Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Systemic sclerosis and COVID-19 vaccines: a SPIN Cohort study

Lancet Rheumatol 2022
Published Online
January 18, 2022
https://doi.org/10.1016/
S2665-9913(21)00416-1

There is little information on the safety of COVID-19 vaccines in patients with autoimmune rheumatic diseases, and patient concerns about possible adverse outcomes in these diseases contribute to vaccine hesitancy.[1–3] One study reported that people with systemic sclerosis (n=104) might be more hesitant to receive a COVID-19 vaccine than those with other rheumatic diseases (n=111).[4] The only large study on vaccine experiences in patients with autoimmune rheumatic diseases (n=2860) found that patient-reported adverse reactions were similar in nature and prevalence to those in the general population;[5] however, results were not reported separately for patients with systemic sclerosis.

We surveyed participants in the international Scleroderma Patient-centered Intervention Network (SPIN) Cohort to evaluate the proportion of participants who were vaccinated against COVID-19, whether changes were made to medications before vaccination, adverse reactions and associated factors, degree of vaccine hesitancy, and perceptions about factors that are potentially important to vaccination decisions.

Detailed methods are provided in the appendix (pp 2–4). The SPIN COVID-19 Patient Advisory Team was involved in survey development. The SPIN COVID-19 Vaccine Survey (appendix pp 7–20) was done between April 9, 2021, and May 15, 2021, in English and French, with the software Qualtrics. Participants from the SPIN Cohort were invited to complete the survey by email and popup invitations for patients who completed routine cohort assessments during the study period. Responses were linked to sociodemographic and clinical data that had been previously collected through the cohort. The study received ethics approval as an amendment to the SPIN Cohort study, and written informed consent was obtained from the participants.

Participants indicated whether they had received zero, one, or two doses of a COVID-19 vaccine, and individuals who had received a vaccine were asked about the brand, vaccination date, any adjustments made to their medication, and any adverse reactions they had after each vaccine dose. Participants who had not been vaccinated were asked how likely they were to be vaccinated on a seven-point Likert scale. Participants who reported that they were unsure, more unlikely than likely, unlikely, or would certainly not get vaccinated were categorised as hesitant. All participants rated factors that were potentially important to vaccine decisions on a five-point Likert scale. Multivariable logistic regression was done to assess associations of local (sore arm) reactions and systemic reactions, separately, with age, sex, race or ethnicity, country, systemic sclerosis disease subtype, immunosuppressant use, vaccine brand, and history of COVID-19 infection.

Of 1410 active participants in the SPIN Cohort, 1000 consented to the survey, and 932 (66%) completed the full survey and were included in analyses. In the appendix (pp 25–26), we show characteristics of individuals who responded to the survey compared with individuals who did not, and of survey participants who had been vaccinated compared with participants who had not received a vaccine. Among survey participants, 699 (75%) received at least one vaccine dose and 358 (38%) received two vaccine doses. Medication was changed in only 42 (6%) of 699 participants before their first dose and 28 (8%) of 358 participants before their second dose.

For more on **SPIN**, see https://www.spinsclero.com/"

Adverse reactions were reported after the first dose by 270 (39%) of 699 participants and after the second dose by 209 (58%) of 358 participants (table). The most common adverse reactions were sore arm (first dose, 211/699 [30%]; second dose, 161/358 [45%]), fatigue (first dose, 157/699 [22%]; second dose, 143/358 [40%]), and muscle ache (first dose, 60/699 [9%]; second dose, 80/358 [22%]). No severe reactions were reported. Worsening of at least one symptom of systemic sclerosis was reported after the first dose by 41 (6%) of 699 participants and after the second dose by 28 (8%) of 358 participants. Variables that were independently associated with a systemic reaction (any reaction other than sore arm) after the first dose (appendix p 27) included age in years (odds ratio 0·97; 95% CI 0·96–0·99), male sex (0·36; 0·19–0·68), AstraZeneca vaccine (reference, Pfizer; 2·30; 1·37–3·84), and history of COVID-19 infection (2·50; 1·32–4·72). For the second dose (appendix p 28), there were independent associations with age (0·96; 0·94–0·98), male sex (0·36; 0·18–0·72), non-White race or ethnicity (0·49; 0·25–0·94), French participants (reference, participants from the USA;

See **Online** for appendix

	First dose (N=699), n (%)	Second dose (N=358), n (%)
No adverse reaction	429 (61%)	149 (42%)
At least one adverse reaction*	270 (39%)	209 (58%)
Sore arm	211 (30%)	161 (45%)
Fatigue	157 (22%)	143 (40%)
Muscle ache	60 (9%)	80 (22%)
Joint pain	42 (6%)	41 (11%)
Influenza-like symptoms	46 (7%)	50 (14%)
Fever	42 (6%)	49 (14%)
Chills	42 (6%)	59 (16%)
Shortness of breath	15 (2%)	9 (3%)
Rash	13 (2%)	10 (3%)
Severe allergy	0	0
Hives	0	3 (1%)
At least one systemic sclerosis symptom worsening	41† (6%)	28‡ (8%)

*Participants could report more than one adverse reaction. †Most common systemic sclerosis symptoms worsening (first dose): fatigue (n=23), muscle weakness (n=13), shortness of breath (n=12), Raynaud's phenomenon (n=11), and arthritis (n=11). ‡Most common systemic sclerosis symptoms worsening (second dose): fatigue (n=19), muscle weakness (n=11), gastrointestinal symptoms (n=11), arthritis (n=11), Raynaud's phenomenon (n=8), and shortness of breath (n=8).

Table: **Self-reported adverse reactions after COVID-19 vaccination**

0·41; 0·23–0·73), immunosuppressant use (0·60; 0·36–0·98), and Moderna vaccine (2·37; 1·34–4·18); only 21 participants received an AstraZeneca vaccine for their second dose.

Of the 932 participants, 90 (10%) were classed as vaccine-hesitant. Hesitancy was significantly associated with younger age (mean 55 years *vs* 60 years for participants who were not vaccine-hesitant), country (France had the highest hesitancy, 44/281 [16%] participants; UK had the lowest hesitancy, 3/86 [3%]), being a current smoker (11/44 [25%]), and history of COVID-19 infection (16/77 [21%]). Hesitancy was greater among men and among participants who did not have interstitial lung disease or pulmonary hypertension, although these associations were not significant (appendix p 29). Compared with participants who were not vaccine-hesitant and had not received a vaccine but planned to, those who were classed as hesitant scored significantly higher on all 16 potential concerns, including items related to COVID-19 vaccine effectiveness, the potential for adverse reactions, the vaccine development process, and the need for COVID-19 vaccination (item scores 1–5; median difference in item means, 1·2 points; appendix p 30).

Regarding considerations in vaccine decision making, the 842 (90%) of 932 participants who received or planned to receive the vaccine rated all eight beliefs about vaccination (eg, effectiveness, collaborative good, and return to normal) as significantly more important than did participants who were vaccine-hesitant (appendix p 31). The greatest difference between these two groups of participants in the ranking of beliefs as important or very important was for vaccination being a civic duty (625/842 [74%] who were not vaccine-hesitant *vs* 12/90 [13%] who were vaccine-hesitant; difference 61%; 95% CI 53–69%). When participants were queried regarding the importance of ten information sources for decision making, the proportion who rated the sources as important or very important was higher among participants who were not vaccine-hesitant for recommendations by their doctors (672/842 [80%] *vs* 45/90 [50%] who were vaccine-hesitant; difference 30%; 19–40%) and the ability to discuss concerns with their doctor (626/842 [74%] who were not vaccine-hesitant *vs* 56/90 [62%] who were vaccine-hesitant; difference 12%; 2–23%). Participants who were vaccine-hesitant placed higher importance than individuals who were not on having sufficient time to assess long-term negative effects of the vaccines (500/842 [59%] who were not vaccine-hesitant *vs* 72/90 [80%] who were vaccine-hesitant; difference 20%; 12–30%) and the experiences of other people with systemic sclerosis with the vaccine (429/842 [51%] who were not vaccine-hesitant *vs* 58/90 [64%] who were vaccine-hesitant; difference 13%; 3–24%).

In summary, 842 (90%) of 932 respondents had been vaccinated by mid-May, 2021, or intended to be vaccinated. Only 42 (6%) of 699 participants made medication changes before their first vaccine dose and 28 (8%) of 358 participants did so before their second vaccine dose. The proportion of participants who had adverse reactions after vaccination was similar to that of the general population in clinical trials[6,7] and self-reports from patients with other autoimmune rheumatic diseases.[5] Self-reported systemic sclerosis flare was uncommon, and there were no serious adverse reactions. The proportion of participants who were vaccine-hesitant was substantially lower in this study than in studies of the general population,[8] which could relate to greater concern about infection among people with systemic sclerosis.

A strength of our study is the high percentage of respondents from a large, multinational cohort in which the participants have similar characteristics to individuals in other major systemic sclerosis cohorts.[9] However, our study has several limitations. The SPIN Cohort is a convenience sample, and the subset of cohort participants who completed the SPIN COVID-19 Vaccine Survey might not be representative of all individuals with systemic sclerosis; adverse reactions were self-reported, and opinions and degree of vaccine hesitancy might evolve over time.

To our knowledge, this is the first large study that details experiences with COVID-19 vaccines in systemic sclerosis. Vaccination was safe in this group with no serious adverse events, a side-effect profile similar to that seen in other populations, and a low rate of reported systemic sclerosis flare.

Funding for this study was provided by the Canadian Institutes of Health Research (CIHR; GA4-177764). Additionally, the Scleroderma Patient-centered Intervention Network (SPIN) has received funding for the SPIN Cohort and to support studies, including the present study, from the Arthritis Society; the Lady Davis Institute for Medical Research of the Jewish General Hospital, Montreal, Canada; the Jewish General Hospital Foundation, Montreal, Canada; McGill University, Montreal, Canada; the Scleroderma Society of Ontario; Scleroderma Canada; Sclérodermie Québec; Scleroderma Manitoba; Scleroderma Atlantic; the Scleroderma Association of BC; Scleroderma SASK; Scleroderma Australia; Scleroderma New South Wales; Scleroderma Victoria; and Scleroderma Queensland. YW was supported by a Fonds de recherche du Québec—Santé Postdoctoral Training Fellowship, RSH was supported by a CIHR Postdoctoral Training Award, and BDT was supported by a Tier 1 Canada Research Chair, all outside of the present work. No sponsor or funder was involved in the study design; in the collection, analysis, and interpretation of the data; in the writing of the report; or in the decision to submit the paper for publication. JKG, KS, LK, M-EC, RSH, CPD, LM, BDT, RFS, and members of the SPIN SARS-CoV-2 Vaccination Patient Advisory Team contributed to the conception and design of study. M-EC, RSH, NØ, JN, AB, MC-A, AC-J, and BDT contributed to oversight and management of data collection. YW and BDT contributed to data analysis and accessed and verified the underlying data. All authors contributed to the interpretation of results. JKG and KS drafted the manuscript. All authors provided a critical review and approved the final manuscript. JKG is the guarantor. A full list of the SPIN investigators is listed in the appendix. JKG and KS are joint first authors; BDT and RFS are joint senior authors. JKG reports grants from Cumberland and Eicos, outside of the submitted work. CPD reports personal fees from Janssen, GlaxoSmithKline (GSK), Bayer, Sanofi-Aventis, Galapagos, Boehringer Ingelheim, Roche, CSL Behring, Corbus Pharmaceuticals, Acceleron Pharma, Horizon Therapeutics, and ARXX Therapeutics, all outside the submitted 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 of the submitted work. RFS reports grants from Roche-Genentech, GSK, Boehringer Ingelheim, Chemocentryx, Corbus Pharmaceuticals, Formation Biologics, InflaRx, Kadmon, AstraZeneca, and Principia Biopharma, and consulting fees from AbbVie, Roche-Genentech, GSK, Sanofi, Janssen, Chemocentryx, Formation Biologics, and Chemomab Therapeutics, all outside the submitted work. All other authors declare no competing interests.

De-identified individual participant data will be made available 12 months after publication upon request to the corresponding author and presentation of a methodologically sound proposal that is approved by the SPIN Data Access and Publications Committee.

Jessica K Gordon, Kimberly Showalter, Yin Wu, Linda Kwakkenbos, Marie-Eve Carrier, Richard S Henry, Nora Østbø, Julia Nordlund, Angelica Bourgeault, Mara Cañedo-Ayala, Andrea Carboni-Jiménez, Christopher P Denton, Luc Mouthon, Brett D Thombs, Robert F Spiera, SPIN COVID-19 Patient Advisory Team on behalf of the SPIN Investigators

gordonj@hss.edu

Department of Rheumatology, Hospital for Special Surgery, New York, NY 10021, USA (JKG, KS, RFS); Lady Davis Institute for Medical Research, Jewish General Hospital, Montreal, QC, Canada (YW, M-EC, RSH, NØ, JN, AB, MC-A, AC-J, BDT); Department of Psychiatry (YW, RSH, BDT), Department of Medicine (BDT), Department of Psychology (BDT), Department of Educational and Counselling Psychology (BDT), and Biomedical Ethics Unit (BDT), McGill University, Montreal, QC, Canada; Department of Clinical Psychology, Radboud University, Nijmegen, Netherlands (LK); Centre for Rheumatology and Connective Tissue Diseases, Division of Medicine, University College London, London, UK (CPD); Service de Médecine Interne, Centre de Référence Maladies Autoimmunes et Systémiques Rares d'Ile de France, Hôpital Cochin, Assistance Publique—Hôpitaux de Paris (APHP), Paris, France (LM); APHP-CUP, Hôpital Cochin, Université de Paris, Paris, France (LM); SPIN COVID-19 Patient Advisory Team: *USA* A Gietzen (Scleroderma Foundation, Tri-State Chapter, Buffalo, NY); *Canada* G Guillot (Sclérodermie Québec, Longueuil, QC), N Lewis (Toronto, ON), K Nielsen (Scleroderma Society of Ontario, Hamilton, ON), M Richard (Scleroderma Atlantic, Halifax, NS), M Sauvé (Scleroderma Society of Ontario and Scleroderma Canada, Hamilton, ON); *Netherlands* J Welling (NVLE Dutch patient organization for systemic autoimmune diseases, Utrecht); *Belgium* J Welling (Federation of European Scleroderma Associations, Brussels)

1 Boekel L, Hooijberg F, van Kempen ZLE, et al. Perspective of patients with autoimmune diseases on COVID-19 vaccination. *Lancet Rheumatol* 2021; **3:** e241–43.

2 D'Silva KM, Jorge A, Cohen A, et al. COVID-19 outcomes in patients with systemic autoimmune rheumatic diseases compared to the general population: a US multicenter, comparative cohort study. *Arthritis Rheumatol* 2021; **73:** 914–20.

3 Felten R, Dubois M, Ugarte-Gil MF, et al. Vaccination against COVID-19: Expectations and concerns of patients with autoimmune and rheumatic diseases. *Lancet Rheumatol* 2021; **3:** e243–45.

4 Ciaffi J, Guiggioli D, Mari A, et al. COVID-19 vaccine hesitancy in systemic sclerosis. *Clin Exp Rheumatol* 2021; **39** (suppl 131)**:** 165–66.

5 Sattui SE, Liew JW, Kennedy K, et al. Early experience of COVID-19 vaccination in adults with systemic rheumatic diseases: results from the COVID-19 Global Rheumatology Alliance Vaccine Survey. *RMD Open* 2021; **7:** e001814.

6 Baden LR, El Sahly HM, Essink B, et al. Efficacy and safety of the mRNA-1273 SARS-CoV-2 vaccine. *N Engl J Med* 2021; **384:** 403–16.

7 Polack FP, Thomas SJ, Kitchin N, et al. Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine. *N Engl J Med* 2020; **383:** 2603–15.

8 Cascini F, Pantovic E, Al-Ajlouni Y, et al. Attitudes, acceptance and hesitancy among the general population worldwide to receive the COVID-19 vaccines and their contributing factors: a systematic review. *EClinicalMedicine* 2021; **40:** 101113.

9 Dougherty DH, Kwakkenbos L, Carrier ME, et al. The Scleroderma Patient-Centered Intervention Network Cohort: baseline clinical features and comparison with other large scleroderma cohorts. *Rheumatology* 2018; **57:** 1623–31.