Mental health symptoms in scleroderma during COVID-19: a Scleroderma Patient-centred Intervention Network (SPIN) cohort longitudinal study

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Abstract

Objective

People with systemic sclerosis (SSc) are vulnerable in COVID-19 and face challenges related to shifting COVID-19 risk and protective restrictions. We evaluated mental health symptom trajectories in people with SSc through March 2022.

Methods

The longitudinal Scleroderma Patient-centred Intervention Network (SPIN) COVID-19 cohort was launched in April 2020 and included participants from the ongoing SPIN Cohort and external enrolees. Analyses included estimated means with 95% CIs for anxiety and depression symptoms pre-COVID-19 for ongoing SPIN Cohort participants and anxiety, depression, loneliness, and fear of COVID-19 for all participants across 28 COVID-19 assessments up to March 2022. We conducted sensitivity analyse including estimating trajectories using only responses from participants who completed ≥90% of items for ≥21 of 28 possible assessments ("completers") and stratified analyses for all outcomes by sex, age, country, and SSc subtype.

Results

Anxiety symptoms increased in early 2020 but returned to pre-COVID-19 levels by mid-2020 and remained stable through March 2022. Depression symptoms did not initially change but were slightly lower by mid-2020 compared to pre-COVID-19 and were stable through March 2022. COVID-19 fear started high and decreased. Loneliness did not change across the pandemic. Results were similar for completers and for all subgroups.

Conclusion

People with SSc continue to face COVID-19 challenges related to ongoing risk, the opening of societies, and removal of protective restrictions. People with SSc, in aggregate, appear to be weathering the pandemic well, but health care providers should be mindful that some individuals may benefit from mental health support.

Key words

anxiety, depression, fear, mental health, systemic sclerosis, COVID-19

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Introduction

People with systemic sclerosis (SSc) have been vulnerable in COVID-19 due to older age, health fragility, immunosuppressant treatment, and interstitial lung disease in >40% (1). Only one study has assessed mental health in SSc during COVID-19 (2). We previously reported that anxiety symptoms were initially moderately elevated in April 2020 (N=435; standardised mean difference [SMD]=0.51; 95% CI 0.37 to 0.64) but returned to pre-COVID-19 levels by March 2021 (SMD=0.05, 95% CI -0.08 to 0.19). Depression symptoms were initially unchanged but then decreased slightly below pre-COVID-19 levels (March 2021 SMD=-0.20, 95% CI -0.35 to -0.06) (1).

No studies have reported trajectories of other important COVID-19 mental health outcomes, including fear (3) and loneliness (4), in people with SSc or have reported more recent outcomes from the pandemic. Since March 2021, people with SSc have been able to be vaccinated (5) but have faced questions about vaccine effectiveness, schedules for immunocompromised individuals, and prophylactic approaches with monoclonal antibodies in addition to COVID-19 vaccination, that may provide additional protection for at-risk patients. There has been greater treatment availability for those infected but also concerns about additional COVID-19 waves, new variants, and possible infection or re-infection among those vaccinated. Many preventive restrictions (*e.g.*, mask mandates, social distancing) have been scaled back or lifted, which may raise fears about safety and the ability to participate in social and other activities among people with SSc. Our objectives were to 1) update previous results that compared pre-COVID-19 and COVID-19 on anxiety and depression symptoms through March 2021 and 2) track symptoms of anxiety, depression, fear, and loneliness across the pandemic through March 2022.

Methods and materials

This was a longitudinal study of participants from the Scleroderma Patient-centred Intervention Network (SPIN) COVID-19 Cohort, including a subset of participants from the ongoing SPIN Cohort (6) who had pre-COVID-19 anxiety and depression symptom data. The SPIN COVID-19 Cohort protocol, with more detailed methods, is available online (https://osf.io/62vut/).

Patient involvement

Patient members of the SPIN Steering Committee prioritised developing research on mental health in COVID-19. Members of the SPIN COVID-19 Patient Advisory Team contributed to SPIN COVID-19 Cohort design and planning, outcome selection, results interpretation, and manuscript review.

Data availability

De-identified individual participant data with a data dictionary and analysis codes that were used to generate the results reported in this article will be made available upon request to the corresponding author and presentation of a methodologically sound proposal that is approved by the Scleroderma Patient-centred Intervention Network Data Access and Publications Committee. Data will be available after publication. Data requesters will need to sign a data transfer agreement.

SPIN COVID-19 cohort

Enrolment for the SPIN COVID-19 cohort was open April 9 to April 27, 2020. Recruitment was done via the ongoing SPIN cohort and externally. The SPIN cohort includes participants from 47 sites (6) in 7 countries who complete assessments every 3 months. SPIN cohort participants must be ≥18 years old and meet 2013 ACR/EULAR SSc criteria (7). Informed consent is obtained for cohort participation and to be contacted about additional studies. Email and popups during regular assessments were used to invite SPIN cohort pariticipants to enrol in the SPIN COVID-19 cohort. Recruitment was also done externally via SPIN's patient organisation partners and via SPIN's Twitter and Facebook. Potential participants were directed to a Qualtrics survey to provide electronic informed consent and complete measures. Participants not enrolled in the ongoing SPIN Cohort had to confirm that they

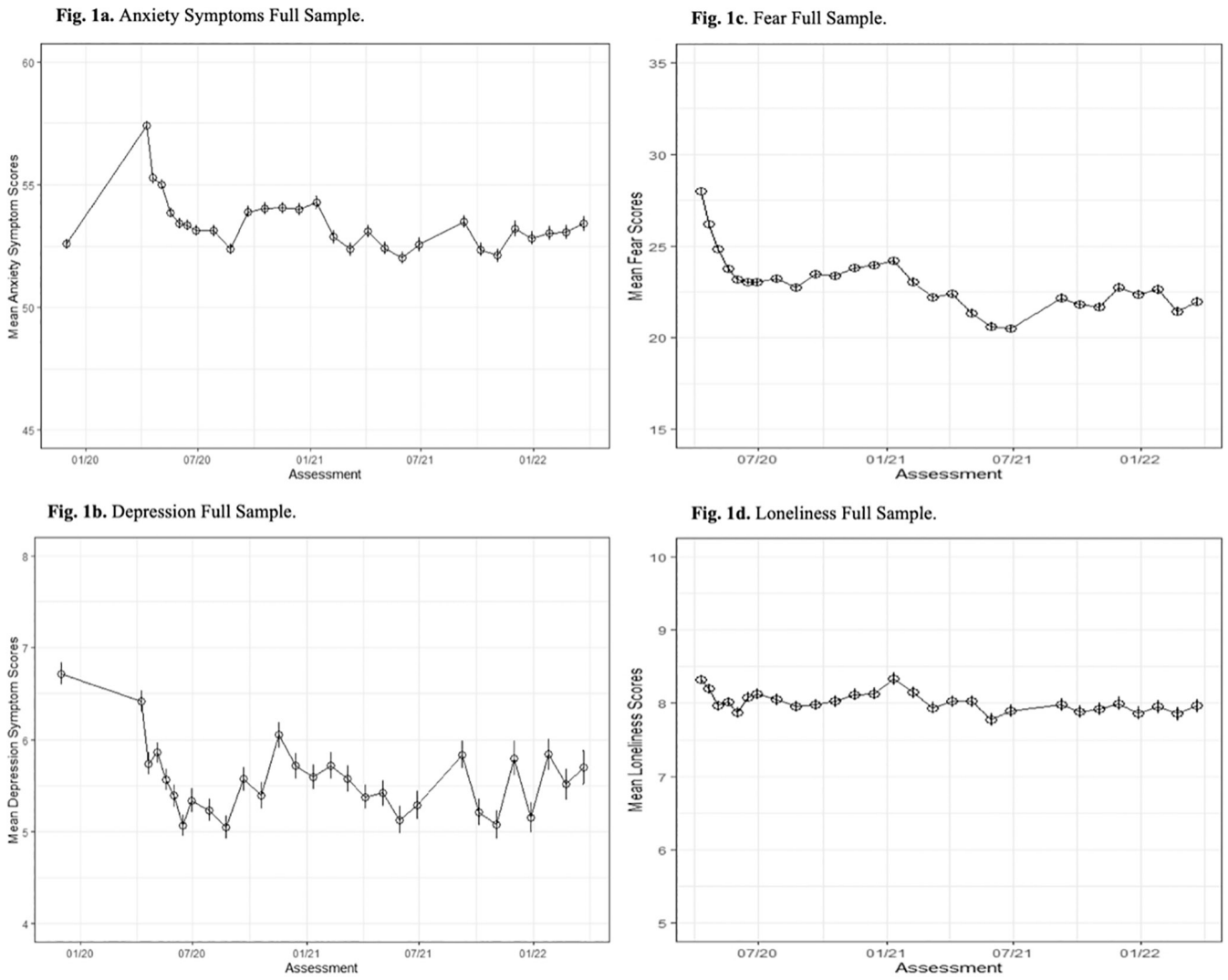

Fig. 1. Figures 1a and 1b show mean anxiety and depression symptom scores with 95% confidence intervals for the ongoing SPIN Cohort subsample (n=435) pre-COVID-19 and at each assessment during COVID-19. Figures 1c and 1d show mean COVID-19 fear and loneliness scores with 95% confidence intervals at each assessment during COVID-19 for the full sample (n=800).
Note: Please see Supplementary Table S3 for number of participants at each time point.

were aged ≥18 years, had physician-diagnosed SSc, and were fluent in English or French.

Participants completed measures via Qualtrics bi-weekly from April 9 through July 22, 2020 then every four weeks from July 27, 2020 onward. The SPIN (#MP-05-2013-150) and SPIN COVID-19 (#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 sites.

Measures

For SPIN Cohort participants, person-level, deterministic linking was used with email addresses to link pre-COVID-19 sociodemographic, medical, and patient-reported outcome data to SPIN COVID-19 Cohort outcome data. Anxiety symptoms (PROMIS Anxiety 4a v.1.0 scale) (8, 9) and depression symptoms (Patient Health Questionaire-8; PHQ-8) (10) were available for SPIN Cohort participants pre-COVID-19 and during COVID-19. For pre-COVID-19 SPIN Cohort measures, we used the last assessment completed July 1 to December 31, 2019 for the PROMIS Anxiety 4a v.1.0 (assessed every 3 months) and PHQ-8 (assessed every 6 months). The COVID-19 Fears Questionnaire for Chronic Medical Conditions (11) and UCLA Loneliness Scale (12) were only available during COVID-19. Detailed information on measures is available in the study protocol (https://osf.io/62vut/).

Statistical analyses

We first estimated means with 95% CIs for anxiety and depression symptoms pre-COVID-19 and across the 28 COVID-19 assessments among SPIN Cohort participants. We then estimated means with 95% CIs for anxiety and depression symptoms, loneliness, and COVID-19 fear across the 28 COVID-19 assessments for all COVID-19 Cohort participants. Missing data were imputed via multivariate imputation by chained equations (MICE) to generate 20 imputed datasets, using 15 cycles per imputed dataset. Variables in the

Table I. Standardised mean difference changes in symptoms and 95% Confidence Intervals for the full sample*.

	Anxiety symptoms	Depression symptoms	COVID-19 Fear	Loneliness
April 2020 *vs*. Pre-COVID-19	0.50 (0.40, 0.60)	-0.06 (-0.15, 0.04)	---	---
March 2021 *vs*. Pre-COVID-19	0.03 (-0.07, 0.13)	-0.18 (-0.28, -0.08)	---	---
March 2022 *vs*. Pre-COVID-19	0.08 (-0.02, 0.18)	-0.18 (-0.28, -0.08)	---	---
March 2021 *vs*. April 2020	-0.48 (-0.58, -0.38)	-0.13 (-0.23, -0.03)	-0.50 (-0.60, -0.40)	-0.05 (-0.15, 0.05)
March 2022 *vs*. April 2020	-0.42 (-0.52, -0.32)	-0.13 (-0.22, -0.03)	-0.63 (-0.73, -0.53)	-0.10 (-0.20, 0.05)

*Standardised mean difference changes were calculated as the difference between mean scores at each time divided by the pooled standard deviation and corrected for sample size using Hedges' g formula. Standardised mean differences may be interpreted as 0.20 = small, 0.50 = medium, and 0.80 = large.

imputation procedure included baseline demographics and medical variables (sex, age, race/ethnicity, country, time since SSc diagnosis, SSc subtype) and patient-reported mental health outcomes (anxiety, depression, fear, boredom, and loneliness) across all timepoints, including pre-COVID-19 for anxiety and depression symptoms.

We conducted two sets of sensitivity analyses. First, for all outcomes, we estimated trajectories using only responses from participants who completed ≥90% of items for ≥21 (≥75%) of the COVID-19 assessments without imputation ("completers"). Second, we conducted stratified analyses for all outcomes by sex, age (median split), country (Canada, United States, France), and SSc subtype (diffuse *vs*. limited). For subgroups by country, we included only countries with >50 participants. All analyses were conducted in R (13) and R packages *mice* (14) for missing data.

Results

There were 1,251 SPIN Cohort participants who completed anxiety and depression measures in the last 6 months of 2019. Of these, 435 (34.8%) separately enrolled in the COVID-19 Cohort. In addition, 365 external participants enrolled in the SPIN COVID-19 Cohort, resulting in 800 participants who completed baseline COVID-19 data (Supplementary Fig. S1). Mean age was 55.6 (SD=12.6) years, most were White (655 of 800, 83.0%) and female (719 of 800, 90.3%). Participant countries included the United States (255 of 800, 31.8%), France (206 of 800, 25.8%), Canada (194 of 800, 24.6%), and the United Kingdom (68 of 800, 8.5%) (Suppl. Table S1). From the COVID-19 Cohort, 303 (38%) completed ≥75% of the 28 assessments.

As shown in Figure 1a, anxiety symptoms increased in early 2020 but returned to pre-COVID-19 levels by mid-2020 and have remained there through March 2022 (SMD=0.08, 95% CI -0.07 to 0.18). Depression symptoms (Fig. 1b) did not initially change but were lower by mid-2020 compared to pre-COVID-19 and have been stable through March 2022 (SMD = -0.18, 95% CI -0.28 to -0.08). COVID-19 fear (Fig. 1c) significantly decreased from April 2020 through March 2021 (SMD = -0.50, 95% CI -0.60 to -0.40) and through March 2022 (SMD = -0.63, 95% CI -0.73 to -0.53) by moderate amounts. Loneliness (Fig. 1d) did not change significantly from April 2020 through March 2021 (SMD = -.05, 95% CI -0.15 to 0.05) and remained stable through March 2022 (SMD = -0.10, 95% CI -0.20 to 0.00). As shown in Appendix Figures 2a-d, results were similar for completers. See Supplementary Tables S2 and S3 for means and standard deviations across assessments. Table I provides SMD and 95% CIs for comparisons over time for all measures (Suppl. Table S4 for completers). Symptom trajectories were similar by subgroups defined by age, sex, country, and SSc subtype (Suppl. Fig. S3-S6).

Discussion

The main finding was that anxiety symptoms in SSc increased substantively in April 2020 then returned to pre-COVID-19 levels by mid-2020 and have been stable through March 2022 despite the length of the pandemic and ongoing challenges faced by people with SSc. Depression symptoms were unchanged initially and have been slightly lower than pre-pandemic levels since then. Loneliness symptoms did not change significantly from early in the pandemic to March 2022. COVID-19 fear started high but decreased quickly and then maintained the lower level across the pandemic. These are aggregate levels, however. Although symptom trajectories were largely stable for the full sample and all subgroups (sex, age, country, disease subtype), individuals within subgroups may have had different experiences. Even though overall levels were stable, some people may have improved, and some people with SSc have likely experienced new mental health challenges and require support from their health care providers, consistent with reports of additional mental health service usage in the pandemic (15).

A recent systematic review (2) compared mental health symptoms in 134 cohorts from the general population and subgroups before COVID-19 and during COVID-19 and found that in the general population, general mental health symptoms (11 studies, n=30,185) and anxiety symptoms (4 studies, n=2,632) did not change, whereas depression symptoms worsened minimally (4 studies, n=3,470; SMD = 0.12, 95% CI 0.01 to 0.24). Among people with pre-existing medical conditions, changes in general mental health (12 studies, n=6,511), anxiety symptoms (11 studies, n=5,775), and depression symptoms (16 studies, n=21,594) were not significantly different from zero. Although symptoms of anxiety initially increased in our cohort, they quickly returned to pre-COVID-19 levels, and depression symptoms did not change, consistent with results from the systematic review. Study strengths include the large, multinational sample and that it is the only study of people with any medical condition (2) that has assessed participants pre-COVID-19 and at regular inter-

vals across the pandemic. Limitations include convenience sampling with most participants from a small number of countries, online questionnaire completion, both of which may reduce generalisability, and loss to follow-up over the pandemic, although results for imputed data and those who completed most assessments were similar. We were not able to address what types of support were received by study participants. We also did not have data for SPIN COVID-19 Cohort participants for specific SSc manifestations. However, among participants in the ongoing SPIN Cohort, we previously reported that disease factors (time since diagnosis, disease subtype, interstitial lung disease, overlap syndrome, immunosuppressant medication use) were not associated with increased anxiety at the beginning of the pandemic compared to pre-pandemic (16).

In sum, anxiety and depression symptoms remained at pre-COVID-19 levels from March 2021 to March 2022. Loneliness did not change from April 2020 through March 2022, while COVID-19 fear decreased. As the world transitions into a new phase of the pandemic, however, medically vulnerable people with SSc face new challenges related to ongoing COVID-19 and the removal of protective restrictions with societies reopening. Many individuals face worry or fear related to COVID-19 concerns (*e.g.*, testing, vaccination, accurate information), decisions about returning to work, whether to manage health care in person or via telehealth, and pressures from family or friends who may not understand or accept their reluctance to socialise in the absence of masking or social distancing requirements. Thus, while people with SSc, in aggregate, appear to be weathering the pandemic well, health care providers should be mindful that some individuals may benefit from mental health assessment and support.

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