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Mental health before and during the pandemic in people with systemic sclerosis

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See Online for appendix

Due to the health, social, and economic consequences[1] of the COVID-19 pandemic, there are concerns about mental health implications, especially among people susceptible to serious illness or death from COVID-19 due to pre-existing medical conditions.[2] A living systematic review (ie, a systematic review that is continually updated) found that general mental health, anxiety, and depression symptoms did not worsen substantively in the general population in the early months of the pandemic.[3] Among people with pre-existing medical conditions, however, anxiety symptoms worsened significantly (three studies; n=2053; standardised mean difference [SMD] 0·27 [95% CI 0·01 to 0·54]) but depression symptoms did not change (three studies; N=2006; SMD 0·01 [–0·15 to 0·17]).[3]

Individuals with systemic sclerosis (also called scleroderma) are at risk of complications if infected with SARS-CoV-2. More than 40% of people with systemic sclerosis have interstitial lung disease, many are frail, and immunosuppressant medication use is common.[4,5] Our Scleroderma Patient-centered Intervention Network (SPIN) Cohort study,[6] which was included in the COVID-19 living systematic review,[3] found that anxiety symptoms increased substantially from before COVID-19 to April 9–27, 2020 (n=435; SMD 0·51 [95% CI 0·37 to 0·64]) but depression symptoms did not (n=388; SMD –0·05 [–0·19 to 0·09]).

To our knowledge, no studies have tracked mental health symptoms among people with pre-existing medical conditions before COVID-19 and at regular intervals throughout the pandemic.[3] The objective of the present study was to follow up our previous systemic sclerosis COVID-19 mental health study, which reported findings up until April 9–27, 2020[6] to describe anxiety and depression symptom trajectories from late-2019 to March, 2021. Detailed methods are provided in the appendix (pp 2–3). Researchers developed study objectives and methods in collaboration with an eight-member patient advisory team.

We performed a longitudinal study, which included participants from the ongoing SPIN Cohort[5,7] who enrolled separately in the SPIN-COVID-19 Cohort from April 9–27, 2020. Deterministic linking (email addresses) was used to merge sociodemographic, medical, and anxiety and depression symptom data before COVID-19 from the SPIN Cohort with anxiety and depression symptom data collected from April 9–27, 2020, to March, 2021, via the SPIN-COVID-19 Cohort. The SPIN (number MP-05-2013-150) and SPIN-COVID-19 (number 2021-2286) Cohorts were approved by the research ethics committee of the Centre intégré universitaire de santé et de services sociaux du Centre-Ouest-de-l'Île-de-Montréal. The SPIN Cohort was also approved by ethics committees of SPIN recruiting sites.

Eligible SPIN Cohort participants are recruited during regular medical visits and must be 18 years or older and meet the 2013 American College of Rheumatology and European League Against Rheumatism systemic sclerosis criteria.[8] SPIN Cohort participants provided written informed consent for participation and to be contacted about additional studies. For pre-COVID-19 SPIN Cohort measures, we used the last anxiety (PROMIS Anxiety 4a version 1.0; assessed every 3 months) and depression (eight-item Patient Health Questionnaire; assessed every 6 months) symptom assessments between July 1 and Dec 31, 2019. We assessed anxiety and depression symptoms during the COVID-19 pandemic with the same measures every 2 weeks from April 9 until July 22, 2020, and then every 4 weeks. We used multivariate imputation via chained equations to account for missing data. Statistical analysis methods are shown in the appendix (p 4).

Of 1251 active SPIN Cohort participants who had completed an assessment during the 6-month period before the COVID-19 pandemic, 435 (35%) enrolled in the separate SPIN COVID-19 Cohort, and all enrolled participants were included in the main analyses. A participant flow chart is shown in the appendix (p 5). Mean age was 56·9 years, most participants were White (360 [83%] of 435) and female (385 [89%]), and mean time since diagnosis was 12·1 years (SD 7·8). Participant countries of residence included France (159 [37%]), the USA (128 [29%]), Canada (98 [23%]), and the UK (50 [11%]). Detailed participant characteristics are shown in the appendix (p 6).

As shown in figure A, mean anxiety symptom scores increased substantially from before the pandemic to April, 2020 (SMD 0·51 [95% CI 0·37 to 0·64]) but decreased again to levels seen before the pandemic by March, 2021 (SMD 0·05 [–0·08 to 0·19]). Depression symptoms (figure C) were not substantively different from before the pandemic to April, 2020 (SMD –0·05 [–0·19 to 0·09]) but were significantly lower subsequently—although minimally—from before the pandemic to March, 2021 (SMD –0·20 [95% CI –0·35 to –0·06]). As shown in figure B and D, results were similar when evaluated only among participants who completed at least ten of 15 assessments during the pandemic period (277 [64%] of 435). Means and SDs across assessments for the full sample, those who completed at least ten of 15 assessments, and the number of participants who completed each assessment are shown in the appendix (p 7). Anxiety symptom patterns were similar across time by subgroups defined by age, sex, country, and systemic sclerosis subtype (appendix pp 8–9).

Compared with before the COVID-19 pandemic, anxiety symptoms increased substantially when assessed April 9–27, 2020, whereas depression symptoms did not. Both anxiety and depression symptoms improved later in 2020, with anxiety symptoms returning to pre-COVID-19 levels and depression symptoms slightly lower than the pre-pandemic level.

To our knowledge, this study is the first to report regular mental health assessments in any population with a pre-existing medical condition before and at regular intervals throughout the pandemic. In contrast to studies conducted in general population samples from several countries, which found negligible to small worsening

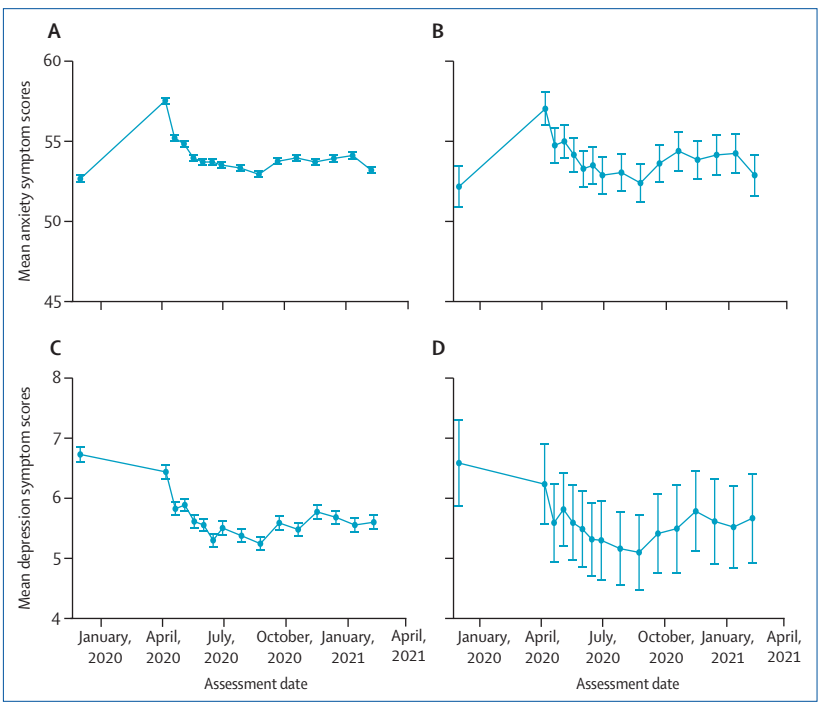

Figure: **Anxiety and depression scores before and during the COVID-19 pandemic**
Mean anxiety (A) and depression (C) symptom scores with 95% CIs for the SPIN Cohort subsample before the COVID-19 pandemic and at each assessment during the pandemic. Mean anxiety (B) and depression (D) symptom scores with 95% CIs for those who completed ten or more assessments. Anxiety was scored with PROMIS Anxiety 4a version 1.0 and depression was scored with the eight-item Patient Health Questionnaire. For number of participants at each timepoint see the appendix (p 7).

of mental health early in the pandemic,[3] people with systemic sclerosis reported a substantial increase in anxiety symptoms, but not in depression symptoms. Among the general population studies, mental health improved by late-2020,[3] which is consistent with findings from our systemic sclerosis cohort.

The finding that anxiety symptoms increased initially during the COVID-19 pandemic among people with systemic sclerosis but depression symptoms did not is consistent with the results of a living systematic review, which synthesised results from studies of participants with pre-existing medical conditions and similarly found that anxiety symptoms, but not depression symptoms, increased.[3] Among studies included in the review, the largest were an initial report of the SPIN-COVID-19 Cohort (n=435)[6] and a study of 1504 people with rheumatoid arthritis (n=1126), osteoarthritis (n=277), or systemic lupus erythematosus (n=101),[9] which found that from 2019, to March to June, 2020, anxiety increased by a SMD of 0·26 (95% CI 0·19 to 0·33; n=1504), whereas depression symptoms were stable (0·04 [–0·03 to 0·11]; n=1504).[9]

These findings were not surprising to patient members of our research team. When we had an initial meeting to prioritise outcomes for the SPIN-COVID-19 Cohort and for an intervention trial to support mental health in COVID-19 among people with systemic sclerosis,[10] members of our patient advisory team were unanimous in encouraging the prioritisation of anxiety for monitoring and for the primary trial outcome, which we did. They believed that people with systemic sclerosis would have increased anxiety due to their susceptibility to poor outcomes if infected with SARS-CoV-2 and due to restrictions in health-care access, which made managing their condition difficult. They thought that depression symptoms would be less influenced because, in their opinion, many people with systemic sclerosis already had to cope with some degree of isolation and had developed resilience.

Strengths of our study include the large, multinational cohort of people with systemic sclerosis, which has similar participant characteristics to other major systemic sclerosis cohorts,[6] and the comparison of pre-COVID-19 mental health symptoms with data collected throughout the pandemic. Some limitations should also be considered. The SPIN Cohort is a convenience sample, and those who enrolled in the SPIN-COVID-19 Cohort were a subset of SPIN Cohort participants; thus, they might not be representative of all people with systemic sclerosis. Furthermore, participants completed questionnaires online, which might further reduce generalisability due to the need to be able to access and complete forms via the internet.

To summarise, anxiety symptoms, but not depression symptoms, increased substantially among people with systemic sclerosis early in the pandemic. Anxiety symptoms decreased quickly thereafter and returned to levels from before the pandemic. This finding, however, is an aggregate pattern. The pandemic has affected individuals in different ways, and some people with systemic sclerosis who did not previously have mental health difficulties are likely to have had new challenges. Health-care providers should understand that, overall, people with systemic sclerosis appear to be resilient, but that there are likely to be some people who are struggling and would benefit from assessment and mental health support.

RSH, LK, M-EC, SP, SJB, LM, JV, ABe, BDT, and members of the SPIN-COVID-19 patient advisory team were responsible for study concept and design. RSH, LK, M-EC, ABo, ABe, and BDT were responsible for data acquisition. RSH and LK directly accessed and verified the data. RSH, ZN, and ABe were responsible for statistical analysis. RSH and BDT drafted the manuscript. All authors provided critical revision of the manuscript for important intellectual content, approved the final version, and agree to be accountable for all aspects of the work. LM reports personal fees from Actelion/Johnson & Johnson; grants from LFB; non-financial support from Octapharma; and non-financial support from Grifols, all outside the submitted work. All other authors declare no competing interests. De-identified individual participant data with a data dictionary and analysis codes that were used to generate the results reported in this Comment will be made available upon request to the corresponding author and presentation of a methodologically sound proposal that is approved by the SPIN data access and publications committee. Data will be available after publication. Data requesters will need to sign a data transfer agreement. The study was funded by the Canadian Institutes of Health Research (number VR4-172745, GA4-177764), McGill Interdisciplinary Initiative in Infection and Immunity Emergency COVID-19 Research Fund; Scleroderma Canada, made possible by an educational grant for patient support programming from Boehringer Ingelheim; Scleroderma Society of Ontario; Scleroderma Manitoba; Scleroderma Atlantic; Scleroderma Australia; Scleroderma New South Wales; Scleroderma Victoria; Scleroderma Queensland; Scleroderma SASK; Scleroderma Association of BC; and Sclérodermie Québec. RSH and ZN were supported by Mitacs post-doctoral fellowship awards, ABe was supported by a Fonds de recherche du Québec—Santé senior researcher salary award, and BDT was supported by a tier 1 Canada Research Chair, all outside of the submitted work. No sponsor had any role in the study design, data collection, data analysis, or interpretation, writing of the report, or in the decision to submit for publication.

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Immunomodulatory and immunosuppressive medication modification among patients with rheumatic diseases at the time of COVID-19 vaccination

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Due to concerns about underlying immune dysregulation and immunosuppression, patients with systemic rheumatic diseases might modify their medications at the time of COVID-19 vaccination to optimise their immune response and mitigate vaccine side-effects. Immunosuppressed patients in New York state were approved for vaccination on Feb 15,2021,[1] soon after the American College of Rheumatology COVID-19 Vaccine Clinical Guidance Task Force issued its first management guidelines on Feb 8, 2021.[2] Whether real-world behaviour was aligned with these guidelines is unknown. Therefore, our study evaluated medication modifications at the time of COVID-19 vaccination by patients with rheumatic diseases at a single centre in New York City.

We emailed a secure web-based survey between March 5 and March 25, 2021, to 7505 patients aged 18 years or older who were evaluated at least once by a rheumatologist between April 1, 2018 and April 21, 2020, at a large rheumatology centre in New York City. We collected data on immunomodulatory and immunosuppressive medications at the time of COVID-19 vaccination, including whether doses were taken earlier than scheduled, delayed, or skipped. We also identified the individual responsible for the medication modification—ie, rheumatologist, other physician, or the patient themselves. This study was approved by the Hospital for Special Surgery, New York, institutional review board and patient consent was obtained via the survey.

As of March 2021, out of 2753 respondents to our COVID-19 vaccine questionnaire (36·7% response rate), 1852 respondents (67·3%) who reported receiving at least one vaccine dose and completed the medication modification questions were included in the current analysis. The mean age of patients receiving at least one vaccine dose was 63·0 (SD 14·2). 1474 (79·6%) of 1852 patients were female, 1619 (87·4%) were White, 58 (3·1%) were Black, and 88 (4·8%) were Hispanic or Latinx. The characteristics of survey recipients and respondents are reported in the appendix (p 5). Out of 1852 patients who received at least one vaccine dose, 998 (53·9%) received the Pfizer vaccine, 821 (44·3%) received the Moderna vaccine, 26 (1·4%) received the Janssen vaccine, and seven (0·4%) received other (six AstraZeneca and one Sinovac). 1173 (64·2%) of 1826 patients who were eligible to receive two vaccine doses reported that they had received both.

See **Online** for appendix

There were 1373 individual reports of using immunomodulatory or corticosteroid medications at the time of the first vaccine dose. Before the first vaccine dose, 215 (15·7%) of 1373 medication schedules were modified; of these, 41 (19·1%) medications were taken earlier than scheduled, and 174 (80·9%) medications were delayed or skipped (table; appendix p 1). Medications accounting for these modifications included: biologics (43·7%), conventional synthetic disease-modifying antirheumatic drugs (DMARDs; 35.3%), hydroxychloroquine (11·2%), corticosteroids (5·1%), and small molecules (4·7%; table).