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# Patient-reported Disease Activity in an Axial Spondyloarthritis Cohort during the COVID-19 Pandemic

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**Objective.** Response to the coronavirus disease 2019 (COVID-19) pandemic has resulted in shelter-in-place orders and major changes to individuals' daily lives. The impact of such stressors on disease activity in individuals with axial spondyloarthritis (axSpA) is unclear. The aim of this study is to examine whether stress, anxiety, and depression are associated with patient-reported disease activity, after accounting for important factors.

**Methods.** We administered a survey to an axSpA cohort from a single center with well-defined demographic and disease characteristics. We included questions about job status changes, exercise, medication use, disease activity (by the Bath Ankylosing Spondylitis Disease Activity Index [BASDAI]), and psychological factors (stress, depressive symptoms, and anxiety). Separate multivariable linear models examined the associations between perceived stress, anxiety, and depression with the BASDAI.

**Results.** After adjustment for potential confounders, those with higher levels of stress had a statistically significant 0.54-point higher BASDAI, on average, compared with those with lower levels of stress (95% confidence interval [CI]: 0.11, 0.97). Those with higher levels of anxiety also had a statistically significant higher BASDAI, on average, compared with those with lower levels of anxiety ($\beta$: 0.95, 95% CI: 0.18, 0.99). The association between depression and BASDAI was not statistically significant. We did not find differences in these associations among subgroups of age, job status, or county of residence.

**Conclusion.** Individuals with axSpA with higher levels of stress and anxiety had significantly higher disease activity levels, although with a difference below clinical importance. Further planned studies will evaluate the trajectory of disease activity.

## INTRODUCTION

Severe acute respiratory syndrome coronavirus 2 is a novel coronavirus that causes coronavirus disease 2019 (COVID-19), which the World Health Organization declared a pandemic in 2020 (1). By early April 2020, there were over 100 000 confirmed cases in the United States, with global cases climbing past a million (2). In response to rising case numbers, San Francisco, California, was placed under a shelter-in-place order on March 17, 2020, with many cities, counties, and states subsequently doing the same (3).

Prior literature in other rheumatic diseases has been conflicting in terms of how major natural disasters, such as hurricanes and earthquakes, impact disease activity (4–9). Stress is implicated as an important factor that affects disease activity, as has been demonstrated in rheumatoid arthritis (RA) (10–12). However, there have been few studies of axial spondyloarthritis (axSpA) that have directly examined the association of stress with disease activity (13), and none them have evaluated the association of major stressors such as natural disasters or pandemics with disease activity. As a shelter-in-place order impacts the entire community and may result in occupational changes (eg, working from home or loss of income), limitations on physical activity (eg, closure of nonessential businesses including gyms), and medication changes (eg, in light of concerns of increased infection risk with immunosuppression), COVID-19 represents a unique situation to study the impact of stress on disease activity in axSpA.

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The purpose of this study is to study the impact of this major event, particularly in light of local shelter-in-place ordinances and major economic changes, on disease activity in an existing natural history cohort of individuals with axSpA. The primary aim is to examine whether stress, anxiety, and depression are associated with a change in disease activity, after accounting for important factors.

## PATIENTS AND METHODS

**Study population.** The natural history of axSpA study is an ongoing prospective cohort of 473 subjects at the University of California, San Francisco (UCSF). Adults who met either the modified New York criteria for ankylosing spondylitis (AS) or the Assessment of Spondyloarthritis International Society (ASAS) criteria for nonradiographic axSpA were enrolled from 2007. The purpose of the cohort study is to explore potential mechanisms responsible for disease, risk factors for the development and progression, associated comorbidities, treatments and treatment complications, and the natural history of spondyloarthritis. Patients are followed at cohort study visits every 6 months.

**Data collection and variables.** For the current study, subjects were emailed a link to a survey hosted online through the HIPAA-compliant platform Qualtrics that was specifically focused on issues surrounding the past 2 months during the COVID-19 pandemic. Survey objectives, risks, benefits, and study team contact information were provided to patients before questions were initiated. This study received internal review board (IRB) approval from UCSF following a modification to the cohort IRB. The University of Washington determined that further IRB review was not needed for the analysis of this study.

*Medication use.* Patients were asked about baseline nonsteroidal anti-inflammatory drug (NSAID) and biologics use, and whether there was any change over the prior two months (increased, decreased, stopped, stayed the same, switched, or did not use at baseline). The interval of 2 months (February to April 2020) was chosen to capture potential changes that patients may have instituted on account of the pandemic.

*Exercise.* Patients were asked about baseline ("six months ago") exercise frequency, duration, and specific type. Then they were asked about change over the prior 2 months (increased, decreased, stopped, stayed the same, or did not exercise at baseline).

*Job status.* Patients were asked for details about their current employment status, including whether they were unemployed, and their current work location if employed.

*COVID-19.* Patients were asked whether they had received a nasal swab or other form of testing for the diagnosis of COVID-19 and whether the results were positive. If testing had been performed, they were asked about symptoms and any treatment received. They were also given the opportunity to provide any concerns they had regarding COVID-19 in an open-ended question.

*Disease activity.* The Bath Ankylosing Spondylitis Disease Activity Index (BASDAI*)* was administered as an assessment of disease activity over the prior week. The BASDAI is a composite measure of AS disease activity and consists of six questions that address five major symptoms in AS: fatigue, spinal pain, peripheral joint pain and swelling, localized tenderness, and morning stiffness (14). Scores range from 0 to 10, with higher scores reflecting greater disease activity.

Psychological factors were measured by the following instruments:

The Perceived Stress scale is a 10-item, self-reported instrument that measures perceived stress in relation to life events over the past month (15). Scores range from 0 to 40, with higher scores indicating greater stress.

The Center for Epidemiologic Studies – Depression (CES-D) scale is a 20-item, self-reported measure of depression symptoms with an emphasis on depressed mood in the past week (16). Scores range from 0 to 60, with higher scores indicating more severe symptoms. A score of 16 or greater is suggestive of possible depression and a score of 20 or greater of probable depression.

The Patient Reported Outcomes Measurement Information System (PROMIS) Anxiety short form is a six-item, self-reported measure of anxiety over the past 7 days (17). Scores are converted to a standardized T-score, with a population mean of 50 and standard deviation of 10. Cutoff scores to define levels

of anxiety have been suggested as none/slight (<55), mild (55.0-59.9), moderate (60.0-69.9), and severe (≥70) levels of anxiety (18).

Baseline measures, including demographics, axSpA disease characteristics, medication use, and comorbidities were obtained from either the cohort database (in the case of time-invariant characteristics) or from the most recent study visit prior to March 2020.

Disease activity was recorded using the BASDAI. NSAID use was recorded as none, low dose, or high dose (19). Biologic use, including tumor necrosis factor inhibitors and interleukin-17 inhibitors, was recorded as a binary variable (using, yes/no). Comorbidities were extracted using information available in the electronic medical record problem list and medication list, as appropriate.

**Table 1.** Baseline characteristics for survey respondents ($n$ = 203) stratified by Perceived Stress Scale score

| Characteristics | Overall $n$ = 203 | Low Stress $n$ = 94 | High Stress $n$ = 109 | $P$ Value |
|---|---|---|---|---|
| Demographics | | | | |
| Age, y | 46.4 ± 12.5 | 47.6 ± 12.3 | 45.4 ± 12.6 | .16 |
| | 44 (55-57) | 45 (38-56) | 43 (36-52) | |
| Male gender | 133 (66%) | 74 (79%) | 59 (54%) | <.01 |
| Race/ethnicity | | | | .52 |
| White | 157 (77%) | 77 (82%) | 80 (73%) | |
| Asian | 27 (13%) | 9 (10%) | 18 (17%) | |
| Hispanic | 6 (3%) | 1 (1%) | 5 (5%) | |
| African American | 1 (2%) | 1 (1%) | 0 (0%) | |
| Other | 12 (3%) | 6 (6%) | 6 (6%) | |
| Residence in California | 178 (88%) | 81 (86%) | 97 (89%) | .54 |
| Any exercise | 180 (89%) | 87 (93%) | 94 (86%) | .19 |
| Disease characteristics | | | | |
| Classification | | | | .65 |
| Nonradiographic | 51 (25%) | 21 (22%) | 30 (28%) | |
| Radiographic/AS | 147 (72%) | 71 (76%) | 76 (70%) | |
| Not classified | 5 (2%) | 2 (2%) | 3 (3%) | |
| HLA-B27 positive | 177 (88%) | 79 (86%) | 98 (90%) | .38 |
| Symptom duration, y | 22.9 ± 12.4 | 24.8 ± 12.7 | 21.3 ± 12.0 | .04 |
| | 20 (14-30) | 23 (15-33) | 19 (13-26) | |
| Abnormal CRP | 29 (15%) | 14 (15%) | 15 (14%) | .85 |
| History of acute anterior uveitis | 96 (47%) | 38 (40%) | 58 (53%) | .07 |
| History of IBD | 36 (18%) | 16 (17%) | 20 (18%) | .81 |
| History of psoriasis | 26 (13%) | 13 (14%) | 13 (12%) | .69 |
| On NSAID | 106 (52%) | 49 (52%) | 54 (50%) | .39 |
| On biologic | 83 (41%) | 83 (41%) | 120 (59%) | .90 |
| BASDAI (0-10) | 2.3 ± 1.8 | 2.0 ± 1.7 | 2.7 ± 1.9 | .01 |
| | 1.9 (0.9-3.4) | 1.4 (0.7-3.2) | 2.3 (1.3-3.6) | |
| Comorbidities identified in the electronic health record | | | | |
| Hypertension | 53 (26%) | 31 (33%) | 22 (20%) | .04 |
| Diabetes | 10 (5%) | 4 (4%) | 6 (6%) | .68 |
| Cardiovascular disease | 7 (3%) | 4 (4%) | 3 (3%) | .56 |
| Other cardiac disease | 15 (7%) | 11 (12%) | 4 (4%) | .32 |
| BMI, kg/m$^2$ | 25.5 ± 4.8 | 25.3 ± 4.33 | 25.7 ± 5.2 | .94 |
| | 24.5 (6.0) | 24.5 (22.3-27.9) | 24.3 (22.0-28.0) | |
| Smoking | | | | |
| Current | 4 (2%) | 0 (0%) | 4 (4%) | .06 |
| Ever | 63 (31%) | 31 (33%) | 32 (29%) | .58 |
| Asthma | 33 (16%) | 12 (12%) | 21 (19%) | .21 |
| Cancer | 18 (9%) | 8 (9%) | 10 (9%) | .87 |
| Depression | 66 (33%) | 16 (17%) | 50 (46%) | <.01 |
| Anxiety | 15 (7%) | 6 (6%) | 9 (8%) | .61 |

*Note.* Continuous variables are reported as mean ± SD and median (interquartile range) and categorical variables as $n$ (%). To assess differences between high- and low-stress level groups, we used $\chi^2$ tests for categorical variables and Mann-Whitney $U$ tests for continuous variables. Data were missing for 43 respondents for BASDAI. Biologic use includes infliximab, etanercept, adalimumab, golimumab, certolizumab pegol, secukinumab, and ixekizumab. Cardiovascular disease is defined as history of myocardial infarction, stroke, or cardiovascular revascularization in the electronic medical record. Other cardiac disease includes heart failure, valvulopathy, arrhythmia, and angina. Cancer includes all but nonmelanoma skin cancers. Hypertension, diabetes, depression, and anxiety are defined by the presence of either problem listed in the problem list and/or medication use in the electronic medical record.

Abbreviations: AS, ankylosing spondylitis; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BMI, body mass index; CRP, C-reactive protein; IBD, inflammatory bowel disease; NSAID, nonsteroidal anti-inflammatory drug.

**Analysis.** We performed descriptive statistics for baseline characteristics and survey responses, which included calculation of pairwise correlation coefficients for stress, anxiety, and depression scales. We used multiple imputation with chained equations with 10 iterations to impute missing values for the BASDAI at baseline (20–22). We included the following variables as predictors in the imputation model: age, gender, race, survey BASDAI, baseline BASDAI, change in NSAID use, change in biologic use, change in exercise, change in job status, total PROMIS Anxiety score, and total CES-D score. Complete case analyses were performed as a secondary analysis.

Because stress, anxiety, and depression may be closely related, we examined correlations among these scores. For the first primary analysis, we compared the survey BASDAI score between those with higher versus lower levels of stress (Perceived Stress Scale dichotomized at the median). We used multivariable linear regression and adjusted for the following potential confounders identified a priori: age (years), gender, race (white versus other), baseline BASDAI, decrease or cessation of NSAID use, decrease or cessation of biologic use, decrease or cessation of exercise, and whether there was a change in job status. For the second analysis, we used multivariable linear regression to compare the survey BASDAI between those with higher versus lower levels of anxiety (PROMIS Anxiety score dichotomized at the median) after adjusting for the same confounders as in the first analysis. For the third analysis, we compared the survey BASDAI between those with higher versus lower scores on the CES-D scale (dichotomized at the cutoff of 16) using multivariable linear regression with adjustment for the same confounders as in the previous two models. In exploratory analyses, we tested interactions ($\alpha = .10$ for statistical significance) in the primary analysis model between perceived stress level and 1) age greater than 65 years, 2) job change, and 3) residence outside of San Francisco.

All analyses were conducted in Stata Software version 15 (StataCorp) using robust standard error estimates and an $\alpha$ level of .05 (with the exception of tests of interaction).

## RESULTS

As of April 2020, there were 473 patients in the cohort. The survey was initially sent on April 2, 2020. Several reminders, including emails, messages through the electronic medical record, and telephone calls, were sent. As of April 28, 2020, the final response rate was 43% with 203 complete responses. Overall, survey respondents had a mean age of 46.4 ± 12.5 years, 66% were male, and 77% were white. Baseline data are described, by stress level based on the Perceived Stress Scale, in Table 1. Groups by stress level were similar, with the exception of a lower proportion of males in the higher stress group (54% versus 79%) and a higher proportion with diagnoses of depression in the higher stress group (46% versus 17%).

**Table 2.** Characteristics of survey respondents compared to nonrespondents[a]

| Variable | Respondents<br>$n$ = 203 | Nonrespondents<br>$n$ = 237 | $P$ Value |
|---|---|---|---|
| Age, y | 46 ± 13<br>44 (55-57) | 44 ± 13<br>41 (35-51) | .03 |
| Male gender | 133 (66%) | 154 (65%) | .91 |
| White race | 157 (77%) | 138 (58%) | <.01 |
| AS classification | 147 (72%) | 157 (68%) | .16 |
| Biologic use at baseline | 83 (41%) | 108 (47%) | .47 |
| NSAID use at baseline | 106 (52%) | 133 (58%) | .32 |
| BASDAI at baseline, (0-10) | 2.3 ± 1.8<br>1.9 (0.9-3.4) | 2.9 ± 2.3<br>2.4 (1.0-4.7) | .08 |

*Note.* Continuous variables are reported as mean ± SD and median (interquartile range) and categorical variables as $n$ (%). To assess differences between high- and low-stress level groups, we used $\chi^2$ tests for categorical variables and Mann-Whitney $U$ tests for continuous variables. Values missing for the following: AS classification ($n = 7$ nonrespondents), biologic use ($n = 7$ nonrespondents), NSAID use ($n = 7$ nonrespondents), baseline BASDAI ($n = 43$ respondents, $n = 102$ nonrespondents).
Abbreviations: AS, ankylosing spondylitis; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; NSAID, nonsteroidal anti-inflammatory drug.
[a] Total cohort of 473. Not included in this table: 26 declined survey participation and 7 who were deceased.

Characteristics of respondents versus nonrespondents are shown in Table 2. Groups were similar in terms of gender, AS classification, and treatment for axSpA. Nonrespondents were older and a higher proportion were white as compared with respondents. Nonrespondents had a numerically higher BASDAI at baseline but also a higher proportion of missing data for the BASDAI.

Survey outcomes are shown in Table 3, stratified by stress level. The majority of respondents did not alter their NSAID or biologic dosing (81% and 88%, respectively). However, 56% reported decreasing or stopping their exercise as compared with 6 months prior, and 13% reported a change in their job. Nine received testing for COVID-19, but none reported a positive test. There were more people who reduced or stopped their NSAIDs (but not biologics) in the high- versus low-stress group; and more people who had job changes and were not currently working in the high- versus low-stress group. The scores for CES-D, anxiety, and BASDAI were higher in the high-stress group compared with the low-stress group. Stress, anxiety, and depression scores were highly correlated (pairwise correlation coefficients ranged from 0.70 to 0.74, Table 4), so separate multivariate regression analyses were conducted for each factor.

There were missing data for the baseline BASDAI for 43 respondents, which were imputed using multiple imputation with chained equations. After adjustment for potential confounders and baseline disease activity, those with higher levels of stress had a statistically significant 0.54-point higher BASDAI, on average, compared with those with lower levels of stress (95% confidence interval [CI]: 0.11, 0.97). Those with higher levels of anxiety had a statistically significant 0.59-point higher BASDAI, on average,

**Table 3.** Survey responses, stratified by dichotomized score on Perceived Stress Scale (*n* = 203)

| Survey items | Overall<br>*n* = 203 | Low stress<br>*n* = 94 | High stress<br>*n* = 109 |
|---|---|---|---|
| Decreased or stopped NSAID | 29 (14%) | 8 (8%) | 19 (17%) |
| Decreased or stopped biologic | 20 (10%) | 9 (9%) | 11 (10%) |
| Decreased or stopped exercise | 116 (57%) | 47 (50%) | 69 (63%) |
| Job changed | 27 (13%) | 10 (10%) | 17 (16%) |
| Current work location | Not working: 55 (27%)<br>Home: 123 (61%)<br>Hospital: 7 (3%)<br>Restaurant: 2 (1%)<br>Other: 16 (8%) | Not working: 21 (22%)<br>Home: 60 (64%)<br>Hospital: 2 (2%)<br>Restaurant: 1 (1%)<br>Other: 10 (11%) | Not working: 34 (31%)<br>Home: 63 (58%)<br>Hospital: 5 (5%)<br>Restaurant: 1 (1%)<br>Other: 6 (6%) |
| Tested for COVID-19 | 9 (4 %) | 4 (4%) | 5 (5%) |
| BASDAI (0-10) | 2.5 ± 1.9<br>1.8 (1.1-3.4) | 1.9 ± 1.7<br>1.4 (0.8-2.5) | 3 ± 2<br>2.3 (1.6-3.9) |
| Perceived Stress Scale (0-40) | 15 ± 8<br>14 (9-20) | 8 ± 3<br>9 (6-11) | 21 ± 5<br>20 (17-24) |
| PROMIS Anxiety scale (39-82) | 54 ± 9<br>54 (49-61) | 49 ± 6<br>49 (46-54) | 59 ± 8<br>61 (54-65) |
| CES-D scale (0-60) | 14 ± 10<br>12 (6-19) | 7 ± 5<br>6 (3-10) | 20 ± 10<br>17 (12-27) |

*Note*. Continuous variables reported as mean ± SD and median (interquartile range); categorical variables reported as *n* (%)
Abbreviations: BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; CES-D, Center for Epidemiologic Studies Depression; COVID-19, coronavirus disease 2019; NSAID, nonsteroidal anti-inflammatory drug; PROMIS, Patient-Reported Outcome Measurement Information System.

compared with those with lower levels of anxiety (95% CI: 0.18, 0.99), after adjustment for potential confounders and baseline disease activity. The average difference in the BASDAI was not significantly different compared with those with higher versus lower scores on the CES-D scale (β: .38, 95% CI: –0.10, 0.85). Results were similar using complete case analysis (data not shown).

In exploratory analyses, the association of stress with disease activity did not differ across subgroups of age, job status, or county of residence (*P* = 0.44, 0.90, and 0.99, respectively), nor did the association of anxiety with disease activity differ by these subgroups (*P* = 0.69, 0.22, and 0.62, respectively).

## DISCUSSION

In this study, higher levels of perceived stress and anxiety, but not depression, were significantly associated with higher disease activity levels among individuals with axSpA. We did not find differences in this association among subgroups of age, job status, or county of residence. To our knowledge, this is the first study to evaluate patient-reported disease activity in relation to psychological factors among individuals with axSpA during a major pandemic. Although the estimated average difference in the BASDAI comparing between stress and anxiety levels was less than the minimal clinically important difference (MCID) of 1.0

**Table 4.** Correlation matrix for stress, anxiety, and depression levels

| | Stress | Anxiety | Depression |
|---|---|---|---|
| Stress | 1.00 | ... | ... |
| Anxiety | 0.70 | 1.00 | ... |
| Depression | 0.77 | 0.74 | 1.00 |

reported by Pavy et al (23), the differences between groups may become more apparent upon longitudinal follow-up of this cohort as the pandemic evolves.

Stress is related to disease activity in rheumatic disease (10–12). However, whether stress is an independent predictor of elevated disease activity has not been definitively demonstrated in axSpA. Jiang et al examined psychological status, sleep quality, and stress due to life events over the prior 12 months in patients with AS and found an association between anxiety/depression and disease activity (13). Previously published studies have evaluated patients with RA, systemic lupus erythematosus (SLE), and inflammatory bowel disease (IBD) following natural disasters (4–9), with inconclusive findings. Wallace et al followed 13 patients with RA and 10 with SLE for 6 months after the 1994 Northridge earthquake, but no flares were documented (4). A study in Japan surveyed 192 women with RA who had experienced a natural disaster (predominantly typhoons, tornados, and torrential rain) between 2004 and 2006. Surveys were administered 1 and 6 months following the event, with the finding that 14% experienced deterioration of functional status, whereas 22% experienced a worsening of self-rated health status (6). In contrast, a study in Taiwan compared patients with SLE inside and outside of the disaster zone following the major earthquake of September 1999. The researchers found that 6 months following the disaster, neither the exposed nor the comparator group had experienced a significant change in the clinical symptoms of SLE (7). Factors affecting short-term and long-term impact can vary. Two studies examined the frequency of disease relapse in IBD immediately following the Great East Japan earthquake of March 2011, and then with follow-up data 1 and 2 years postdisaster. The authors found that the factors that influenced long-term relapse were

different from those that influenced short-term relapse (8,9). However, many of these studies were small, some did not have adequate comparators, and there was high potential for unmeasured confounding.

The COVID-19 pandemic represents a unique universal stressor on our patient population, as the shelter-in-place orders affected multiple cities, counties, and entire states in the United States, with impacts on job status, the ability to exercise, and access to health care. Information on COVID-19 risk for people living with rheumatic disease was also scarce in the early days of the pandemic, as these comorbidities were not reported in the initial large case series published from China, Europe, or the United States (24–29). Larger reports from a global rheumatology registry are forthcoming (30). At the end of March 2020, Michaud et al surveyed a large US registry of patients with rheumatic disease (FORWARD) and found that common themes relating to COVID-19 were concerns over risk of infection and how best to manage immunosuppressive medications (31).

The strengths of this study include the use of a well-defined axSpA cohort with detailed baseline data on important confounders as well as baseline data on disease activity. We were able to administer a survey with disease-specific questions, capturing a fairly homogenous population of rheumatic disease. The survey had a moderate response rate of 43%. Additionally, we used validated measures of anxiety, stress, and depression with mean levels in our cohort that were similar to those in other rheumatic disease cohorts (32,33).

There are limitations of this study that we must acknowledge. First, this is an observational study limited to two time intervals: before and after the pandemic. There is potential selection bias regarding survey responses, as those with lower stress levels and disease activity may be more inclined to respond to the survey. Generalizability may be limited, as all of the patients in this study were under the care of one rheumatologist. During the survey period, most of the patients were living in the Bay Area of California, which had shelter-in-place implementation that differed from other areas of the country. Unmeasured confounding and measurement error are also possible, as we were limited in the granularity of detail that we could include in our survey. We did not have stress or anxiety measures in prior surveys, so we could not measure changes in these variables. Finally, our use of the BASDAI as a patient-reported measure of disease activity is limited by its use of subjective, rather than objective, questions.

Our survey-based study of an axSpA cohort at a single US center found that stress and anxiety were significantly associated with patient-reported disease activity, independent of confounding factors. Although the average difference in BASDAI was below the MCID, these findings suggest that the COVID-19 pandemic may have had an impact on axSpA disease activity through increased stress and anxiety. We will continue this study with further iterations of the survey as a repeated measure. This

will allow us to look at both population- and subject-level trajectories over time.

## AUTHOR CONTRIBUTIONS

All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be published. Dr. Liew had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study conception and design. Liew, Castillo, Katz, Haroon, Gensler. Acquisition of data. Castillo, Gensler. Analysis and interpretation of data. Liew, Zaccagnino, Katz, Haroon, Gensler.

## REFERENCES

1. World Health Organization. Coronavirus disease (COVID-19) pandemic. URL: https://www.who.int/emergencies/diseases/novel-coronavirus-2019.

2. Johns Hopkins Coronavirus Resource Center. URL: https://coronavirus.jhu.edu/

3. San Francisco Department of Public Health. Order of the Health Officer No. C19-07b. March 31, 2020. URL: https://oewd.org/file/17367 (accessed on September 2, 2020.)

4. Wallace DJ, Metzger AL. Can an earthquake cause flares of rheumatoid arthritis or lupus nephritis? [concise communications]. Arthitis Rheum 1994;37:1826–8.

5. Grady KE, Reisine ST, Fifield J, Lee NR, McVay J, Kelsey ME. The impact of Hurricane Hugo and the San Francisco earthquake on a sample of people with rheumatoid arthritis. Arthritis Care Res 1991;4:106–10.

6. Tomio J, Sato H, Mizumura H. Impact of natural disasters on the functional and health status of patients with rheumatoid arthritis. Mod Rheumatol 2011;21:381–90.

7. Chou CT, Hwang CM. Changes in the clinical and laboratory features of lupus patients after the big earthquake in Taiwan. Lupus 2002;11:109–13.

8. Miyazawa T, Shiga H, Kinouchi Y, Takahashi S, Tominaga G, Takahashi H, et al. Long-term course of inflammatory bowel disease after the Great East Japan Earthquake. J Gastroenterol Hepatol 2018;33:1956–60.

9. Shiga H, Miyazawa T, Kinouchi Y, Takahashi S, Tominaga G, Takahashi H, et al. Life-event stress induced by the Great East Japan Earthquake was associated with relapse in ulcerative colitis but not Crohn's disease: a retrospective cohort study. BMJ Open 2013;3:e002294.

10. Evers AW, Verhoeven EW, van Middendorp H, Sweep FC, Kraaimaat FW, Donders AR, et al. Does stress affect the joints? Daily stressors, stress vulnerability, immune and HPA axis activity, and short-term disease and symptom fluctuations in rheumatoid arthritis. Ann Rheum Dis 2014;73:1683–8.

11. Hassett AL, Clauw DJ. The role of stress in rheumatic diseases. Arthritis Res Ther 2010;12:123.

12. Brouwer SJ, Kraaimaat FW, Sweep FC, Creemers MC, Radstake TR, Laarhoven AI, et al. Experimental stress in inflammatory rheumatic diseases: a review of psychophysiological stress responses. Arthritis Res Ther 2010;12:R89.

13. Jiang Y, Yang M, Wu H, Song H, Zhan F, Liu S, et al. The relationship between disease activity measured by the BASDAI and psychological status, stressful life events, and sleep quality in ankylosing spondylitis. Clin Rheumatol 2015;34:503–10.

14. Garrett S, Jenkinson T, Kennedy LG, Whitelock H, Gaisford P, Calin A. A new approach to defining disease status in ankylosing

spondylitis: the Bath Ankylosing Spondylitis Disease Activity Index. J Rheumatol 1994;21:2286–91.

15. Cohen S. Perceived stress scale. 1994. URL: https://www.mind garden.com/132-perceived-stress-scale.

16. Radloff LS. The CES-D scale: A self-report depression scale for research in the general population. Appl Psychol Meas 1977;1:385–401.

17. Health Measures. Patient Reported Outcomes Measurement Information System (PROMIS). URL: www.nihpromis.org.

18. Health Measures. PROMIS Anxiety Scoring Manual. URL: http://www.healthmeasures.net/images/PROMIS/manuals/PROMIS_Anxiety_Scoring_Manual.pdf.

19. Dougados M, Simon P, Braun J, Burgos-Vargas R, Maksymowych WP, Sieper J, et al. ASAS recommendations for collecting, analysing and reporting NSAID intake in clinical trials/epidemiological studies in axial spondyloarthritis. Ann Rheum Dis 2011;70:249–51.

20. Rubin D. Introduction in multiple imputation for nonresponse in surveys. New York: John Wiley & Sons; 1987.

21. Van Buuren S. Flexible imputation of missing data. Boca Raton (FL): Chapman & Hall/CRC; 2012.

22. Moons KG, Donders RA, Stijnen T, Harrell FE Jr. Using the outcome for imputation of missing predictor values was preferred. J Clin Epidemiol 2006;59:1092–101.

23. Pavy S, Brophy S, Calin A. Establishment of the minimum clinically important difference for the bath ankylosing spondylitis indices: a prospective study. J Rheumatol 2005;32:80–5.

24. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 2020;395:P497–506.

25. Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. JAMA 2020;323(13):1239–1242. https://doi.org/10.1001/jama.2020.2648

26. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med 2020;382:1708–20.

27. Grasselli G, Zangrillo A, Zanella A, Antonelli M, Cabrini L, Castelli A, et al. Baseline characteristics and outcomes of 1591 patients infected with SARS-CoV-2 admitted to ICUs of the Lombardy region, Italy. JAMA 2020;323:1574–81.

28. Goyal P, Choi JJ, Pinheiro LC, Schenck EJ, Chen R, Jabri A, et al. Clinical characteristics of Covid-19 in New York City. N Engl J Med 2020;382:2372–4.

29. Richardson S, Hirsch JS, Narasimhan M, Crawford JM, McGinn T, Davidson KW, et al. Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized with COVID-19 in the New York City Area. JAMA 2020;323:2052–9.

30. Gianfrancesco MA, Hyrich KL, Gossec L, Strangfeld A, Carmona L, Mateus EF, et al. Rheumatic disease and COVID-19: initial data from the COVID-19 Global Rheumatology Alliance provider registries. Lancet Rheumatol 2020;2:E250–3.

31. Michaud K, Wipfler K, Shaw Y, Simon TA, Cornish A, England BR, et al. Experiences of patients with rheumatic diseases in the US during early days of the COVID-19 pandemic. ACR Open Rheumatol 2020;2:335–43.

32. Lee YC, Bingham CO III, Edwards RR, Marder W, Phillips K, Bolster MB, et al. Association between pain sensitization and disease activity in patients with rheumatoid arthritis: a cross-sectional study. Arthritis Care Res (Hoboken) 2018;70:197–204.

33. Da Costa D, Zummer M, Fitzcharles MA. Determinants of sleep problems in patients with spondyloarthropathy. Musculoskeletal Care 2009;7:143–61.