P = 0.036$ ) compared to other time periods.

In the multivariate linear regression (Table 3), we also found that impaired PF was significantly common among Saudi patients ( $P = 0.001$ ) who were older, married, and educated ( $P < 0.001$ ), as well as employed ( $P = 0.003$ ). Moreover, rheumatic patients experiencing active disease activity ( $B = -0.37$ ,  $P = 0.021$ ), without having any comorbidities,

except diabetes, ( $B = -0.80$ ,  $P = 0.018$ ) were likely to have impaired physical health. Additionally, the reduction of physical activity was associated with higher FTG, PI, and PL ( $P < 0.001$ ). Furthermore, patients with increased rheumatic disease activity ( $B = 0.789$ ,  $P < 0.001$ ) and/or diagnosed with psychological disorders ( $B = 0.755$ ,  $P = 0.002$ ) were predictive of them feeling fatigued during the pandemic. We found that increased FTG was positively correlated with DEP symptoms and PI ( $P < 0.001$ ).

Additionally, the SD and PI experiences by rheumatic patients were reported to be within normal limits ( $T$ -score mean = 53.07 [ $\pm$  3.45] and 59.09 [ $\pm$  2.34], respectively). Of note, patients' PL was considered moderate (mean 4.69 [ $\pm$  0.31]). The mean SD score did not differ over time,  $F(2,1275) = 1.20$ ,  $P = 0.301$ . Meanwhile, the mean PI significantly increased over time,  $F(2,1275) = 4.49$ ,  $P = 0.011$  (Table 2). The Bonferroni adjusted post-hoc pairwise comparison test showed that there was a significant difference between times 1 and 3 ( $P = 0.020$ ) compared to other time periods.

In a multivariate analysis, all marital and educational statuses significantly converged with patients' lower sleep quality ( $P < 0.050$ ). Age and comorbidity did not converge with sleep quality (Table 3). Moreover, patients with active rheumatic disease, particularly ankylosing spondylarthritis (AS), were likely to experience sleep disturbances ( $P < 0.050$ ). Interestingly, rheumatic patients with COVID-19 infection were also likely to experience poorer sleep

**Table 3** Multivariate linear regression for functional patient-reported outcomes ( $N=1278$ )

Predictor	Unstandardized coefficient $B$ (95% CI)			
	Physical function (PF)	Fatigue (FTG)	Sleep quality (SLP)	Pain interference (PI)
Age	-0.05 (-0.07, -0.04)**	0.01 (-0.01, 0.02)	-0.01 (-0.02, 0.01)	0.04 (0.03, 0.06)**
Male	-0.34 (-0.76, 0.09)	-0.50 (-0.93, -0.08)*	0.08 (-0.21, 0.37)	-0.14 (-0.59, 0.32)
Saudi	0.67 (0.27, 1.08)**	-	-	-0.65 (-1.10, -0.20)*
Marital status (single)	-0.64 (-0.29, -0.98)**	-	-0.48 (-0.82, -0.15)*	-
Education level (elementary)	-1.43 (-2.17, -0.69)**	-1.41 (-2.17, -0.65)**	-0.62 (-1.14, -0.10)*	-0.97 (-1.81, -0.13)*
Employed	0.47 (0.16, 0.79)*	-	-	-
Smoker	-	-	-0.30 (-0.74, 0.14)	-
Psychological disorder	-	0.76 (0.28, 1.23)*	-	-
Comorbidity	-0.80 (-1.46, -0.14)*	-2.20 (-4.78, 0.38)	-	0.56 (0.23, 0.88)**
Confirmed COVID-19 infection	-	-	-0.43 (-0.84, -0.02)*	-
Disease diagnosis	-	-	0.89 (0.08, 1.70)* (AS)	-0.81 (-1.16, -0.46)** (BD)
Active disease activity	-0.37 (-0.68, -0.06)*	0.23 (-0.10, 0.57)	0.27 (0.06, 0.48)*	0.59 (0.23, 0.95)**
Disease duration (years)	-	-	-	0.04 (0.017, 0.062)**
Difficulty accessing health-care	-	-	-	-
Difficulty obtaining medication	-	-0.34 (-0.63, -2.27)*	-	-
Worsening disease activity	-	0.79 (0.40, 1.17)**	-	0.73 (0.31, 1.14)**
Contracting COVID infection	-	-	-	0.30 (-0.03, 0.63)
Deteriorating disease, if infected	-0.24 (-0.55, 0.067)	-	-	-
Losing a job	-	-	-	-
Physical function	-	-	-	-
Social participation	-	-0.07 (-0.15, 0.02)	-	-
Anxiety	-	-	-	0.05 (0.00, 0.10)*
Depression	-	0.27 (0.23, 0.31)**	-0.02 (-0.05, 0.01)	-
Fatigue	-0.13 (-0.18, -0.08)**	-	-0.03 (-0.07, 0.00)	0.69 (0.65, 0.73)**
Sleep disturbance	-	-	-	-0.12 (-0.21, -0.03)*
Pain interference	-0.43 (-0.48, -0.38)**	0.57 (0.53, 0.61)**	-0.04 (-0.07, -0.01)*	-
Pain intensity (levels)	-	-	-	-

AS Ankylosing spondylarthritis; BD Behçet's syndrome; \*\*Correlation is significant at the 0.01 level (2-tailed); \*Correlation is significant at the 0.05 level (2-tailed)

quality ( $B = -0.430$ ,  $P = 0.041$ ). We also found that sleep quality was negatively and independently associated with PL and PI. A patient's score for PI tended to rise incrementally, corresponding to declining sleep quality ( $B = -0.38$ ,  $P = 0.025$ ).

Moreover, the majority of rheumatic patients indicated experiencing pain within normal limits that were not debilitating in their daily lives during the pandemic. Though our results showed that the mean scores for PL significantly increased over time,  $F(2,1275) = 6.50$ ,  $P = 0.002$ . Consistently, a patient experiencing heightened PI was likely to be older, with active rheumatic disease, one or more comorbidity, increased disease activity, and longer disease duration ( $P = 0.001$ ), according to the multivariate model (Table 3).

However, patients diagnosed with SLE ( $P < 0.001$ ) or beçet's syndrome ( $P = 0.048$ ) measured significantly lower PI compared to other rheumatic patients. Additionally, a rheumatic patient who is anxious, fatigued, and sleep disturbed was predictive of increased PI during the pandemic ( $P < 0.050$ ).

As for their mental health, rheumatic patients indicated mild ANX and DEP symptoms ( $T$ -score mean = 57.47 [ $\pm 3.38$ ] and 55.17 [ $\pm 3.34$ ], respectively). The mean ANX and DEP scores increased over time, but results did not show significant statistical difference between the three time periods (Table 2).

Interestingly, greater depression symptoms were common in younger, single individuals, whereas increased anxiety

was common among men who were not single ( $P < 0.050$ ). The linear regression model showed that anxiety and depression were interrelated significantly and positively with many factors related to patients' health behaviors and perceptions (Table 4). We identified that rheumatic patients (more likely those diagnosed with sjögren syndrome but less likely behçet's syndrome) and/or with a psychological diagnosis were at a higher risk of depressive symptoms ( $B = 1.62, P < 0.001$ ). Also, patients who did or did not contract COVID-19 infection were likely to feel more anxious and fearful ( $B = 1.20, P < 0.001$ ) during the pandemic.

Furthermore, a significant decrease was found in the social health domain ( $P = 0.028$ ), though the overall mean for patients' SP was within normal limits over time ( $T$ -score mean = 47.68 [ $\pm 2.72$ ]). The mean SP score significantly decreased over time,  $F(2,1275) = 3.60, P = 0.028$

(Table 2). The Bonferroni adjusted post hoc pairwise comparison test showed that there was a significant difference between times 1 and 3 ( $P = 0.050$ ) compared to other time periods.

Our results from the multivariate analysis showed that employed patients ( $B = 0.39, P = 0.023$ ) who were not able to access healthcare services ( $B = -0.46, P < 0.005$ ) during the pandemic were likely to be unable to perform their usual social roles and activities (Table 4). Age also seemed to play a factor such that for each additional one year rise in a patient's age, the model predicted that their scores for the ability to participate in social roles decreased by a factor equal to 0.050 points less on average ( $P < 0.001$ ). Furthermore, the inability to participate in social activities negatively correlated with DEP ( $P = 0.054$ ), FTG ( $P < 0.001$ ), and PI ( $P < 0.001$ ), even after adjustment for other covariates.

**Table 4** Multivariate linear regression for psychosocial patient-reported outcomes ( $N = 1278$ )

Predictor	Unstandardized coefficient $B$ (95% CI)		
	Anxiety (ANX)	Depression (DEP)	Social participation (SP)
Age	- 0.02 (- 0.04, 0.00)	- 0.09 (- 0.11, - 0.07)**	- 0.05 (- 0.06, - 0.03)**
Male	0.50 (0.02, 0.98)*	- 0.26 (- 0.80, 0.27)	- 0.31 (- 0.77, 0.15)
Saudi	-	-	-
Marital status (single)	- 0.47 (- 0.85, - 0.09)*	0.48 (0.05, 0.90)*	-
Education level (elementary)	-	-	-
Employed	-	-	-
Smoker	- 0.57 (- 1.28, 0.15)	0.58 (- 0.22, 1.38)	-
Psychological disorder	-	1.62 (1.06, 2.19)**	-
Comorbidity	-	0.19 (- 0.18, 0.55)	-
Confirmed COVID-19 infection	0.66 (- 0.01, 1.34)*	-	-
Disease diagnosis	-	1.82 (0.61, 3.03)* (SS)	- 0.51 (- 1.05, 0.03) (RA)
Active disease activity	-	-	-
Disease duration (years)	-	-	-
Difficulty accessing healthcare	0.49 (0.16, 0.82)*	-	- 0.46 (- 0.79, - 0.14)*
Difficulty obtaining medication	-	-	-
Worsening disease activity	-	- 0.39 (- 0.84, 0.06)	-
Contracting COVID infection	1.20 (0.84, 1.56)**	0.83 (0.47, 1.19)**	-
Deteriorating disease, if infected	0.62 (0.23, 1.00)*	-	-
Losing a job	0.35 (0.02, 0.69)*	0.84 (0.39, 1.29)**	-
Physical function	-	-	-
Social participation	-	-	-
Anxiety	-	-	-
Depression	0.50 (0.46, 0.55)**	-	- 0.05 (- 0.09, 0.00)*
Fatigue	0.14 (0.09, 0.18)**	0.37 (0.31, 0.44)**	- 0.19 (- 0.25, - 0.13)**
Sleep disturbance	-	- 0.08 (- 0.18, 0.03)	-
Pain interference	-	0.17 (0.11, 0.23)**	- 0.50 (- 0.56, - 0.45)**
Pain intensity (levels)	-	-	-

RA Rheumatoid arthritis, SS Sjögren syndrome

\*\*Correlation is significant at the 0.01 level (2-tailed); \*Correlation is significant at the 0.05 level (2-tailed)

## Discussion

This study assessed the quality of life in people with rheumatic diseases living in SA during the COVID-19 pandemic. Significant changes in some PROMIS® domains were observed among patients warranting rheumatologists' attention. It was also noticed that these domains were not just transient in nature during the COVID-19 pandemic and its corresponding public health interventions, but instead persistent over time and likely to reflect the complexity of their long-term care.

### Physical health (PF and FTG)

Our findings showed that the reduction in the overall physical health significantly correlated with increased fatigue and pain. Particularly for the older female patients, who had a lower physical function and established marriage, education, and employment, it meant that they had difficulty juggling their daily duties/responsibilities alongside managing their own diseases during the pandemic. Supporting this result is the observation of women living with fibromyalgia, where reduced levels of daily lifestyle resulted in impaired physical function, worsened quality of life, and more fatigue [8]. This suggests that rheumatic patients experiencing functional difficulties might need personalized support to manage their symptoms, considering demographical factors, such as age, gender, and societal roles, as well as their history of physical function. One way perhaps by using a frailty screening assessment (e.g., Reported Edmonton Frail Scale) that could equip the rheumatologist with a multidimensional approach to identifying older patients at risk of negative outcomes due to physical weakness.

Moreover, we found that fatigue was positively correlated with high depressive and pain symptoms, which might be explained by the presence of pre-existing comorbidity and psychological disorder(s). The reduced physical energy was also common as a new symptom in rheumatic patients and the general population during the pandemic [9, 10]. The relationship between physical dysfunction and cognitive abnormalities coupled with heightened stressors has been well established in rheumatic diseases [11, 12]. This suggests that a prolonged worry and stress brought by stringent COVID-19 measures (e.g., restricted access to healthcare services) might worsen patients' disease and treatment outcomes [13]. Thus, effective fatigue management education should include a neuropsychic examination and stress-controlling strategies.

Furthermore, approximately 20% of our study population had a negative perception of disease activity that

persisted during the pandemic. In conjunction with worsened symptoms of disease activity, we found increased impairment of functional ability. Such deterioration was also significantly associated with increased fatigue scores. These findings indicate a complex interrelationship between physical activity and disease activity. However, much of our understanding of this relationship remains unclear. It would be interesting to observe how physical impairment and fatigue would resolve after the pandemic.

Although fatigue is a common symptom in rheumatic diseases, fatigue complaints might be neglected at a clinical visit and often misinterpreted as a non-disease-related symptom (i.e., comorbidity or medication). As a result, discrepancies between patient and physician perspectives might negatively impact decision-making and health outcomes. Thus, recognizing patients' concerns and providing 'structural communication' in addressing physical health might provide an opportunity for mitigating poor quality of life.

### Physical health (SD and PI)

Sleeping abnormalities are commonly experienced by rheumatic patients [14]. Some studies conducted during the pandemic found that 30–40% of the participants experienced insomnia during isolation [9, 15]. Loss of a sleeping routine can lead to sleeping difficulties and a reduction in sleep quality [16, 17], particularly for rheumatic patients [13, 18]. In our study, significant sleep abnormalities were associated with subjective sleep quality, such as sleep duration, habitual sleep efficiency, and sleep disturbance.

Interestingly, in many of the first COVID-19 cases, new-onset of health problems related to sleeping difficulties emerged, including physical exhaustion and daytime dysfunction [19, 20]. In addition, several studies suggested that insomnia predisposes individuals to chronic pain or increased pain [21–23]. Our results were consistent with evidence found in the literature, where people suffering from rheumatic pain had the most significant impact on their sleep quality. Similarly, individuals with RA commonly reported (60–75%) that arthritic pain interfered with their sleep to some degree [24]. Furthermore, a significant, positive correlation ( $r=0.612$ ,  $P<0.001$ ) between disease activity and impaired sleep quality was found in a study of 55 patients with AS compared to age and gender-matched healthy controls [25].

The worsening of pain might hamper a patient's ability to cope with it and contribute to the reliance on maladaptive health behaviors, such as medication non-adherence, drug alteration, and self-medicating [5]. In addition, the restricted healthcare services and medications potentially contribute to worsening pain [26]. The current psychological approach is heavily therapist-dependent [27, 28]. To mitigate COVID-related impact on the psychosocial status,

perhaps, it's important to identify affected patients and offer innovative healthcare techniques [29–31] that can optimize empowerment in self-managing their rheumatic conditions and resilience to overcome pandemic challenges [32].

### Mental health (ANX and DEP)

We found that intrinsic and extrinsic factors might have influenced the mental states during the pandemic. For instance, most of our participants were unemployed and felt anxious and depressed; even among employed individuals, we found many were fearful and distressed about losing their jobs. Our findings mirrored another study on the employment history of rheumatic patients during the pandemic [33]. Similarly, significant anxiety was associated with low monthly income (OR = 1.79, 95% CI = 1.07, 3.01,  $P < 0.026$ ) [18]. In fact, inadequate financial resources were independently associated with increased anxiety and depressive symptoms [34].

Also, the severity of anxiety and depression over time might be related to the extent (magnitude and duration) of exposure to COVID-related stressors. In our study, we found patients worried about contracting COVID-19 infection and losing their job at the same time were almost as depressed as those living with pre-existing psychological disorders. Also, patients who had already contracted the COVID-19 infection were no more anxious than those who were not infected and were still worried about it throughout the pandemic. Frontera and colleagues also found that anxiety, depression, and fatigue levels were similar between subjects with and without COVID-19 infection; however, those with the infection were at risk of long-term psychological impairment [35]. These findings indicate that the chronic coexistence of stressors might have a combined effect on the risk of developing psychiatric-like states or exacerbating the pre-existing symptoms.

We also identified that some rheumatic patients experienced poorer mental health than others, even after adjusting for neuropsychiatric and comorbid disorders. For instance, patients, more likely those living with sjögren's syndrome but less likely with behçet's syndrome, felt more depressed and experienced increased fatigue and pain symptoms during the pandemic. Similarly, the SPIN COVID-19 Cohort revealed a considerable increase in anxiety symptoms among people with scleroderma, but depressive symptoms had minimally increased compared to before the pandemic [34]. This might or might not be attributed to the nature of their disease [36, 37]. However, emerging evidence revealed that depression and rheumatic diseases might share common pathophysiological mechanisms potentially linking peripheral and brain immune responses [38–41].

Thus, experiencing environmental stressors during the pandemic (e.g., difficulty obtaining the needed healthcare

services and resources) could negatively affect patients' mental health long-term. The poor mental state, in turn, might potentially impact patients' health perception and behavior [42]. This reflects a potential health risk that warrants physicians' attention during clinical assessments.

### Social health (SP)

A statistically significant change was found in the social function domain, as more than half of the participants had mildly to severely impaired social function that was worsening over time. Older rheumatic patients with multiple morbidities and who could not access healthcare services during the pandemic were likely to be unable to participate in social roles. An in-depth analysis of participants' responses revealed no significant difference regarding their experience in 'doing leisure activities with others,' 'doing usual personal work at home,' and 'doing regular activities with friends.' However, participants consistently scored lower in 'doing family activities.' For the older patients who scored lower SP, this could presumably mean that they could not get the family support they needed during the pandemic. However, more younger patients seem to be experiencing a similar social deprivation [43]. These findings were not entirely unsuspected, but one might question whether participation in social roles during the pandemic can be considered a valid construct in the context of COVID-19 restrictions.

Nevertheless, the forced social isolation implemented to mitigate the spread of COVID-19 might trigger long-term health impacts in rheumatic patients. The inability to participate in social activities due to the COVID-19 measures may worsen some patients' mental health. We found that the failure to participate in social activities significantly correlated with depression, fatigue, and pain levels, even after adjustment for confounding factors. Our results were consistent with findings from other studies [29, 44], where older rheumatic patients with strict social distancing measures showed a negative impact on mental well-being compared to patients with flexible social distancing [29, 45]. Other studies reported that participants prevented from social gatherings suffered loneliness and sadness early during the pandemic [10], whereas social support made individuals less stressed about their health and the infection [44, 46]. This is important because social isolation potentially makes transitory loneliness chronic, which might impact cardiovascular health in the long term [47].

Undoubtedly, social distancing with effective communication has been valued as beneficial protection of rheumatic patients during the pandemic, as individuals declared that social support made them less stressed about their health and the infection [44, 46]. However, it is important to investigate during follow-ups whether patients maintain the limitation of social activity long-term.



## Strengths and limitations

Our study provides a glimpse into the experience of patients living with chronic diseases under strict COVID-19 public health measures. We used a validated tool to capture various domains related to the overall well-being of individuals. Using a time-series design allowed us to examine trends of important patient-reported outcomes, considering the natural experiment generated by public health intervention measures. Yet, the limitations were as follows: First, the inclusion criteria allowing for the collection of heterogeneous data might have introduced unexpected confounding variables. However, exploring all these relationships was beyond the scope of our present study. Thus, specific predictors were selected for regression modeling based on our literature review of relevance. Second, the nature of the survey-based study might have allowed for the misclassification of patients and their diseases. Hence, we tried to avoid disease-based analysis and focused on our population as a whole. Third, the online survey might have caused patients with no e-technology to be marginalized. This then raises the question of whether the PROMIS® questionnaire is reliable as an online survey. To the best of our knowledge, no study has investigated this problem, but it is worth exploring. Fourth, the scores may have been generalized for some rheumatic patients as emerging evidence suggests changing the PROMIS® fatigue scores threshold, particularly for RA patients [48]. Lastly, the change in response rate due to participants' dropout might have been influenced by the 'situational demand' brought by the COVID-19 crisis. The faced health risk during the early days of the pandemic likely drove respondents to participate in our survey. However, as the local restrictions eased and more information surfaced about the nature of COVID-19, it probably affected participants' interest/decision to respond to the surveys. Thus, we have included all observed data and applied multiple imputation method to deal with non-response bias. Nevertheless, results should be interpreted with caution.

## Conclusion

The involuntary social isolation brought by the COVID-19 pandemic upon rheumatic patients might trigger a vicious cycle of physical and mental distress leading to a worsening perception of their rheumatic diseases. Other factors, such as age, gender, comorbidity, and psychological disorders, exacerbate the problem. Probable subsequent waves of COVID-19 put increasing psychological demand and pressure on coping mechanisms employed by rheumatic patients. We recommend planning before the next pandemic wave, implementing effective physician–patient communication during and after a pandemic, and employing a more

holistic approach to social-mental-physical post-pandemic interventions.

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## Declarations

**Conflict of interest** The authors declared that they have no conflict of interest.

**Ethical approval** All procedures performed in this study involving human participants were in accordance with the ethical standards of the Institution Review Board of King Saud University, Riyadh, SA (Approval No. E-20-4787) and with the 1964 Helsinki declaration and its later amendments.

**Informed consent** Informed consent was obtained from all participants included in the study.

## References

1. Voelker, R. (2000). Rheumatic disease burden. *JAMA*, 283(14), 1816. <https://doi.org/10.1001/jama.283.14.1816-jwm00002-2-1>
2. Anyfanti, P., Triantafyllou, A., Panagopoulos, P., Triantafyllou, G., Pырpasopoulou, A., Chatzimichailidou, S., Koletsos, N., Botis, I., Aslanidis, S., & Douma, S. (2016). Predictors of impaired quality of life in patients with rheumatic diseases. *Clinical Rheumatology*, 35(7), 1705–1711. <https://doi.org/10.1007/s10067-015-3155-z>
3. Callahan, L. F. (2016). The history of patient-reported outcomes in rheumatology. *Rheumatic Diseases Clinics of North America*, 42(2), 205–217. <https://doi.org/10.1016/j.rdc.2016.01.012>
4. Arvidsson, S., Arvidsson, B., Fridlund, B., & Bergman, S. (2011). 2011 Factors promoting health-related quality of life in people with rheumatic diseases: a 12 month longitudinal study. *BMC Musculoskeletal Disorders*, 12, 102. <https://doi.org/10.1186/1471-2474-12-102>
5. Hassen, L. M., Almaghlouth, I. A., Hassen, I. M., Daghestani, M. H., Almohisen, A. A., Alqurtas, E. M., Alkhalaf, A., Bedaiwi, M. K., Omair, M. A., Almogairen, S. M., & Alarfaj, H. F. (2020). Impact of COVID-19 outbreak on rheumatic patients' perceptions and behaviors: A cross-sectional study. *International Journal of Rheumatic Disease*, 23(11), 1541–1549. <https://doi.org/10.1111/1756-185X.13959>
6. von Elm, E., Altman, D. G., Egger, M., Pocock, S. J., Gøtzsche, P. C., & Vandenbroucke, J. P. (2014). The strengthening the reporting of observational studies in epidemiology (STROBE) statement: Guidelines for reporting observational studies. *International Journal Surgery*, 12(12), 1495–1499. <https://doi.org/10.1016/j.ijssu.2014.07.013>
7. Rothrock, N. E., Amtmann, D., & Cook, K. F. (2020). Development and validation of an interpretive guide for PROMIS scores. *Journal of Patient Reported Outcomes*, 4(1), 16. <https://doi.org/10.1186/s41687-020-0181-7>

8. Merriwether, E. N., Frey-Law, L. A., Rakel, B. A., Zimmerman, M. B., Dailey, D. L., Vance, C. G., Golchha, M., Geasland, K. M., Chimenti, R., Crofford, L. J., & Sluka, K. A. (2018). Physical activity is related to function and fatigue but not pain in women with fibromyalgia: baseline analyses from the fibromyalgia activity study with TENS (FAST). *Arthritis Research Therapy*, *20*(1), 199. <https://doi.org/10.1186/s13075-018-1671-3>
9. Stanton, R., To, Q. G., Khalesi, S., Williams, S. L., Alley, S. J., Thwaite, T. L., Fenning, A. S., & Vandelanotte, C. (2020). 2020 Depression, anxiety and stress during COVID-19: Associations with changes in physical activity, sleep, tobacco and alcohol use in Australian adults. *International Journal of Environmental Research Public Health*, *17*(11), 4065. <https://doi.org/10.3390/ijerph17114065>
10. Michaud, K., Wipfler, K., Shaw, Y., Simon, T. A., Cornish, A., England, B. R., Ogdie, A., & Katz, P. (2020). Experiences of patients with rheumatic diseases in the United States during early days of the COVID-19 pandemic. *ACR Open Rheumatology*, *2*(6), 335–343. <https://doi.org/10.1002/acr2.11148>
11. de Brouwer, S. J., Kraaimaat, F. W., Sweep, F. C., Creemers, M. C., Radstake, T. R., van Laarhoven, A. I., van Riel, P. L., & Evers, A. W. (2010). Experimental stress in inflammatory rheumatic diseases: a review of psychophysiological stress responses. *Arthritis Research Therapy*, *12*(3), R89. <https://doi.org/10.1186/ar3016>
12. van Middendorp, H., & Evers, A. W. (2016). The role of psychological factors in inflammatory rheumatic diseases: From burden to tailored treatment. *Best Practice & Research Clinical Rheumatology*, *30*(5), 932–945. <https://doi.org/10.1016/j.berh.2016.10.012>
13. Mancuso, C. A., Duculan, R., Jannat-Khah, D., Barbhayya, M., Bass, A. R., & Mehta, B. (2020). Rheumatic disease-related symptoms during the height of the COVID-19 pandemic. *HSS Journal*, *16*(Suppl 1), 36–44. <https://doi.org/10.1007/s11420-020-09798-w>
14. Ingegnoli, F., Buoli, M., Posio, C., Di Taranto, R., Lo Muscio, A., Cumbo, E., Ostuzzi, S., & Caporali, R. (2021). COVID-19 related poor mental health and sleep disorders in rheumatic patients: A citizen science project. *BMC Psychiatry*, *21*(1), 385. <https://doi.org/10.1186/s12888-021-03389-7>
15. Shi, L., Lu, Z. A., Que, J. Y., Huang, X. L., Liu, L., Ran, M. S., Gong, Y. M., Yuan, K., Yan, W., Sun, Y. K., & Shi, J. (2020). 2020 prevalence of and risk factors associated with mental health symptoms among the general population in china during the coronavirus disease 2019 pandemic. *JAMA Network Open.*, *3*(7), e2014053. <https://doi.org/10.1001/jamanetworkopen.2020.14053>
16. Xiao, H., Zhang, Y., Kong, D., Li, S., & Yang, N. (2020). The Effects of Social Support on Sleep Quality of Medical Staff Treating Patients with Coronavirus Disease 2019 (COVID-19) in January and February 2020 in China. *Medical Science Monitor*. <https://doi.org/10.12659/MSM.923549>
17. Deng, J., Zhou, F., Hou, W., Silver, Z., Wong, C. Y., Chang, O., Huang, E., & Zuo, Q. K. (2021). The prevalence of depression, anxiety, and sleep disturbances in COVID-19 patients: a meta-analysis. *Annals of New York Academy Science*, *1486*(1), 90–111. <https://doi.org/10.1111/nyas.14506>
18. Adnine, A., Nadiri, K., Soussan, I., Coulibaly, S., Berrada, K., Najdi, A., & Abourazzak, F. E. (2021). Mental health problems experienced by patients with rheumatic diseases during COVID-19 pandemic. *Current Rheumatology Reviews*, *17*(3), 303–311. <https://doi.org/10.2174/1573397117666210127124544>
19. Kang, L., Li, Y., Hu, S., Chen, M., Yang, C., Yang, B. X., & Liu, Z. (2020). The mental health of medical workers in Wuhan, China dealing with the 2019 novel coronavirus. *Lancet Psychiatry*, *7*(3), e14. [https://doi.org/10.1016/S2215-0366\(20\)30047-X](https://doi.org/10.1016/S2215-0366(20)30047-X)
20. Wang, C., Pan, R., Wan, X., Tan, Y., Xu, L., Ho, C. S., & Ho, R. C. (2020). Immediate Psychological Responses and Associated Factors during the Initial Stage of the 2019 Coronavirus Disease (COVID-19) Epidemic among the General Population in China. *International Journal of Environmental Research Public Health*, *17*(5), 1729. <https://doi.org/10.3390/ijerph17051729>
21. Andersen, M. L., Araujo, P., Frange, C., & Tufik, S. (2018). Sleep Disturbance and Pain: A Tale of Two Common Problems. *Chest*, *154*(5), 1249–1259. <https://doi.org/10.1016/j.chest.2018.07.019>
22. Menefee, L. A., Cohen, M. J., Anderson, W. R., Doghramji, K., Frank, E. D., & Lee, H. (2000). Sleep disturbance and nonmalignant chronic pain: A comprehensive review of the literature. *Pain Medicine*, *1*(2), 156–172. <https://doi.org/10.1046/j.1526-4637.2000.00022.x>
23. Nicassio, P. M., & Wallston, K. A. (1992). Longitudinal relationships among pain, sleep problems, and depression in rheumatoid arthritis. *Journal of Abnormal Psychology*, *101*(3), 514–520. <https://doi.org/10.1037//0021-843x.101.3.514>
24. Lavie, P., Epstein, R., Tzischinsky, O., Gilad, D., Nahir, M., Lorber, M., & Scharf, Y. (1992). Actigraphic measurements of sleep in rheumatoid arthritis: comparison of patients with low back pain and healthy controls. *The Journal of Rheumatology*, *19*(3), 362–365.
25. Aydin, E., Bayraktar, K., Turan, Y., Omurlu, I., Tastaban, E., & Sendur, O. F. (2015). Qualidade do sono em pacientes com espondilite anquilosante [Sleep quality in patients with ankylosing spondylitis]. *Revista Brasileira de Reumatologia*, *55*(4), 340–345. <https://doi.org/10.1016/j.rbr.2014.12.007>
26. Blyth, F. M., March, L. M., Brnabic, A. J., & Cousins, M. J. (2004). Chronic pain and frequent use of health care. *Pain*, *111*(1–2), 51–58. <https://doi.org/10.1016/j.pain.2004.05.020>
27. Knoerl, R., Lavoie Smith, E. M., & Weisberg, J. (2016). Chronic pain and cognitive behavioral therapy: An integrative review. *Western Journal of Nursing Research*, *38*(5), 596–628. <https://doi.org/10.1177/0193945915615869>
28. Sharpe, L. (2016). Psychosocial management of chronic pain in patients with rheumatoid arthritis: challenges and solutions. *Journal of Pain Research*. <https://doi.org/10.2147/JPR.S83653>
29. Cleaton, N., Raizada, S., Barkham, N., Venkatachalam, S., Sheeran, T., Adizie, T., Sapkota, H., Singh, B., & Bateman, J. (2020). COVID-19 prevalence and the impact on quality of life from stringent social distancing in a single large UK rheumatology centre. *Annals of the Rheumatic Diseases*. <https://doi.org/10.1136/annrheumdis-2020-218236>
30. Blaney, C., Hitchon, C. A., Marrie, R. A., Mackenzie, C., Holens, P., & El-Gabalawy, R. (2021). Support for a non-therapist assisted, Internet-based cognitive-behavioral therapy (iCBT) intervention for mental health in rheumatoid arthritis patients. *Internet Interventions*. <https://doi.org/10.1016/j.invent.2021.100385>
31. Kluck, J. P., Stoyanova, F., & Krämer, N. C. (2021). Putting the social back into physical distancing: The role of digital connections in a pandemic crisis. *International Journal of Psychology*, *56*(4), 594–606. <https://doi.org/10.1002/ijop.12746>
32. Evers, A. W., Kraaimaat, F. W., Geenen, R., Jacobs, J. W., & Bijlsma, J. W. (2003). Pain coping and social support as predictors of long-term functional disability and pain in early rheumatoid arthritis. *Behaviour Research and Therapy*, *41*(11), 1295–1310. [https://doi.org/10.1016/s0005-7967\(03\)00036-6](https://doi.org/10.1016/s0005-7967(03)00036-6)
33. Jetha, A., Tucker, L. B., Chen, C., & Gignac, M. A. M. (2021). Impact of the COVID-19 Pandemic on the employment of Canadian young adults with rheumatic disease: Findings from a longitudinal survey. *Arthritis Care & Research*, *73*(8), 1146–1152. <https://doi.org/10.1002/acr.24617>
34. Thombs, B. D., Kwakkenbos, L., Henry, R. S., Carrier, M. E., Patten, S., Harb, S., Bourgeault, A., Tao, L., Bartlett, S. J., Moulton, L., & Varga, J. (2020). Changes in mental health symptoms from pre-COVID-19 to COVID-19 among participants with systemic sclerosis from four countries: A Scleroderma Patient-centered Intervention Network (SPIN) Cohort study. *Journal of*

- Psychosomatic Research*, 139, 110262. <https://doi.org/10.1016/j.jpsychores.2020.110262>
35. Frontera, J. A., Lewis, A., Melmed, K., Lin, J., Kondziella, D., Helbok, R., Yaghi, S., Meropol, S., Wisniewski, T., Balcer, L., & Galetta, S. L. (2021). Prevalence and predictors of prolonged cognitive and psychological symptoms following COVID-19 in the United States. *Frontiers in Aging Neuroscience*. <https://doi.org/10.3389/fnagi.2021.690383>
  36. AlEnzi, F., Alqahtani, B., Alhamad, E. H., Daghestani, M., Tashkandy, Y., Othman, N., Alshahrani, K., Paramasivam, M. P., Halwani, R., & Omair, M. A. (2020). Fatigue in Saudi patients with primary Sjögren's syndrome and its correlation with disease characteristics and outcome measures: A cross-sectional study. *Open Access Rheumatology*, 12, 303–308. <https://doi.org/10.2147/OARRR.S284985>
  37. Seyahi, E., Poyraz, B. C., Sut, N., Akdogan, S., & Hamuryudan, V. (2020). The psychological state and changes in the routine of the patients with rheumatic diseases during the coronavirus disease (COVID-19) outbreak in Turkey: A web-based cross-sectional survey. *Rheumatology International*, 40(8), 1229–1238. <https://doi.org/10.1007/s00296-020-04626-0>
  38. Nerurkar, L., Siebert, S., McInnes, I. B., & Cavanagh, J. (2019). Rheumatoid arthritis and depression: An inflammatory perspective. *Lancet Psychiatry*, 6(2), 164–173. [https://doi.org/10.1016/S2215-0366\(18\)30255-4](https://doi.org/10.1016/S2215-0366(18)30255-4)
  39. Albeltagy, E. S., Elaziz, S. Y. A., Abozaid, S. Y., El Zomor, H. M., & Elhamed, S. S. A. (2021). Interleukin 6, interleukin 17, disease-related and contextual factor association with depression, and its severity in patients with rheumatoid arthritis. *Clinical Rheumatology*, 40(3), 895–904. <https://doi.org/10.1007/s10067-020-05326-7>
  40. Smesam, H. N., Qazmooz, H. A., Khayoon, S. Q., Almulla, A. F., Al-Hakeim, H. K., & Maes, M. (2022). Pathway phenotypes underpinning depression, anxiety, and chronic fatigue symptoms due to acute rheumatoid arthritis: A precision nomothetic psychiatry analysis. *Journal of Personalized Medicine*. <https://doi.org/10.3390/jpm12030476>
  41. Cao, L. H., Zhao, Y. Y., Bai, M., Geliebter, D., Geliebter, J., Tiwari, R., He, H. J., Wang, Z. Z., Jia, X. Y., Li, J., & Li, X. M. (2022). Mechanistic Studies of Gypenosides in Microglial State Transition and its Implications in Depression-Like Behaviors: Role of TLR4/MyD88/NF-κB Signaling. *Front Pharmacology*, 13, 838261. <https://doi.org/10.3389/fphar.2022.838261>
  42. Hausmann, J. S., Kennedy, K., Simard, J. F., Liew, J. W., Sparks, J. A., Moni, T. T., Harrison, C., Larché, M. J., Levine, M., Sattui, S. E., Semalulu, T., Foster, G., Surangiwal, S., Thabane, L., Beesley, R. P., Durrant, K. L., Mateus, E. F., Mingolla, S., Nudel, M., ... Sirotych, E. (2021). Immediate effect of the COVID-19 pandemic on patient health, health-care use, and behaviours: results from an international survey of people with rheumatic diseases. *Lancet Rheumatol.*, 3(10), e707–e714. [https://doi.org/10.1016/S2665-9913\(21\)00175-2](https://doi.org/10.1016/S2665-9913(21)00175-2)
  43. Beam, C. R., & Kim, A. J. (2020). Psychological sequelae of social isolation and loneliness might be a larger problem in young adults than older adults. *Psychological Trauma*, 12(S1), S58–S60. <https://doi.org/10.1037/tra0000774>
  44. Sloan, M., Gordon, C., Lever, E., Harwood, R., Bosley, M. A., Pilling, M., Brimicombe, J., Naughton, F., Blane, M., Walia, C., & D'Cruz, D. (2021). COVID-19 and shielding: Experiences of UK patients with lupus and related diseases. *Rheumatology Advances Practice*. <https://doi.org/10.1093/rap/rkab003>
  45. Garrido-Cumbrera, M., Marzo-Ortega, H., Christen, L., Plazuelo-Ramos, P., Webb, D., Jacklin, C., Irwin, S., Grange, L., Makri, S., Mateus, E. F., & Mingolla, S. (2021). Assessment of impact of the COVID-19 pandemic from the perspective of patients with rheumatic and musculoskeletal diseases in Europe: results from the REUMAVID study (phase 1). *RMD Open*, 7(1), e001546. <https://doi.org/10.1136/rmdopen-2020-001546>
  46. Rathi, M., Singh, P., Bi, H. P., Shivanna, A., Kavadiachanda, C., Tripathy, S. R., Parthasarathy, J., Tota, S., Maurya, S., Vishnu-priya Vijayalekshmi, D., Bhavani, A. J., Gupta, R., Danda, D., Rajasekhar, L., Negi, V. S., Shobha, V., Das, B., & Aggarwal, A. (2021). Impact of the COVID-19 pandemic on patients with systemic lupus erythematosus: Observations from an Indian inception cohort. *Lupus*, 30(1), 158–164. <https://doi.org/10.1177/0961203320962855>
  47. Courtin, E., & Knapp, M. (2017). Social isolation, loneliness and health in old age: A scoping review. *Health and Social Care in the Community*, 25(3), 799–812. <https://doi.org/10.1111/hsc.12311>
  48. Bingham, C. O., Butanis, A. L., Orbai, A. M., Jones, M., Ruffing, V., Lyddiatt, A., Schrandt, M. S., Bykerk, V. P., Cook, K. F., & Bartlett, S. J. (2021). Patients and clinicians define symptom levels and meaningful change for PROMIS pain interference and fatigue in RA using bookmarking. *Rheumatology (Oxford)*, 60(9), 4306–4314. <https://doi.org/10.1093/rheumatology/keab014>

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