The Role of Resilience in Systemic Sclerosis: A Comprehensive Investigation using the Scleroderma Patient-centered Intervention Network (SPIN) Cohort

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July 2023

A thesis submitted to McGill University in partial fulfillment of the requirements of the degree of Master of Science in Psychiatry.

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ABSTRACT

Objective: Systemic sclerosis (SSc), a rare, chronic autoimmune disease, can profoundly impact physical and psychological well-being. Resilience, the ability to maintain mental health despite adverse circumstances, remains understudied in SSc. This thesis presents two studies within the Scleroderma Patient-centered Intervention Network (SPIN) Cohort. Study 1 examined the validity, reliability, and differential item functioning (DIF) between English- and French-language versions of the 10-item Connor-Davidson Resilience Scale (CD-RISC-10) in SSc. Study 2 investigated the association of resilience in SSc with patient-important outcomes, including mental health.

Methods: Study 1 used confirmatory factor analysis (CFA) to evaluate the CD-RISC-10 factor structure and conducted DIF analysis across languages with Multiple-Indicator Multiple-Cause models. We tested convergent validity with another measure of resilience and measures of self-esteem, depression, and anxiety symptoms. We assessed internal consistency and test-retest reliability using Cronbach's alpha and intraclass correlation coefficient (ICC).

In Study 2, we built upon a previous study from the SPIN Cohort that identified five latent classes ("low," "normal," "high," "very high," and "high/low") based on patient-reported outcomes (pain, fatigue, sleep, anxiety, and depression). We employed latent profile modeling to re-identify these classes using a different SPIN dataset. To compare resilience levels between the "high" and "high/low" groups and across all classes, we calculated each class's mean total CD-RISC-10 resilience and mean item scores and performed multiple linear regression analyses to compare resilience levels, controlling for sociodemographic and disease variables.

Results: In Study 1 (N = 962), CFA supported a single-factor structure (Tucker Lewis Index = 0.99, Comparative Fit Index = 0.99, Root Mean Square Error of Approximation = 0.08, 90%

confidence interval 0.07 to 0.09). We found no meaningful DIF, meaning the scale performed similarly in English and French. Internal consistency was high (α =0.93, 95% confidence interval [CI] 0.92 to 0.94), and we found correlations with other measures of psychological functioning were moderate to large (|r| = 0.57 to 0.78), confirming study hypotheses. The scale showed good 1-2-week test-retest reliability (ICC = 0.80, 95% CI 0.75 to 0.85) in a subsample of 230 participants. In Study 2 (N =1054), we re-identified the five latent classes from the previous study. Resilience decreased with higher disease severity and mental health issues for 4 of the classes. However, the "high/low" class showed high resilience (mean = 30.2, standard deviation [SD] = 6.1), despite high disease severity similar to the "high" class. Similarly, the results of the multiple regression showed that the "high" class exhibited a lower resilience score (regression coefficient = -6.00, 95% CI: -7.12 to -4.87) and standardized mean difference (SMD) of -0.83 (95% CI: -0.98 to -0.67) compared to the "high/low" class.

Conclusion: The CD-RISC-10 is a valid and reliable measure of resilience in SSc with score comparability across English and French versions, suitable for SSc research and clinical applications. Resilience may play a role in mitigating the impact of SSc symptoms on psychological well-being, suggesting the potential for developing effective resilience-focused interventions. Future research should further explore factors of resilience in SSc.

RÉSUMÉ

Contexte : La sclérose systémique (SSc), une maladie auto-immune rare et chronique, a un impact profond sur le bien-être physique et psychologique. La résilience, la capacité à maintenir une santé mentale malgré des circonstances défavorables, reste peu étudiée pour la SSc. Cette thèse présente 2 études de la cohorte SPIN (Scleroderma Patient-centered Intervention Network). L'étude 1 a examiné la validité, la fiabilité et le fonctionnement différentiel des versions anglaise et française de l'échelle de résilience Connor-Davidson à 10 énoncés (CD-RISC-10). L'étude 2 a étudié la résilience en lien avec la gravité de la maladie et la santé mentale.

Méthodes : L'étude 1 a utilisé l'analyse factorielle confirmatoire (AFC) pour évaluer la structure factorielle de la CD-RISC-10 et a réalisé une analyse du fonctionnement différentiel des énoncés entre les langues à l'aide de modèles à indicateurs et causes multiples. Nous avons testé la validité convergente avec une autre mesure de résilience et des mesures d'estime de soi, de dépression et d'anxiété. Nous avons évalué la cohérence interne et la fiabilité test/re-test en utilisant l'alpha de Cronbach et le coefficient de corrélation intraclasse (CCI). Dans l'étude 2, nous nous sommes appuyés sur une étude précédente SPIN, qui a identifié 5 classes latentes ("faible", "normale", "élevée", "très élevée" et "élevée/faible") basées sur les résultats rapportés par les patient.e.s (douleur, fatigue, sommeil, anxiété et dépression). Nous avons utilisé la modélisation de profil latent pour réidentifier ces classes. Pour comparer les niveaux de résilience entre les classes "élevée" et "élevée/faible" et entre toutes les classes, nous avons calculé la moyenne totale de résilience de la CD-RISC-10 et les scores moyens des énoncés, et nous avons effectué une analyse de régression linéaire multivariable pour comparer les niveaux de résilience en contrôlant les variables sociodémographiques et médicales.

Résultats : Dans l'étude 1 (N = 962), l'AFC a confirmé une structure unifactorielle (indice de Tucker-Lewis = 0,99, indice de validité comparative = 0,99, racine carrée de l'erreur d'approximation = 0,08, intervalle de confiance à 90 % de 0,07 à 0,09). Nous n'avons trouvé aucun fonctionnement différentiel significatif, ce qui signifie que l'échelle a une performance similaire en anglais et en français. La cohérence interne était élevée (α =0,93, intervalle de confiance à 95 % de 0,92 à 0,94), et nous avons observé des corrélations modérées à élevées avec d'autres mesures du fonctionnement psychologique, confirmant les hypothèses de l'étude. L'échelle a montré une bonne fiabilité test/re-test sur une période de 1 à 2 semaines (CCI = 0,80, intervalle de confiance à 95 % de 0,75 à 0,85) dans un sous-échantillon de 230 participant.e.s. Dans l'étude 2 (N =1054), nous avons réidentifié les 5 classes latentes. La résilience diminuait avec la gravité de la maladie et les problèmes de santé mentale pour 4 des classes. Cependant, la classe "élevée/faible" présentait une résilience élevée (moyenne = 30,2, écart-type [SD] = 6,1), malgré une gravité similaire à celle de la classe "élevée". De même, les résultats de la régression multiple ont montré que la classe "élevée" présentait un score de résilience inférieur (coefficient de régression = -6,00, intervalle de confiance à 95 % : -7,12 à -4,87) et une différence moyenne standardisée (DMS) de -0,83 (intervalle de confiance à 95 % : -0,98 à -0,67) par rapport à la classe "élevée/faible".

Conclusion : L'échelle CD-RISC-10 est une mesure valide et fiable de résilience au sein de la SSc, adaptée à la recherche et aux applications cliniques. Les résultats de la deuxième étude indiquent que la résilience pourrait jouer un rôle dans l'atténuation de l'impact des symptômes de la SSc sur le bien-être psychologique, suggérant des bénéfices potentiels des interventions axées sur la résilience. Des études futures devraient approfondir les facteurs de résilience pour la SSc.

ACKNOWLEDGEMENTS

I would like to express my sincere appreciation to my supervisor, Dr. Brett Thombs, for his unwavering support, belief in my abilities, and exceptional mentorship. You motivated me to push boundaries and explore new avenues of research. Your dedication to scientific rigour, the importance of open discussions, and standing up for one's interests have been invaluable lessons that I will carry with me throughout my career. I am genuinely grateful for the opportunities you have provided and the knowledge I have gained under your guidance.

I extend my heartfelt appreciation to Dr. Richard Henry – I am profoundly grateful for your continuous support and invaluable contributions throughout my academic journey. Your presence and guidance, despite geographical distances and time zones, have been instrumental in my growth and development.

To my co-authors, I am sincerely grateful for your expertise, constructive critiques, and collaborative efforts. Your contributions have significantly enhanced the content and quality of this thesis, and our enriching discussions have shaped my research journey.

I am incredibly thankful for the financial support I received through the PROMOS Scholarship, the Mitacs Globalink Graduate Fellowship Award, and the McGill Graduate Fellowship. These funding sources have been pivotal in supporting my research endeavours.

To my parents, Susanne Begemann and Matthias Neyer, and my partner, Lennard Trippensee, your loving support, belief in my dreams, and continuous encouragement have been indispensable. Danke! Lastly, I want to express my heartfelt thanks to the entire team in the SPIN office. Your camaraderie and positive work environment have made my time in Canada an incredible and rewarding experience. I will forever cherish the friendships and memories created during this period.

CONTRIBUTIONS OF AUTHORS

Manuscript #1: *Validity, Reliability, and Differential Item Functioning of English and French Versions of the 10-Item Connor-Davidson Resilience Scale in Systemic Sclerosis: A Scleroderma Patient-centered Intervention Network (SPIN) Cohort Study*

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Manuscript #2: *The Association of Resilience and Positive Mental Health in Systemic Sclerosis: A Scleroderma Patient-centered Intervention Network (SPIN) Cohort Cross-Sectional Study*

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CHAPTER 1

Introduction: Relevance of Resilience in Scleroderma

1.1. What is Scleroderma?

Systemic sclerosis (SSc) is a rare, chronic, autoimmune rheumatic disease characterized by vascular abnormalities and fibrosis of the skin and internal organs (1,2). In North America, approximately 13.5-44.3 per 100,000 people are affected (3), with the disease being 2-3 times more common in women than in men (2,3). While the etiology of the condition is unclear (1), a combination of genetic and environmental factors is thought to contribute to its development (2).

SSc is typically diagnosed later in life, usually between the ages of 34 and 60 (3). Initial symptoms are nonspecific in most cases but often include Raynaud's phenomenon, which is distinguished by the development of digital ulceration, scarring, and gangrene (4,5). During the later stages of the disease, common disease manifestations include joint deformity, reductions in mobility, dyspnea, gastrointestinal symptoms, fatigue, pain, and sleep disturbances (1,6–12).

Three SSc subtypes can be identified based on the extent of affected skin using the modified Rodnan skin score (2). The most frequently diagnosed subtypes in SSc patients are limited cutaneous systemic sclerosis (lcSSc) and diffuse cutaneous systemic sclerosis (dcSSc), with the latter being defined by a more rapid disease progression (4).

In addition to the physical manifestations, SSc can significantly impact mental health and well-being. Due to limited research on SSc and mental health, it is difficult to estimate an exact prevalence. However, a recent systematic review by Nassar et al., 2023 (N = 6) (13) found that based on 3 studies from France, Canada, and India (N = 93 to 345), current or 30-day major depressive disorder prevalence ranged from 4 to 29%, while current or 30-day prevalence of any anxiety disorder ranged from 49% to 51%. The review also found that in 3 studies from Iran,

Canada, and the Netherlands (N = 114 to 376) that examined factors associated with depression, pulmonary involvement, breathing problems, and tender joint counts were associated with higher symptoms of depression in SSc. Other studies also found that mental health issues in SSc often arise from the symptoms associated with the disease, such as fatigue, pain, pruritus, sleep problems, and sexual impairments (14,15). Moreover, a systematic review conducted by Hudson et al. in 2009 (16), which included an international dataset of 1,127 SSc patients, reported significantly lower scores of health-related quality of life on the Medical Outcomes Trust Short Form 36 (SF-36) (mean = 38.3, 95% CI: 35.2 to 41.5) compared to the general population (mean = 50, SD = 10). In addition, Park et al. (17) found that participants with SSc from South Korea (N=120) reported lower mental component summary (MCS) scores, a subscore of the SF-36 that summarizes mental well-being (mean = 43.0, SD = 0.9) compared to individuals with rheumatoid arthritis (N = 120) (mean = 48.9, SD = 0.9). Collectively, this evidence suggests high levels of mental health issues among individuals with SSc.

1.2. What is Resilience?

Resilience has been defined as a dynamic process of positive adjustment or the ability to preserve or restore mental health despite adverse circumstances, such as living with a chronic illness (18,19).

The ability to cultivate resilience is thought to be influenced by many factors, including genetic, epigenetic, developmental, and psychological variables (20–22). Psychological attributes closely associated with resilience include optimism, cognitive reappraisal, social support, humour, physical exercise, prosocial behaviour, and coping (23,24). Coping refers to specific strategies used to manage stress and negative emotions, such as accepting the reality of the

situation (25). It plays a crucial role in building resilience, as resilient individuals effectively employ these strategies to navigate and overcome stressors (22,26).

Conversely, vulnerability factors, such as economic, social, or environmental hardships, can impede an individual's ability to develop resilience in the face of adverse experiences (27,28). For example, maltreatment during childhood can modify an individual's risk response and increase their susceptibility to undesirable outcomes.

In research, resilience is often measured using self-report questionnaires, and several instruments have been developed for this purpose (29). One commonly used instrument is the 10-item Connor-Davidson Resilience scale (CD-RISC-10) (30). The scale was initially validated in a sample of English-speaking undergraduate students (30) and has since been widely applied, including in individuals with systemic lupus erythematous (31) and cancer (32).

1.3. Why is Resilience important?

Research conducted in cancer, rheumatic diseases, rare diseases, and other medical contexts has consistently demonstrated that individuals with medical conditions who exhibit higher levels of resilience also report lower levels of anxiety and depression symptoms (23,24,33).

A systematic review from 2020 (34) examined resilience interventions across over 250 studies with 78,567 participants. The authors identified six types of interventions, including alternative, evidence-based, mindfulness, physical activity, psychoeducation, and social support. Their findings demonstrated that these interventions can enhance resilience and improve various patient-important outcomes. The meta-analysis revealed a small yet significant overall effect size (Hedges' g = 0.48, SE = 0.04, 95% CI = [0.40, 0.56]). The interventions targeted both at-risk groups and the general population across all ages.

Understanding resilience in the context of SSc can thus have far-reaching implications. By exploring resilience in larger samples of individuals with SSc, researchers can evaluate whether resilience may play a role in maintaining positive mental health in SSc. In the future, researchers might also be able to develop targeted interventions and strategies that increase the overall resilience of individuals with SSc. However, questions remain about what type of intervention would work best in SSc patients and how this should be measured.

1.4. Previous Research on Resilience in Scleroderma

To date, limited research has examined resilience in the context of scleroderma. Only two small-scale studies, each involving fewer than 50 participants, have measured resilience in individuals with SSc (35,36). Rojas et al. (35) investigated the association between cytokines, proteins important for the immune system, and resilience, while Ciaffi et al. (36) examined resilience in SSc patients following the first COVID-19 wave in Italy. Both applied common resilience measures, the Brief Resilience Scale (37) and the 14-item Resilience Scale (38). However, neither study explored the validation of these or other resilience measures in the SSc population. The lack of a validated scale thus hinders research on resilience in SSc.

Although not originally about resilience, a recent study by the Scleroderma Patient-centered Intervention Network (SPIN) investigated clusters of commonly experienced patient-important outcomes and found five latent classes based on fatigue, sleep, pain, anxiety, and depression in >2,000 individuals with SSc (39). The first 4 classes were characterized by "low," "normal," "high," or "very high" patient-reported outcome levels, and class membership was robustly associated with overall SSc disease severity and prevalence of disease characteristics (e.g., diffuse subtype, joint contractures, gastrointestinal symptoms). A fifth class ("high/low") had similarly high levels of fatigue, sleep, pain and SSc disease characteristics as the "high" class

but low anxiety and depression. The presence of the "high/low" class, we hypothesized, might be due to higher resilience in that group (18,19).

1.5. Objectives of this Thesis

The objectives of the present research were carried out over two studies focussing on resilience in individuals with SSc.

The objectives of the first study were to evaluate (1a) the validity and (1b) reliability of the CD-RISC-10 within the SSc population, (1c) assess its internal consistency, and (1d) test-retest reliability, and (1e) examine its convergent validity by comparing scores with other measures of resilience, self-esteem, depression, and anxiety symptoms.

The objectives of the second study were to (2a) re-identify the previously found 5 classes of patient-reported outcome-based classes of individuals with SSc ("low," "normal," "high," "very high," "high/low"), (2b) evaluate resilience across the five classes using scores obtained from the CD-RISC-10, (2c) compare levels of resilience between members of the "high" class with high disease severity and high mental health symptoms and the "high/low" class with high disease severity but low mental health symptoms, controlling for sociodemographic and disease variables. We hypothesized that resilience would be higher among participants in the "high/low" class compared to the "high" symptom class.

1.6. Connecting Text

Some people with SSc report positive mental health, despite severe disease manifestations (39), which may be associated with resilience. However, the lack of a validated resilience measure in SSc has hindered comprehensive research in this area. A methodological review (17) examining various tools to measure resilience found that more than 15 scales had

been developed in the past. Among these, the 25-item Connor-Davidson Resilience Scale (CD-RISC) (21) emerged as one of the three measures with the strongest ratings for measurement properties based on predefined criteria for overall quality and usability (29). The 10-item short version of the scale, the CD-RISC-10, which researchers initially validated in English-speaking undergraduate students (30), reduces the burden on study participants and has similar measurement properties as the CD-RISC (29,40).

The present manuscript titled '*Validity, Reliability, and Differential Item Functioning of English and French Versions of the 10-Item Connor-Davidson Resilience Scale in Systemic Sclerosis: A Scleroderma Patient-centered Intervention Network (SPIN) Cohort Study*' aims to address the critical gap in resilience measurement within the SSc population by validating the CD-RISC-10.

CHAPTER 2

Manuscript 1

2.1. Validity, Reliability, and Differential Item Functioning of English and French Versions of the 10-Item Connor-Davidson Resilience Scale in Systemic Sclerosis: A Scleroderma Patient-Centered Intervention Network Cohort Study

Published paper:

Neyer MA, Henry RS, Carrier ME, et al. Validity, reliability, and differential item functioning of English and French versions of the 10-item Connor-Davidson Resilience Scale in systemic sclerosis: a Scleroderma Patient-Centered Intervention Network Cohort study [published online ahead of print, 2023 May 2]. Arthritis Care Res (Hoboken). 2023;10.1002/acr.25139. doi:10.1002/acr.25139

INTRODUCTION

Systemic sclerosis (SSc, scleroderma) is a rare, chronic autoimmune disorder characterized by vascular abnormalities and fibrosis of the skin and internal organs, including the gastrointestinal tract, lungs, heart, and kidneys (1,2). Disease manifestation is heterogeneous, and course is unpredictable (1,3). Researchers have estimated the standardized mortality rate to be almost three times as high as sex- and age-matched peers (4), and people with SSc report substantially lower quality of life compared to those with other rheumatic diseases (5) and the general population (6). Symptoms often include impaired function and mobility, breathing problems, gastrointestinal symptoms, fatigue, pain, pruritus, sleep disturbances, body image distress from disfigurement (e.g., skin tightening, pigment changes, hand contractures, telangiectasias), and reduced mental health (3,7–10).

A recent cross-sectional study (11) of more than 2,000 participants in the Scleroderma Patient-centered Intervention Network (SPIN) Cohort found that five latent classes characterized patterns of patient-reported outcomes, including fatigue, sleep, pain, anxiety symptoms, and depression symptoms. Four classes separated participants into low, normal, high, and very high symptom severity classes, and levels of patient-reported symptoms in these classes tracked closely with the severity or presence of specific disease manifestations. The fifth class, however, identified people with high fatigue, sleep, and pain symptoms but low mental health problems, even though members of this class had underlying disease burdens similar to the high class. The difference between people in this class and others with similarly severe SSc might be associated with resilience (12,13).

Research has defined resilience as positive adjustment or the ability to preserve or restore mental health despite adverse circumstances (14,15). Psychological factors associated with

resilience include self-efficacy, self-esteem, optimism, hardiness, determination, an internal locus of control, and a sense of self-empowerment and mastery (12,13). People with chronic medical conditions who score higher on resilience measures report lower anxiety and depression symptoms and better quality of life (12,13). In addition, researchers have found that intervention strategies that enhance resilience and adaptive coping improve psychological adaptation and reduce symptom burden (16).

No resilience measure has been validated in scleroderma, and there are no studies on resilience in people with SSc. A methodological review (17) of tools to measure resilience reported that more than 15 scales had been developed and that, based on a set of predefined criteria to assess overall quality and usability, the 25-item Connor-Davidson Resilience Scale (CD-RISC) (18) was among 3 measures with the strongest ratings for measurement properties. It was the only measure that researchers had successfully used to evaluate change in response to an intervention. Researchers originally developed the CD-RISC in English and simultaneously validated it in a general population sample, primary care outpatients, mixed psychiatry outpatients, anxiety patients, and people with post-traumatic stress disorder (18). The 10-item short version of the scale, the CD-RISC-10, which researchers initially validated in English-speaking undergraduate students (19), reduces burden on study participants and has similar measurement properties as the CD-RISC (17,20). Additionally, compared to the original CD-RISC, the factor structure of the 10-item version may be more stable across studies and different cultural groups (21). The CD-RISC-10 has been validated in multiple languages (22,23), including French (22), and is therefore well-suited for use in international cohorts.

The objectives of the present study were to evaluate the validity and reliability of the 10-item CD-RISC-10 for use in SSc by 1) testing its unidimensional structure; 2) performing a

differential item functioning (DIF) analysis to identify possible differences in measurement properties between English- and French-language respondents and assess the magnitude of any DIF; 3) evaluating internal consistency and test-retest reliability; and 4) evaluating convergent validity by comparing scores to another measure of resilience, the Resilience Scale (RS14) (24); a measure of self-esteem, the Rosenberg Self-Esteem Scale (25); and measures of depression and anxiety symptoms, using Patient Reported Outcomes Measurement Information System (PROMIS) Anxiety 4a v2.0 and Depression 4a v2.0 scales (26). For convergent validity, we hypothesized that the CD-RISC-10 would be correlated moderately to highly with all other measures and that the magnitude of correlation with the RS14, another measure of resilience, would be the largest.

METHODS

We evaluated cross-sectional data collected from regular Scleroderma Patient-centered Intervention Network (SPIN) Cohort assessments to evaluate English- (19) and French-language (22) versions of the CD-RISC-10 for factor structure, language-based DIF, internal consistency reliability, and convergent validity. We administered the CD-RISC-10 a second time to a subset of participants 1-2 weeks after their first assessment to assess test-retest validity. A protocol was published online prior to study initiation (https://osf.io/dx3b6/). We reported the study consistent with the COnsensus-based Standards for the selection of health status Measurement INstruments (COSMIN) reporting guideline for studies on properties of patient-reported outcome measures (27).

Participants and Procedure

The SPIN Cohort (28,29) is a convenience sample of participants recruited from 47 sites in 7 countries (Australia, Canada, France, Mexico, Spain, the United Kingdom, and the United

States). To be eligible for the SPIN Cohort, participants must be aged ≥ 18 years, fluent in English, French, or Spanish, have access to and be able to respond to questionnaires via the Internet, and meet the 2013 American College of Rheumatology/European League Against Rheumatism criteria for systemic sclerosis (30) verified by a physician at a SPIN site. Participants are invited to participate in the SPIN Cohort by attending physicians or nurse coordinators at recruiting sites. Site personnel obtain written informed consent, including consent to be contacted by the SPIN team about additional studies, and submit an electronic medical form to enrol participants. Participants then receive an email with a unique, secure link to complete baseline measurements online in English, French, or Spanish. Subsequent online assessments are conducted by SPIN at 3-month intervals (28,29). The study included SPIN participants who completed all study measures in English or French during a regular assessment between August 2022 and January 2023, when the CD-RISC-10 was included in the SPIN Cohort. We did not include Spanish-language participants in this study because there were not enough individuals to conduct all study analyses.

To examine test-retest reliability, we administered the CD-RISC-10 to a subsample of participants 1-2 weeks following their routine cohort assessment. We invited English- and French-speaking SPIN Cohort participants who completed the CD-RISC-10 as part of their regular SPIN Cohort assessment by email 7 days (31,32) later to complete the scale a second time via the online survey website Qualtrics. Invited participants had access to the questionnaire for 7 days, and they completed the retest assessments between 7 and 14 days after the initial assessment. We sent a reminder email to non-responders 4 days after the initial invitation. As an incentive, we randomly selected 10 questionnaire respondents to win an Amazon gift card worth

$100 CAD or the equivalent in their local currency. We emailed invitations until we reached our targeted sample size for test-retest reliability.

The SPIN Cohort study was approved by the Research Ethics Committee of the Centre intégré universitaire de santé et de services sociaux du Centre-Ouest-de-l'Île-de-Montréal (#MP-05-2013-150) and by the ethics committees of all recruiting sites. The present study was approved as an amendment.

Measures

At baseline, SPIN Cohort participants report sociodemographic variables, including race or ethnicity, country, language, education, and marital status. Physician-reported data from the baseline data assessment include age, sex, height, weight, date of initial onset of non-Raynaud phenomenon symptoms, SSc subtype, presence of gastrointestinal involvement, digital ulcers anywhere on the fingers, current tendon friction rubs, presence of joint contractures, history of renal crisis, presence of pulmonary arterial hypertension, presence of interstitial lung disease, presence of primary biliary cirrhosis, and presence of overlap syndromes (rheumatoid arthritis, Sjögren's syndrome, systemic lupus erythematosus, idiopathic inflammatory myositis, autoimmune thyroid disease).

CD-RISC-10

CD-RISC-10 scores reflect multiple aspects of resilience, including flexibility, self-efficacy, regulation of emotion, optimism, and the ability to maintain focus under stress. Items assess the ability to tolerate and cope with experiences such as change, personal problems, illness, pressure, failure, and painful feelings (19). Item response options range from 0 (not true at all) to 4 (true nearly all the time). Participants respond to each statement in reference to the previous month. Evaluators score the scale by totalling item scores, resulting in possible scores

of 0-40, with higher scores reflecting greater resilience. The correlation of the CD-RISC-10 with the 25-item CD-RISC was 0.92 in a sample of N > 500 undergraduates (19). Researchers have validated a French version of the scale (22).

RS14

The 25-item Resilience Scale was initially developed by researchers in a sample of older women who had recently experienced but successfully coped with a loss (e.g., loss of a spouse) (33). The scale received the second-highest score level in the review of resilience measures (17) and the highest possible rating for content and construct validity. The shortened form of the RS25, the RS14 (24), is based on a one-factor structure and focuses on aspects of resilience such as self-reliance, purpose, equanimity, perseverance, and authenticity. Items are rated using a 7-point Likert scale, ranging from 1 (strongly disagree) to 7 (strongly agree). Evaluators sum item scores to a total (possible range 14-98), and higher scores reflect greater resilience. Researchers have validated the RS14 in numerous populations. It exhibits similar measurement properties to the original Resilience Scale, including evidence of high reliability and good validity in clinical and non-clinical settings (24). The correlation of the RS14 with the original 25-item Resilience Scale was 0.97 in a sample of 776 middle-aged and older adults (24). A French version of the scale has been validated by researchers (34).

Rosenberg Self-Esteem Scale

The Rosenberg Self-Esteem Scale (25) assesses self-esteem, which reflects confidence in one's abilities or worth. It measures both positive and negative feelings about the self. Researchers originally developed the scale in a sample of high school juniors and seniors (25). Since then, the scale has been applied by studies across a wide range of samples and has demonstrated high reliability and good validity (35). The scale contains 10 items rated on a 4-

point Likert scale, with response options from 0 (strongly disagree) to 3 (strongly agree). Evaluators calculate scoring of the scale by first reverse scoring the negatively worded items (items 2, 5, 6, 8, 9) and then totalling item scores, resulting in a possible range of 0-30, with higher scores reflecting greater self-esteem. Researchers previously validated a French version of the scale (36).

PROMIS Depression 4a v2.0 and Anxiety 4a v2.0

The PROMIS Depression 4a v2.0 and Anxiety 4a v2.0 scales (26) measure patient-reported depression and anxiety symptoms over the past 7 days. Participants rate four statements for each domain on a 5-point scale ranging from 1 ("Never") to 5 ("Always"). The sum of item scores for each domain yields a score ranging from 4 to 20, which is converted by evaluators into a T-score adjusted to the United States general population (mean = 50, standard deviation [SD] = 10). Higher scores indicate greater severity of depression or anxiety symptoms. The SPIN research team previously validated the English and French versions of PROMIS Depression 4a v2.0 and Anxiety 4a v2.0 in SSc (37).

Statistical Analyses

We calculated descriptive sample statistics as the mean (SD) for continuous variables and frequencies and percentages for categorical variables for the total sample and separately for the English and French-speaking samples.

Confirmatory factor analysis (CFA)

We conducted a CFA to evaluate the single-factor structure of the CD-RISC-10 (19). Item responses for the CD-RISC-10 are ordinal Likert data. We modelled the responses using a weighted least squares estimator, a diagonal weight matrix, and robust standard errors. We used the Tucker-Lewis Index (TLI), Comparative Fit Index (CFI), and Root Mean Square Error of

Approximation (RMSEA) to assess model fit. Well-fitting models are indicated by a TLI and CFI ≥ 0.95 and RMSEA ≤ 0.06 (38), although a CFI of ≥ 0.90 and an RMSEA of ≤ 0.08 (39) are often regarded as indicators of acceptable model fit. We used modification indices to identify pairs of items for which model fit would improve if error estimates were freed to covary and for which there were theoretically justifiable shared method effects (e.g., similar wording) if the original model did not achieve adequate model fit.

DIF analysis

We performed a DIF analysis using the Multiple-Indicator Multiple-Cause (MIMIC) model to identify possible differences in measurement properties between English and French versions of the CD-RISC-10. DIF analysis compares patterns of item responses in subgroups and tests whether individuals with similar levels of a latent construct respond to each item similarly, regardless of group affiliation. MIMIC models for DIF assessment are based on structural equation models, in which the group variable (English versus French) is added to the basic CFA model as an observed variable. Thus, the base MIMIC model consists of the CFA factor model with the additional regression of the latent factor on group to control for group differences on the level of the latent factor. We then identified DIF by first separately regressing items, one at a time, on group. If there was DIF for one or more items in this first step, the item with the largest magnitude of statistically significant DIF was considered to have DIF, and the link between the language group variable and that item was included in the model. In a second step, we again separately regressed remaining items on group one at a time and included the item with the largest DIF in the model. This procedure was repeated until none of the remaining items showed significant DIF. Once all items with significant DIF had been identified, the potential magnitude

of DIF items collectively was evaluated by comparing the difference on the latent factor between language groups in the baseline CFA model and after controlling for DIF.

Because we did not encounter DIF of a meaningful magnitude, item analyses and reliability and convergent validity were done with the whole sample and not separated by language.

Item analyses

We reported means, SDs, item intercorrelations, and item-rest correlations for each item of the CD-RISC-10. The item-rest correlation is the correlation of an item score with the total score after removing the item from the total score. In addition, we examined floor and ceiling effects, defined as ≥ 15% of the participants having the lowest or highest possible score (40).

Reliability and convergent validity

We computed Cronbach's alpha to determine the internal consistency (41) and an intraclass correlation coefficient (ICC) to measure test-retest reliability (42). We chose the ICC as the measure of test-retest reliability because it reflects both the degree of correlation and agreement between measurements (43). We calculated ICC estimates and 95% confidence intervals (CIs) based on absolute-agreement and a 2-way mixed-effects model.

To examine the convergent validity of the CD-RISC-10, we formulated hypotheses on the direction and magnitude of Pearson's correlations with other outcome measures a priori based on existing evidence from convergent validity comparisons for the CD-RISC-10 (21). The magnitude of correlations was interpreted as small ($|r| \leq 0.3$), moderate ($0.3 < |r| < 0.5$), or large ($|r| \geq 0.5$) (44). We hypothesized that all correlations between measures would be moderate to large and that the CD-RISC-10 would be more strongly related to another resilience measure, the RS14, than with other measures.

We conducted the CFA and the DIF using Mplus7 (45). All other statistical analyses we performed using SPSS (Version 29) (46).

Sample Size Calculation

Confirmatory factor analysis

Recommendations for CFA sample size vary. In the present study, we performed a single-factor CFA with 10 indicators using a sample that we expected to include approximately 1,000 participants. This number substantially exceeds the minimum recommended by all established recommendations and standards (47–49) for a sample size necessary to achieve excellent agreement between true model characteristics and estimates.

Convergent validity

Stable estimates of correlations are typically achieved with a sample size of 250 or greater, although smaller correlations require larger samples. To assess a Pearson's correlation with a 95% CI with a width of 0.10, a sample size of ≥ 403 is required for a correlation of 0.30 and ≥ 275 for a correlation of 0.50 (41).

Test-retest reliability

Although an ICC value of 0.70 is considered acceptable for test-retest reliability, a coefficient approaching or exceeding 0.80 is preferable (50). A test-retest sample size of 200 people would be required for a precision level of 95% CI with a width of 0.10 for an estimated ICC of 0.80 (32). Therefore, we aimed for a retest sample size of 200 participants.

RESULTS

Sample Characteristics

In total, 962 participants completed all items of the CD-RISC-10, RS14, Rosenberg Self-esteem Scale, and PROMIS Depression 4a v2.0 and Anxiety 4a v2.0. Sociodemographic and

disease characteristics were similar across English- and French-language samples, as shown in Table 1. The total sample consisted of 848 (88%) female participants with a mean age of 61.1 years (SD = 11.6). Mean time since onset of first non-Raynaud's symptoms was 15.7 years (SD = 9.6), and 345 individuals (36%) had diffuse SSc. Participants were from France (37%), Canada (26%), the United States (25%), the United Kingdom (9%), and Australia (2%). Just over half (N = 549, 57%) completed assessments in English.

CD-RISC Measurement Properties

Confirmatory factor analysis

The results of the CFA are shown in Table 2. In the initial CFA, the model fit for the hypothesized single-factor model was somewhat suboptimal (TLI = 0.97, CFI = 0.98, RMSEA = 0.11). Our examination of modification indices showed that freeing the error terms of Items 1 and 2 to covary would improve model fit. Items 1 and 2 evaluate how well people can adapt to changes or deal with things coming their way, which are closely related experiences. Therefore, we refitted the model to allow these items' error terms to covary, resulting in a good fit to the data (TLI = 0.99, CFI = 0.99, RMSEA = 0.08).

DIF analysis

The one-factor model, which included regression of the latent resilience factor on language, demonstrated good fit (CFI = 0.99, TLI = 0.99, RMSEA = 0.07). Table 3 shows baseline CFA model parameters before correcting for DIF. We identified six items with statistically significant language-based DIF. Compared to English-language participants, French-language participants had higher scores than would be expected on item 3 (β = 0.14, 95% CI 0.04 to 0.23) and item 9 (β = 0.13, 95% CI 0.04 to 0.21) and lower scores on item 1 (β = -0.17, 95% CI -0.27 to -0.08), item 4 (β = -0.12, 95% CI -0.23 to -0.03), item 5 (β = -0.22, 95% CI -

0.32 to -0.14), and item 6 (β = -0.17, 95% CI -0.26 to -0.08). The difference between the two language groups (English – French) on the mean latent factor level was not meaningfully different between the model with DIF adjustment (standardized mean differences [SMD] = 0.31, 95% CI 0.17 to 0.43) and without adjustment (SMD = 0.26, 95% CI 0.13 to 0.37). See Table 3.

Item analysis

Table 4 includes the mean item and total CD-RISC-10 scores for the full sample. Mean item scores ranged from 2.5 for Item 4 ("Having to cope with stress can make me stronger") to 3.1 for Item 1 ("I am able to adapt when changes occur"). Correlations between items ranged from r = 0.44 (p < 0.001, Items 3 and 8) to r = 0.73 (p < 0.001, Items 1 and 2). Item-rest correlations ranged from r = 0.62 (item 8) to r = 0.80 (item 2). There were 2 participants (0.2%) with the lowest possible score (0) on the scale and 48 (5.0%) with the highest possible score (40). Supplementary Table S1 shows item response frequencies.

Reliability

Cronbach's alpha was 0.93 (95% CI 0.92 to 0.94). We assessed test-retest reliability in a subsample of 230 participants, whose characteristics were similar to the full sample (see Table S2 in supplementary material for subsample sociodemographic and medical data), resulting in an ICC of 0.80 (95% CI 0.75 to 0.85), indicating good one- to two-week test-retest reliability.

Convergent validity

As shown in Table 5, there were moderate to large correlations between the CD-RISC-10 and measures of resilience (RS14), self-esteem (Rosenberg Self-esteem Scale), depression (PROMIS Depression 4a v2.0), and anxiety (PROMIS Anxiety 4a v2.0). All correlations were consistent with convergent validity hypotheses.

DISCUSSION

We tested the unidimensional structure of the CD-RISC-10, examined whether there were meaningful differences in measurement properties between English- and French-language versions of the scale, and evaluated internal consistency, test-retest reliability, and convergent validity. We found that the hypothesized single-factor structure of the scale fit well, supporting the use of a single total score for the CD-RISC-10 scale. There was statistically significant DIF for six items between English- and French-language participants. However, the cumulative effect of DIF was minimal and did not meaningfully influence estimates of differences in resilience between English- and French-language respondents in unadjusted (SMD = 0.26, 95% CI 0.17 to 0.43) versus DIF-adjusted models (SMD = 0.31, 95% CI 0.17 to 0.43), allowing us to conclude that CD-RISC-10 scores of English- and French-language participants can be compared and aggregated without concerns of language-based bias.

Internal consistency reliability (α = 0.93, 95% CI 0.92 to 0.94) and test-retest reliability (ICC = 0.80, 95% CI 0.75 to 0.85) were good, and there were no floor or ceiling effects. In addition, indices of convergent validity were consistent with study hypotheses; the CD-RISC-10 was correlated moderately to highly with all measurements (Rosenberg Self-esteem: r = 0.69; PROMIS Depression: r = -0.60; PROMIS Anxiety: r = -0.57) and the magnitude of correlation with the RS14, another measure of resilience, was the largest (r = 0.78).

Researchers initially validated the CD-RISC-10 in a sample of 1,743 undergraduates from the United States (19). The present study is the first to validate the scale among people with SSc and, to our knowledge, the first comparison of measurement properties between English- and French-language versions. The overall outcomes of our study were consistent with results from previous studies that examined measurement properties of the CD-RISC Scale in other

samples, including among people with chronic diseases (19,22,23). We believe that this is the first study to examine language-based DIF in the CD-RISC-10.

The findings of our study have important implications for research. We found that the CD-RISC-10 provides a valid and reliable method for evaluating resilience in individuals with SSc. A previous study (11) used latent profile analysis and found that some people with SSc report positive mental health, despite experiencing severe disease manifestations and high levels of pain, fatigue, and sleep disturbance, which could be associated with resilience (12,13). Resilience, using the CD-RISC-10, should be compared between classes of people with SSc who differ in mental health despite having similar disease burdens to elucidate further the possible role of resilience in the mental health of people with SSc. We plan to conduct these analyses in a second study, using a sample from the SPIN Cohort. In addition, researchers could conduct similar analyses in other chronic illness populations, and validation of the CD-RISC-10 in people with SSc may support measurement of resilience in other similar autoimmune rheumatic diseases.

The results of our DIF analysis demonstrate the comparability and combinability of CD-RISC-10 scores across English and French languages in SSc, presenting opportunities for broader utilization in international patient cohorts, including the SPIN Cohort (28,29). Among people with chronic medical conditions, intervention strategies that improve resilience and adaptive coping have been found to be effective in improving psychological adaptation and reducing symptom burden (16). The CD-RISC-10 presents a valid outcome measure for testing similar interventions in SSc.

Our study has several notable strengths, including its international cohort with participants from 47 clinical sites, its large sample size, its assessment of test-retest reliability,

and the comparison of measurement properties in English- and French-language participants with SSc. There are also limitations to consider. First, the SPIN Cohort is a convenience sample of people with SSc receiving treatment at SPIN recruiting centres who can complete online measures, as SPIN collects data digitally only. However, a comparison with the European Scleroderma Trials and Research and Canadian Scleroderma Research Group cohorts indicated broad comparability of participant characteristics, which supports generalizability in SSc (28). Second, the examination of DIF was limited to English- and French-language versions of the CD-RISC-10 and adults with SSc, and the generalisability of the results to other populations is not known. Third, the MIMIC approach to DIF evaluates uniform, but not non-uniform, DIF.

Overall, the results of this study indicate that the CD-RISC is a valid and reliable measure of resilience in English and French languages in SSc, supporting its use as an outcome measure to assess resilience in this population. In addition, we found DIF to be negligible, suggesting that CD-RISC-10 scores are comparable across English- and French-language versions.

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Table 1. Sample sociodemographic and disease characteristics for the full sample and by assessment language

	Full Sample (N = 962)		English (N = 549)		French (N = 413)	
	N	Mean (SD) or N (%)	N	Mean (SD) or N (%)	N	Mean (SD) or N (%)
Sociodemographic Variables						
Age (years)	962	61.1 (11.6)	549	62.4 (10.7)	413	59.4 (12.5)
Female sex	962	848 (88%)	549	488 (89%)	413	360 (87%)
White race or ethnicity	955	816 (85%)	546	471 (86%)	409	345 (84%)
Country	962		549		413	
Canada		254 (26%)		197 (36%)	57	57 (14%)
United States		245 (25%)		245 (45%)		
United Kingdom		85 (9%)		85 (16%)		
France		358 (37%)		2 (<1%)	356	356 (86%)
Australia		20 (2%)		20 (4%)		
Language (English)	962	549 (57%)				
Education (years)	960	15.1 (3.6)	549	15.6 (3.0)	411	14.4 (4.1)
Marital status single	960	106 (11%)	549	54 (10%)	411	52 (13%)
BMI	962	25.1 (5.2)	549	25.6 (5.4)	413	24.4 (5.0)
Disease Characteristics						
Time since first non-Raynaud's symptom	892	15.7 (9.6)	505	17.6 (9.9)	387	13.3 (8.8)
Diffuse subtype	955	345 (36%)	543	221 (41%)	412	124 (30%)
Gastrointestinal involvement	962	828 (86%)	549	480 (88%)	413	348 (84%)
Digital ulcers	914	124 (14%)	513	72 (14%)	401	52 (13%)
Current tendon friction rubs	846	86 (10%)	468	46 (10%)	378	40 (11%)
Large joint contractures (moderate or severe)	891	98 (11%)	499	41 (8%)	392	57 (15%)
Small joint contractures (moderate or severe)	906	224 (25%)	504	107 (21%)	402	117 (29%)
History of SSc renal crisis	945	40 (4%)	539	25 (5%)	406	15 (4%)
Interstitial lung disease	941	296 (32%)	534	159 (30%)	407	137 (34%)
Pulmonary arterial hypertension	931	70 (8%)	525	41 (8%)	406	29 (7%)
Primary biliary cirrhosis	926	18 (2%)	527	10 (2%)	399	8 (2%)
Any overlap syndrome[a]	962	195 (20%)	549	113 (21%)	413	82 (20%)
Psychological Assessments						
CD-RISC-10	962	27.8 (7.3)	549	28.6 (7.2)	413	26.8 (7.18)
RS14	962	78.6 (15.1)	549	80.2 (14.3)	413	76.6 (15.9)
Rosenberg Scale	962	20.8 (5.5)	549	21.6 (5.7)	413	19.9 (5.2)
PROMIS Depression	962	51.5 (9.2)	549	50.6 (9.0)	413	52.8 (9.4)
PROMIS Anxiety	962	53.6 (9.8)	549	52.8 (9.6)	413	54.6 (10.0)

SD = standard deviation; CD-RISC-10 = 10-item Connor-Davidson Resilience Scale; RS14 = 14-item Resilience-Scale; PROMIS = Patient Reported Outcomes Measurement Information System.
[a]Participant had at least one of rheumatoid arthritis, Sjogren's syndrome, systemic lupus erythematosus, or idiopathic inflammatory myositis.

Table 2. Factors Loadings of the CD-RISC-10

Item[a]	**CFA Factor Loading[b]**	**95% CIs**
1. I am able to adapt when changes occur	0.76	0.73 to 0.80
2. I can deal with whatever comes my way	0.87	0.85 to 0.89
3. I try to see the humorous side of things when I am faced with problems	0.74	0.71 to 0.77
4. Having to cope with stress can make me stronger	0.76	0.74 to 0.80
5. I tend to bounce back after illness, injury, or other hardships	0.84	0.82 to 0.86
6. I believe I can achieve my goals, even if there are obstacles	0.85	0.83 to 0.87
7. Under pressure, I stay focused and think clearly	0.83	0.80 to 0.85
8. I am not easily discouraged by failure	0.70	0.67 to 0.73
9. I think of myself as a strong person when dealing with life's challenges and difficulties	0.87	0.85 to 0.89
10. I am able to handle unpleasant or painful feelings like sadness, fear, and anger	0.83	0.81 to 0.86

[a]On a 5-point scale, where 0 = not true at all and 4 = true nearly all the time.
[b]Error terms of Items 1 and 2 were freed to covary.

Table 3. Factor loadings for the CD-RISC-10 in combined English and French samples and DIF evaluation

Item	Base model[a]		DIF corrected model[b]	
	CFA Factor Loading	**95% CIs**	**CFA Factor Loading**	**95% CIs**
1. I am able to adapt when changes occur	0.77	0.74 to 0.79	0.77	0.74 to 0.79
2. I can deal with whatever comes my way	0.87	0.85 to 0.88	0.87	0.85 to 0.88
3. I try to see the humorous side of things when I am faced with problems	0.74	0.70 to 0.76	0.74	0.70 to 0.76
4. Having to cope with stress can make me stronger	0.76	0.74 to 0.79	0.76	0.74 to 0.79
5. I tend to bounce back after illness, injury, or other hardships	0.84	0.82 to 0.86	0.84	0.82 to 0.86
6. I believe I can achieve my goals, even if there are obstacles	0.85	0.83 to 0.87	0.85	0.83 to 0.87
7. Under pressure, I stay focused and think clearly	0.82	0.80 to 0.84	0.82	0.80 to 0.84
8. I am not easily discouraged by failure	0.70	0.66 to 0.72	0.70	0.66 to 0.72
9. I think of myself as a strong person when dealing with life's challenges and difficulties	0.87	0.85 to 0.89	0.87	0.85 to 0.89
10. I am able to handle unpleasant or painful feelings like sadness, fear, and anger	0.83	0.81 to 0.85	0.83	0.81 to 0.85
Direct effects on items attributable to the French language				
1. I am able to adapt when changes occur			-0.17	-0.27 to -0.08
3. I try to see the humorous side of things when I am faced with problems			0.14	0.04 to 0.23
4. Having to cope with stress can make me stronger			-0.12	-0.23 to -0.03
5. I tend to bounce back after illness, injury, or other hardships			-0.22	-0.32 to -0.14
6. I believe I can achieve my goals, even if there are obstacles			-0.17	-0.26 to -0.08
9. I think of myself as a strong person when dealing with life's challenges and difficulties			0.13	0.04 to 0.21
Standardized mean difference (English – French) on latent resilience factor	0.26	0.13 to 0.37	0.31	0.17 to 0.43

CFA = confirmatory factor analysis; CI = confidence interval; DIF = differential item functioning.
[a]Unstandardized model with fixed variance, regression of the latent resilience factor on language, not corrected for DIF.
[b]Unstandardized model with fixed variance, regression of the latent resilience factor on language, corrected for DIF on items 1, 3, 4, 5, 6, and 9.

Table 4. Characteristics of the CD-RISC-10

Item	**Mean (SD) Score[a]**	**Item-Rest Correlation**
1. I am able to adapt when changes occur	3.1 (0.84)	0.70
2. I can deal with whatever comes my way	2.9 (0.86)	0.80
3. I try to see the humorous side of things when I am faced with problems	2.7 (0.97)	0.67
4. Having to cope with stress can make me stronger	2.5 (1.00)	0.69
5. I tend to bounce back after illness, injury, or other hardships	3.0 (0.88)	0.75
6. I believe I can achieve my goals, even if there are obstacles	2.8 (0.88)	0.76
7. Under pressure, I stay focused and think clearly	2.6 (0.97)	0.75
8. I am not easily discouraged by failure	2.6 (0.98)	0.62
9. I think of myself as a strong person when dealing with life's challenges and difficulties	3.0 (0.92)	0.78
10. I am able to handle unpleasant or painful feelings like sadness, fear, and anger	2.7 (0.97)	0.75
Total score	27.8 (7.3)	

[a]On a 5-point scale, where 0 = not true at all and 4 = true nearly all the time.

Table 5. Correlation of measures with the CD-RISC-10 to assess convergent validity

Convergent Validity[a]	**Pearson correlation**	**95% CIs**	**Hypothesis Confirmed**
Large positive correlation			
Resilience (RS14)	0.78	0.76 to 0.81	Yes
Moderate to large positive correlation			
Self-esteem (Rosenberg Self-esteem Scale)	0.69	0.65 to 0.72	Yes
Moderate to large negative correlation			
Depression (PROMIS Depression)	-0.60	-0.64 to -0.56	Yes
Anxiety (PROMIS Anxiety)	-0.57	-0.61 to -0.52	Yes

CI = confidence interval; RS14 = 14-item Resilience-Scale; PROMIS = Patient Reported Outcomes Measurement Information System.

[a]Magnitude of correlations was defined as small = $|r| \leq 0.3$, moderate = $0.3 < |r| < 0.5$, and large = = $|r| \geq 0.5$.

SUPPLEMENTARY MATERIAL

Table S1. Item responses distributions for each item of the CD-RISC-10 (N = 962)

Item	Item responses				
	not true at all (0)	**rarely true (1)**	**sometimes true (2)**	**often true (3)**	**true nearly all the time (4)**
	N (%)	**N (%)**	**N (%)**	**N (%)**	**N (%)**
1. I am able to adapt when changes occur	6 (<1%)	24 (3%)	209 (22%)	400 (42%)	323 (34%)
2. I can deal with whatever comes my way	12 (1%)	22 (2%)	254 (26%)	404 (42%)	268 (28%)
3. I try to see the humorous side of things when I am faced with problems	18 (2%)	86 (9%)	283 (29%)	363 (38%)	212 (22%)
4. Having to cope with stress can make me stronger	27 (3%)	124 (13%)	320 (33%)	349 (36%)	142 (15%)
5. I tend to bounce back after illness, injury, or other hardships	9 (1%)	43 (5%)	213 (22%)	415 (43%)	282 (29%)
6. I believe I can achieve my goals, even if there are obstacles	9 (1%)	49 (5%)	277 (29%)	407 (42%)	220 (23%)
7. Under pressure, I stay focused and think clearly	26 (3%)	87 (9%)	272 (28%)	403 (42%)	174 (18%)
8. I am not easily discouraged by failure	24 (3%)	95 (10%)	308 (32%)	359 (37%)	176 (18%)
9. I think of myself as a strong person when dealing with life's challenges and difficulties	12 (1%)	52 (5%)	200 (21%)	392 (41%)	306 (32%)
10. I am able to handle unpleasant or painful feelings like sadness, fear, and anger	25 (3%)	71 (7%)	274 (29%)	391 (41%)	201 (21%)

Table S2. Sociodemographic and disease characteristics for retest sample (N = 230)

	Test-Retest Sample (N = 230)	
	N	**Mean (SD) or N (%)**
Sociodemographic Variables		
Age (years)	230	62.1 (11.2)
Female sex	230	199 (87%)
White race or ethnicity	229	203 (89%)
Country	230	
Canada		62 (27%)
United States		75 (33%)
United Kingdom		19 (8%)
France		69 (30%)
Australia		5 (2%)
Language (English)	230	147 (64%)
Education (years)	230	15.2 (3.3)
Marital status single	230	27 (12%)
BMI	230	25.6 (5.5)
Disease Characteristics		
Time since first non-Raynaud's symptom	211	15.5 (8.4)
Diffuse subtype	230	83 (36%)
Gastrointestinal involvement	230	202 (88%)
Digital ulcers	224	27 (12%)
Current tendon friction rubs	205	18 (9%)
Large joint contractures (moderate or severe)	215	22 (10%)
Small joint contractures (moderate or severe)	220	45 (21%)
History of SSc renal crisis	226	8 (4%)
Interstitial lung disease	226	67 (30%)
Pulmonary arterial hypertension	224	20 (9%)
Primary biliary cirrhosis	223	3 (1%)
Overlap syndrome[a]	230	43 (19%)
Psychological Assessments		
CD-RISC-10	230	28.1 (7.0)
RS14	230	79.62 (14.8)
Rosenberg Scale	230	20.9 (5.8)
PROMIS Depression	230	51.4 (9.0)
PROMIS Anxiety	230	53.4 (9.2)

SD = standard deviation; CD-RISC-10 = 10-item Connor-Davidson Resilience Scale; RS14 = 14-item Resilience-Scale; PROMIS = Patient Reported Outcomes Measurement Information System.

[a]Participant had at least one of rheumatoid arthritis, Sjogren's syndrome, systemic lupus erythematosus, or idiopathic inflammatory myositis.

2.2. Connecting Text

Our study findings provide robust evidence supporting the use of the CD-RISC-10 (30) within the SSc population. Through a comprehensive examination involving 962 participants, our study demonstrated that the CD-RISC-10 exhibited good reliability and validity, with comparable measurement properties for both English and French-language participants.

A single-factor structure was supported by confirmatory factor analysis (CFA) (Tucker Lewis Index [TLI] = 0.99, Comparative Fit Index [CFI] = 0.99, Root Mean Square Error of Approximation [RMSEA] = 0.08, 90% confidence interval [CI] 0.07 to 0.09). Furthermore, no meaningful DIF was found, indicating measurement equivalence across language groups. Internal consistency was high ($\alpha = 0.93$, 95% CI 0.92 to 0.94), and correlations with other measures of psychological functioning supported our hypotheses ($|r| = 0.57$ to 0.78). Test-retest reliability was also good (intraclass correlation coefficient [ICC] = 0.80, 95% CI 0.75 to 0.85) in a subsample of 230 participants.

As the first study to validate a resilience measure in SSc, our research establishes a vital foundation for future investigations into resilience within the SSc population. The CD-RISC-10 can now be used to evaluate resilience in people with SSc, including in international studies with English- and French-language participants. However, despite this progress, our understanding of resilience in SSc remains limited due to a lack of comprehensive research. Exploring resilience and its associations within SSc is crucial, as studies in other chronic diseases have shown the positive impact of resilience on mental health outcomes (23,41,42).

A previous study by Wojeck et al. (39) conducted a latent class analysis and identified 5 classes based on patient-reported outcomes. Their findings revealed a pattern of individuals with SSc that report positive mental, despite experiencing high levels of pain, fatigue, and sleep

disturbance. Their results indicate that this pattern might be because of resilience and its potential protective effect on mental well-being.

Building upon these preliminary insights, the subsequent manuscript: "*The Association of Resilience and Positive Mental Health in Systemic Sclerosis: A Scleroderma Patient-centered Intervention Network (SPIN) Cohort Cross-Sectional Study*," aims to further examine the role of resilience in individuals with SSc. We sought to re-identify the five classes found by Wojeck et al. (39) and analyze resilience levels across the classes, using the validated CD-RISC (30) as a comprehensive measure of resilience.

CHAPTER 3

Manuscript 2

3.1. The Association of Resilience and Positive Mental Health in Systemic Sclerosis: A Scleroderma Patient-centered Intervention Network (SPIN) Cohort Cross-Sectional Study

Submitted paper:

Neyer MA, Henry RS, Carrier ME, et al. The association of resilience and positive mental health in systemic sclerosis: a Scleroderma Patient-centered Intervention Network (SPIN) Cohort cross-sectional study.

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INTRODUCTION

Systemic sclerosis (SSc, scleroderma) is a rare chronic autoimmune disorder characterized by fibrosis and vascular abnormalities of the skin, internal organs, and blood vessels (1,2). People with SSc experience substantially lower health-related quality of life compared to the general population (3) and individuals with other rheumatic diseases (4). Common challenges faced by people with SSc include fatigue, pain, difficulty sleeping (1,5–11) and mental health concerns, including depression and anxiety (12–16).

A recent cross-sectional study (17) of more than 2,000 individuals with SSc in the Scleroderma Patient-centered Intervention Network (SPIN) Cohort investigated clusters of commonly experienced patient-important outcomes and found five latent classes based on fatigue, pain, sleep disturbance, anxiety symptoms, and depression symptoms. The first four classes separated participants into "low," "normal," "high," and "very high" symptom severity classes. The levels of patient-reported symptoms in these classes were strongly associated with overall disease severity and specific disease manifestations, including gastrointestinal symptoms, small and large joint contractures, and tendon friction rubs. Members of a fifth class had similarly high levels of fatigue, pain, and sleep disturbance scores, as the "high" class, and disease burden and symptom manifestations were also similar; they, however, reported low levels of anxiety and depression symptoms ("high/low" class). The difference in mental health symptoms between people in this class and others with similarly severe SSc might be explained by resilience.

Resilience has been defined as positive adjustment or the ability to preserve or restore mental health despite adverse circumstances, such as living with a burdensome and potentially fatal chronic illness (18,19). Psychological factors associated with resilience include self-efficacy, self-esteem, optimism, hardiness, and a sense of self-empowerment and mastery (20,21). Resilience can be measured

through self-report measures, including the 10-item Connor-Davidson Resilience Scale (CD-RISC-10) (22), which we recently validated among individuals with SSc (23).

People with medical conditions who score higher on resilience measures also report lower levels of anxiety and depression symptoms and better quality of life (20,21,24). A systematic review of over 200 studies found that interventions that promote resilience can improve resilience and other patient-important outcomes (25). However, only two small studies (N < 50) (26,27) have evaluated resilience in SSc, and evidence is needed to evaluate whether resilience may play a role in maintaining positive mental health in SSc.

The objectives of this study were to (1) evaluate resilience across the five previously delineated patient-reported outcome-based classes of people with SSc using scores on the CD-RISC-10 (22) and (2) compare resilience levels between members of the "high" (high fatigue, pain, sleep disturbance and SSc disease severity and high mental health symptoms) and "high/low" (high fatigue, pain, sleep disturbance and SSc disease severity but low mental health symptoms) classes, as well as the other classes, controlling for sociodemographic and disease variables. We hypothesized that resilience would be higher among participants in the "high/low" class compared to the "high" symptom class.

METHODS

We evaluated cross-sectional data collected from participants in the SPIN Cohort (28,29) during routine online assessments. First, to assign latent class membership, we applied Wojeck et al.'s latent profile analysis, which was done with SPIN Cohort baseline data collected between 2014 and 2020 in our study sample of follow-up assessments conducted between August 2022 and January 2023. Second, we compared resilience across classes, adjusting for sociodemographic and disease variables. We posted a protocol online prior to initiating the study (available at: https://osf.io/dx3b6/).

Participants and Procedure

The SPIN Cohort (28,29) is a convenience sample of participants from 7 countries: Australia, Canada, France, Mexico, Spain, the United Kingdom, and the United States. Eligible participants are recruited at 53 SPIN clinical sites during regular physician visits and must be aged ≥ 18 years, fluent in English, French, or Spanish, have access to and be able to respond to questionnaires via the Internet and meet the 2013 American College of Rheumatology/European League Against Rheumatism criteria for systemic sclerosis (30) verified by a SPIN site physician. Participants are invited to participate in the SPIN Cohort by attending physicians or nurse coordinators. Onsite staff obtain written informed consent and submit an electronic medical form to enrol participants. Participants then receive an email with a unique, secure link to complete baseline measurements online in English, French, or Spanish. SPIN conducts subsequent online assessments at 3-month intervals (28). Analyses in the present study included SPIN participants who completed the CD-RISC-10 and the domains of Patient-reported Outcomes Measurement Information System (PROMIS)-29 v2.0 (31) for fatigue, pain interference, sleep disturbance, anxiety symptoms, and depression symptoms in English or French during a regular assessment between August 2022 and January 2023, when the CD-RISC-10 was included in the SPIN Cohort since the CD-RISC-10 was only administered in English and French.

The SPIN Cohort study was approved by the Research Ethics Committee of the Centre intégré universitaire de santé et de services sociaux du Centre-Ouest-de-l'Île-de-Montréal (#MP-05-2013-150) and by the ethics committees of all recruiting sites. The present study was approved as an amendment.

Measures

At baseline, SPIN Cohort participants report sociodemographic variables, including race or ethnicity, country, language, education, and marital status. Physician-reported data from the baseline data assessment include age, sex, height, weight, date of initial onset of non-Raynaud phenomenon symptoms, SSc subtype, presence of gastrointestinal (esophageal; stomach; intestinal) involvement, digital ulcers anywhere on the fingers, current tendon friction rubs, presence of large or small joint contractures, presence of pulmonary arterial hypertension, and presence of interstitial lung disease.

CD-RISC-10

CD-RISC-10 (22) scores reflect multiple aspects of resilience, including flexibility, self-efficacy, emotion regulation, optimism, and the ability to maintain focus under stress. Items assess the ability to tolerate and cope with experiences such as change, personal problems, illness, pressure, failure, and painful feelings (22). Item response options range from 0 (not true at all) to 4 (true nearly all the time). Participants respond to each statement in reference to the previous month. Item scores are summed (possible total scores 0 to 40, with higher scores reflecting greater resilience). The correlation of the CD-RISC-10 with the full 25-item version of the CD-RISC was 0.92 in a sample of N > 500 undergraduates (32). We previously validated the CD-RISC-10 in English- and French-speaking SSc patients (N = 962) (23). The results of that study supported a single-factor structure, internal consistency was high (α =0.93, 95% confidence interval 0.92 to 0.94), and we found that correlations with other measures of psychological functioning were consistent with study hypotheses. The scale showed good 1–2-week test-retest reliability (ICC = 0.80, 95% confidence interval 0.75 to 0.85) in a subsample of 230 participants. In addition, we found DIF to be negligible, suggesting that CD-RISC-10 scores are comparable across English- and French-language versions.

PROMIS-29 (depression, anxiety, fatigue, sleep disturbance, pain interference domains)

PROMIS-29 v2.0 (31) domains assess patient-reported outcomes over the last 7 days. Items are rated on a 5-point Likert scale. Domain scores are obtained by totalling item scores (range 4 to 20) and then converting total scores into a T-score adjusted to the United States general population (mean = 50, standard deviation [SD] = 10). Higher scores in each domain represent greater depression symptoms, anxiety symptoms, fatigue, sleep disturbance, or pain interference. The English and French versions of all PROMIS-29v2.0 domains have been validated in the SPIN Cohort (33). Additional information on individual domain items is reported in the Supplemental Methods.

Statistical Analyses

Assignment of Class Membership and Descriptive Statistics

We applied the latent profile model used by Wojeck et al. (17) to our sample of people with SSc to re-identify the five classes previously found based on levels of fatigue, pain, sleep disturbance, anxiety symptoms, and depression symptoms, specifying the analysis to extract a 5-class solution. In their study, Wojeck et al. identified this model as the best-fitting model with the optimal number of classes based on the Akaike Information Criteria, Bayesian Information Criteria, Bootstrapped Likelihood Ratio Test, sample size adjusted Bayesian Information Criteria, and the Vuong-Lo-Mendell-Rubin likelihood ratio test model fit indicators and considerations of clinical interpretability. We confirmed that the pattern of increasing patient-reported outcomes was observed across four classes in our sample and that there was, similarly, a fifth class with high fatigue, pain, and sleep disturbance but low anxiety and depression symptoms. We performed the latent class analysis in Mplus version 8.3 (34).

We computed descriptive statistics of sociodemographic variables and disease characteristics for the total sample and each of the five classes separately.

Comparison of Resilience Between Members of Five Classes

We calculated mean total CD-RISC resilience scores and mean item scores for members of each class. We used multiple linear regression to compare CD-RISC resilience scores across classes, controlling for sociodemographic and disease variables. The "high/low" class was designated as the reference class to facilitate comparisons. We standardized continuous predictor variables prior to entering variables into the model. We report unstandardized model regression coefficients with 95% confidence intervals (CIs). We conducted all regression analyses in R version 4.3.0 (35), RStudio Version 2023.03.0+386 (36).

Before conducting regression analyses, we used multiple imputations via chained equations using the mice package (37) in R to address missing covariate data. We generated 20 imputed datasets using 15 cycles per dataset using all variables in the main regression model in the mice procedure. We included categorical variables in the mice procedure with all possible levels for each variable). We performed collapsing of variable categories (e.g., race or ethnicity, marital status) and standardization (e.g., age) after the imputation procedure.

We additionally conducted a complete case sensitivity analysis of our main model for resilience by including only participants without any missing covariate data.

RESULTS

Sample Characteristics

Sample Characteristics

A total of 1466 SPIN Cohort participants completed SPIN measures at least once in the year prior to initiating the present study. Of these, 1098 logged in to complete assessments during the study, and 1054 completed all items for the CD-RISC-10 and PROMIS-29 v2.0 fatigue, pain interference, sleep disturbance, anxiety symptoms, and depression symptom

domains. Of the 1054 participants, 926 (88%) were female, and the mean age was 60.9 years (SD = 11.7). Most participants were white (N = 764, 86%). Participants were from France (N = 392, 37%), the United States (N = 277, 26%), Canada (N = 269, 26%), the United Kingdom (N = 95, 9%), and Australia (N = 21, 2%). Mean time since onset of non-Raynaud's symptoms was 15.7 years (SD = 9.6), and 380 individuals (36%) had diffuse SSc. See Table 1.

Latent Classes

We re-identified the 5 latent classes previously found by Wojeck et al. (17) based on patient-reported outcomes (fatigue, pain interference, sleep disturbance, anxiety symptoms, and depression symptoms) and verified that the 5 classes were similarly characterized by 4 classes with “low,” “normal,” “high,” and “very high,” levels of all outcomes plus a distinct fifth class with high, fatigue, pain interference, and sleep disturbance and low anxiety and depression symptoms (“high/low”). Characteristics of members of the 5 classes in the present study and the study by Wojeck et al. (17) were similar (Supplemental Table 2.1).

Resilience

CD-RISC-10 Scores by Class

Table 2 shows total CD-RISC-10 resilience score and item scores for the full sample and each class separately. Mean total score for the full sample was 27.7 (SD = 7.3). Resilience scores decreased from the "low" class to the "very high" class with an average decrease of 4.7 points at each step (range 4.5 to 5.2 points). For the “high/low” class, the mean total score was 30.2 (SD = 6.1), which was substantially higher than the mean total score for the “high” class (24.2, SD = 5.9; difference = 6.0, standardized mean difference = 0.82). For each of the 10 CD-RISC-10 items, the “high/low” class scored higher than the “high” class by 0.5 to 0.7 points.

Multiple Linear Regression Analysis

Regression results are presented in Table 3 for unadjusted and adjusted multiple regression models. Consistent with the descriptive analyses, compared to the “high/low” class, resilience scores decreased consistently from the “low” (2.9 points higher, 95% CI 1.7 to 4.1 higher) to the “very high” class (11.1 points lower, 95% CI 9.5 to 12.6 lower). Mean resilience score for the “high” class was 6.0 points (95% CI 4.9 to 7.1) lower than the “high/low” class. Supplemental Table 2 shows multiple linear regression results with all covariate parameters. Results of the complete case analysis were similar to the imputed multiple linear regression with the full sample (see Supplemental Table 3).

DISCUSSION

We evaluated resilience in 5 classes of people with SSc defined by levels of patient-important outcomes, including fatigue, pain interference, sleep disturbance, anxiety and depression symptoms. Levels of impairment increased for all outcomes across 4 of these classes (“low,” “normal,” “high,” “very high”), as did indicators of overall SSc severity and prevalence of SSc symptoms. In the fifth class, “high/low,” SSc severity and fatigue, pain interference, and sleep disturbance outcomes were similar to the “high” class, but anxiety and depression symptoms were similar to the “low” class. Across the “low,” “normal,” “high,” and “very high” classes, resilience was closely tied to disease severity and all patient-reported outcomes. The “low” class exhibited the highest resilience (mean = 33.2, SD = 5.3), whereas the "very high" class, characterized by the highest SSc symptom burden and worst patient-reported outcomes, displayed the lowest resilience (mean = 19.0, SD = 7.9). The fifth subgroup deviated from this pattern. Resilience scores among people in the “high/low” class (mean = 30.2, SD = 6.1) were similar to the “low” and “normal” classes, despite symptom severity and fatigue, pain interference, and sleep disturbance outcomes that were similar to the “high” class. In the multiple

regression analysis that controlled for sociodemographic and disease variables, resilience in the "high" class was significantly lower compared to the "high/low" class (SMD = 0.83, 95% CI 0.67 to 0.98).

Our finding that perceived resilience decreases with increasing self-reported disease burden is consistent with the definition of resilience. Resilience reflects the ability to adapt despite adverse circumstances (18,19). However, if the magnitude of adverse circumstances increases, it becomes more difficult to adapt, and thus, perceived resilience is lower. As we found in the present study in SSc, studies in other diseases have also reported that patient-reported outcomes are associated with resilience (38–41). In two studies of participants in a cohort of cancer outpatients receiving chemotherapy, lower resilience was associated with higher fatigue, sleep disturbance, pain, symptoms of depression and anxiety and lower levels of energy and cognitive function (N = 957 and 1326) (38,39) In inflammatory bowel disease lower resilience scores were correlated with higher disease activity and lower quality of life (N = 229) (40). Similarly, in Parkinson's disease, lower resilience was linked to higher fatigue, disability, apathy and lower quality of life (N = 83) (41).

Our finding that there were substantial differences in resilience among some individuals with SSc with the same high levels of disease severity and that those differences were associated with differences in mental health is also consistent with how resilience is understood and research from other diseases. From a conceptual perspective, high levels of resilience can protect against adverse mental health outcomes and preserve positive mental health (18,19). Therefore, people with high resilience would be expected to have better mental health. A 2018 meta-analysis (42) of 55 studies (N = 15,003) of people with a range of somatic illnesses found that, overall, resilience scores were correlated with mental health scores (r = 0.43, 95% CI 0.39 to

0.48). Similarly, a 2021 systematic review of resilience in adults with cancer (20) found that higher resilience scores were consistently linked to lower anxiety (15 studies, 2329 participants) and depression symptom scores (12 studies, N = 2554).

There is a substantial amount of evidence that establishes an association between resilience and mental health, but much less is known about the specific factors that contribute to the development of resilience and the impact of those factors on mental health in the context of SSc. Future research should focus on learning how individuals with high and low resilience cope with their disease. Investigating people with SSc who have high symptom burden and low anxiety and depression ("high/low" class) and high symptom burden and high anxiety and depression ("high" class) could provide valuable insights into perceptions of resilience, its development, and the identification and implementation of coping strategies within each group. Identifying effective strategies would facilitate the development of interventions that promote resilience. A systematic review of over 200 studies found that interventions that promote resilience can improve resilience and other patient-important outcomes in other disease contexts (25).

Our study has several important strengths, including its international cohort and large sample size. There are also limitations to consider. First, the SPIN Cohort is a convenience sample of people with SSc receiving treatment at SPIN recruiting centres who can complete online measures, as SPIN collects data via the internet only. However, a comparison with the European Scleroderma Trials and Research and Canadian Scleroderma Research Group cohorts indicated that participant characteristics were similar (28). Second, the study relies on self-report measures for assessing resilience and mental health symptoms. Self-report measures are subject to biases, such as social desirability or recall bias, which may affect accuracy (43). We used

measures that were previously validated in SSc, though, which may mitigate this concern (23,33). Third, despite controlling for sociodemographic and disease variables, we measured both resilience and mental health cross-sectionally, and there may be other unmeasured confounding variables that could influence the relationship between resilience and mental health symptoms in SSc patients (44).

This study investigated resilience in relation to mental health and disease severity among individuals with SSc. We found a general trend of decreasing resilience with higher disease severity for most participants. However, we identified a distinct subgroup of individuals with SSc that reported low levels of mental health symptoms despite experiencing high symptom severity. This subgroup also reported substantially greater resilience compared to those with high-severity SSc symptoms and high mental health problems, even after considering other sociodemographic and disease-related factors. Overall, these results are consistent with research on resilience in other diseases (20,38–41,42). Our findings underscore the need for further investigation of the resilience construct and strategies to support resilience in SSc.

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Table 1. Sample sociodemographic and disease characteristics for the full sample and by class

	Full Sample (N = 1054)		Low (N = 208)		Normal (N = 286)		High (N = 307)		Very High (N = 84)		High Fatigue/Sleep/Pain & Low Anxiety/Depression (N = 169)	
	N	Mean (SD) or N (%)	N	Mean (SD) or N (%)	N	Mean (SD) or N (%)	N	Mean (SD) or N (%)	N	Mean (SD) or N (%)	N	Mean (SD) or N (%)
Sociodemographic Variables												
Age (years)	1053	60.9 (11.7)	208	61.1 (10.9)	286	62.8 (12.6)	306	61.8 (11.4)	84	59.3 (12.6)	169	60.3 (11.0)
Sex	1054		208		286		307		84		169	
Female		926 (88%)		168 (81%)		251 (88%)		279 (91%)		77 (92%)		151 (89%)
Male		128 (12%)		40 (19%)		35 (12%)		28 (9%)		7 (8%)		18 (11%)
Race or Ethnicity	888		173		244		254		70		147	
White		764 (86%)		154 (89%)		213 (87%)		217 (85%)		55 (79%)		125 (85%)
Black		45 (5%)		6 (3%)		10 (4%)		12 (5%)		5 (7%)		12 (8%)
Other		79 (9%)		13 (8%)		21 (9%)		25 (10%)		10 (14%)		10 (7%)
Country	1054		208		286		307		84		169	
Canada		269 (26%)		57 (28%)		63 (22%)		82 (27%)		23 (27%)		44 (26%)
United States		277 (26%)		67 (32%)		85 (30%)		65 (21%)		9 (11%)		51 (30%)
United Kingdom		95 (9%)		11 (5%)		15 (5%)		31 (10%)		15 (18%)		23 (14%)
France		392 (37%)		71 (34%)		115 (40%)		123 (40%)		36 (43%)		47 (28%)
Australia		21 (2%)		2 (1%)		8 (3%)		6 (2%)		1 (1%)		4 (2%)
Education (years)	892	15.0 (4.0)	175	15.4 (3.8)	245	15.6 (3.7)	254	13.8 (4.0)	70	15.0 (4.5)	148	15.6 (3.3)
Marital status single	895	102 (11%)	176	20 (11%)	245	24 (10%)	255	28 (11%)	70	14 (20%)	149	16 (11%)
Disease Characteristics												
Time since first non-Raynaud's symptom	978	15.7 (9.6)	190	15.5 (9.0)	263	16.7 (10.4)	287	14.9 (9.0)	78	15.2 (10.5)	160	15.9 (9.5)
Diffuse subtype	1047	380 (36%)	208	77 (37%)	282	96 (34%)	305	106 (35%)	83	36 (43%)	169	65 (38%)
Digital ulcers	1004	139 (14%)	197	18 (9%)	274	36 (13%)	293	47 (16%)	80	19 (24%)	160	19 (12%)
Current tendon friction rubs	926	98 (11%)	185	15 (8%)	257	33 (13%)	267	26 (10%)	68	10 (15%)	149	14 (9%)
Large joint contractures (moderate or severe)	976	112 (11%)	193	20 (10%)	268	31 (12%)	280	35 (13%)	78	11 (14%)	157	15 (10%)
Small joint contractures (moderate or severe)	992	252 (25%)	194	49 (25%)	273	66 (24%)	288	69 (24%)	78	28 (36%)	159	40 (25%)
Esophageal gastrointestinal symptoms	1038	874 (84%)	204	165 (81%)	283	231 (82%)	305	269 (88%)	80	67 (84%)	166	142 (86%)
Stomach gastrointestinal symptoms	1015	268 (26%)	196	39 (20%)	276	68 (25%)	299	85 (28%)	80	25 (31%)	164	51 (31%)
Intestinal gastrointestinal symptoms	1027	349 (34%)	197	45 (23%)	278	91 (33%)	304	108 (36%)	82	33 (40%)	166	72 (43%)
Interstitial lung disease	1032	336 (33%)	203	65 (32%)	278	88 (32%)	305	102 (33%)	80	29 (36%)	166	52 (31%)
Pulmonary arterial hypertension	1020	82 (8%)	202	9 (5%)	274	27 (10%)	296	23 (8%)	81	9 (11%)	167	14 (8%)
PROMIS29 Variables in Symptom Cluster												
Fatigue T-score	1054	54.4 (10.8)	208	41.5 (6.9)	286	53.6 (8.3)	307	60.2 (8.0)	84	67.8 (7.2)	169	54.5 (7.0)
Pain Interference T-Score	1054	55.3 (9.4)	208	45.2 (5.8)	286	53.3 (8.4)	307	60.5 (7.3)	84	65.4 (7.8)	169	56.6 (6.0)
Sleep Disturbance T-score	1054	52.4 (8.5)	208	45.2 (6.8)	286	51.4 (7.5)	307	55.7 (7.3)	84	60.5 (7.6)	169	53.0 (7.6)
Anxiety T-score	1054	53.5 (9.8)	208	42.2 (4.3)	286	53.1 (5.8)	307	60.7 (5.2)	84	68.6 (6.3)	169	47.5 (7.3)
Depression T-score	1054	51.5 (9.3)	208	41.0 (1.1)	286	51.9 (2.7)	307	59.0 (2.8)	84	69.0 (3.79)	169	41.0 (0.0)

SD = standard deviation; PROMIS29 = Patient Reported Outcomes Measurement Information System 29-item Health Profile. T-scores standardized for the United States general population (mean=50, standard deviation=10).

Table 2. Total CD-RISC-10 resilience score and item scores for full sample and each class separately

	Full Sample (N = 1054)	Low (N = 208)	Normal (N = 286)	High (N = 307)	Very High (N = 286)	High Fatigue/Sleep/Pain & Low Anxiety/Depression (N = 169)	High/Low - High
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean Score Difference (SD)
Total CD-RISC-10 Score (Range from 0-40)	27.7 (7.3)	33.2 (5.3)	28.7 (5.8)	24.2 (5.9)	19.0 (7.9)	30.2 (6.1)	6.0
CD-RISC-10 Item Scores (Range from 0-5)							
1. I am able to adapt when changes occur	3.1 (0.8)	3.6 (0.6)	3.2 (0.7)	2.7 (0.7)	2.1 (1.0)	3.2 (0.7)	0.5
2. I can deal with whatever comes my way	2.9 (0.9)	3.5 (0.6)	3.1 (0.7)	2.5 (0.8)	2.0 (1.0)	3.2 (0.8)	0.7
3. I try to see the humorous side of things when I am faced with problems	2.7 (1.0)	3.2 (0.8)	2.7 (0.9)	2.3 (0.9)	1.8 (1.1)	3.0 (0.9)	0.7
4. Having to cope with stress can make me stronger	2.5 (1.0)	3.1 (0.9)	2.5 (0.9)	2.1 (0.9)	1.6 (1.1)	2.7 (0.9)	0.6
5. I tend to bounce back after illness, injury, or other hardships	2.9 (0.9)	3.5 (0.6)	3.0 (0.8)	2.6 (0.9)	2.0 (1.0)	3.1 (0.8)	0.5
6. I believe I can achieve my goals, even if there are obstacles	2.8 (0.9)	3.4 (0.6)	2.9 (0.7)	2.4 (0.7)	1.9 (0.9)	3.1 (0.7)	0.7
7. Under pressure, I stay focused and think clearly	2.6 (1.0)	3.3 (0.7)	2.8 (0.9)	2.2 (0.9)	1.8 (1.1)	2.8 (0.8)	0.6
8. I am not easily discouraged by failure	2.6 (1.0)	3.0 (1.0)	2.6 (0.9)	2.3 (0.9)	1.9 (1.0)	2.9 (1.0)	0.6
9. I think of myself as a strong person when dealing with life's challenges and difficulties	3.0 (0.9)	3.4 (0.7)	3.0 (0.8)	2.7 (0.9)	2.1 (1.2)	3.2 (0.8)	0.5
10. I am able to handle unpleasant or painful feelings like sadness, fear, and anger	2.7 (1.0)	3.3 (0.7)	2.8 (0.8)	2.3 (0.9)	1.9 (1.1)	3.0 (0.9)	0.7

SD = standard deviation

Table 3. CD-RISC-10 resilience scores in low, normal, high, and very high classes compared to the high/low class (N = 1054)

	Unadjusted Multiple Regression Model		Adjusted Multiple Regression Model[a]	
	Regression Coefficient (95% CI)	**Standardized Mean Difference (95% CI)**	**Regression Coefficient (95% CI)**	**Standardized Mean Difference (95% CI)**
Classes (Reference High Fatigue/Sleep/Pain & Low Anxiety/Depression Class)				
Low	2.92 (1.70, 4.14)	0.35 (0.22, 0.47)	2.92 (1.69, 4.14)	0.40 (0.23, 0.57)
Normal	-1.56 (-2.70, -0.42)	-0.22 (-0.37, -0.06)	-1.56 (-2.70, -0.42)	-0.22 (-0.37, -0.06)
High	-6.04 (-7.17, -4.92)	-0.83 (-0.99, -0.68)	-6.00 (-7.12, -4.87)	-0.83 (-0.98, -0.67)
Very High	-11.20 (-12.77, 9.63)	-1.55 (-1.76, -1.33)	-11.06 (-12.64, 9.49)	-1.53 (-1.74, -1.31)

[a]Adjusted for sociodemographic variables and disease characteristics. All regression coefficients are unstandardized. Standardized variables were calculated by subtracting raw scores from the mean and dividing by standard deviation. See Supplemental Table 2 for full results with all covariates in the model.

SUPPLEMENTAL MATERIAL

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PROMIS-29 v2.0 items for fatigue, pain interference, sleep disturbance, anxiety and depression domains

Scale	(1)	(2)	(3)	(4)	(5)
Anxiety					
In the past 7 days...					
I felt fearful	Never	Rarely	Sometimes	Often	Always
I found it hard to focus on anything other than my anxiety	Never	Rarely	Sometimes	Often	Always
My worries overwhelmed me	Never	Rarely	Sometimes	Often	Always
I felt uneasy	Never	Rarely	Sometimes	Often	Always
Depression					
In the past 7 days...					
I felt worthless	Never	Rarely	Sometimes	Often	Always
I felt helpless	Never	Rarely	Sometimes	Often	Always
I felt depressed	Never	Rarely	Sometimes	Often	Always
I felt hopeless	Never	Rarely	Sometimes	Often	Always
Pain Interference					
In the past 7 days...					
How much did pain interfere with your day to day activities?	Not at all	A little bit	Somewhat	Quite a bit	Very much
How much did pain interfere with work around the home?	Not at all	A little bit	Somewhat	Quite a bit	Very much
How much did pain interfere with your ability to participate in social activities?	Not at all	A little bit	Somewhat	Quite a bit	Very much
How much did pain interfere with your household chores?	Not at all	A little bit	Somewhat	Quite a bit	Very much
Sleep Disturbance					
In the past 7 days...					
My sleep quality was	Very good	Good	Fair	Poor	Very poor
My sleep was refreshing	Very much	Quite a bit	Somewhat	A little bit	Not at all
I had a problem with my sleep	Not at all	A little bit	Somewhat	Quite a bit	Very much
I had difficulty falling asleep	Not at all	A little bit	Somewhat	Quite a bit	Very much
Fatigue					
In the past 7 days...					
How run-down did you feel on average?	Not at all	A little bit	Somewhat	Quite a bit	Very much
How fatigued were you on average?	Not at all	A little bit	Somewhat	Quite a bit	Very much

SD = standard deviation; PROMIS29 = Patient Reported Outcomes Measurement Information System 29-item Health Profile. T-scores standardized for the United States general population (mean=50, standard deviation=10).

Supplemental Table 1. Comparison of latent classes based on PROMIS-29 variables with Wojeck et al.

PROMIS29 Variables in Symptom Cluster	Fatigue T-score	Pain Interference T-Score	Pain Intensity Score[a]	Sleep Disturbance T-score	Anxiety T-score	Depression T-score
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)
Neyer et al. (N = 1054)						
Low (N = 208)	41.5 (6.9)	45.2 (5.8)		45.2 (6.8)	42.2 (4.3)	41.0 (1.1)
Normal (N = 286)	53.6 (8.3)	53.3 (8.4)		51.4 (7.5)	53.1 (5.8)	51.9 (2.7)
High (N = 307)	60.2 (8.0)	60.5 (7.3)		55.7 (7.3)	60.7 (5.2)	59.0 (2.8)
Very High (N = 84)	67.8 (7.2)	65.4 (7.8)		60.5 (7.6)	68.6 (6.3)	69.0 (3.79)
High Fatigue/Sleep/Pain & Low Anxiety/Depression (N = 169)	54.5 (7.0)	56.6 (6.0)		53.0 (7.6)	47.5 (7.3)	41.0 (0.0)
Wojeck et al. (N = 2212)						
Low (N = 565)	43.3 (7.5)		1.4 (1.5)	46.3 (7.2)	42.7 (4.9)	41.1 (0.8)
Normal (N = 651)	53.9 (8.6)		3.1 (2.2)	51.3 (7.8)	50.8 (6.9)	52.0 (2.7)
High (N = 569)	61.7 (7.8)		5.0 (2.3)	56.1 (7.0)	60.1 (5.4)	59.4 (2.8)
Very High (N = 193)	66.9 (6.6)		6.3 (2.1)	60.7 (7.2)	67.7 (5.7)	69.0 (3.9)
High Fatigue/Sleep/Pain & Low Anxiety/Depression (N = 234)	59.1 (7.3)		5.0 (2.0)	54.7 (7.6)	47.0 (7.3)	41.0 (0.0)

SD = standard deviation; PROMIS29 = Patient Reported Outcomes Measurement Information System 29-item Health Profile. T-scores standardized for the United States general population (mean=50, standard deviation=10).
[a]T-scores are not available for the pain intensity item (possible range 0 to 10 with higher scores representing greater pain intensity).

Supplemental Table 2. Association of class membership, sociodemographic variables, and disease characteristics with resilience (full sample, N = 1054)

	Bivariate Regression Model	Multiple Regression Model[a]	
	Regression Coefficient (95% CI)	Regression Coefficient (95% CI)	Standardized Mean Difference (95% CI)
Sociodemographic Variables			
Age (years)	0.28 (-0.15, 0.72)	0.08 (-0.31, 0.46)	0.01 (-0.04, 0.06)
Male sex	0.70 (-0.64, 2.04)	-0.43 (-1.57, 0.72)	-0.06 (-0.22, 0.10)
Race or ethnicity other than White	-0.59 (-1.98, 0.80)	0.15 (-1.03, 1.33)	0.02 (-0.14, 0.18)
Country			
Canada	-1.30 (-2.50, -0.11)	-0.36 (-1.38, 0.66)	-0.05 (-0.19, 0.09)
United Kingdom	-3.92 (-5.58, -2.26)	-1.76 (-3.20, -0.32)	-0.24 (-0.44, -0.04)
France	-3.10 (-4.20, -2.01)	-1.75 (-2.72, -0.78)	-0.24 (-0.38, -0.11)
Australia	-1.86 (-5.02, 1.30)	-0.52 (-3.21, 2.17)	-0.07 (-0.44, 0.30)
Education (years)	-0.39 (-0.83, 0.04)	-0.28 (-0.64, 0.08)	-0.04 (-0.09, 0.01)
Marital status single	-0.29 (-1.3, 0.72)	0.88 (0.00, 1.76)	0.12 (0.00, 0.24)
Disease Characteristics			
Time since first non-Raynaud's symptom	0.67 (0.22, 1.12)	0.37 (-0.03, 0.78)	0.05 (0.00, 0.11)
Diffuse subtype	0.03 (-0.88, 0.94)	-0.13 (-1.02, 0.75)	-0.02 (-0.14, 0.10)
Digital ulcers	-0.59 (-1.90, 0.71)	0.71 (-0.46, 1.88)	0.10 (-0.06, 0.26)
Current tendon friction rubs	-0.82 (-2.30, 0.65)	-0.40 (-1.67, 0.87)	-0.05 (-0.23, 0.12)
Large joint contractures (moderate or severe)	-0.47 (-1.90, 0.96)	0.61 (-0.75, 1.98)	0.08 (-0.10, 0.27)
Small joint contractures (moderate or severe)	-0.68 (-1.70, 0.35)	-0.35 (-1.39, 0.68)	-0.05 (-0.19, 0.09)
Esophageal gastrointestinal symptoms	0.01 (-1.21, 1.22)	0.54 (-0.48, 1.56)	0.07 (-0.07, 0.22)
Stomach gastrointestinal symptoms	-0.80 (-1.80, 0.20)	-0.50 (-1.44, 0.44)	-0.07 (-0.20, 0.06)
Intestinal gastrointestinal symptoms	-0.49 (-1.43, 0.45)	-0.19 (-1.07, 0.70)	-0.03 (-0.15, 0.10)
Interstitial lung disease	0.62 (-0.33, 1.56)	0.76 (-0.06, 1.59)	0.11 (-0.01, 0.22)
Pulmonary arterial hypertension	-0.56 (-2.18, 1.07)	-0.17 (-1.54, 1.20)	-0.02 (-0.21, 0.17)
Classes (Reference High Fatigue/Sleep/Pain & Low Anxiety/Depression Class)			
Low	2.92 (1.70, 4.14)	2.92 (1.69, 4.14)	0.40 (0.23, 0.57)
Normal	-1.56 (-2.70, -0.42)	-1.56 (-2.70, -0.42)	-0.22 (-0.37, -0.06)
High	-6.04 (-7.17, -4.92)	-6.00 (-7.12, -4.87)	-0.83 (-0.98, -0.67)
Very High	11.20 (-12.77, -9.63)	-11.06 (-12.64, 9.49)	-1.53 (-1.74, -1.31)

[a]Adjusted for sociodemographic variables and disease characteristics. All regression coefficients are unstandardized. Standardized variables were calculated by subtracting raw scores from mean and dividing by standard deviation.

Supplemental Table 3. Sensitivity analysis of association of class membership with resilience (complete cases, N = 669)

	Adjusted Multiple Regression Model[a]	
	Regression Coefficient (95% CI)	**Standardized Mean Difference (95% CI)**
Sociodemographic Variables		
Age (years)	-0.07 (-0.58, 0.44)	-0.01 (-0.08, 0.06)
Male sex	0.26 (-1.16, 1.68)	0.04 (-0.16, 0.23)
Race or ethnicity other than White	0.14 (-1.23, 1.50)	0.02 (-0.17, 0.20)
Country		
Canada	-0.02 (-1.38, 1.34)	0.00 (-0.19, 0.18)
United Kingdom	-1.78 (-3.79, -0.23)	-0.24 (-0.52, -0.03)
France	-2.00 (-3.27, -0.73)	-0.27 (-0.45, -0.10)
Australia	-0.74 (-3.95, 2.48)	-0.10 (-0.54, 0.34)
Education (years)	0.14 (-0.35, 0.63)	0.02 (-0.05, 0.09)
Marital status single	0.81 (-0.23, 1.85)	0.11 (-0.03, 0.25)
Disease Characteristics		
Time since first non-Raynaud's symptom	0.40 (-0.11, 0.91)	0.05 (-0.02, 0.12)
Diffuse subtype	-0.05 (-1.18, 1.08)	-0.01 (-0.16, 0.15)
Digital ulcers	1.14 (-0.42, 2.69)	0.15 (-0.06, 0.37)
Current tendon friction rubs	-0.33 (-1.90, 1.24)	-0.05 (-0.26, 0.17)
Large joint contractures (moderate or severe)	0.96 (-0.82, 2.73)	0.13 (-0.11, 0.37)
Small joint contractures (moderate or severe)	-0.31 (-1.66, 1.04)	-0.04 (-0.23, 0.14)
Esophageal gastrointestinal symptoms	0.71 (-0.60, 2.02)	0.10 (-0.08, 0.28)
Stomach gastrointestinal symptoms	-0.89 (-2.09, 0.30)	-0.12 (-0.29, 0.04)
Intestinal gastrointestinal symptoms	0.01 (-1.12, 1.15)	0.00 (-0.15, 0.16)
Interstitial lung disease	0.90 (-0.15, 1.96)	0.12 (-0.02, 0.27)
Pulmonary arterial hypertension	0.35 (-1.51, 2.22)	0.05 (-0.21, 0.30)
Classes (Reference High Fatigue/Sleep/Pain & Low Anxiety/Depression Class)		
Low	3.36 (1.80, 4.91)	0.46 (0.25, 0.67)
Normal	-1.13 (-2.57, 0.30)	-0.15 (-0.35, -0.04)
High	-5.72 (-7.14, -4.29)	-0.78 (-0.97, -0.59)
Very High	-11.06 (-13.12, -9.00)	-1.51 (-1.79, -1.23)

[a]Adjusted for sociodemographic variables and disease characteristics. All regression coefficients are unstandardized. Standardized variables were calculated by subtracting raw scores from mean and dividing by standard deviation.

3.2. Connecting Text

We re-identified 5 latent classes based on patient-reported outcomes, previously found by Wojeck et al. (39), to examine resilience across these different classes. Our study identified two distinct resilience patterns. First, the results indicate a general trend of decreasing resilience with higher disease severity and mental health issues for most participants. Second, we identified a subgroup of individuals with SSc that report low mental health problems despite experiencing high symptom severity. This subgroup demonstrated greater resilience (mean = 30.2, standard deviation [SD] = 6.1) compared to those with high-severity SSc symptoms and high mental health problems (24.2, SD = 5.9). These patterns persisted even when controlling for sociodemographic and disease-related factors in the multiple linear regression. Our results suggest an association between resilience and mental health and a possible protective effect of resilience against mental health issues due to disease-associated symptoms.

However, despite the recognition that there is a link between resilience and mental health, more information is needed about the specific factors that influence resilience and their impact on mental health in the context of SSc. It would be important to explore how people with SSc that have higher resilience deal with their disease and what skills and strategies people who report lower resilience might be able to cultivate, such as active coping mechanisms or an optimistic outlook on life (30,43). This type of research could also pave the way for the development of resilience-building interventions in SSc in the future.

CHAPTER 4

General Discussion

4.2. Summary of Findings

In the first study, we validated the 10-item CD-RISC-10 (30) in a sample of 962 participants for use in the SSc population. The results demonstrated that the CD-RISC-10 is a valid and reliable measure of resilience in SSc. Confirmatory factor analysis supported a single-factor structure, indicating its suitability for measuring resilience. The differential item functioning found no meaningful difference between the English and French versions of the scale. The CD-RISC-10 showed high internal consistency ($\alpha = 0.93$) and good test-retest reliability (ICC = 0.80, 95% CI: 0.75 to 0.85) in a subsample of 230 participants. Convergent validity was supported by moderate to large correlations with other measures of psychological functioning ($|r| = 0.57$ to 0.78).

In the second study, we examined patterns of resilience and associated factors among a sample of 1054 SSc participants. We built upon earlier work by Wojeck et al. (39) and investigated resilience in relation to mental health and disease severity in individuals with SSc using the CD-RISC-10 (30). Wojeck et al. (39) previously identified five latent classes based on patient-reported outcomes (pain, fatigue, sleep, anxiety, and depression). We employed latent profile modeling and re-identified these classes ("low," "normal," "high," "very high," "high/low") to analyse resilience scores across the classes using the CD-RISC. The results of our descriptive analyses showed that resilience decreased as disease severity and mental health issues increased across four of the classes. However, the "high/low" class showed higher resilience (mean = 30.2, standard deviation [SD] = 6.1) than the "high" class (mean = 24.2, SD = 5.9), despite having similar disease severity. We found the same pattern in the results of the multiple

linear regression. Resilience decreased with higher levels of impairment compared to the “high/low” class. Furthermore, the "high" class exhibited a significantly lower resilience score (regression coefficient = -6.00, 95% CI: -7.12 to -4.87) and standardized mean difference (SMD) (-0.83, 95% CI: -0.98 to -0.67) compared to the "high/low" class.

4.3. Limitations

The following limitations should be noted in interpreting the research findings from both of our studies. First, the SPIN Cohort, from which our data for both manuscripts were drawn, is a convenience sample of people with SSc receiving treatment at SPIN recruiting centres who can complete online measures, as SPIN collects data digitally only. However, a comparison with the European Scleroderma Trials and Research and Canadian Scleroderma Research Group cohorts indicated broad comparability of participant characteristics, which supports generalizability in SSc (44). Second, both studies rely on self-report measures for assessing resilience and mental health symptoms. Self-report measures are subject to biases, such as social desirability or recall bias, which may affect the accuracy of the data collected (45). Nevertheless, it is important to note that we only used previously validated measures within SSc for the primary outcomes (46,47).

In addition, each study had individual limitations. In the first study, the DIF analysis employed the MIMIC approach, which evaluates uniform DIF but not non-uniform DIF, meaning that we could not assess potential variations in item functioning specific to certain groups or characteristics within the sample. Finally, in the second study, despite controlling for sociodemographic and disease variables, there remains a possibility of unmeasured confounding factors that could influence the relationship between resilience and mental health symptoms in individuals with SSc, such as spirituality (43). Although it is not possible for a single study to

include all potential confounding factors, our focus on patterns across symptom groups allowed us to identify clear associations. Future research can expand upon these patterns and incorporate additional factors that may influence resilience in individuals with SSc.

4.4. Conclusions

The present research consists of two studies focusing on resilience in individuals with SSc. The first study aimed to assess the validity, reliability, and DIF of the CD-RISC-10 in English- and French-speaking participants with SSc. The second study explored resilience levels within distinct latent classes (“low,” “normal,” “high,” “very high,” and “high/low”) and their relationship with disease severity and mental health outcomes.

We found that the CD-RISC-10 is a reliable and valid measure of resilience in SSc across languages. Furthermore, the second study revealed that resilience levels were closely tied to disease severity and mental health issues for most participants. However, one distinct subgroup, the 'high/low' class, exhibited resilience scores and mental health similar to the 'low' and 'normal' classes despite indicating symptom severity comparable to the 'high' class.

These findings hold significant implications. The validated CD-RISC-10 can now serve as a valuable tool for assessing resilience in this population, both in research and clinical contexts. Additionally, our results suggest a potentially protective effect of resilience against mental health issues arising from the impact of SSc, including high symptom severity. Moving forward, exploring resilience within the 'high/low' and 'high' classes is crucial to gain a deeper understanding of resilience factors and their impact on mental health in individuals with SSc. Moreover, research on coping strategies used by individuals with high resilience is needed to advance our knowledge of resilience in SSc and potentially pave the way for developing resilience-promoting interventions.

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