

Fatigue and Its Association With Social Participation, Functioning, and Quality of Life in Systemic Sclerosis

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Objective. Fatigue is consistently ranked as one of the most problematic symptoms of systemic sclerosis (SSc), but the impact of fatigue on daily life is not well characterized. The purpose of this study was to examine the contribution of fatigue to deficits in social participation, functioning, and quality of life.

Methods. Baseline data from a sample undertaking a clinical trial were utilized ($n = 267$). Fatigue, pain interference, depressive symptoms, physical function, and social participation were assessed by measures from the Patient-Reported Outcomes Measurement Information System. Hierarchical linear regressions were performed to determine the unique contribution of fatigue to social participation, physical function, and quality of life above and beyond the effects of demographic and clinical variables, pain interference, and depressive symptoms.

Results. The sample was predominantly female (91%), with an average age of 53.7 years, average disease duration of 9 years, and a mean fatigue T score of 58.7. Of all outcomes, fatigue was most strongly associated with deficits in social participation, explaining 48% of the variance beyond demographic and clinical factors, which is similar to the amount of variance contributed by pain interference and depressive symptoms combined (49%). Fatigue also accounted for significant amounts of variance in physical function and quality of life ($R^2 = 0.27$ and 0.33 , respectively) above and beyond the effects of demographic and clinical factors.

Conclusion. Fatigue is an important clinical problem in SSc and is strongly associated with decreased participation in social roles and activities. Rehabilitation interventions that focus on fatigue management may be necessary to maximize participation.

INTRODUCTION

Systemic sclerosis (SSc) is a rare autoimmune disease associated with vascular damage and tissue fibrosis that affects the skin and internal organs (1–3). In the US, it affects between 13.5 and 39.9 per 100,000 people (4). In addition to the classic skin hardening that restricts movement, a major complaint of individuals with SSc is the substantial symptom burden. Symptoms such as fatigue, pain, and depressive symptoms are common, and because SSc is diagnosed in early to middle age and has no cure, individuals with SSc face many years of managing the manifestations of a complex and progressive condition (5).

Symptoms of SSc significantly disrupt daily activities and diminish quality of life (6–9). Of the symptoms experienced, fatigue has been consistently ranked as one of the most problematic (6,7,10–12). Fatigue in SSc is significantly greater than what is experienced by the general population, which is similar to other rheumatologic conditions and those who are actively receiving cancer treatment (8,9,12). Fatigue affects many facets of life, diminishing the ability to perform usual tasks (7,13), engage in meaningful activities (7,14), perform work duties (15,16), and fulfill family responsibilities (14,17,18). The debilitating nature of fatigue has prompted a call for research to better understand fatigue and its correlates (6,7,9,14) in order

The statements made herein are solely the responsibility of the authors and do not necessarily represent the views of the Patient-Centered Outcomes Research Institute, its board of governors, or its methodology committee.

Supported by the Patient-Centered Outcomes Research Institute (grant CER-1310-08323 to Drs. Poole and Khanna as co-principal investigators). Dr. Khanna's work was supported by the NIH (National Institute of Arthritis and Musculoskeletal and Skin Diseases grant K24-AR-063129).

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Dr. Khanna has received consulting fees, speaking fees, and/or honoraria from AbbVie, Acceleron, Actelion, Blade Therapeutics, Boehringer Ingelheim, Cytori, Galapagos, GlaxoSmithKline, Mitsubishi Tanabi, Sanofi-Aventis/Genzyme, UCB Pharma (less than \$10,000 each), Bayer, Bristol Myers Squibb, and Genentech/Roche (more than \$10,000 each) and owns stock in Eicos Sciences. No other disclosures relevant to this article were reported.

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Submitted for publication August 7, 2019; accepted in revised form December 10, 2019.

SIGNIFICANCE & INNOVATIONS

- Fatigue is associated with physical function, quality of life, and social participation. Individuals with systemic sclerosis and higher levels of fatigue had reduced ability to participate in social roles and activities.
- Fatigue explains the same amount of variance in social participation as pain and depressive symptoms combined. With pain and depressive symptoms included in the model, fatigue explains an additional 9% of variance in social participation.
- Fatigue was a significant predictor of physical function and quality of life, although pain interference and depressive symptoms accounted for more variability, suggesting that different symptoms have variable effects depending on the functional domain.

to better address this symptom, reduce disability, and improve quality of life.

To better understand the contribution of fatigue to functioning and quality of life in SSc, we examined baseline data from a sample of participants in a clinical trial investigating the effectiveness of an internet-based, self-management program (19). The purpose of this study was to examine the contribution of fatigue to deficits in social participation, functioning, and quality of life in individuals with SSc. We hypothesized that fatigue would be the strongest unique contributor to each of these outcomes in multivariable models that included other symptoms (pain interference and depressive symptoms), clinical variables, and demographics.

PATIENTS AND METHODS

Procedure. Adults with SSc were recruited to participate in a randomized controlled trial designed to evaluate the efficacy of an internet-based, chronic disease self-management program (19). Participants were recruited from 2 universities (in the Midwest and Southeast US) as well as from websites and social media from national SSc foundations. To be included in the trial, participants needed to be US residents, report a diagnosis of SSc, be age 18 years or older, have basic computer literacy and access to a computer with internet and email capabilities, be able to communicate in English, and be willing to complete the study procedures. All participants provided informed consent. After informed consent was obtained, participants were sent a Qualtrics survey to complete baseline assessments examined in this secondary data analysis. The study was approved by institutional human subjects review boards at the University of New Mexico, University of Michigan, and the Medical University of South Carolina.

Measures. Fatigue was measured using the 4 items from the fatigue subscale of the Patient-Reported Outcomes Measurement Information System (PROMIS)-29, version 2.0. The PROMIS-29 contains several scales used in this analysis that have been vali-

dated in a large international sample of individuals with SSc (20). Referenced for the past 7 days and rated on a scale from 1 (not at all) to 5 (very much), the 4 items are as follows: 1) I feel fatigued; 2) I have trouble starting things because I am tired; 3) How run-down did you feel on average?; and 4) How fatigued were you on average? Ratings were converted to a T score metric that standardized the ratings to the US population, in which the mean \pm SD ages were 50 \pm 10 years. A higher score indicates worse fatigue.

Outcomes. *Social participation.* The Ability to Participate in Social Roles and Activities scale was part of the PROMIS-29 and consists of 4 items. On a scale of 5 (never) to 1 (always), participants were asked to rate the following: 1) I have trouble doing all of my regular leisure activities with others; 2) I have trouble doing all of the family activities that I want to do; 3) I have trouble doing all of my usual work (including work at home); and 4) I have trouble doing all of the activities with friends that I want to do. Scores were converted to T scores for analysis. A higher score indicates better ability.

Physical function. The PROMIS-29 has a physical function scale with 4 items. On a scale of 5 (without any difficulty) to 1 (unable to do), participants were asked to rate the following: 1) Are you able to do chores such as vacuuming or yard work?; 2) Are you able to go up and down stairs at a normal pace?; 3) Are you able to go for a walk of at least 15 minutes?; and 4) Are you able to run errands and shop? A higher score indicates better physical function.

Quality of life. The 5-level EuroQoL 5-domain instrument is a generic health-related, quality of life assessment commonly used in populations with various chronic conditions (21,22). It has domains of mobility, self-care, activity, pain, and anxiety. Participants are asked to rate their health state on a scale of no problems, slight problems, moderate problems, severe problems, and extreme problems. Responses are then transformed to a metric of health utility using an algorithm in which scores range from 0.0 (death) to 1.0 (full/optimal health).

Demographic and clinical characteristics. Demographic information included age, race, ethnicity, sex, education level, marital status, and employment status. Clinical characteristics included scleroderma type (limited/CREST syndrome [calcinosis, Raynaud's phenomenon, esophageal dysmotility, sclerodactyly, telangiectasias]/sine, diffuse, or overlap) and disease duration (measured as the year diagnosed). Self-rated health was ascertained using 1 question, in which participants rated their overall health as excellent, very good, good, fair, or poor.

Other symptoms. *Pain interference and depressive symptoms.* Both of these symptoms were assessed from the PROMIS scales of the PROMIS-29. Pain interference was assessed by 4 items. For the previous 7 days, participants rated pain interference on a scale of 1 (not at all) to 5 (very much) for the following questions: 1) How much did pain interfere with your day to day activities?; 2) How much did pain interfere with work

Table 1. Sample-reported symptoms, functioning, and quality of life (n = 267 participants)*

Measures	Overall sample	Diffuse cutaneous SSc (n = 115)	Limited cutaneous SSc (n = 120)	Overlap SSc (n = 31)
Fatigue†	58.7 ± 10.4	57.5 ± 10.1	58.4 ± 10.4	63.7 ± 10.1
Pain interference	58.0 ± 9.3	56.9 ± 9.7	58.0 ± 8.8	61.4 ± 8.9
Pain intensity (0–10 NRS)	4.2 ± 2.2	3.9 ± 2.3	4.2 ± 2.1	4.9 ± 2.2
Depressive symptoms	51.3 ± 9.8	51.3 ± 10.1	51.3 ± 10.0	51.6 ± 8.7
Anxiety	54.0 ± 10.0	53.4 ± 9.9	54.4 ± 10.1	54.7 ± 10.5
Sleep disturbance†	53.7 ± 6.5	53.9 ± 6.5	52.5 ± 5.7	57.0 ± 8.2
Social participation	45.0 ± 8.2	44.9 ± 8.0	45.8 ± 8.5	43.3 ± 7.2
Quality of life, EQ-5D-5L	0.78 ± 0.08	0.78 ± 0.08	0.79 ± 0.08	0.77 ± 0.07
Self-rated health, no. (%)†				
Excellent	3 (1.1)	3 (2.6)	0 (0)	0 (0)
Very good	33 (12.4)	16 (13.9)	15 (12.5)	1 (3.2)
Good	114 (42.7)	38 (33.0)	62 (51.7)	14 (45.2)
Fair	100 (37.5)	51 (44.4)	36 (30.0)	13 (41.9)

* Values are the mean ± SD unless indicated otherwise. We used the Patient-Reported Outcomes Measurement Information System–29, version 2, which comprises scales for fatigue, pain interference, pain intensity, depressive symptoms, anxiety, sleep disturbance, ability to participate in social roles (social participation), and physical function. EQ-5D-5L = 5-level EuroQol 5-domain instrument; NRS = numerical rating scale; SSc = systemic sclerosis.

† $P \leq 0.05$ difference among SSc subtypes.

around the home?; 3) How much did pain interfere with your ability to participate in social activities?; and 4) How much did pain interfere with your household chores? Depressive symptoms were also assessed for the past 7 days. On a scale of 1 (never) to 5 (always), participants rated the following: 1) I felt worthless; 2) I felt helpless; 3) I felt depressed; and 4) I felt hopeless. Higher scores on these scales indicated worse symptoms.

Statistical analysis. Descriptive statistics were used to characterize the sample. We used frequency and proportion for categorical variables, means and SDs for normally distributed continuous data, and median and interquartile ranges for nonnormally distributed continuous data. The association between fatigue (T score from the PROMIS measure) and 3 outcome variables was investigated in 3 separate, hierarchical, multivariable linear regression analyses with the following outcome variables: social participation, physical function, and quality of life. For each outcome, 3 models were constructed to examine the relative contributions of fatigue and other symptoms (pain interference and depressive symptoms) above and beyond demographic and clinical variables. This method allowed us to examine the unique contribution of fatigue and the set of other symptoms, respectively, to the model variance without the influence of each other. It also allowed for comparison across models given the difference in order of entry. In Model 1, demographic and clinical variables (age, sex, race, scleroderma subtype, and years since scleroderma diagnosis) were entered in block 1, and fatigue was entered in block 2. In Model 2, demographic and clinical variables were entered in block 1, fatigue in block 2, and pain interference and depressive symptoms in block 3. Model 2 was performed to examine how much the symptom of fatigue explained the variance in each outcome above and beyond clinical factors, and how much unique variance is then explained

by pain interference and depressive symptoms. In Model 3, the order of entry of the pain interference and depressive symptoms block and the fatigue block were reversed. Model 3 was performed to examine how much unique variance fatigue adds to the model above and beyond demographic and clinical variables and symptoms of pain interference and depressive symptoms. R^2 values indicated the amount of variance in the outcomes attributable to the variable blocks entered into the models. To depict the unadjusted relationship between fatigue and social participation, a scatter plot with overlaid best-fitting lines was constructed, estimated using ordinary least squares piecewise regression. We prespecified a cut point of 1 SD below the sample fatigue T score mean.

RESULTS

The characteristics of the sample have been reported in detail elsewhere (19). Briefly, the sample was predominantly female (91%), the mean ± SD age was 53.7 ± 11.7 years, and the sample consisted of 17% racial/ethnic minorities (nonwhite). Approximately three-fourths of the sample (74%) had academic degrees or professional qualifications, with a mean of 16 years of education; 64% were married, and 42% reported working part or full time. For the scleroderma subtype reported by participants, 45% had limited cutaneous SSc or sine scleroderma; 43% had diffuse cutaneous SSc; 12% had scleroderma overlapping with another rheumatic disease, and 0.4% (n = 1) did not know the subtype. Time since diagnosis was a median of 9 years, with an interquartile range of 5–16 years.

Table 1 shows the values for reported functioning, health, and symptom measures. In total, 43.9% of the sample rated their overall health to be fair or poor. Fatigue was the symptom rated to be worst (mean T score 58.7 or 0.87 SD above the US population), followed

Table 2. Association of fatigue with ability to participate in social roles*

	Model 1			Model 2			Model 3		
	Block	β	ΔR^2	Block	β	ΔR^2	Block	β	ΔR^2
Constant		82.83†			94.93†			94.93†	
Demographic/clinical factors	1		0.02	1		0.02	1		0.02
Age		-0.10†			-0.12†			-0.12†	
Female		1.62			1.51			1.51	
Minority		1.03			1.51			1.51	
Diffuse SSc‡		-1.49†			-1.65†			-1.65†	
Overlap SSc‡		0.10			-0.19			-0.19	
Diagnosis year		-0.04			-0.03			-0.03	
Fatigue	2	-0.56†	0.48†	2	-0.32†	0.48†	3	-0.28†	0.09†
Pain interference				3	-0.28†	0.11†	2	-0.16†	0.49†
Depressive symptoms					-0.16†			0.32†	
Total model R^2			0.50			0.61			0.60

* Fatigue, ability to participate in social roles and activities, pain interference, and depressive symptoms are scales from the Patient-Reported Outcomes Measurement Information System–29, version 2. Hierarchical regression models were constructed with variable(s) entered in blocks. Beta coefficients are from full models. ΔR^2 is shown for pain interference and depressive symptoms in combination, as they were entered together in a block. N = 266 in all models (1 participant had missing data for systemic sclerosis [SSc] type).

† $P \leq 0.05$.

‡ Reference group: limited or sine scleroderma.

by pain interference (mean T score 58.0). Mean anxiety, sleep disturbance, and depressive symptoms scores were all within 0.5 SDs of the normative sample mean (T score 50). Using 1-way analyses of variance or chi-square tests to examine differences across SSc subtype, only fatigue, sleep disturbance, and self-rated health were significantly different ($P \leq 0.05$). Participants with overlap SSc had the highest levels of fatigue and sleep disturbance and comprised the highest proportion of those who rated their health as fair or poor (51.6%). Participants with diffuse cutaneous SSc also comprised a

high proportion of individuals who rated their health as fair or poor (50.5%), but their mean fatigue and sleep disturbance levels were similar to those with limited cutaneous SSc or sine scleroderma.

Fatigue and social participation. Table 2 shows results from hierarchical regression models in which fatigue and other variables were examined as predictors of social participation. In Model 1, 50% of the variance in social participation was explained by demographic and clinical factors, which contributed a negligible

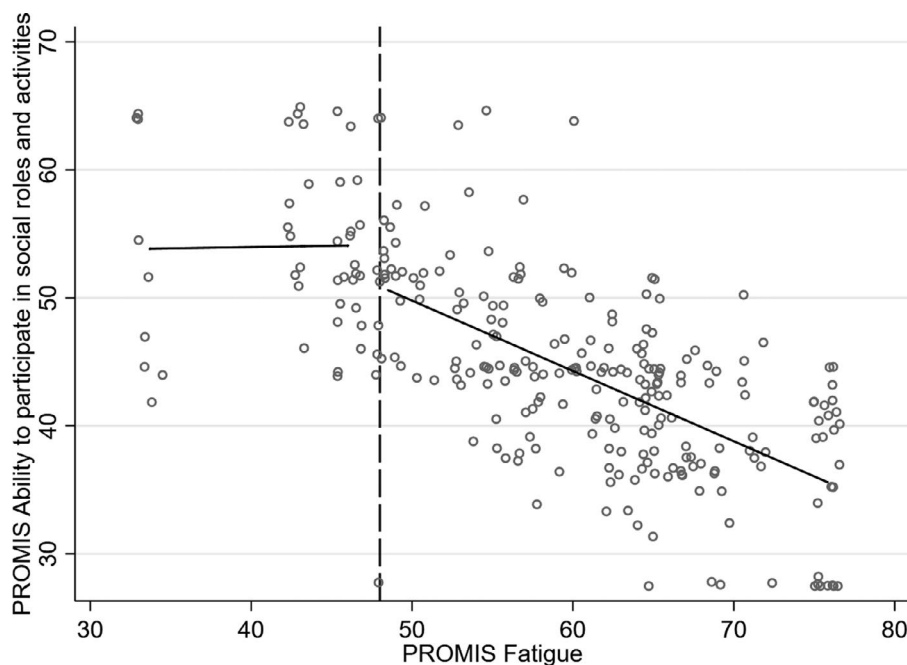


Figure 1. Unadjusted relationship between fatigue and social participation. Social participation is measured by the Patient-Reported Outcomes Measurement Information System (PROMIS), using the Ability to Participate in Social Roles and Activities subscale. Both axes depict T scores. The cut point used (dotted line) is 1 SD below the sample mean for the PROMIS fatigue subscale (T score 48). Solid lines depict the best-fit (ordinary least squares regression) lines above and below the cut point. Symbols show data points for individual participants.

Table 3. Association of fatigue with physical function*

	Model 1			Model 2			Model 3		
	Block	β	ΔR^2	Block	β	ΔR^2	Block	β	ΔR^2
Constant		66.41†			76.51†			76.51†	
Demographic/clinical factors	1		0.03	1		0.03	1		0.03
Age		-0.07†			-0.09†			-0.09†	
Female		0.84			1.13			1.13	
Minority		0.47			1.00			1.00	
Diffuse SSc‡		-1.84†			-2.05†			-2.05†	
Overlap SSc‡		-1.23			-1.15			-1.15	
Diagnosis year		-0.07			-0.06			-0.06	
Fatigue	2	-0.36†	0.27†	2	-0.16†	0.27†	3	-0.16†	0.03†
Pain interference				3	-0.35†	0.13†	2	-0.35†	0.37†
Depressive symptoms					-0.03			-0.03	
Total model R ²			0.30			0.43			0.43

* Fatigue, physical function, pain interference, and depressive symptoms are scales from the Patient-Reported Outcomes Measurement Information System–29, version 2. Hierarchical regression models were constructed with variable(s) entered in blocks. Beta coefficients included in the table are from full models. ΔR^2 is shown for pain interference and depressive symptoms in combination, as they were entered together in a block. N = 266 in all models (1 participant had missing data for systemic sclerosis [SSc] type).

† $P \leq 0.05$.

‡ Reference group: limited or sine scleroderma.

amount (2%) of variance, and by fatigue, which accounted for nearly one-half (48%) of the variance. Of the demographic and clinical factors, age and the diffuse cutaneous SSc subtype demonstrated significant independent negative associations with social participation. When pain interference and depressive symptoms were added in a block after fatigue (Model 2), a further increase of 11% of variance in the outcome was explained by these symptoms. In Model 3, fatigue accounted for a significant amount of variance (9%) above and beyond the effects of pain interference and depressive symptoms combined (49% of variance). Regardless of the order of entry, the models accounted for ~60% of the variance in social participation.

Figure 1 shows the unadjusted association between fatigue and social participation, with the best-fit line segmented at 1 SD below the sample mean (fatigue mean T score 48). In this graph, the negative association between fatigue and social participation is only seen when patients have fatigue that is approximately at the mean or greater (T score of 48 or higher). Fatigue was not associated with social participation for individuals with low fatigue.

Fatigue and physical function. Table 3 shows the results from the hierarchical regression models in which physical function was the outcome. In Model 1, 30% of the variance in physical function was explained by demographic and clinical factors (3% combined) and fatigue (27% of the variance). Age and diffuse cutaneous SSc were significantly negatively associated with physical function and depressive symptoms. In Model 2, fatigue accounted for a significant and substantial amount of variance in physical function (27%); pain and depressive symptoms added a significant amount of variance above and beyond the effect of fatigue on physical function. In Model 3, pain interference and depressive symptoms accounted for a substantial and significant amount of

variance in physical function (37%); fatigue added a statistically significant, although small amount of variance in physical functioning when added in the third step. The models accounted for 43% of the variance in self-reported physical function.

Fatigue and quality of life. Table 4 shows the results from the hierarchical regression models in which quality of life was the outcome. In Model 1, 35% of the variance in quality of life was explained by demographic and clinical factors and fatigue; as in prior models, demographic and clinical variables accounted for very small amounts of the variance in quality of life (2%), whereas fatigue accounted for 33% of the variance. Of the demographic factors, diffuse cutaneous SSc was significantly associated with lower quality of life. In Model 2, pain interference and depressive symptoms contributed an additional 21% variance in quality of life above and beyond the effects of fatigue. In contrast, in Model 3, fatigue only contributed an additional 1% variance in quality of life above the variance explained by pain interference and depressive symptoms, which accounted for 53% of the variance in quality of life. These models explained 56% of the variance in quality of life and depressive symptoms.

DISCUSSION

Fatigue is a symptom often described in the literature as debilitating by individuals with SSc (6,10,11), but it is not yet clear what aspects of functioning and quality of life are most affected by fatigue and other symptoms. In this study, our objective was to examine the contribution of fatigue to deficits in social participation, functioning, and quality of life. To accomplish this, we examined the relative contributions of fatigue above and beyond demographics and clinical factors and other symptoms (pain interference and depression).

Table 4. Association of fatigue with quality of life*

	Model 1			Model 2			Model 3		
	Block	β	ΔR^2	Block	β	ΔR^2	Block	β	ΔR^2
Constant		1.05†			1.22†			1.22†	
Demographic/clinical factors	1		0.02	1		0.02	1		0.02
Age		-0.0001			-0.0004			-0.0004	
Female		0.02			0.02			0.02	
Minority		-0.004			0.002			0.002	
Diffuse SSc‡		-0.01			-0.02†			-0.02†	
Overlap SSc‡		-0.004			-0.008			-0.008	
Diagnosis year		-0.0004			-0.0003			-0.0003	
Fatigue	2	-0.005†	0.33†	2	-0.001†	0.33†	3	-0.001†	0.01†
Pain interference				3	-0.004†	0.21†	2	-0.004†	0.53†
Depressive symptoms					-0.002†			-0.002†	
Total model R^2			0.35			0.56			0.56

* Quality of life was measured using the 5-level EuroQol 5-domain instrument. Fatigue, pain interference, and depressive symptoms are scales from the Patient-Reported Outcomes Measurement Information System–29, version 2. Hierarchical regression models were constructed with variable(s) entered in blocks. Beta coefficients included in the table are from full models. ΔR^2 is shown for pain interference and depressive symptoms in combination, as they were entered together in a block. N = 266 in all models (1 participant had missing data for systemic sclerosis [SSc] type).

† $P \leq 0.05$.

‡ Reference group: limited or sine scleroderma.

There are 3 main findings of this study. First, of all outcomes assessed, fatigue was most strongly associated with decreased ability to participate in social roles and activities. Fatigue alone accounted for nearly the same amount of variance in social participation ($R^2 = 0.48$) (Table 2) as pain interference and depressive symptoms combined ($R^2 = 0.49$) (Table 2). Furthermore, the substantial amount of unique variance that fatigue explained over and above symptoms of pain interference and depressive symptoms suggests that fatigue is particularly influential with regard to reduced social participation. These findings are in contrast to those of Sandusky et al, who reported that fatigue was not a significant correlate for social participation after controlling for depressive symptoms (7), and Poole et al (23), who used a single visual analog scale measure for fatigue and reported no difference in social participation with higher levels of fatigue. However, there are several key differences in the measurement of social participation between the current study and those studies. Sandusky et al measured social participation via social networks and relationships as opposed to participation in particular activities, and Poole et al measured social participation by ascertaining frequency of performance of activities, such as gardening, household maintenance, and shopping, and also counted higher frequency as better participation.

In the current study, social participation was measured using the PROMIS social participation scale, which assesses difficulty in usual activities and whether participation is above or below what the individual wants to do. In addition, the PROMIS social participation scale has been validated and has stronger psychometric properties compared to the instruments used in the prior studies. Last, differences between this study's sample and the samples in those studies may also affect the comparisons. For instance, in the study by Sandusky et al, a higher proportion of individuals reported having a high school education or less (32%) in relation to the current sample (20%).

One reason why fatigue may have a strong negative association with social participation is because work limitations are included in the social participation measure. In SSc, fatigue is a strong correlate of work disability (24,25), and baseline fatigue severity was a main predictor of work disability in a longitudinal study (16). This study's findings, showing a strong negative association between fatigue and social participation, are similar to those of studies of another chronic condition: multiple sclerosis (26,27). In those studies, pain and depressive symptoms are also important factors in decreased physical function and quality of life.

Our findings have implications for both assessment and intervention development. While clinical assessment often includes measures of physical function, it appears important to include measures of social participation when assessing patients with SSc, especially if they report high fatigue. In addition, the assessment used to measure fatigue is an important consideration, as some assessments, such as the Multidimensional Fatigue Inventory and Multidimensional Assessment of Fatigue Scale, include items asking about the impact of fatigue on participation. Assessment of social participation may reveal areas for intervention that would be appropriate for rehabilitation professionals to address, such as workplace adaptation, and also supports the idea that fatigue management is necessary in this population, which is similar to the recommendations in other studies (6,7,9,12,14).

Second, although fatigue accounted for approximately one-third of the variance in physical function and quality of life outcomes when entered in the models prior to the addition of pain interference and depressive symptoms, fatigue did not significantly contribute to the variance in physical function and quality of life after these symptoms were included in the models (only 1% and 3%, respectively). The findings suggest that interventions to impact physical function and quality of life need to be multifaceted

and include strategies to reduce pain and depressive symptoms in addition to fatigue management. Indeed, other studies have confirmed this relationship between fatigue, pain, depressive symptoms, and function (7,12,28).

Third, this finding extends the understanding of how demographic and clinical factors relate to symptoms, functioning, and quality of life in SSc. Neither age nor disease subtype was associated with the outcomes measured. Interestingly, individuals with SSc all have relatively high symptom severity compared to normative populations, and individuals with the 2 main subtypes of SSc (diffuse and limited) have somewhat similar fatigue levels (T scores 57 and 58, respectively). This is similar to a previous study that showed no significant differences in fatigue by subtype (7). Although fatigue severity was similar in these groups, individuals with diffuse cutaneous SSc have greater deficits in their ability to participate in social roles and activities, suggesting that fatigue management is particularly important in this group. Moreover, lung, gastrointestinal, and muscle involvement, more common with diffuse cutaneous SSc, have been reported to be predictors of fatigue (12).

In regard to limitations, this study utilized cross-sectional data, so causality between fatigue and outcomes cannot be assumed. Furthermore, participants comprised a national sample and self-reported all measures via survey, so clinical variables could not be corroborated by medical records. In addition, other measures of health status, such as number and types of comorbidities, were not collected, and this information could have further explained variance in the functioning and quality of life outcomes. Future studies should examine longitudinal associations between fatigue and social participation.

In conclusion, this study showed that fatigue related strongly to deficits in the ability to participate in social roles and activities. Intervention development for fatigue management may be particularly needed to maximize social participation in this population.

AUTHOR CONTRIBUTIONS

All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be submitted for publication. Dr. Murphy had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study conception and design. Murphy, Kratz, Whibley, Poole, Khanna.

Acquisition of data. Murphy, Poole, Khanna.

Analysis and interpretation of data. Murphy, Kratz, Whibley, Poole, Khanna.

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