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Factors Associated with Patient-reported Likelihood of Using Online Self-care Interventions: A Scleroderma Patient-centered Intervention Network (SPIN) Cohort Study

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Factors Associated with Patient-reported Likelihood of Using Online Self-care Interventions: A Scleroderma Patient-centered Intervention Network (SPIN) Cohort Study

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ABSTRACT

Objectives: The Scleroderma Patient-centered Intervention Network (SPIN) Cohort was constituted as a framework for conducting multiple trials of online self-care interventions for people living with systemic sclerosis (SSc, scleroderma), utilizing the cohort multiple randomised controlled trial design. In order to offer interventions to patients interested in using them, participants complete signalling items that query about the likelihood that patients would agree to participate in 9 different hypothetical online programs addressing problems common in SSc. It is not known, however, what factors influence patient-reported interest in participating in a particular online intervention and if intervention-specific signalling questions provide unique information or replicate broader characteristics, such as overall willingness to participate in interventions or self-efficacy. The objective of this study was to determine factors that explain responses to intervention-specific signalling items.

Design: Cross-sectional survey.

Setting: SPIN Cohort participants enrolled at 42 centres from Canada, the United States, the United Kingdom, France, Spain, and Mexico who completed study questionnaires from March 2014 through January 2018 were included.

Participants: In total, 1,060 participants had complete baseline data for all variables included in regression analyses and were included in the analyses, including 128 men (12%).

Results: For all individual signalling questions, controlling for other variables, the mean of the remaining signalling questions was the strongest predictor (standardized regression coefficient β from 0.61 (sleep) to 0.80 (self-management). Smaller, but statistically significant, associations were found with the symptom associated with the respective signalling question and with general patient self-efficacy for 7 of 9 signalling questions.

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Conclusions: The main factor associated with patients' interest in participating in a disease-specific online self-care intervention is their general interest in participating in online interventions. Factors that may influence this general interest should be explored and may be taken into consideration when inviting patients to try online interventions.

Keywords: clinical trials; cmRCT; cohort multiple RCT; systemic sclerosis; scleroderma

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STRENGTHS AND LIMITATIONS OF THIS STUDY

- This is the first study to evaluate factors associated with patients indicating likelihood of using specific online interventions as part of signalling questions sometimes used in the cohort multiple randomised controlled trial design.
- A large, international sample of patients with SSc was analysed.
- Factors examined included sociodemographic variables, general likelihood of using online interventions, and symptoms or problems that would be addressed by the specific intervention.
- The SPIN Cohort constitutes a convenience sample of SSc patients receiving treatment at a SPIN recruiting centre, and patients at these centres may differ from those in other settings.
- SSc patients in the SPIN Cohort complete questionnaires online, which may limit the generalizability of findings.

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INTRODUCTION

Well-designed and conducted randomised controlled trials (RCTs) provide the best mechanism for evaluating the benefits and harms of healthcare interventions.[1,2] Large-scale RCTs, however, are complex and expensive to conduct. Concerns have been raised that many RCTs have difficulty recruiting and enrolling patients, consent procedures do not reflect how patients make decisions in real clinical practice, long-term outcomes are often not available, many trials have limited real-world generalizability, and the infrastructure needed for individual trials is prohibitively expensive.[3-11]

In response to these concerns, new approaches to RCTs have been proposed, including trial designs that utilize routinely collected health data or create data sources to facilitate patient recruitment and outcome assessment.[4,12-16] One example is the cohort multiple RCT (cmRCT) design.[4] In the cmRCT design, researchers set up an ongoing observational cohort that is designed from inception to serve as a framework for conducting trials. Participants who enrol in the cohort complete outcome measurements at regular intervals. When a trial is conducted using the cohort, a random selection of patients eligible for the trial is contacted and offered access to the intervention being tested. Patients who are eligible but not selected are not notified that the trial is occurring and therefore receive usual care. Outcomes for the two groups are compared post-trial using the cohort's routine data collection procedures. In most examples of cmRCTs, prior to enrolment in the cohort, patients are informed and consent to the possibility that they may be participants in trials but would not be notified about the trial if they are assigned to usual care.[17-22]

Participants sometimes enrol in trials in order to receive a new intervention that would not be available to them as part of their usual care. In conventional trial designs in which participants

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consent to randomisation to a specific intervention or usual care, this may lead to withdrawal from the trial or disappointment bias reflected in patient-reported outcomes.[1,4] In order to reduce this possibility, in the cmRCT design, cohort participants are not notified about specific trials being planned or conducted, except when they are offered access to an intervention as part of a trial. A potential problem with this approach is that a substantial number of patients offered an intervention that is undergoing testing may not accept it, since they did not enrol in the cohort with any expectation that it would be offered to them. This would dilute intervention effects estimated on an intention-to-treat basis, potentially substantially if the rate of accepted offers is low, as the intervention arm then includes a large proportion of patients receiving care as usual.[23] A possible solution that has been suggested to reduce non-acceptance of intervention offers is to present cohort patients with a list of possible interventions as part of regular cohort data collection and ask if they would agree to use them if offered.[4] Using this as a criteria for eligibility to participate in the trial is thought to increase the likelihood of accepting an intervention offer without disclosing the actual intervention that will be offered.

Systemic sclerosis (SSc), also known as scleroderma, is a rare autoimmune connective tissue disease characterized by vascular injury, immune dysfunction and an abnormal fibrotic process that can affect multiple organ systems including the skin, lungs, gastrointestinal tract and cardiovascular system.[24,25] SSc is notable for the range of problems faced by people living with the disease, including limitations in physical mobility and hand function, pain, fatigue, sleep disturbance, depression, sexual dysfunction, and body image distress from disfiguring changes in appearance.[17,26-28] The Scleroderma Patient-centered Intervention Network (SPIN) was formed to develop, test, and disseminate interventions to improve the health and quality of life of patients with SSc, and to serve as a model for doing this in other rare diseases. To do this, SPIN

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utilizes the cmRCT design and maintains a large international cohort used to collect information about problems important to patients and as a framework for RCTs of internet-based rehabilitation, education, self-management, and psychological interventions.[17]

As part of routine data collection via the SPIN Cohort, SPIN administers a series of signalling items that query about patients' self-reported likelihood of using 9 different online programs that would address problems common in SSc, including fatigue, hand function and mobility, sleep difficulty, emotions and stress, concerns about body image and appearance, pain, low self-efficacy for managing different problems common in scleroderma, nutrition and diet, and difficulty exercising. It is not clear, however, what factors are associated with patient-reported likelihood of using interventions and whether responses reflect a general willingness to use online interventions versus the desire to address specific problems or symptoms. The objective of this study was to identify characteristics of SPIN Cohort participants associated with a greater reported likelihood that they would agree to use an online intervention if it were offered through SPIN, including sociodemographic characteristics, disease characteristics, a general willingness to use online interventions, and symptoms or problems that would be presumed to be addressed by each specific intervention.

PATIENTS AND METHODS

Patients and Procedure

The study sample consisted of participants enrolled in the SPIN Cohort [17] who completed study questionnaires from March 2014 through January 2018. Patients were enrolled at 42 centres from Canada, the United States, the United Kingdom, France, Spain, and Mexico. To be eligible for the SPIN Cohort, participants must be classified as having SSc according to 2013 ACR/EULAR criteria,[29] be ≥ 18 years of age, be fluent in English, French, or Spanish,

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and be able to respond to questionnaires via the Internet. The SPIN sample is a convenience sample. Eligible participants are invited by attending physicians or supervised nurse coordinators from SPIN centres to participate, and written informed consent is obtained. The local SPIN investigator provides medical data, which triggers an email invitation to participants with instructions for activating their SPIN account and completing SPIN Cohort measures online. Participants complete outcome measures upon enrolment and subsequently every 3 months. Participants with limited or diffuse SSc who completed all study variables at baseline were included in the present study. The SPIN Cohort study was approved by the Research Ethics Committee of the Jewish General Hospital, Montréal, Canada and by the research ethics committees of each participating centre.

Measures

Sociodemographic and Medical Data. Patients provided demographic data, including age, sex and years of education. SPIN recruiting physicians provided medical data, including time since first non-Raynaud's phenomenon symptoms, onset of Raynaud's phenomenon, and SSc diagnosis; SSc subtype (limited or diffuse cutaneous SSc);[30] and modified Rodnan Skin Score.[31]

Signalling Items. Nine signalling items were developed specifically for use in the SPIN Cohort to assess the self-reported likelihood that Cohort participants would agree to use online programs designed to address one of nine problems related to living with scleroderma, including fatigue, hand function and mobility, sleep problems, emotions and stress, concerns about body image and appearance, pain, low self-efficacy for disease management, nutrition/diet, and exercise. Each item ("*Please indicate how likely you would be to participate in an online*

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program that addresses […]") is rated on a numerical scale ranging from 0 (*not likely at all*) to 10 (*very likely*).

Self-Efficacy to Manage Chronic Disease Scale (SEMCD). The 6-item SEMCD Scale measures confidence in one's ability to manage fatigue, pain, emotional distress and other symptoms as well as to reduce the need for medical care and reliance on medications.[32] Respondents are asked to rate their current confidence in their ability to perform certain tasks regularly. Each item is rated on a 10-point rating scale ranging from 1 (*not confident at all*) to 10 (*totally confident*). The score for the scale is the mean of all items, with higher scores reflecting greater self-efficacy. The SEMCD scale has been validated in patients with SSc.[33]

Patient-Reported Outcomes Measurement Information System-29 (PROMIS-29v2). The PROMIS-29 profile version 2.0 (PROMIS-29v2) [34] measures patient-reported health status over the past 7 days, with 4 items for each of 7 domains (physical function, anxiety, depression, fatigue, sleep disturbance, ability to participate in social roles and activities, pain interference) plus a single pain intensity item. Items are scored on a 5-point scale (range 1-5), with different response options for different domains. The single pain intensity item is measured on an 11-point rating scale (0 = *no pain*, 11= *worst imaginable pain*). Higher scores represent more of the domain being measured; that is, better physical function and ability to participate in social roles and activities, but higher levels of anxiety, depression, fatigue, sleep disturbance, pain interference, and pain intensity. Raw domain scores are obtained by summing item scores for each domain, which are converted into T-scores standardized for the general US population (mean=50, standard deviation [SD]=10). The PROMIS-29v2 has been validated in patients with SSc.[35]

Cochin Hand Function scale (CHFS). The 18-item CHFS [36,37] measures the ability to

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perform daily hand-related activities. Items are scored on a scale from 0 (*yes, without difficulty*) to 5 (*impossible*) and are grouped into five content categories: kitchen, dressing oneself, hygiene, the office, and other. Total scores range from 0 to 90, and higher scores indicate more hand disability. The CHFS has been validated in SSc.[37]

Social Appearance Anxiety Scale (SAAS). The SAAS is a 16-item measure examining fear of situations in which one's appearance will be evaluated.[38] Response options range from 1 (*not at all*) to 5 (*extremely*). To calculate a total score, the first item is reverse coded and then all items are summed. Total scores range from 16 to 80, with higher scores indicating greater fear. The SAAS has been validated in SSc.[39]

Interference from gastrointestinal problems. Interference with daily activities from gastrointestinal problems was assessed using an 11-point numerical rating scale (range 0-10), with higher scores indicating more limitations.

Physical activity. Physical activity was assessed using a single item "*Compared to other people your age, how would you rate your physical activity during the past year?*". Response options ranged from 1 (*physically inactive*) to 5 (*very active*).

Statistical Analyses

Descriptive statistics were used to calculate the mean and standard deviation (SD) for each signalling item. To assess what factors were associated with self-reported likeliness of participating in an online program, multiple linear regression analyses were conducted for each of the 9 signalling questions separately. Independent variables included in the regression models were determined a-priori. For each regression analysis, the following independent variables were included: (a) demographic and disease characteristics including age, sex, disease duration (time since onset of first non-Raynaud symptom), modified Rodnan Skin Score, years of education; (b)

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the mean score of the remaining signalling questions to reflect general likelihood of using online interventions; (c) self-efficacy to manage chronic disease; and (d) the symptom or problem corresponding with the intervention in each signalling item. The intervention-specific symptoms or problems were measured with the relevant PROMIS-29 domains for fatigue, sleep, depression, and pain signalling items; physical activity for the exercise signalling item on exercise, CHFS for the hand function signalling item, the SAAS for the body image signalling item, and a single-item numerical rating scale item on intestinal problems for the nutrition and diet signalling item. Standardized regression coefficients beta (β) are reported, as well as the total explained variance for each model (R^2).

In addition to the main regression model, based on our findings, we conducted hierarchical regression models to quantify the amount of additional variance explained by the mean score of the remaining signalling questions and the intervention-specific symptom or problem variable. In these models, in step 1, the demographic and disease characteristics, and self-efficacy to manage chronic disease were included as independent variables. In step 2, the mean score of the remaining signalling questions was added and the magnitude of the change in R^2 was examined. In step 3, the symptom or problem corresponding with the intervention in each signalling item was added.

The assumption of normal distribution of residuals in the regression model was tested using a normal probability plot. Additionally, correlations between independent variables and tolerances were calculated to check for multicollinearity. Linearity of the model was assessed using partial residual plot. All analyses were conducted using Stata version 14.2 (StataCorp, College Station, TX, USA).

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RESULTS

Sample Characteristics

Of 1,704 participants with submitted baseline self-report data, n=228 had no data for the SAAS, as SPIN stopped collecting data for this measure in English-speaking Cohort participants after November 7, 2016. Of the 1,476 eligible participants, there were 416 (28.2%) missing one or more variables. A commonly missing value was the time since the onset of the first non-Raynaud's symptom (n=103). The remaining patients (n=313) were missing one or more demographic or patient-reported outcome measures (i.e., signalling or symptom measures).

In total, 1,060 participants had complete data for all variables and were included in regression analyses, including 128 men (12%) and 932 women (88%; Table 1). Most patients (71%) were married or living as married. Mean time since Raynaud's onset was 14.6 (SD=11.6) years; mean time since first non-Raynaud's symptoms was 11.3 (SD=8.5) years; mean time since diagnosis was 9.4 (SD=7.8) years. The mean signalling question scores ranged from 5.1 (body image) to 7.0 (exercise). As shown in Table 2, correlations between signalling question scores ranged from 0.43 (sleep problems with exercise) to 0.71 (body image with emotions and stress).

Correlates of Signalling Items

Results from the multiple linear regression analyses are shown in Table 3. R^2 for the models ranged from 0.46 (exercise) to 0.64 (self-management). In all models, controlling for other variables, the mean of the remaining signalling questions was most strongly associated with a greater likelihood to participate in an intervention, with standardized regression coefficients ranging from $\beta = 0.61$ (sleep) to $\beta = 0.80$ (self-management). The symptom or problem corresponding with the respective signalling question was significantly associated with higher scores on 7 of the 9 the signalling questions: fatigue ($\beta = 0.30$, $p < 0.001$), hand ($\beta = 0.21$,

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p < 0.001), sleep (β = 0.43, p < 0.001), emotions and stress (β = 0.18, p < 0.001), body image (β = 0.28, p < 0.001), pain (β = 0.32, p < 0.001), and nutrition/diet (β = 0.07, p = 0.004). For the remaining two signalling questions, self-efficacy was not statistically associated with reported likelihood of participating in a self-management program (β = -0.03, p = 0.124), and physical activity level was not associated with the exercise intervention signalling question (β = -0.04, p = 0.130). Higher self-efficacy was significantly associated with higher scores on the signalling questions for 7 items, including fatigue (β = 0.10, p < 0.001), hand (β = 0.11, p < 0.001), sleep (β = 0.13, p < 0.001), body image (β = 0.09, p < 0.001), pain (β = 0.04, p = 0.047), nutrition/diet (β = 0.09, p < 0.001), and exercise (β = 0.16, p < 0.001), but not for emotions and stress (β = 0.03, p = 0.131) or self-management (β = -0.03, p = 0.124). Finally, there were 6 sociodemographic and disease variables included in each regression; between 0 and 2 were significantly associated with signalling question scores, but β ≤ 0.08 in all cases. Unstandardized regression coefficients (B) and their 95% confidence intervals from the multivariate linear regression analyses are shown in Appendix Tables A1-A9.

In the hierarchical analyses, R^2-change was assessed for all 9 models separately (Appendix Tables A1-A9). The amount of additional variance explained by adding the mean of the other signalling items to the model ranged from 0.41 (hand function problems) to 0.60 (self-management). The amount of additional variance explained by adding the symptom or problem corresponding with the signalling item ranged from <0.01 (exercise) to 0.14 (sleep).

Regression diagnostics found no evidence for deviation from the assumption of normal distribution of residuals for any of the regression models based on a normal probability plot. All tolerance values were between 0.56 and 0.97, indicating that multicollinearity was not an issue

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for any of the regression models. Partial residual plots did not show any violation of the linearity assumption for any of the regression models.

DISCUSSION

The main finding of this study was that the most important factor influencing patient-reported interest in using disease-specific online self-care interventions is general interest in using online interventions, which explained a substantial amount of additional variance for each model, ranging from 43% to 60%. The symptom or problem corresponding with the respective signalling question and higher self-efficacy was significantly associated with higher scores on 7 of the 9 the signalling questions, but added between < 1% and 14% of additional explained variance.

Results from our study suggest that there is a generic factor determining interest in participation in online self-care interventions. Across settings, it has been shown that the intention to use technology and the uptake and implementation of technological innovations in practice are mainly predicted by general factors, including the perceived usefulness, the perceived ease of use, experience, and greater technology confidence.[40-42] Identifying if these underlying factors are indeed driving the general interest in our sample of SSc patients could be useful, as these factors could then be taken into consideration in future trials when patients are invited to try novel online interventions in SPIN's research context or in other research programs.

To reduce non-acceptance of intervention offers in the cmRCT design, it has been suggested that cohort participants can be presented with a list of possible interventions as part of regular cohort data collection and asked if they would agree to use them if offered.[4] It has been hypothesized that this process would identify the potential accepters in advance and

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consequently reduce dilution of the intervention effects. The results of our study suggest that such a signalling question may not need to be intervention-specific, as a higher general interest in interventions was the main factor associated with higher scores on all signalling items.

Identifying factors associated with responses, however, cannot predict actual use of interventions. Recently, the suggested process of including patients with a high indicated interest on the cohort's signalling item was applied in the SPIN-HAND feasibility trial, which was conducted via the SPIN Cohort. SPIN-HAND is an online hand exercise program to improve hand function for SSc patients. SPIN Cohort participants with at least mild hand function limitations (CHFS ≥ 3) and an indicated interest in using an online hand-exercise intervention (hand signalling question ≥ 7) were randomised to be offered to use the SPIN-HAND program or usual care for 3 months. Of the 40 SPIN Cohort participants that were included in the SPIN-HAND feasibility trial, 24 were allocated to the intervention arm, and 16 to the control group. Patients in the intervention arm were offered to try the SPIN-HAND program and, afterwards, to participate in an interview collecting their feedback. In total, 15 of 24 (62.5%) patients consented to use the SPIN-HAND intervention.[43] Thus, uptake of the offer to try the intervention was low despite selecting patients based on their indicated interest. This result raises important questions about using signalling items as an eligibility criterion for participation in RCTs conducted using the cmRCT design, and it needs to be carefully evaluated how effective these items are at identifying potential accepters of interventions in advance. Since the SPIN-HAND feasibility trial with its small sample size provides only preliminary evidence, additional RCTs using the cmRCT design with larger samples are necessary to confirm this finding.

The present study has limitations that should be considered in interpreting its results. First, the SPIN Cohort constitutes a convenience sample of SSc patients receiving treatment at a

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SPIN recruiting centre, and patients at these centres may differ from those in other settings. Additionally, SSc patients in the SPIN Cohort complete questionnaires online, which may further limit the generalizability of findings, as all participants already have Internet access and are comfortable using it in a research setting. Third, 28% of the enrolled patients were excluded from the analyses due to missing data. Fourth, the SPIN interventions under development to be tested through the Cohort are all online self-care programs, and this is reflected in the signalling questions that query about these online interventions. Based on our data, however, is not possible to distinguish whether patients respond to the signalling items based on their interest in the content of the proposed programs (e.g., their interest in self-management or non-pharmacological treatments), or whether the online nature of the program drive their responses. Finally, this study explored an indicated interest (intention) in potentially trying an online intervention, but not the patients' actual participation in an intervention when it was offered to them. It remains to be elucidated to what degree these signalling questions may reflect actual acceptance of the offer when participants are invited to participate in an intervention. Recent experiences with the SPIN-HAND feasibility trial indicate that the predictive value of these questions may be lower than anticipated.

In sum, findings of the present study suggest that the main factor influencing patients' interest in participating in a disease-specific online self-care intervention is their general interest in participating in these types of interventions. It should be further explored what factors may drive this general interest, as these factors may be taken into consideration when inviting patients to try novel (online) interventions in a research context.

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AUTHORS' CONTRIBUTIONS

LK and BDT were responsible for the study conception. LM and the SPIN Investigators contributed to data collection. LK, JC, MEC, IB, SJB, VLM, LM, WRN, JW and BDT contributed to data analysis and interpretation. LK, JC and BDT contributed to drafting the manuscript. All authors provided a critical revision of the manuscript and approved the final version of the manuscript. BDT is the guarantor.

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COMPETING INTERESTS STATEMENT

The authors have read and understood the BMJ policy on declaration of interests and declare that they have no competing interests.

DATA SHARING STATEMENT

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Data used in the present study and other SPIN data can be requested via the corresponding author. All requests to use SPIN data will be evaluated per the SPIN Data Sharing and Publication Policy.

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Table 1. Demographic characteristics (N=1,060)

Variable	Value
Demographic	
Age in years, mean (SD)	54.6 (12.2)
Female sex, n (%)	932 (88)
Education in years, mean (SD)	15.0 (3.6)
Married or living as married, n (%)	751 (71)
Country, n (%)	
Canada	273 (26)
United States	416 (39)
United Kingdom	117 (11)
France	218 (21)
Spain	32 (3)
Mexico	4 (0)
Disease characteristics	
Time since onset first non-Raynaud's symptom or sign in years, mean (SD)	11.3 (8.5)
Time since onset Raynaud's in years, mean (SD)[a]	14.6 (11.6)
Time since diagnosis in years, mean (SD)[b]	9.4 (7.8)
Diffuse disease subtype, n (%)	439 (41.4)
Modified Rodnan Skin Score, mean (SD)[c]	8.1 (8.6)
Signalling question scores:	
Fatigue, mean (SD)	6.8 (3.2)
Hand function and mobility, mean (SD)	6.8 (3.4)
Sleep problems, mean (SD)	6.0 (3.7)
Emotions and stress, mean (SD)	5.8 (3.6)
Body image and appearance, mean (SD)	5.1 (3.7)

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Pain, mean (SD)	6.3 (3.4)
Self-management/ coping strategies, mean (SD)	6.6 (3.3)
Nutrition/Diet, mean (SD)	6.9 (3.2)
Exercise, mean (SD)	7.0 (2.9)

Due to missing data: [a]N=986, [b]N=1,053, [c]N=879

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Table 2. Correlations between signalling items (n = 1,060)

	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)
(1) Fatigue	1.00								
(2) Hand function and mobility	0.55	1.00							
(3) Sleep problems	0.63	0.46	1.00						
(4) Emotions and stress	0.60	0.47	0.61	1.00					
(5) Concerns about body image	0.49	0.46	0.52	0.71	1.00				
(6) Pain	0.62	0.59	0.58	0.61	0.53	1.00			
(7) Self-management	0.60	0.63	0.53	0.65	0.60	0.69	1.00		
(8) Nutrition and diet	0.53	0.49	0.48	0.57	0.52	0.52	0.65	1.00	
(9) Exercise	0.47	0.52	0.43	0.50	0.48	0.46	0.60	0.70	1.00

*All correlations are significant with $p<0.001$

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Table 3. Multiple linear regression analyses of the relationship between sociodemographic and disease variables with the signalling questions (n = 1,060)

	Fatigue[1]	Hand function and mobility[2]	Sleep problems[3]	Emotions and stress[4]	Body image[5]	Pain[6]	Self-management	Nutrition and diet[7]	Exercise[8]
	β (P-value)	β (P-value)	β (P-value)	β (P-value)	β (P-value)	β (P-value)	β (P-value)	β (P-value)	β (P-value)
Age in years	0.05 (0.03)	0.02 (0.41)	0.08 (<0.01)	-0.08 (<0.01)	-0.05 (0.02)	0.01 (0.70)	0.03 (0.18)	<-0.01 (0.95)	0.01 (0.73)
Male sex	0.06 (<0.01)	0.02 (0.43)	0.01 (0.60)	-0.02 (0.26)	-0.03 (0.11)	0.04 (0.03)	<0.01 (0.84)	-0.05 (0.01)	-0.02 (0.31)
Disease duration	-0.02 (0.44)	-0.01 (0.58)	<-0.01 (0.94)	-0.03 (0.10)	-0.02 (0.35)	0.01 (0.47)	-0.01 (0.78)	-0.02 (0.36)	<-0.01 (0.98)
Diffuse disease	-0.05 (0.02)	0.02 (0.31)	-0.04 (0.08)	-0.02 (0.42)	0.01 (0.63)	-0.03 (0.19)	0.02 (0.34)	-0.01 (0.62)	0.03 (0.27)
Education in years	<0.01 (0.87)	<-0.01 (0.99)	0.03 (0.10)	0.01 (0.60)	-0.06 (0.01)	-0.05 (<0.01)	-0.01 (0.47)	0.06 (0.01)	0.07 (<0.01)
Married or living as married	0.03 (0.21)	0.03 (0.19)	<-0.01 (0.95)	-0.04 (0.03)	<0.01 (0.88)	0.02 (0.43)	0.01 (0.45)	-0.01 (0.61)	-0.01 (0.69)
Self-efficacy	0.10 (<0.01)	0.11 (<0.01)	0.13 (<0.01)	0.03 (0.13)	0.09 (<0.01)	0.04 (0.05)	-0.03 (0.12)	0.09 (<0.01)	0.16 (<0.01)
Symptom measure	0.30 (<0.01)	0.21 (<0.01)	0.43 (<0.01)	0.18 (<0.01)	0.28 (<0.01)	0.32 (<0.01)	---	0.07 (<0.01)	-0.04 (0.13)
Mean of remaining signalling items	0.65 (<0.01)	0.63 (<0.01)	0.61 (<0.01)	0.72 (<0.01)	0.64 (<0.01)	0.67 (<0.01)	0.80 (<0.01)	0.71 (<0.01)	0.70 (<0.01)
R^2	0.58	0.47	0.61	0.62	0.55	0.64	0.64	0.51	0.46

β: standardized regression coefficient
Symptom measures for the models: [1]PROMIS-29 Fatigue; [2]Cochin Hand Function; [3]PROMIS-29 sleep; [4]PROMIS-29 depression; [5]SAAS score; [6]PROMIS-29 Pain; [7]Interference of GI symptoms; [8]Activity level

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APPENDIX

Table A1. Multiple linear regression of the relationship between sociodemographic and disease variables with signalling question on fatigue (n = 1,060)

	B (95% CI)	β	P
Step 1:			
Age in years	0.01 (0.00 to 0.02)	0.05	0.031
Male sex	0.64 (0.24 to 1.03)	0.06	0.002
Disease duration	-0.01 (-0.02 to 0.01)	-0.02	0.442
Diffuse disease	-0.31 (-0.58 to -0.04)	-0.05	0.023
Education in years	0.00 (-0.03 to 0.04)	<0.01	0.867
Married or living as married	0.18 (-0.10 to 0.47)	0.03	0.208
Self-efficacy	0.14 (0.07 to 0.22)	0.10	<0.001
Total R^2	0.04		
Step 2:			
Mean of remaining signalling items	0.80 (0.75 to 0.85)	0.65	<0.001
Total R^2	0.53		
R^2 change	0.49		<0.001
Step 3:			
PROMIS-29 Fatigue	0.09 (0.08 to 0.11)	0.30	<0.001
Total R^2	0.58		
R^2 change	0.05		<0.001

B (95% CI): raw regression coefficient and 95% confidence interval; β: standardized regression coefficient
All B and β values are for the Step 3 model.

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Table A2. Multiple linear regression of the relationship between sociodemographic and disease variables with signalling question on hand function and mobility (n = 1,060)

	B (95% CI)	β	P
Step 1:			
Age in years	0.01 (-0.01 to 0.02)	0.02	0.407
Male sex	0.19 (-0.27 to 0.65)	0.02	0.425
Disease duration	-0.01 (-0.02 to 0.01)	-0.01	0.578
Diffuse disease	0.17 (-0.16 to 0.49)	0.02	0.311
Education in years	0.00 (-0.04 to 0.04)	<-0.01	0.986
Married or living as married	0.22 (-0.11 to 0.56)	0.03	0.190
Self-efficacy	0.16 (0.09 to 0.24)	0.11	<0.001
Total R^2	0.03		
Step 2:			
Mean of remaining signalling items	0.80 (0.75 to 0.86)	0.63	<0.001
Total R^2	0.44		
R^2 change	0.41		<0.001
Step 3:			
Cochin Hand function	0.04 (0.03 to 0.05)	0.21	<0.001
Total R^2	0.47		
R^2 change	0.03		<0.001

B (95% CI): raw regression coefficient and 95% confidence interval; β: standardized regression coefficient
All B and β values are for the Step 3 model.

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Table A3. Multiple linear regression of the relationship between sociodemographic and disease variables with signalling question on sleep problems (n = 1,060)

	B (95% CI)	β	P
Step 1:			
Age in years	0.02 (0.01 to 0.03)	0.08	<0.001
Male sex	0.12 (-0.32 to 0.55)	0.01	0.596
Disease duration	0.00 (-0.02 to 0.02)	<-0.01	0.936
Diffuse disease	-0.26 (-0.56 to 0.03)	-0.04	0.080
Education in years	0.03 (-0.01 to 0.07)	0.03	0.098
Married or living as married	-0.01 (-0.32 to 0.30)	<-0.01	0.949
Self-efficacy	0.21 (0.14 to 0.28)	0.13	<0.001
Total R^2	0.03		
Step 2:			
Mean of remaining signalling items	0.85 (0.80 to 0.91)	0.61	<0.001
Total R^2	0.46		
R^2 change	0.43		<0.001
Step 3:			
PROMIS-29 sleep	0.18 (0.16 to 0.20)	0.43	<0.001
Total R^2	0.61		
R^2 change	0.14		<0.001

B (95% CI): raw regression coefficient and 95% confidence interval; β: standardized regression coefficient
All B and β values are for the Step 3 model.

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Table A4. Multiple linear regression of the relationship between sociodemographic and disease variables with signalling question on emotions and stress (n = 1,060)

	B (95% CI)	β	P
Step 1:			
Age in years	-0.02 (-0.03 to -0.01)	-0.08	<0.001
Male sex	-0.24 (-0.65 to 0.17)	-0.02	0.257
Disease duration	-0.01 (-0.03 to 0.00)	-0.03	0.096
Diffuse disease	-0.11 (-0.39 to 0.16)	-0.02	0.421
Education in years	0.01 (-0.03 to 0.05)	0.01	0.597
Married or living as married	-0.33 (-0.62 to -0.03)	-0.04	0.032
Self-efficacy	0.05 (-0.02 to 0.13)	0.03	0.131
Total R^2	0.08		
Step 2:			
Mean of remaining signalling items	0.99 (0.93 to 1.04)	0.72	<0.001
Total R^2	0.60		
R^2 change	0.52		<0.001
Step 3:			
PROMIS-29 depression	0.07 (0.05 to 0.08)	0.18	<0.001
Total R^2	0.63		
R^2 change	0.02		<0.001

B (95% CI): raw regression coefficient and 95% confidence interval; β: standardized regression coefficient
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Table A5. Multiple linear regression of the relationship between sociodemographic and disease variables with signalling question on concerns about body image (n = 1,060)

	B (95% CI)	β	P
Step 1:			
Age in years	-0.02 (-0.03 to 0.00)	-0.05	0.023
Male sex	-0.38 (-0.85 to 0.09)	-0.03	0.109
Disease duration	-0.01 (-0.03 to 0.01)	-0.02	0.350
Diffuse disease	0.08 (-0.24 to 0.40)	0.01	0.627
Education in years	-0.06 (-0.10 to -0.01)	-0.06	0.009
Married or living as married	0.03 (-0.31 to 0.36)	<0.01	0.879
Self-efficacy	0.16 (0.08 to 0.23)	0.09	<0.001
Total R^2	0.07		
Step 2:			
Mean of remaining signalling items	0.91 (0.85 to 0.97)	0.64	<0.001
Total R^2	0.49		
R^2 change	0.43		<0.001
Step 3:			
SAAS score	0.08 (0.06 to 0.09)	0.28	<0.001
Total R^2	0.55		
R^2 change	0.06		<0.001

B (95% CI): raw regression coefficient and 95% confidence interval; β: standardized regression coefficient
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Table A6. Multiple linear regression of the relationship between sociodemographic and disease variables with signalling question on pain (n = 1,060)

	B (95% CI)	β	P
Step 1:			
Age in years	0.00 (-0.01 to 0.01)	0.01	0.696
Male sex	0.42 (0.04 to 0.81)	0.04	0.032
Disease duration	0.01 (-0.01 to 0.02)	0.01	0.467
Diffuse disease	-0.17 (-0.44 to 0.09)	-0.03	0.193
Education in years	-0.05 (-0.09 to -0.02)	-0.05	0.005
Married or living as married	0.11 (-0.17 to 0.39)	0.02	0.426
Self-efficacy	0.07 (0.00 to 0.14)	0.04	0.047
Total R^2			
Step 2:			
Mean of remaining signalling items	0.86 (0.81 to 0.91)	0.67	<0.001
Total R^2	0.07		
R^2 change	0.57		<0.001
Step 3:			
PROMIS-29 Pain	0.12 (0.10 to 0.13)	0.32	<0.001
Total R^2	0.64		
R^2 change	0.07		<0.001

B (95% CI): raw regression coefficient and 95% confidence interval; β: standardized regression coefficient
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Table A7. Multiple linear regression of the relationship between sociodemographic and disease variables with signalling question on self-management (n = 1,060)

	B (95% CI)	β	P
Step 1:			
Age in years	0.01 (0.00 to 0.02)	0.03	0.176
Male sex	0.04 (-0.34 to 0.41)	<0.01	0.843
Disease duration	0.00 (-0.02 to 0.01)	-0.01	0.775
Diffuse disease	0.12 (-0.13 to 0.38)	0.02	0.335
Education in years	-0.01 (-0.05 to 0.02)	-0.01	0.466
Married or living as married	0.10 (-0.17 to 0.37)	0.01	0.453
Self-efficacy	-0.04 (-0.10 to 0.01)	-0.03	0.124
Total R^2	0.04		
Step 2:			
Mean of remaining signalling items	1.01 (0.96 to 1.06)	0.80	<0.001
Total R^2	0.64		
R^2 change	0.60		<0.001

B (95% CI): raw regression coefficient and 95% confidence interval; β: standardized regression coefficient
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Table A8. Multiple linear regression of the relationship between sociodemographic and disease variables with signalling question on nutrition/diet (n = 1,060)

	B (95% CI)	β	P
Step 1:			
Age in years	0.00 (-0.01 to 0.01)	<-0.01	0.949
Male sex	-0.53 (-0.94 to -0.11)	-0.05	0.014
Disease duration	-0.01 (-0.02 to 0.01)	-0.02	0.356
Diffuse disease	-0.07 (-0.35 to 0.21)	-0.01	0.621
Education in years	0.05 (0.01 to 0.09)	0.06	0.011
Married or living as married	-0.08 (-0.38 to 0.22)	-0.01	0.613
Self-efficacy	0.12 (0.06 to 0.19)	0.09	<0.001
Total R^2	0.03		
Step 2:			
Mean of remaining signalling items	0.84 (0.79 to 0.89)	0.71	<0.001
Total R^2	0.51		
R^2 change	0.48		<0.001
Step 3:			
Interference of GI symptoms	0.07 (0.02 to 0.12)	0.07	0.004
Total R^2	0.51		
R^2 change	<0.01		<0.001

B (95% CI): raw regression coefficient and 95% confidence interval; β: standardized regression coefficient
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Table A9. Multiple linear regression of the relationship between sociodemographic and disease variables with signalling question on exercise (n = 1,060)

	B (95% CI)	β	P
Step 1:			
Age in years	0.00 (-0.01 to 0.01)	0.01	0.725
Male sex	-0.21 (-0.62 to 0.20)	-0.02	0.313
Disease duration	0.00 (-0.02 to 0.02)	<-0.01	0.981
Diffuse disease	0.15 (-0.12 to 0.43)	0.03	0.273
Education in years	0.06 (0.02 to 0.09)	0.07	0.003
Married or living as married	-0.06 (-0.35 to 0.23)	-0.01	0.689
Self-efficacy	0.21 (0.14 to 0.27)	0.16	<0.001
Total R^2	0.02		
Step 2:			
Mean of remaining signalling items	0.74 (0.69 to 0.79)	0.70	<0.001
Total R^2	0.46		
R^2 change	0.44		<0.001
Step 3:			
Activity level	-0.10 (-0.24 to 0.03)	-0.04	0.130
Total R^2	0.46		
R^2 change	<0.01		0.13

B (95% CI): raw regression coefficient and 95% confidence interval; β: standardized regression coefficient
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Factors Associated with Patient-reported Likelihood of Using Online Self-care Interventions: A Scleroderma Patient-centered Intervention Network (SPIN) Cohort Study

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Factors Associated with Patient-reported Likelihood of Using Online Self-care Interventions: A Scleroderma Patient-centered Intervention Network (SPIN) Cohort Study

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ABSTRACT

Objectives: The Scleroderma Patient-centered Intervention Network (SPIN) Cohort utilizes the cohort multiple randomised controlled trial design to embed trials of online self-care interventions for people living with systemic sclerosis (SSc, scleroderma). To offer interventions to patients interested in using them, participants complete signalling items that query about the likelihood that patients would agree to participate in 9 different hypothetical online programs addressing common SSc-related problems. It is not known what factors influence patient-reported interest in participating in a particular online intervention and if intervention-specific signalling questions provide unique information or replicate broader characteristics, such as overall willingness to participate or self-efficacy. This study assessed factors that explain responses to intervention-specific signalling items.

Design: Cross-sectional survey.

Setting: SPIN Cohort participants enrolled at 42 centres from Canada, the United States, the United Kingdom, France, Spain, and Mexico who completed study questionnaires from March 2014 through January 2018 were included.

Measures: Demographic and disease characteristics, self-efficacy, and symptoms related to each specific intervention were completed in addition to signalling items. General likelihood of using interventions was calculating by taking the mean score of the remaining signalling questions.

Participants: 1,060 participants with complete baseline data were included in the analyses.

Results: For all individual signalling questions, controlling for other variables, the mean of the remaining signalling questions was the strongest predictor (standardized regression coefficient β from 0.61 (sleep) to 0.80 (self-management). Smaller, but statistically significant, associations were found with the symptom associated with the respective signalling question and with general

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self-efficacy for 7 of 9 signalling questions.

Conclusions: The main factor associated with patients' interest in participating in a disease-specific online self-care intervention is their general interest in participating in online interventions. Factors that may influence this general interest should be explored and taken into consideration when inviting patients to try online interventions.

Keywords: clinical trials; cmRCT; cohort multiple RCT; systemic sclerosis; scleroderma

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STRENGTHS AND LIMITATIONS OF THIS STUDY

- This is the first study to evaluate factors associated with patients indicating likelihood of using specific online interventions as part of signalling questions sometimes used in the cohort multiple randomised controlled trial design.
- A large, international sample of patients with SSc was analysed.
- Factors examined included sociodemographic variables, general likelihood of using online interventions, and symptoms or problems that would be addressed by the specific intervention.
- The SPIN Cohort constitutes a convenience sample of SSc patients receiving treatment at a SPIN recruiting centre, and patients at these centres may differ from those in other settings.
- SSc patients in the SPIN Cohort complete questionnaires online, which may limit the generalizability of findings.

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INTRODUCTION

Well-designed and conducted randomised controlled trials (RCTs) provide the best mechanism for evaluating the benefits and harms of healthcare interventions.[1,2] Large-scale RCTs, however, are complex and expensive to conduct. Concerns have been raised that many RCTs have difficulty recruiting and enrolling patients, consent procedures do not reflect how patients make decisions in real clinical practice, long-term outcomes are often not available, many trials have limited real-world generalizability, and the infrastructure needed for individual trials is prohibitively expensive.[3-11]

In response to these concerns, new approaches to RCTs have been proposed, including trial designs that utilize routinely collected health data or create data sources to facilitate patient recruitment and outcome assessment.[4,12-16] One example is the cohort multiple RCT (cmRCT) design.[4] In the cmRCT design, researchers set up an ongoing observational cohort that is designed from inception to serve as a framework for conducting trials. Participants who enrol in the cohort complete outcome measurements at regular intervals. When a trial is conducted using the cohort, a random selection of patients eligible for the trial is contacted and offered access to the intervention being tested. Patients who are eligible but not selected are not notified that the trial is occurring and therefore receive usual care. Outcomes for the two groups are compared post-trial using the cohort's routine data collection procedures. In most examples of cmRCTs, prior to enrolment in the cohort, patients are informed and consent to the possibility that they may be participants in trials but would not be notified about the trial if they are assigned to usual care.[17-22]

Participants sometimes enrol in trials in order to receive a new intervention that would not be available to them as part of their usual care. In conventional trial designs in which participants

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consent to randomisation to a specific intervention or usual care, this may lead to withdrawal from the trial or disappointment bias reflected in patient-reported outcomes.[1,4] In order to reduce this possibility, in the cmRCT design, cohort participants are not notified about specific trials being planned or conducted, except when they are offered access to an intervention as part of a trial. A potential problem with this approach is that a substantial number of patients offered an intervention that is undergoing testing may not accept it, since they did not enrol in the cohort with any expectation that it would be offered to them. This would dilute intervention effects estimated on an intention-to-treat basis, potentially substantially if the rate of accepted offers is low, as the intervention arm then includes a large proportion of patients receiving care as usual.[23] A possible solution that has been suggested to reduce non-acceptance of intervention offers is to present cohort patients with a list of possible interventions as part of regular cohort data collection and ask if they would agree to use them if offered.[4] Using this as a criteria for eligibility to participate in the trial is thought to increase the likelihood of accepting an intervention offer without disclosing the actual intervention that will be offered.

Systemic sclerosis (SSc), also known as scleroderma, is a rare autoimmune connective tissue disease characterized by vascular injury, immune dysfunction and an abnormal fibrotic process that can affect multiple organ systems including the skin, lungs, gastrointestinal tract and cardiovascular system.[24,25] SSc is notable for the range of problems faced by people living with the disease, including limitations in physical mobility and hand function, pain, fatigue, sleep disturbance, depression, sexual dysfunction, and body image distress from disfiguring changes in appearance.[17,26-28] The Scleroderma Patient-centered Intervention Network (SPIN) was formed to develop, test, and disseminate interventions to improve the health and quality of life of patients with SSc, and to serve as a model for doing this in other rare diseases. To do this, SPIN

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utilizes the cmRCT design and maintains a large international cohort used to collect information about problems important to patients and as a framework for RCTs of internet-based rehabilitation, education, self-management, and psychological interventions.[17]

As part of routine data collection via the SPIN Cohort, SPIN administers a series of signalling items that query about patients' self-reported likelihood of using 9 different online programs that would address problems common in SSc, including fatigue, hand function and mobility, sleep difficulty, emotions and stress, concerns about body image and appearance, pain, low self-efficacy for managing different problems common in scleroderma, nutrition and diet, and difficulty exercising. It is not clear, however, what factors are associated with patient-reported likelihood of using interventions and whether responses reflect a general willingness to use online interventions versus the desire to address specific problems or symptoms. The objective of this study was to identify characteristics of SPIN Cohort participants associated with a greater reported likelihood that they would agree to use an online intervention if it were offered through SPIN, including sociodemographic characteristics, disease characteristics, a general willingness to use online interventions, and symptoms or problems that would be presumed to be addressed by each specific intervention.

PATIENTS AND METHODS

Patients and Procedure

The study sample consisted of participants enrolled in the SPIN Cohort [17] who completed study questionnaires from March 2014 through January 2018. Patients were enrolled at 42 centres from Canada, the United States, the United Kingdom, France, Spain, and Mexico. To be eligible for the SPIN Cohort, participants must be classified as having SSc according to 2013 ACR/EULAR criteria,[29] be ≥ 18 years of age, be fluent in English, French, or Spanish,

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and be able to respond to questionnaires via the Internet. The SPIN sample is a convenience sample. Eligible participants are invited by attending physicians or supervised nurse coordinators from SPIN centres to participate, and written informed consent is obtained. The local SPIN investigator provides medical data, which triggers an email invitation to participants with instructions for activating their SPIN account and completing SPIN Cohort measures online. Participants complete outcome measures upon enrolment and subsequently every 3 months. Participants with limited or diffuse SSc who completed all study variables at baseline were included in the present study. The SPIN Cohort study was approved by the Research Ethics Committee of the Jewish General Hospital, Montréal, Canada and by the research ethics committees of each participating centre.

Measures

Sociodemographic and Medical Data. Patients provided demographic data, including age, sex and years of education. SPIN recruiting physicians provided medical data, including time since first non-Raynaud's phenomenon symptoms, onset of Raynaud's phenomenon, and SSc diagnosis; SSc subtype (limited or diffuse cutaneous SSc);[30] and modified Rodnan Skin Score.[31]

Signalling Items. Nine signalling items were developed specifically for use in the SPIN Cohort to assess the self-reported likelihood that Cohort participants would agree to use online programs designed to address one of nine problems related to living with scleroderma, including fatigue, hand function and mobility, sleep problems, emotions and stress, concerns about body image and appearance, pain, low self-efficacy for disease management, nutrition/diet, and exercise. Each item ("*Please indicate how likely you would be to participate in an online*

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program that addresses […]") is rated on a numerical scale ranging from 0 (*not likely at all*) to 10 (*very likely*).

Self-Efficacy to Manage Chronic Disease Scale (SEMCD). The 6-item SEMCD Scale measures confidence in one's ability to manage fatigue, pain, emotional distress and other symptoms as well as to reduce the need for medical care and reliance on medications.[32] Respondents are asked to rate their current confidence in their ability to perform certain tasks regularly. Each item is rated on a 10-point rating scale ranging from 1 (*not confident at all*) to 10 (*totally confident*). The score for the scale is the mean of all items, with higher scores reflecting greater self-efficacy. The SEMCD scale has been validated in patients with SSc.[33]

Patient-Reported Outcomes Measurement Information System-29 (PROMIS-29v2). The PROMIS-29 profile version 2.0 (PROMIS-29v2) [34] measures patient-reported health status over the past 7 days, with 4 items for each of 7 domains (physical function, anxiety, depression, fatigue, sleep disturbance, ability to participate in social roles and activities, pain interference) plus a single pain intensity item. Items are scored on a 5-point scale (range 1-5), with different response options for different domains. The single pain intensity item is measured on an 11-point rating scale (0 = *no pain*, 11= *worst imaginable pain*). Higher scores represent more of the domain being measured; that is, better physical function and ability to participate in social roles and activities, but higher levels of anxiety, depression, fatigue, sleep disturbance, pain interference, and pain intensity. Raw domain scores are obtained by summing item scores for each domain, which are converted into T-scores standardized for the general US population (mean=50, standard deviation [SD]=10). The PROMIS-29v2 has been validated in patients with SSc.[35]

Cochin Hand Function scale (CHFS). The 18-item CHFS [36,37] measures the ability to

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perform daily hand-related activities. Items are scored on a scale from 0 (*yes, without difficulty*) to 5 (*impossible*) and are grouped into five content categories: kitchen, dressing oneself, hygiene, the office, and other. Total scores range from 0 to 90, and higher scores indicate more hand disability. The CHFS has been validated in SSc.[37]

Social Appearance Anxiety Scale (SAAS). The SAAS is a 16-item measure examining fear of situations in which one's appearance will be evaluated.[38] Response options range from 1 (*not at all*) to 5 (*extremely*). To calculate a total score, the first item is reverse coded and then all items are summed. Total scores range from 16 to 80, with higher scores indicating greater fear. The SAAS has been validated in SSc.[39]

Interference from gastrointestinal problems. Interference with daily activities from gastrointestinal problems was assessed using an 11-point numerical rating scale (range 0-10), with higher scores indicating more limitations.

Physical activity. Physical activity was assessed using a single item "*Compared to other people your age, how would you rate your physical activity during the past year?*". Response options ranged from 1 (*physically inactive*) to 5 (*very active*).

Statistical Analyses

Descriptive statistics were used to calculate the mean and standard deviation (SD) for each signalling item. Pearson correlations between signalling question scores were calculated. To assess factors associated with self-reported likelihood of participating in an online program, we conducted multiple linear regression analysis for each signalling question and entered sets of variables hierarchically. Independent variables included in the regression models were determined a-priori, and included: (a) demographic and disease characteristics including age, sex, disease duration (time since onset of first non-Raynaud symptom), modified Rodnan Skin

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Score, years of education; (b) general likelihood of using online interventions, calculating by taking the mean score of the remaining signalling questions; (c) self-efficacy to manage chronic disease; and (d) the symptom or problem corresponding with the intervention in each signalling item. The intervention-specific symptoms or problems were measured with the relevant PROMIS-29 domains for fatigue, sleep, depression, and pain signalling items; physical activity for the exercise signalling item on exercise, CHFS for the hand function signalling item, the SAAS for the body image signalling item, and a single-item numerical rating scale item on intestinal problems for the nutrition and diet signalling item. Standardized regression coefficients beta (β) are reported, as well as the total explained variance for each model (R^2).

In addition to the main regression model, based on our findings, we conducted hierarchical regression models to quantify the amount of additional variance explained by the mean score of the remaining signalling questions and the intervention-specific symptom or problem variable. In these models, in step 1, the demographic and disease characteristics, and self-efficacy to manage chronic disease were included as independent variables. In step 2, the mean score of the remaining signalling questions was added and the magnitude of the change in R^2 was examined. In step 3, the symptom or problem corresponding with the intervention in each signalling item was added.

The assumption of normal distribution of residuals in the regression model was tested using a normal probability plot. Additionally, correlations between independent variables and tolerances were calculated to check for multicollinearity. Linearity of the model was assessed using partial residual plot. All analyses were conducted using Stata version 14.2 (StataCorp, College Station, TX, USA).

Patient and Public Involvement

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Since SPIN was conceived, SPIN Patient Advisory Board members have been involved in all stages of SPIN's research (https://www.spinsclero.com/en/Team?teamID=f120d6a6-8bee-62ed-b515-ff0000ce1efe). They have engaged in projects that have helped to better understand important problems faced by people with SSc [e.g., 17, 27, 28], to prioritize educational, psychosocial, and rehabilitation tools to address these problems and to evaluate how best to develop, test, and deliver interventions in a rare disease context [e.g., 17, 40]. Members of the SPIN Patient Advisory Board initially participated in the selection of topics to include in the SPIN Cohort assessments including the development of signalling items to include. Team members provided input on the use of the cmRCT design and were involved in decisions related to which international scleroderma treatment centres to approach for enrolment of patients.

RESULTS

Sample Characteristics

Of 1,704 participants with submitted baseline self-report data, n=228 had no data for the SAAS, as SPIN stopped collecting data for this measure in English-speaking Cohort participants after November 7, 2016. Of the 1,476 eligible participants, there were 416 (28.2%) missing one or more variables. A commonly missing value was the time since the onset of the first non-Raynaud's symptom (n=103). The remaining patients (n=313) were missing one or more demographic or patient-reported outcome measures (i.e., signalling or symptom measures).

In total, 1,060 participants had complete data for all variables and were included in regression analyses, including 128 men (12%) and 932 women (88%; Table 1). Most patients (71%) were married or living as married. Mean time since Raynaud's onset was 14.6 (SD=11.6) years; mean time since first non-Raynaud's symptoms was 11.3 (SD=8.5) years; mean time since diagnosis was 9.4 (SD=7.8) years. The mean signalling question scores ranged from 5.1 (body

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image) to 7.0 (exercise). Response frequencies for signalling items are shown in Appendix Table A. Responses for each signaling question were skewed towards willingness to participate, with score 10 (very likely to participate) being most frequently given for all 9 items (range 22-36%). As shown in Table 2, correlations between signalling question scores ranged from 0.43 (sleep problems with exercise) to 0.71 (body image with emotions and stress).

Correlates of Signalling Items

Results from the multiple linear regression analyses are shown in Table 3. R^2 for the models ranged from 0.46 (exercise) to 0.64 (self-management). In all models, controlling for other variables, the mean of the remaining signalling questions was most strongly associated with a greater likelihood to participate in an intervention, with standardized regression coefficients ranging from $\beta = 0.61$ (sleep) to $\beta = 0.80$ (self-management). The symptom or problem corresponding with the respective signalling question was significantly associated with higher scores on 7 of the 9 the signalling questions: fatigue ($\beta = 0.30$, $p < 0.001$), hand ($\beta = 0.21$, $p < 0.001$), sleep ($\beta = 0.43$, $p < 0.001$), emotions and stress ($\beta = 0.18$, $p < 0.001$), body image ($\beta = 0.28$, $p < 0.001$), pain ($\beta = 0.32$, $p < 0.001$), and nutrition/diet ($\beta = 0.07$, $p = 0.004$). For the remaining two signalling questions, self-efficacy was not statistically associated with reported likelihood of participating in a self-management program ($\beta = -0.03$, $p = 0.124$), and physical activity level was not associated with the exercise intervention signalling question ($\beta = -0.04$, $p = 0.130$). Higher self-efficacy was significantly associated with higher scores on the signalling questions for 7 items, including fatigue ($\beta = 0.10$, $p < 0.001$), hand ($\beta = 0.11$, $p < 0.001$), sleep ($\beta = 0.13$, $p < 0.001$), body image ($\beta = 0.09$, $p < 0.001$), pain ($\beta = 0.04$, $p = 0.047$), nutrition/diet ($\beta = 0.09$, $p < 0.001$), and exercise ($\beta = 0.16$, $p < 0.001$), but not for emotions and stress ($\beta = 0.03$, $p = 0.131$) or self-management ($\beta = -0.03$, $p = 0.124$). Finally, there were 6 sociodemographic and

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disease variables included in each regression; between 0 and 2 were significantly associated with signalling question scores, but $\beta \leq 0.08$ in all cases. Unstandardized regression coefficients (B) and their 95% confidence intervals from the multivariate linear regression analyses are shown in Appendix Tables B1-B9.

In the hierarchical analyses, R^2-change was assessed for all 9 models separately (Appendix Tables B1-B9). The amount of additional variance explained by adding the mean of the other signalling items to the model ranged from 0.41 (hand function problems) to 0.60 (self-management). The amount of additional variance explained by adding the symptom or problem corresponding with the signalling item ranged from <0.01 (exercise) to 0.14 (sleep).

Regression diagnostics found no evidence for deviation from the assumption of normal distribution of residuals for any of the regression models based on a normal probability plot. All tolerance values were between 0.56 and 0.97, indicating that multicollinearity was not an issue for any of the regression models. Partial residual plots did not show any violation of the linearity assumption for any of the regression models.

DISCUSSION

The main finding of this study was that the most important factor influencing patient-reported interest in using disease-specific online self-care interventions is general interest in using online interventions, which explained a substantial amount of additional variance for each model, ranging from 43% to 60%. The symptom or problem corresponding with the respective signalling question and higher self-efficacy was significantly associated with higher scores on 7 of the 9 the signalling questions, but added between < 1% and 14% of additional explained variance.

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Results from our study suggest that there is a generic factor determining interest in participation in online self-care interventions. Across settings, it has been shown that the intention to use technology and the uptake and implementation of technological innovations in practice are mainly predicted by general factors, including the perceived usefulness, the perceived ease of use, experience, and greater technology confidence.[41-43] Identifying if these underlying factors are indeed driving the general interest in our sample of SSc patients could be useful, as these factors could then be taken into consideration in future trials when patients are invited to try novel online interventions in SPIN's research context or in other research programs.

To reduce non-acceptance of intervention offers in the cmRCT design, it has been suggested that cohort participants can be presented with a list of possible interventions as part of regular cohort data collection and asked if they would agree to use them if offered.[4] It has been hypothesized that this process would identify the potential accepters in advance and consequently reduce dilution of the intervention effects. The results of our study suggest that such a signalling question may not need to be intervention-specific, as a higher general interest in interventions was the main factor associated with higher scores on all signalling items.

Identifying factors associated with responses, however, cannot predict actual use of interventions. Recently, the suggested process of including patients with a high indicated interest on the cohort's signalling item was applied in the SPIN-HAND feasibility trial, which was conducted via the SPIN Cohort. SPIN-HAND is an online hand exercise program to improve hand function for SSc patients. SPIN Cohort participants with at least mild hand function limitations (CHFS ≥ 3) and an indicated interest in using an online hand-exercise intervention (hand signalling question ≥ 7) were randomised to be offered to use the SPIN-HAND program or

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usual care for 3 months. Of the 40 SPIN Cohort participants that were included in the SPIN-HAND feasibility trial, 24 were allocated to the intervention arm, and 16 to the control group. Patients in the intervention arm were offered to try the SPIN-HAND program and, afterwards, to participate in an interview collecting their feedback. In total, 15 of 24 (62.5%) patients consented to use the SPIN-HAND intervention.[43] Thus, uptake of the offer to try the intervention was low despite selecting patients based on their indicated interest. This result raises important questions about using signalling items as an eligibility criterion for participation in RCTs conducted using the cmRCT design, and it needs to be carefully evaluated how effective these items are at identifying potential accepters of interventions in advance. Since the SPIN-HAND feasibility trial with its small sample size provides only preliminary evidence, additional RCTs using the cmRCT design with larger samples are necessary to confirm this finding.

The present study has limitations that should be considered in interpreting its results. First, the SPIN Cohort constitutes a convenience sample of SSc patients receiving treatment at a SPIN recruiting centre, and patients at these centres may differ from those in other settings. Additionally, SSc patients in the SPIN Cohort complete questionnaires online, which may further limit the generalizability of findings, as all participants already have Internet access and are comfortable using it in a research setting. Third, 28% of the enrolled patients were excluded from the analyses due to missing data. Fourth, the SPIN interventions under development to be tested through the Cohort are all online self-care programs, and this is reflected in the signalling questions that query about these online interventions. Based on our data, however, is not possible to distinguish whether patients respond to the signalling items based on their interest in the content of the proposed programs (e.g., their interest in self-management or non-pharmacological treatments), or whether the online nature of the program drive their responses. Finally, this study

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explored an indicated interest (intention) in potentially trying an online intervention, but not the patients' actual participation in an intervention when it was offered to them. It remains to be elucidated to what degree these signalling questions may reflect actual acceptance of the offer when participants are invited to participate in an intervention. Recent experiences with the SPIN-HAND feasibility trial indicate that the predictive value of these questions may be lower than anticipated.

In sum, findings of the present study suggest that the main factor influencing patients' interest in participating in a disease-specific online self-care intervention is their general interest in participating in these types of interventions. It should be further explored what factors may drive this general interest, as these factors may be taken into consideration when inviting patients to try novel (online) interventions in a research context.

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AUTHORS' CONTRIBUTIONS

LK and BDT were responsible for the study conception. LM and the SPIN Investigators contributed to data collection. LK, JC, MEC, FR, SJB, VLM, LM, WRN, JW and BDT contributed to data analysis and interpretation. LK, JC and BDT contributed to drafting the manuscript. All authors provided a critical revision of the manuscript and approved the final version of the manuscript. BDT is the guarantor.

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COMPETING INTERESTS STATEMENT

The authors have read and understood the BMJ policy on declaration of interests and declare that they have no competing interests.

DATA SHARING STATEMENT

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Data used in the present study and other SPIN data can be requested via the corresponding author. All requests to use SPIN data will be evaluated per the SPIN Data Sharing and Publication Policy.

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Table 1. Demographic characteristics (N=1,060)

Variable	Value
Demographic	
Age in years, mean (SD)	54.6 (12.2)
Female sex, n (%)	932 (88)
Education in years, mean (SD)	15.0 (3.6)
Married or living as married, n (%)	751 (71)
Country, n (%)	
Canada	273 (26)
United States	416 (39)
United Kingdom	117 (11)
France	218 (21)
Spain	32 (3)
Mexico	4 (0)
Disease characteristics	
Time since onset first non-Raynaud's symptom or sign in years, mean (SD)	11.3 (8.5)
Time since onset Raynaud's in years, mean (SD)[a]	14.6 (11.6)
Time since diagnosis in years, mean (SD)[b]	9.4 (7.8)
Diffuse disease subtype, n (%)	439 (41.4)
Modified Rodnan Skin Score, mean (SD)[c]	8.1 (8.6)
Signalling question scores:	
Fatigue, mean (SD)	6.8 (3.2)
Hand function and mobility, mean (SD)	6.8 (3.4)
Sleep problems, mean (SD)	6.0 (3.7)
Emotions and stress, mean (SD)	5.8 (3.6)
Body image and appearance, mean (SD)	5.1 (3.7)

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Pain, mean (SD)	6.3 (3.4)
Self-management/ coping strategies, mean (SD)	6.6 (3.3)
Nutrition/Diet, mean (SD)	6.9 (3.2)
Exercise, mean (SD)	7.0 (2.9)
Patient-reported outcome measures:	
Self-Efficacy to Manage Chronic Disease Scale, mean (SD)	6.3 (2.2)
PROMIS-29 fatigue, mean (SD)	55.9 (10.7)
PROMIS-29 sleep, mean (SD)	52.8 (8.6)
PROMIS-29 depression, mean (SD)	51.7 (9.3)
PROMIS-29 pain, mean (SD)	56.4 (9.3)
Cochin Hand Function Scale, mean (SD)	14.7 (16.4)
Social Appearance Anxiety Scale, mean (SD)	29.6 (13.7)
Interference from gastrointestinal problems, mean (SD)	2.7 (3.0)
Physical Activity, mean (SD)	1.7 (1.1)

Due to missing data: [a]N=986, [b]N=1,053, [c]N=879

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Table 2. Correlations between signalling items (n = 1,060)

	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)
(1) Fatigue	1.00								
(2) Hand function and mobility	0.55	1.00							
(3) Sleep problems	0.63	0.46	1.00						
(4) Emotions and stress	0.60	0.47	0.61	1.00					
(5) Concerns about body image	0.49	0.46	0.52	0.71	1.00				
(6) Pain	0.62	0.59	0.58	0.61	0.53	1.00			
(7) Self-management	0.60	0.63	0.53	0.65	0.60	0.69	1.00		
(8) Nutrition and diet	0.53	0.49	0.48	0.57	0.52	0.52	0.65	1.00	
(9) Exercise	0.47	0.52	0.43	0.50	0.48	0.46	0.60	0.70	1.00

*All correlations are significant with $p<0.001$

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Table 3. Multiple linear regression analyses of the relationship between sociodemographic and disease variables with the signalling questions (n = 1,060)

	Fatigue[1]	Hand function and mobility[2]	Sleep problems[3]	Emotions and stress[4]	Body image[5]	Pain[6]	Self-management	Nutrition and diet[7]	Exercise[8]
	β (P-value)	β (P-value)	β (P-value)	β (P-value)	β (P-value)	β (P-value)	β (P-value)	β (P-value)	β (P-value)
Age in years	0.05 (0.03)	0.02 (0.41)	0.08 (<0.01)	-0.08 (<0.01)	-0.05 (0.02)	0.01 (0.70)	0.03 (0.18)	<-0.01 (0.95)	0.01 (0.73)
Male sex	0.06 (<0.01)	0.02 (0.43)	0.01 (0.60)	-0.02 (0.26)	-0.03 (0.11)	0.04 (0.03)	<0.01 (0.84)	-0.05 (0.01)	-0.02 (0.31)
Disease duration	-0.02 (0.44)	-0.01 (0.58)	<-0.01 (0.94)	-0.03 (0.10)	-0.02 (0.35)	0.01 (0.47)	-0.01 (0.78)	-0.02 (0.36)	<-0.01 (0.98)
Diffuse disease	-0.05 (0.02)	0.02 (0.31)	-0.04 (0.08)	-0.02 (0.42)	0.01 (0.63)	-0.03 (0.19)	0.02 (0.34)	-0.01 (0.62)	0.03 (0.27)
Education in years	<0.01 (0.87)	<-0.01 (0.99)	0.03 (0.10)	0.01 (0.60)	-0.06 (0.01)	-0.05 (<0.01)	-0.01 (0.47)	0.06 (0.01)	0.07 (<0.01)
Married or living as married	0.03 (0.21)	0.03 (0.19)	<-0.01 (0.95)	-0.04 (0.03)	<0.01 (0.88)	0.02 (0.43)	0.01 (0.45)	-0.01 (0.61)	-0.01 (0.69)
Self-efficacy	0.10 (<0.01)	0.11 (<0.01)	0.13 (<0.01)	0.03 (0.13)	0.09 (<0.01)	0.04 (0.05)	-0.03 (0.12)	0.09 (<0.01)	0.16 (<0.01)
Symptom measure	0.30 (<0.01)	0.21 (<0.01)	0.43 (<0.01)	0.18 (<0.01)	0.28 (<0.01)	0.32 (<0.01)	---	0.07 (<0.01)	-0.04 (0.13)
Mean of remaining signalling items	0.65 (<0.01)	0.63 (<0.01)	0.61 (<0.01)	0.72 (<0.01)	0.64 (<0.01)	0.67 (<0.01)	0.80 (<0.01)	0.71 (<0.01)	0.70 (<0.01)
R^2	0.58	0.47	0.61	0.62	0.55	0.64	0.64	0.51	0.46

β: standardized regression coefficient

Symptom measures for the models: [1]PROMIS-29 Fatigue; [2]Cochin Hand Function; [3]PROMIS-29 sleep; [4]PROMIS-29 depression; [5]SAAS score; [6]PROMIS-29 Pain; [7]Interference of GI symptoms; [8]Activity level

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APPENDIX

Table A. Frequencies for signaling item responses (N=1,060)

	Fatigue	Hand function	Sleep problems	Emotions and stress	Body image	Pain	Self-management	Nutrition and diet	Exercise
Response	**N (%)**	**N (%)**	**N (%)**	**N (%)**	**N (%)**	**N (%)**	**N (%)**	**N (%)**	**N (%)**
0	55 (5.2)	76 (7.2)	153 (14.4)	122 (11.5)	182 (17.2)	88 (8.3)	76 (7.2)	48 (4.5)	0 (0.0)
1	57 (5.4)	56 (5.3)	51 (4.8)	72 (6.8)	87 (8.2)	57 (5.4)	59 (5.6)	53 (5.0)	64 (6.0)
2	45 (4.3)	40 (3.8)	43 (4.1)	66 (6.2)	78 (7.4)	55 (5.2)	34 (3.2)	36 (3.4)	40 (3.8)
3	46 (4.3)	53 (5.0)	49 (4.6)	51 (4.8)	66 (6.2)	58 (5.5)	48 (4.5)	49 (4.6)	59 (5.6)
4	30 (2.8)	29 (2.7)	39 (3.7)	36 (3.4)	36 (3.4)	35 (3.3)	32 (3.0)	33 (3.1)	47 (4.4)
5	119 (11.2)	110 (10.4)	124 (11.7)	141 (13.3)	133 (12.6)	132 (12.5)	128 (12.1)	137 (12.9)	167 (15.8)
6	50 (4.7)	48 (4.5)	40 (3.8)	56 (5.3)	47 (4.4)	60 (5.7)	69 (6.5)	53 (5.0)	54 (5.1)
7	89 (8.4)	92 (8.7)	77 (7.3)	88 (8.3)	64 (6.0)	88 (8.3)	90 (8.5)	82 (7.7)	78 (7.4)
8	132 (12.5)	105 (9.9)	101 (9.5)	87 (8.2)	82 (7.7)	113 (10.7)	118 (11.1)	116 (10.9)	118 (11.1)
9	69 (6.5)	83 (7.8)	69 (6.5)	66 (6.2)	56 (5.3)	75 (7.1)	72 (6.8)	74 (7.0)	69 (6.5)
10	368 (34.7)	368 (34.7)	314 (29.6)	275 (25.9)	229 (21.6)	299 (28.2)	334 (31.5)	379 (35.8)	364 (34.3)

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Table B1. Multiple linear regression of the relationship between sociodemographic and disease variables with signalling question on fatigue (n = 1,060)

	B (95% CI)	β	P
Step 1:			
Age in years	0.01 (0.00 to 0.02)	0.05	0.031
Male sex	0.64 (0.24 to 1.03)	0.06	0.002
Disease duration	-0.01 (-0.02 to 0.01)	-0.02	0.442
Diffuse disease	-0.31 (-0.58 to -0.04)	-0.05	0.023
Education in years	0.00 (-0.03 to 0.04)	<0.01	0.867
Married or living as married	0.18 (-0.10 to 0.47)	0.03	0.208
Self-efficacy	0.14 (0.07 to 0.22)	0.10	<0.001
Total R^2	0.04		
Step 2:			
Mean of remaining signalling items	0.80 (0.75 to 0.85)	0.65	<0.001
Total R^2	0.53		
R^2 change	0.49		<0.001
Step 3:			
PROMIS-29 Fatigue	0.09 (0.08 to 0.11)	0.30	<0.001
Total R^2	0.58		
R^2 change	0.05		<0.001

B (95% CI): raw regression coefficient and 95% confidence interval; β: standardized regression coefficient
All B and β values are for the Step 3 model.

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Table B2. Multiple linear regression of the relationship between sociodemographic and disease variables with signalling question on hand function and mobility (n = 1,060)

	B (95% CI)	β	P
Step 1:			
Age in years	0.01 (-0.01 to 0.02)	0.02	0.407
Male sex	0.19 (-0.27 to 0.65)	0.02	0.425
Disease duration	-0.01 (-0.02 to 0.01)	-0.01	0.578
Diffuse disease	0.17 (-0.16 to 0.49)	0.02	0.311
Education in years	0.00 (-0.04 to 0.04)	<-0.01	0.986
Married or living as married	0.22 (-0.11 to 0.56)	0.03	0.190
Self-efficacy	0.16 (0.09 to 0.24)	0.11	<0.001
Total R^2	0.03		
Step 2:			
Mean of remaining signalling items	0.80 (0.75 to 0.86)	0.63	<0.001
Total R^2	0.44		
R^2 change	0.41		<0.001
Step 3:			
Cochin Hand function	0.04 (0.03 to 0.05)	0.21	<0.001
Total R^2	0.47		
R^2 change	0.03		<0.001

B (95% CI): raw regression coefficient and 95% confidence interval; β: standardized regression coefficient
All B and β values are for the Step 3 model.

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Table B3. Multiple linear regression of the relationship between sociodemographic and disease variables with signalling question on sleep problems (n = 1,060)

	B (95% CI)	β	P
Step 1:			
Age in years	0.02 (0.01 to 0.03)	0.08	<0.001
Male sex	0.12 (-0.32 to 0.55)	0.01	0.596
Disease duration	0.00 (-0.02 to 0.02)	<-0.01	0.936
Diffuse disease	-0.26 (-0.56 to 0.03)	-0.04	0.080
Education in years	0.03 (-0.01 to 0.07)	0.03	0.098
Married or living as married	-0.01 (-0.32 to 0.30)	<-0.01	0.949
Self-efficacy	0.21 (0.14 to 0.28)	0.13	<0.001
Total R^2	0.03		
Step 2:			
Mean of remaining signalling items	0.85 (0.80 to 0.91)	0.61	<0.001
Total R^2	0.46		
R^2 change	0.43		<0.001
Step 3:			
PROMIS-29 sleep	0.18 (0.16 to 0.20)	0.43	<0.001
Total R^2	0.61		
R^2 change	0.14		<0.001

B (95% CI): raw regression coefficient and 95% confidence interval; β: standardized regression coefficient
All B and β values are for the Step 3 model.

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Table B4. Multiple linear regression of the relationship between sociodemographic and disease variables with signalling question on emotions and stress (n = 1,060)

	B (95% CI)	β	P
Step 1:			
Age in years	-0.02 (-0.03 to -0.01)	-0.08	<0.001
Male sex	-0.24 (-0.65 to 0.17)	-0.02	0.257
Disease duration	-0.01 (-0.03 to 0.00)	-0.03	0.096
Diffuse disease	-0.11 (-0.39 to 0.16)	-0.02	0.421
Education in years	0.01 (-0.03 to 0.05)	0.01	0.597
Married or living as married	-0.33 (-0.62 to -0.03)	-0.04	0.032
Self-efficacy	0.05 (-0.02 to 0.13)	0.03	0.131
Total R^2	0.08		
Step 2:			
Mean of remaining signalling items	0.99 (0.93 to 1.04)	0.72	<0.001
Total R^2	0.60		
R^2 change	0.52		<0.001
Step 3:			
PROMIS-29 depression	0.07 (0.05 to 0.08)	0.18	<0.001
Total R^2	0.63		
R^2 change	0.02		<0.001

B (95% CI): raw regression coefficient and 95% confidence interval; β: standardized regression coefficient
All B and β values are for the Step 3 model.

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Table B5. Multiple linear regression of the relationship between sociodemographic and disease variables with signalling question on concerns about body image (n = 1,060)

	B (95% CI)	β	P
Step 1:			
Age in years	-0.02 (-0.03 to 0.00)	-0.05	0.023
Male sex	-0.38 (-0.85 to 0.09)	-0.03	0.109
Disease duration	-0.01 (-0.03 to 0.01)	-0.02	0.350
Diffuse disease	0.08 (-0.24 to 0.40)	0.01	0.627
Education in years	-0.06 (-0.10 to -0.01)	-0.06	0.009
Married or living as married	0.03 (-0.31 to 0.36)	<0.01	0.879
Self-efficacy	0.16 (0.08 to 0.23)	0.09	<0.001
Total R^2	0.07		
Step 2:			
Mean of remaining signalling items	0.91 (0.85 to 0.97)	0.64	<0.001
Total R^2	0.49		
R^2 change	0.43		<0.001
Step 3:			
SAAS score	0.08 (0.06 to 0.09)	0.28	<0.001
Total R^2	0.55		
R^2 change	0.06		<0.001

B (95% CI): raw regression coefficient and 95% confidence interval; β: standardized regression coefficient
All B and β values are for the Step 3 model.

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Table B6. Multiple linear regression of the relationship between sociodemographic and disease variables with signalling question on pain (n = 1,060)

	B (95% CI)	β	P
Step 1:			
Age in years	0.00 (-0.01 to 0.01)	0.01	0.696
Male sex	0.42 (0.04 to 0.81)	0.04	0.032
Disease duration	0.01 (-0.01 to 0.02)	0.01	0.467
Diffuse disease	-0.17 (-0.44 to 0.09)	-0.03	0.193
Education in years	-0.05 (-0.09 to -0.02)	-0.05	0.005
Married or living as married	0.11 (-0.17 to 0.39)	0.02	0.426
Self-efficacy	0.07 (0.00 to 0.14)	0.04	0.047
Total R^2			
Step 2:			
Mean of remaining signalling items	0.86 (0.81 to 0.91)	0.67	<0.001
Total R^2	0.07		
R^2 change	0.57		<0.001
Step 3:			
PROMIS-29 Pain	0.12 (0.10 to 0.13)	0.32	<0.001
Total R^2	0.64		
R^2 change	0.07		<0.001

B (95% CI): raw regression coefficient and 95% confidence interval; β: standardized regression coefficient
All B and β values are for the Step 3 model.

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Table B7. Multiple linear regression of the relationship between sociodemographic and disease variables with signalling question on self-management (n = 1,060)

	B (95% CI)	β	P
Step 1:			
Age in years	0.01 (0.00 to 0.02)	0.03	0.176
Male sex	0.04 (-0.34 to 0.41)	<0.01	0.843
Disease duration	0.00 (-0.02 to 0.01)	-0.01	0.775
Diffuse disease	0.12 (-0.13 to 0.38)	0.02	0.335
Education in years	-0.01 (-0.05 to 0.02)	-0.01	0.466
Married or living as married	0.10 (-0.17 to 0.37)	0.01	0.453
Self-efficacy	-0.04 (-0.10 to 0.01)	-0.03	0.124
Total R^2	0.04		
Step 2:			
Mean of remaining signalling items	1.01 (0.96 to 1.06)	0.80	<0.001
Total R^2	0.64		
R^2 change	0.60		<0.001

B (95% CI): raw regression coefficient and 95% confidence interval; β: standardized regression coefficient
All B and β values are for the Step 3 model.

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Table B8. Multiple linear regression of the relationship between sociodemographic and disease variables with signalling question on nutrition/diet (n = 1,060)

	B (95% CI)	β	P
Step 1:			
Age in years	0.00 (-0.01 to 0.01)	<-0.01	0.949
Male sex	-0.53 (-0.94 to -0.11)	-0.05	0.014
Disease duration	-0.01 (-0.02 to 0.01)	-0.02	0.356
Diffuse disease	-0.07 (-0.35 to 0.21)	-0.01	0.621
Education in years	0.05 (0.01 to 0.09)	0.06	0.011
Married or living as married	-0.08 (-0.38 to 0.22)	-0.01	0.613
Self-efficacy	0.12 (0.06 to 0.19)	0.09	<0.001
Total R^2	0.03		
Step 2:			
Mean of remaining signalling items	0.84 (0.79 to 0.89)	0.71	<0.001
Total R^2	0.51		
R^2 change	0.48		<0.001
Step 3:			
Interference of GI symptoms	0.07 (0.02 to 0.12)	0.07	0.004
Total R^2	0.51		
R^2 change	<0.01		<0.001

B (95% CI): raw regression coefficient and 95% confidence interval; β: standardized regression coefficient
All B and β values are for the Step 3 model.

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Table B9. Multiple linear regression of the relationship between sociodemographic and disease variables with signalling question on exercise (n = 1,060)

	B (95% CI)	β	P
Step 1:			
Age in years	0.00 (-0.01 to 0.01)	0.01	0.725
Male sex	-0.21 (-0.62 to 0.20)	-0.02	0.313
Disease duration	0.00 (-0.02 to 0.02)	<-0.01	0.981
Diffuse disease	0.15 (-0.12 to 0.43)	0.03	0.273
Education in years	0.06 (0.02 to 0.09)	0.07	0.003
Married or living as married	-0.06 (-0.35 to 0.23)	-0.01	0.689
Self-efficacy	0.21 (0.14 to 0.27)	0.16	<0.001
Total R^2	0.02		
Step 2:			
Mean of remaining signalling items	0.74 (0.69 to 0.79)	0.70	<0.001
Total R^2	0.46		
R^2 change	0.44		<0.001
Step 3:			
Activity level	-0.10 (-0.24 to 0.03)	-0.04	0.130
Total R^2	0.46		
R^2 change	<0.01		0.13

B (95% CI): raw regression coefficient and 95% confidence interval; β: standardized regression coefficient
All B and β values are for the Step 3 model.

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STROBE Statement

Checklist of items that should be included in reports of observational studies

Section/Topic	Item No	Recommendation	Reported on Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	9,10
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	12,13,14
Objectives	3	State specific objectives, including any prespecified hypotheses	14
Methods			
Study design	4	Present key elements of study design early in the paper	14,15
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	14,15
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	15
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	15, 16, 17
Data sources/measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	15, 16, 17
Bias	9	Describe any efforts to address potential sources of bias	N/A
Study size	10	Explain how the study size was arrived at	19
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	17,18
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	17,18
		(*b*) Describe any methods used to examine subgroups and interactions	N/A
		(*c*) Explain how missing data were addressed	19
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	N/A
		(*e*) Describe any sensitivity analyses	N/A

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Section/Topic	Item No	Recommendation	Reported on Page No
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	19
		(b) Give reasons for non-participation at each stage	19
		(c) Consider use of a flow diagram	N/A
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	20 and Table 1
		(b) Indicate number of participants with missing data for each variable of interest	19
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	20
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Table 3 and supplementary tables
		(*b*) Report category boundaries when continuous variables were categorized	N/A
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	N/A
Discussion			
Key results	18	Summarise key results with reference to study objectives	11
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	21,22
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	22,23,24
Generalisability	21	Discuss the generalisability (external validity) of the study results	24
Other Information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	25

**Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.*

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Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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