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ORIGINAL ARTICLE

Multinational Qualitative Research Study Exploring the Patient Experience of Raynaud's Phenomenon in Systemic Sclerosis

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Objective. **Raynaud's phenomenon (RP) is the most common manifestation of systemic sclerosis (SSc). RP is an episodic phenomenon, not easily assessed in the clinic, leading to reliance on self-report. A thorough understanding of the patient experience of SSc-RP is essential to ensuring that patient-reported outcome (PRO) instruments capture domains important to the target patient population. We report the findings of an international qualitative research study investigating the patient experience of SSc-RP.**

Methods. **Focus groups of SSc patients were conducted across 3 scleroderma centers in the US and UK, using a topic guide and a priori purposive sampling framework devised by qualitative researchers, SSc patients, and SSc experts. Focus groups were audio recorded, transcribed, anonymized, and analyzed using inductive thematic analysis. Focus groups were conducted until thematic saturation was achieved.**

Results. **Forty SSc patients participated in 6 focus groups conducted in Bath (UK), New Orleans (Louisiana), and Pittsburgh (Pennsylvania). Seven major themes were identified that encapsulate the patient experience of SSc-RP: physical symptoms, emotional impact, triggers and exacerbating factors, constant vigilance and self-management, impact on daily life, uncertainty, and adaptation. The interrelationship of the 7 constituent themes can be arranged within a conceptual map of SSc-RP.**

Conclusion. **We have explored the patient experience of SSc-RP in a diverse and representative SSc cohort and identified a complex interplay of experiences that result in significant impact. Work to develop a novel PRO instrument for assessing the severity and impact of SSc-RP, comprising domains/items grounded in the patient experiences of SSc-RP identified in this study, is underway.**

INTRODUCTION

The term Raynaud's phenomenon (RP) is generally used to describe episodic acral vasospasm manifesting as digital discoloration and pain (1). The majority of people experiencing RP symptoms have primary RP, a syndrome of benign but intrusive exaggerated digital microvascular responses to cold and/or emotional stress, affecting approximately 5% of the healthy population (1,2). The term secondary RP is applied when the symptoms are the consequence of underlying pathology; an important cause is autoimmune rheumatic diseases such as systemic sclerosis (SSc), in which functional vascular disturbances are compounded by a progressive obliterative microangiopathy (1). RP is the most common

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Significance & Innovations

- Raynaud's phenomenon comprises a complex interplay of patient experiences that result in significant morbidity for patients living with systemic sclerosis.
- Our findings challenge the accepted paradigm of Raynaud's attacks, with not all systemic sclerosis patients identifying with this concept.
- Existing patient-reported outcome instruments do not fully capture the patient experience of Raynaud's phenomenon in systemic sclerosis.

disease-specific manifestation of SSc, affecting approximately 96% of patients (3). SSc-RP is consistently ranked highest in patient surveys exploring the frequency and impact of disease-related complications of SSc (4,5). RP is an episodic phenomenon, not easily assessed in the clinic setting, leading to a reliance on patient-reported outcome (PRO) instruments. The patient perspective captured by PRO instruments provides valuable insight into the patient condition, not always captured by clinician-reported assessment tools (6). However, no studies to date have explored the domains that form the patient perspective of SSc-RP, yet a thorough understanding of the patient experience of SSc-RP is essential if PRO instruments assessing the severity and impact of SSc-RP are to fully capture experiences important to patients (7). The aim of the present study was to fully explore the themes and subthemes that comprise the patient experience of SSc-RP.

PATIENTS AND METHODS

Study management. The study development and conduct was overseen by a steering committee comprising 9 SSc experts (JDP, RTD, LAS, TMF, FI, NJM, ALH, MMC, and DK), 2 patient research partners (JW and HJ), a vasculitis expert with experience in PRO instrument development (JR), and an experienced team of qualitative researchers (CA, ED, and SH). Ethical approval was obtained from independent ethics committees by chief investigators at each patient-participating site in Bath (UK), New Orleans (Louisiana), and Pittsburgh (Pennsylvania) (JDP, RTD, and LAS, respectively), with all participants providing informed consent before taking part.

Study design. An international multicenter qualitative research study comprising patient focus groups in Bath, Pittsburgh, and New Orleans was developed to ensure experiences were sought from a broad geographical, cultural, and ethnic cross-section of patients. Focus group meetings enable open discussion and debate among participants, allowing convergent and divergent views to be clarified where necessary during the discussion (8). The dynamic nature of focus group interactions facilitates capture of patient experiences not always expressed in 1:1 interview settings.

Participants. All patients fulfilled the 2013 American College of Rheumatology/European League Against Rheumatism classification criteria for SSc (9), were ages >18 years, had sufficient English language skills to participate in group discussions, and had the capacity to provide informed consent. Enrollment decisions were based on an a priori purposive sampling framework developed by the project steering committee and designed to ensure a representative patient cohort with respect to disease subtype (aiming for 60:40 split between limited and diffuse cutaneous SSc), disease duration with early and established disease (≤3 and >3 years since first non-RP symptom), history of digital ulcer disease (as a proxy for peripheral vascular disease severity, aiming for approximately 50:50 split to be representative of digital ulcer prevalence in SSc), sex (aiming for 5:1 female predominance), and ethnicity (with white, African American, and Hispanic representation). A clinician case-report form facilitated subsequent participant selection against the requirements of the purposive sampling framework (10). The size of each focus group was limited to a maximum of 9 participants, to ensure all participants had the opportunity to express their personal views and could confidently challenge alternative/opposing experiences expressed within the group. A minimum of 3 focus groups was originally planned, with an intention to undertake additional focus groups until thematic saturation was achieved (11).

Data collection. Each focus group lasted approximately 1 hour, was cofacilitated by JDP and at least 1 other member of the steering committee and was audio-recorded, transcribed, and anonymized. An initial topic guide was developed by the steering committee (see Supplementary Appendix A, available on the *Arthritis Care & Research* web site at http://onlinelibrary.wiley.com/doi/10.1002/acr.23475/abstract), with each focus group commencing with broad open questions enquiring how patients would describe their RP experiences, before progressing to more focused discussions, sometimes targeting incompletely explored emergent themes from earlier focus groups, ensuring thematic saturation was achieved. At each focus group, efforts were made to create a relaxed, open environment in which the expression of individual and shared experiences was encouraged and everybody's opinion respected.

Data analysis. Qualitative analysis of the focus group transcripts was undertaken by experienced qualitative researchers (SH, ED, and CA). Inductive thematic analysis was adopted to ensure the findings were grounded in shared patient experiences rather than imposed from existing concepts (12). In the first stage, qualitative data were coded by reading the anonymized transcript multiple times, making notes of words and short phrases that captured important experiences. Units of meaning were identified and given descriptive labels (codes). In the second stage, the codes from the transcript were reduced (removing duplications and merging overlapping codes) and explored to see how conceptually related codes could be grouped to form subthemes, and finally subthemes were grouped to form overarching themes (12). The themes were then independently and systematically applied to each transcript by other team members to ensure a rigorous analysis and to minimize researcher bias (with amendments

Table 1. Demographics and clinical phenotype of enrolled participants according to purposive sampling framework*

Demographics/clinical phenotype	Bath	Pittsburgh	New Orleans	Overall
Participants, no. (no. in each focus group held)	17 (8,9)	6 (6)	17 (7,7,3)	40
Age, mean ± SD years	62.5 ± 11.5	50.8 ± 17.7	52.7 ± 12	56.6 ± 13.4
Disease duration, mean ± SD years†	13.8 ± 11.3	8.8 ± 6.6	7.7 ± 6.3	10.5 ± 9.1
Disease subtype				
Limited cutaneous SSc	15 (88)	5 (83)	4 (24)	24 (60)
Diffuse cutaneous SSc	2 (12)	1 (17)	13 (76)	16 (40)
Disease duration†				
≤3 years	2 (12)	2 (33)	5 (29)	9 (23)
>3 years	15 (88)	4 (67)	12 (71)	31 (77)
Sex				
Female	16 (94)	5 (83)	13 (76)	34 (85)
Male	1 (6)	1 (17)	4 (24)	6 (15)
Ethnicity				
White	17 (100)	6 (100)	3 (18)	26 (65)
Black/African American	0 (0)	0 (0)	12 (71)	12 (30)
Hispanic	0 (0)	0 (0)	2 (12)	2 (5)
Vasodilator medication use‡				
None	3 (18)	2 (33)	2 (12)	7 (18)
Calcium channel blocker	9 (54)	2 (33)	14 (82)	25 (63)
Phosphodiesterase inhibitor	5 (29)	4 (67)	3 (18)	12 (30)
Prostanoids	0 (0)	0 (0)	1 (6)	1 (3)
Angiotensin II antagonists	4 (24)	1 (17)	0 (0)	5 (13)
Selective serotonin reuptake inhibitor	2 (12)	0 (0)	0 (0)	2 (5)
Endothelin receptor antagonist	1 (6)	1 (17)	2 (12)	4 (10)
Combination therapy	3 (18)	3 (50)	3 (18)	9 (23)
History of digital ulcer disease				
Yes	7 (41)	4 (33)	12 (71)	23 (58)
No	10 (59)	2 (67)	5 (29)	17 (42)

* Values are the number (%) unless indicated otherwise. SSc = systemic sclerosis.
† Since first non-Raynaud's symptom.
‡ Indication not specified and includes SSc-Raynaud's phenomenon, SSc-digital ulcer, SSc-pulmonary arterial hypertension, and/or systemic hypertension/cardiovascular risk.

made if new codes emerged). This process was an iterative one, undertaken concurrently with data collection, allowing emerging themes to be explored and/or challenged in subsequent groups. After a preliminary independent analysis of the data, an analysis de-briefing meeting was convened, attended by the qualitative research team (SH, CA, and ED), SSc patient research partners (JW and HJ), an experienced PRO developer (JR), and an SSc expert (JDP) to derive consensus on the theme groupings (and applicable subthemes) and the conceptual map describing the interrelationship of the respective themes.

RESULTS

Forty SSc patients participated in 6 focus groups conducted in Bath (n = 2), New Orleans, (n = 3), and Pittsburgh (n = 1). The a priori purposive sampling framework ensured broad and representative participation in terms of clinical phenotype, age, sex, and disease duration. The multicenter design ensured diverse geographic, cultural, and ethnic participation (Table 1). The composition of individual groups differed as deliberate efforts were made to include missing cases in the latter focus groups. A 7th planned focus group in Bath was cancelled, as thematic saturation had been achieved.

Seven major themes emerged, that together constitute the patient experience of SSc-RP: physical symptoms, emotional impact, triggers and exacerbating factors, constant vigilance and self-management, impact on daily life, uncertainty, and adaptation. The interrelationship between the 7 constituent themes can be arranged within a conceptual map of the patient experience of SSc-RP (Figure 1). Each theme and subtheme will be described.

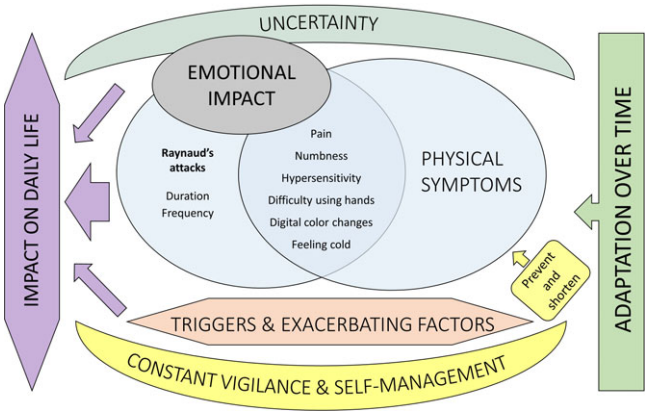

Figure 1. A conceptual map comprising the 7 major interrelated themes that constitute the patient experience of systemic sclerosis–Raynaud's phenomenon.

Table 2. Physical symptoms and emotional impact themes of the patient experience of systemic sclerosis–Raynaud's phenomenon (SSc-RP)

Theme and subtheme Q: location, subject*	Quotation
Physical symptoms	
Pain	
1: P1, S2	How do I feel when it happens? Oh, my fingers start to hurt, they turn white, and it hurts not only on the surface but all the way down to the bone.
2: P1, S5	When you say the word Raynaud's, I just think the word pain.
Numbness/tingling	
3: B2, S1	I have tingling at times, but it's the numbness and not being able to feel and touch I think is the main thing, really from the symptom point of view, as opposed to what it looks like.
4: P1, S6	They get very numb. It's not exactly pain, it's like that really, really deep numbness, like it almost hurts, but to me it's not exactly the same as pain.
Burning/hypersensitivity	
5: N1, S4	I think stinging, the stinging sensation that you feel whenever something like your leg falls asleep or something. I will get that sensation.
6: N1, S6	They were so sensitive, so tender, the fingertips. I did have an office job so I did a lot of typing, and I actually could not…type like you normally type.
7: B1, S6	[I have] a loss of sensation and then I get severe tingling, pain, and then black hands, would be the quick way of describing it.
Feeling cold	
8: N1, S2	I would describe it as your hands are extremely cold.
9: B1, S3	My hands and my feet go like, well, they're like ice. I can't even touch myself when I get a bad attack of it. I can't put my hand on my arm, I'm so cold.
Difficulty using hands	
10: B1, S2	When the sensation kicks in you can't…you can't pick things up and you can't knit or get the money out of your purse.
11: N3, S2	When you're going through a serious episode of Raynaud's your hands are pretty much useless to you.
Color changes	
12: B1, S1	In those days it was very much marbling. Now it is straight to the white.
13: B2, S5	I find with myself if I get cold, I get purple lips, my hands, my toes, and even my knees go purple.
14: N2, S3	But it was my fingers. They would be real, I mean black, numb.
Body sites	
15: P1, S1	I think of purple fingers. That's usually how it manifests. I do get it in my toes a little bit, even knee caps will turn purple, but hands have always been the worst.
16: B1, S3	And my lips at the same time, like you said, you know, they've turned round and said my "lips have gone purple and blue, am I all right?"
Duration of attacks	
17: B1, S6	It may take anything from 5 minutes to an hour to get the circulation back in.
18: B2, S1	Other times if you've gone into a cold place, I think that my fingers haven't gone completely normal all afternoon really.
Frequency of attacks	
19: P1, S1	I probably have maybe a handful of days a year where I don't have any attacks, but it's always got to be in the summer and it kind of has to be the perfect conditions.
Emotional impact	
Distress	
20: B2, S8	Last time when I went shopping…I couldn't open the boot of my car to put the shopping in. I had to ask the lady in the next car to me to do it and when I got in the car I just started crying. I couldn't take it.
Annoyance	
21: P1, S4	By the time I got to checkout, I couldn't pull my charge card out of my wallet because I had no feeling then. And it's just…All the time I'm in there…I just think I can't wait 'til I get back outside, I can't wait 'til I get to my car, I can't wait 'til my fingers are warm again.
22: B2, S4	For me it's the frustration of not being able to do what I want to do while you've got an attack, because you can't move your hands, and you can't do anything, and I think that's even worse than the pain.
23: B1, S1	Things like when you do go out, try to do your shopping, drop a coin and realize you cannot get it up again. You can no longer close your purse which you've opened to get your money out, and silly little things like that. And you sometimes get so frustrated, tears come to your eyes with it.

(continued)

Table 2. *(Cont'd)*

Theme and subtheme Q: location, subject*	Quotation
Despair	
24: N3, S2	Once it [SSc-RP] sets in, the pain could be, oh, just so miserable, I mean, just absolutely intolerable. . .Oh, I could go into hysterics it can get that bad. I've felt like I want these hands off of me.
Embarrassment	
25: P1, S1	It's like you're at work and you're going in for a performance review and you want to look your best and be confident, but your hands are purple, and it's because of the stress of the situation and you feel stupid. It's not really like the life or death, but it still does have some effect on you.
26: B2, S1	My hands were that bad the signature didn't look anything like my signature, and she [shop keeper] embarrassed me, she called the manager over, they wouldn't let me have my shopping, and I walked out of the shop in tears.
27: P1, S6	People make fun of me a lot at work. It's a silly thing, but like it's annoying. I'd rather not have attention for that reason.
28: N3, S3	But keeping the gloves and wearing the gloves in summer time used to bother me, because people stared at me, people laughed at me, and that was embarrassing.

* Q indicates the numbered quote cited in the text. P1 indicates Pittsburgh group 1; N1, N2, N3 indicate New Orleans groups 1, 2, and 3; B1, B2 indicate Bath groups 1 and 2; S number indicates the subject/participant within each focus group.

Theme 1: physical symptoms. The physical symptoms of SSc-RP differed between participants (Table 2). For some, pain was the predominant sensation (quotations 1,2), whereas others described the predominant symptoms as numbness and/or tingling (quotations 3,4), or even burning/stinging/hypersensitivity (quotations 5,6). Many patients reported a combination of symptoms (quotation 7), sometimes evolving as episodes of digital ischemia would develop and abate. Patients are aware that their peripheries are cold to touch, and many patients associate physical symptoms of pain and numbness as feeling cold (quotations 8,9). A combination of pain and altered tactile sensation result in difficulty using the hands (quotations 10,11), particularly concerning fine motor function (quotation 10), which can be further impaired by the need to wear gloves (quotation 60). The oft-cited "red, white, and blue" digital color changes of SSc-RP were described, as expected, but patients preferentially adopted other terms such as purple (quotations 13,15), marbling (quotation 12), and black to report the cutaneous discoloration of SSc-RP (quotations 7,14). The fingers are the predominant body site considered by patients when discussing SSc-RP, in part because the fingers are the most significantly affected area (quotation 15), but also owing to the importance of the fingers for activities of daily living and the fact that the fingers (unlike the toes, nose, and lips) are typically exposed, both to the elements and the visible attention of the patient (quotation 16). Discoloration of the knees, not a body site usually associated with SSc-RP, was mentioned by more than 1 participant (quotation 15). Color changes in the lips, nose, and knees do not appear to result in the same sensory changes as the fingers and toes. For many participants, the notion of attacks was consistent with their experiences of SSc-RP, but some expressed difficulty distinguishing attacks of SSc-RP, as the following passage attests: "I'm not really 100% sure what an 'attack' is because it's just so cold, and then they come back tingling. But I can't say 'Oh, I've got an attack'. . .I can't say 'Oh, they went white,' although they do change color sometimes. . .I've just taken it for granted and lived with it" (New Orleans second focus group, subject 4).

The duration of SSc-RP attacks differed between individuals and varied within individual patients according to exposure to cold and the capacity of patients to either take positive steps to warm their hands or extract themselves from an environment conducive to SSc-RP symptoms (quotations 17,18). The frequency of SSc-RP attacks was also largely dependent on exposure to exacerbating triggers, but the majority reported attacks occurring several times per day and seldom experienced days completely free of SSc-RP symptoms (quotation 19).

Theme 2: emotional impact of SSc-RP. Experiences of SSc-RP have a significant emotional impact on patients, encompassing feelings of distress (quotation 20), annoyance (quotations 21–23) and, for some, desperation (quotation 24) (Table 2). Loss of normality and the restrictive nature of SSc-RP on social participation and leisure pursuits is a particular source of frustration. For some, emotional distress resulted in irritability that impacts on relationships (see below). Unwanted attention toward cutaneous discoloration, the need to wear extra clothing/gloves in ambient conditions, and difficulty using hands due to SSc-RP were highlighted as a source of embarrassment, particularly in the workplace and/or public places (quotations 25–28). Actual body image dissatisfaction related to the visible discoloration of SSc-RP was not a common theme, and many patients had come to accept the appearance of SSc-RP (quotation 42, see below).

Theme 3: triggers and exacerbating factors. Cold exposure was the principal exacerbating factor for all participants (Table 3). Defining a temperature threshold at which RP attacks were more likely was volunteered by some participants (quotation 29), whereas for most it was

Table 3. Triggers and exacerbating factors and constant vigilance and self-management themes of the patient experience of systemic sclerosis–Raynaud's phenomenon (SSc-RP)

Theme and subtheme Q: location, subject*	Quotation
Triggers and exacerbating factors	
Cold	
29: N1, S4	Now, the medication has helped to the point of where. . .I can handle temperatures down to about around 50 [°F] or so. If it's 50 or below, I will have issues when I go outside into the cold.
30: B2, S4	Even the tiniest draught and that's me gone, even if it's blazing sunshine and I've got a draught. It's the regulation of the body temperature. . .it just can't cope with change.
31: P1, S2	It would be 90 something degrees [°F]. You come out, you're in the sun, and a breeze goes by, and right away your hands start turning colors.
32: N1, S7	But when I go into a situation of a grocery store when you go by the freezer section, you know, I can tell, I start turning purple, my fingers start turning purple.
33: P1, S1	The meat department or anything that's refrigerated. A lot of it is . . .It almost feels like you're helpless when you're trying to warm them up, but you don't really know if it's going to work or not.
34: N2, S7	And every time I would go in a grocery store around the freezer part I could not. . .I mean the minute I'd get to there. . .[voices murmur agreement]. It would actually turn so black.
Stress	
35: B2, S6	My hands don't necessarily have to be cold, I can be in a situation like this, just nerves can make mine go.
36: B2, S5	Yes, stress, very much if you're put in a stressed environment, then that will bring the purpleness on the fingers.
37: N2, S5	I don't know how much. . .is like psychological or not, but I know that when I'm feeling more relaxed I, physically, I feel as though I'm doing better. But when I'm stressed for whatever reason like, it's harder to manage my symptoms.
38: N3, S3	I haven't noticed it, maybe it could be something I'm not aware of, stress bringing on the condition.
Unpredictability	
39: N1, S6	And I'll get attacks and it's like I'm not cold, what is causing me to have a Raynaud's attack? And like I'm totally not cold, it's hot, it's in the summer, so that, I don't know what sets that off, I really don't.
Constant vigilance and self management	
Maintaining warmth (preventative measure)	
40: B1, S6	And then if I know that I'm going to be outside shooting, then I make sure I've got, you know, hot pads and gloves and everything else, so you just kind of adapt to it really.
41: B2, S7	I have the heating on day and night and I've always got a thick coat and gloves and then I sort of forget about it really, I've done all I think I can do.
42: P1, S2	I have mittens all over my house. I have great friends who knit me mittens and so I go to the grocery store with mittens on. People look at me like I'm really dumb, but that's life. Who cares if they think I'm dumb wearing mittens, but they work.
43: P1, S1	The first 5–10 years [were] really rough, and I was stubborn. I just wanted to wear a T-shirt and a jacket and some gloves, and you have to accept, no, I need to have a T-shirt, a longer shirt and a hoodie, and a jacket and mittens, and everyone else is wearing some lighter clothes and I'm there totally bundled up, but at this point that's kind of just my daily life, so I think it's actually gotten easier over time.
Seeking warmth (alleviating measure)	
44: N3, S2	If it sets in, just putting a glove on, putting gloves on, just won't do it. . .I have to put heat to my hands somehow with something, to apply heat to get that pain to go away.
45: P1, S1	Like everyone's said, they'll pretty much stay that color until I do something; run them under hot water or put some gloves on or put a jacket on, especially in the grocery store, I notice that all the time.
46: N3, S1	Oh no, you'd have to do something in order to warm them up, and you can't just, like when your fingers or hands go numb, you shake them out, it's not a shake-it-out kind of scenario, it's a "I got to do something."
47: B1, S5	Well one thing that is quite easy I find is a wash basin of warm water, you know, in an emergency if you've obviously got nothing else. . .It comes back you know, all right I find.

(continued)

Table 3. *(Cont'd)*

Theme and subtheme Q: location, subject*	Quotation
Avoiding cold	
48: B1, S4	I tend not to leave the house if I don't have to in the winter.
49: P1, S6	My brother lives in XX and I just won't visit him unless it's like the height of summer, because it's freezing up there, and there's nothing I can do to get warm enough, so I just don't go there.
50: P1, S4	I don't ski anymore, either, 'cos you're taking your gloves off, if your ski falls off or whatever, so even if you have something in your gloves to keep them warm, no, so I avoid winter activities, let's put it that way.
Limited effectiveness of self management	
51: B1, S2	I had 3 pairs of gloves on the other day, and I still got cold hands.
52: P1, S3	I think I could possibly prevent attacks all day, but nobody would be able to live with me [in] the house at 90 degrees [°F].
53: B2, S5	I find that there's nothing you can do to stop the attack because with me there's no tell-tale sign, there's no tingling, it's just I'm here and you're gonna have to deal with it, whether it takes 10 minutes, 20 minutes, it is as long as it lasts.
54: P1, S2	I can't prevent them, but as soon as they [SSc-RP symptoms] start I try to do something about it, try to warm them up.
55: B2, S4	The best thing is to get out of the environment that's causing it, but you can't always do that, you know, so at that stage there is no hope.

* Q indicates the numbered quote cited in the text. P1 indicates Pittsburgh group 1; N1, N2, N3 indicate New Orleans groups 1, 2, and 3; B1, B2 indicate Bath groups 1 and 2; S number indicates the subject/participant within each focus group.

a change (typically a reduction) in temperature or a draft that was most likely to precipitate SSc-RP symptoms (quotations 30–31). Exposure to domestic refrigeration appliances (quotations 32–34) and air conditioning were very frequent exacerbating factors, with visits to the grocery store being particularly likely to trigger SSc-RP symptoms (quotations 32–34), perhaps owing to less easily mitigated sporadic fluctuations in temperature that grocery shopping results in. For many, emotional stress was an important trigger (quotations 35,36), sometimes exacerbated by feelings of embarrassment caused by digital discoloration (quotation 25), and some patients reported their SSc-RP symptoms were less intrusive and more manageable when they felt relaxed (quotation 37). For others, and in contrast to cold exposure, stress had no discernible impact on their SSc-RP (quotation 38). Some participants reported a high level of unpredictability, with SSc-RP attacks occurring for no apparent reason (quotation 39). Rarely reported exacerbating factors included gripping tightly and passive smoke inhalation.

Theme 4: constant vigilance and self-management. Patients described a life of constant vigilance and self-management that, for patients, means that nothing is simple anymore, and everything must be planned and prepared for. All patients reported taking positive steps to maintain warmth to prevent and/or reduce the impact of SSc-RP (quotations 40–42), and patients reported such behavior helping them manage their symptoms better as time had progressed (quotation 43) (Table 3). Abating attacks of SSc-RP necessitates the application of local warmth, and many patients reported strategies they had adopted to achieve this, such as using heat packs, submerging in a basin of warm water, etc. (quotations 44–47). Patients with SSc make significant sacrifices to avoid cold exposure that, while helpful, negatively influence social participation, relationships, and leisure activities (quotations 48–50). Despite the adoption of such measures, complete avoidance of SSc-RP symptoms was an unachievable goal and many participants accepted the limits of self-management (quotations 51–55).

Theme 5: impact on daily life. Each of the preceding themes makes its own specific contribution to the broader impact of SSc-RP on daily life (evident from a number of quotations provided in Tables 4 and 5). Specific aspects of daily life that are commonly affected include shopping (quotation 56), household chores (quotations 57,58) and self-care (quotation 59). The need to wear gloves the majority of time exacerbates the impaired functional capacity, making everyday activities harder to complete (quotation 60). Participation and enjoyment in social and leisure activities are either directly affected by SSc-RP symptoms (quotations 61–64) or lead to tradeoffs taken to avoid cold exposure (quotation 50). Participants provided examples when work participation was challenging because of an inability to control their work environment to suit their needs (quotation 65). An inability to complete work tasks due to SSc-RP was a source of guilt for some (quotations 66,67). Some reported negative experiences in the workplace from colleagues ignorant of or unsympathetic to their needs (quotation 68), while others expressed concerns about the effect of SSc-RP on job security (quotation 69). Several examples were given of the impact of SSc-RP on family life, which included being irritable around family members (quotations 70,71), having difficulty fulfilling family roles (quotations 72,73), and having a sense that family members do not fully appreciate the extent of their problems (quotation 74). Many participants expressed sorrow relating

Table 4. Impact on daily life theme of the patient experience of systemic sclerosis–Raynaud's phenomenon

Theme and subtheme Q: location, subject*	Quotation
Impact on daily life	
Daily activities	
56: B2, S1	You can't sort of feel things properly, trying to do shopping, trying to get cards out of your purse and things, you can't touch it, trying to sign your name when you didn't have to do the push button for the cards.
57: B2, S6	I can't even change the bed, I can't take the sheets off the bed, I can't put them back on the bed. Trying to put a pillow case on, especially because it's cold, you just can't, your fingers just can't do it, even though you're willing them to do it, you just can't do it.
58: N1, S5	Housework. . .the biggest problem was mopping the floors and sweeping the floors. It's almost like I cannot get a grip of the mop stick and the broom to actually sweep right, because I tend to close my hand real tight around it when it. . .That's when it affects the most.
59: B2, S9	I say, and I say to him, don't put the toothpaste back tight, don't put the washing up liquid back tight, because I can't click it to get the washing up liquid out. I mean some things I can still undo with my teeth, but not jars. I haven't got that big a mouth to do a jar, but little bottles, and water bottles I do with my teeth because I can't undo them.
60: B2, S1	I think sometimes with the gloves. . .it actually makes it more difficult anyway for holding. You know, you wear the gloves to warm your hands up, but then you can't grip properly.
Social and leisure	
61: B2, S6	I can't walk my dogs, because I can't hold the lead, I'm frightened that I'll get so far and my fingers won't be able to hold the lead once you get going. Even with the gloves on.
62: N2, S2	I love going out to eat, but when I go I bring the thickest coat and gloves that I can find, and I'll still be miserable. I can't even really enjoy myself. I'll be like, "I've got to get out of here. It's so cold."
63: B1, S6	I used to climb 2 or 3 times a week, and I had to stop that because it kept happening while I was climbing. I had a couple of quite nasty falls, so I had to stop that. And that was basically just loss of sensation when you're clinging to a rock face.
64: N1, S4	If it's real cold, obviously, it does. It affects it [social life] severely, I mean, you know, you can't. . .There's certain hobbies like playing videogames, or maybe woodworking or things like that, where it just doesn't. It just doesn't work like it used to.
Work	
65: B2, S6	I work in a library, and like you say with the air conditioning, if I get under the air conditioning and suddenly go straight there, I've walked from a nice warm place out of the office into the library, smack straight away it goes. You can't move the books, you can't get the book back in because your fingers just can't physically move because it's that sore.
66: B1, S4	I felt really bad because I'd been there longer, but there was staff coming in, I'm on more money than them, and I'm waiting for them to finish their job off for them to come and help me start my jobs. So I actually left last year.
67: N1, S3	Well, by the time I was sick, I was self-employed, I had started a little business of my own. But yes, it shut me down. I had to employ other people to do what I was doing, so yes.
68: N3, S3	I had a supervisor and I had to put gloves on and I learned to type in the gloves. . .She called me into her office and. . .she grabbed her phone and said "now I've got a picture." I looked at her, she said, "Huh, it's not that cold, I can't believe you have gloves on in here." And I'm like "Okay, what did you call me for?" Because I had to learn to deal with people's reactions. . .I had to just stop being embarrassed about that and just walk around and put your gloves on wherever you go, if they look, they laugh.
69: B2, S5	Well I just never told my employer, because I wouldn't have been able to do my work. . .I used to put 3 lots of thermal linings on in gloves, and I used to freeze, but I had to do it because that's what my job was.
INT: B2, S5	So were you worried about telling your employers in case? Yes, because they would have said well don't bother coming back Monday.
Family	
70: P1, S5	I feel very bad, because then I get angry, I get cranky with my family, my poor husband, you know, just because it's hurting so bad and he's never going to understand that pain of just going into a grocery store.
71: P1, S4	Especially if he's [spouse] with me and I have episodes. . .I'm just, come on, I'm just very short with him or whatever. . .if I'm alone I just deal with it, but sometimes I do tend to take it out on him maybe a little bit.
72: B2, S9	I used to take him up and give him a bath, and now he says, "No, not nanny, let mummy and daddy do it, not nanny, she's too cold." So I can't bath him because my hands are too blue and they start as soon as I'm going up the stairs. . .So I don't bath him anymore, it's a shame. That's a big thing to lose that is, yes.

(continued)

Table 4. *(Cont'd)*

Theme and subtheme Q: location, subject*	Quotation
73: N3, S1	I won't ever show that to them, because I'm supermomma, but you know, when they've gone to school, I kind of think about it and, you know, it's getting to the point I can't even tie a shoestring.
74: B1, S1	My daughter is just laughing at me. She understands to a point but she doesn't understand the pain and I think the frustration of it.
Loss of normality	
75: B2, S5	It's a combination of the pain and the numbness, the not being able to do normal things. It would be lovely to sort of turn the clock back and. . .be back to what I was like when I was 18, 19 [years old], go in the sea and not come out blue, sit in the garden after the sun goes down at 6 o'clock.

* Q indicates the numbered quote cited in the text. P1 indicates Pittsburgh group 1; N1, N2, N3 indicate New Orleans groups 1, 2, and 3; B1, B2 indicate Bath groups 1 and 2; S number indicates the subject/participant within each focus group; INT = interviewer.

to a loss of normality and inability to do things they took for granted previously (quotation 75).

Theme 6: uncertainty. All of the preceding themes result in having to manage a life that is filled with uncertainty. This broad-ranging theme encompassed a number of aspects relevant to SSc-RP, ranging from the aforementioned uncertainty over the labels we use to describe attacks of SSc-RP, uncertainty regarding future disease progression (particularly concerning the development of digital ulcers in patients with prior experience of this complication [quotations 76–78]), the relevance of SSc-RP symptoms to the aging process (quotation 79), and/or uncertainty regarding the likely efficacy of current/future drug treatments for controlling their SSc-RP (quotation 80). A change in routine can provoke uncertainty and anxiety regarding the likely impact on the participants' ability to manage their SSc-RP symptoms (quotations 81,82). Indeed, a generalized anxiety at finding themselves in an environment in which their symptoms were poorly controlled, and the need to make adequate preparation for activities that might impact on SSc-RP symptoms, was a recurring theme across the focus groups (quotations 83,84).

Theme 7: adaptation. In spite of all the aforementioned unpleasant experiences and challenges, participants reported many examples that demonstrated a remarkable capacity to adapt to life with SSc-RP. Examples included adaptations made in the home environment (quotation 85), tradeoffs accepted in daily activities and social participation (quotations 86–89), and scenarios in which they might seek help from others (quotation 90). Acceptance of the need to continue life despite SSc-RP, supported by a strong sense of "not letting it beat you," emerged within each focus group, and a number of quotations highlight the resilience and fortitude with which many patients face their illness (quotations 91–94).

DISCUSSION

We report the outcome of the first study to specifically examine the patient experience of SSc-RP. The multicenter design and comprehensive purposive sampling framework has ensured that we have captured experiences from a representative cohort of SSc patients in terms of age, sex, disease duration, and clinical phenotype, while also ensuring diverse geographic, cultural, and ethnic participation. Thematic analysis of the anonymized focus group transcripts was led by qualitative researchers without direct experience of managing SSc, ensuring an unbiased appraisal of the experiences expressed. The involvement of patient research partners in decision-making has ensured that each stage of the study (from devising the focus group topic guide to the interpretation of thematic analysis) was appropriate and suitable for achieving the project's stated aims. We chose focus groups over individual patient interviews to allow participants to respond to the opinions of others, challenging and/or validating the views of other group members. Focus groups can result in a propensity for participants to conform to majority opinion, but deliberate efforts were made to create an environment that avoided this conformity. We feel the focus groups facilitated the capture of relevant and generalizable experiences across the diverse spectrum of SSc, which might not have emerged from 1:1 patient interviews.

Inductive thematic analysis has identified 7 major interrelated themes (and encompassing subthemes) constituting the patient experience of SSc-RP that can be arranged within a conceptual map of SSc-RP. Unsurprisingly, the physical symptoms of SSc-RP are positioned at the heart of our conceptual map and featured prominently when participants were asked to describe their RP experiences. Specific physical symptoms of SSc-RP differed between patients, with some experiencing a predominance of pain, whereas for others, numbness was a more relevant description of their experiences of SSc-RP. The physical symptoms of SSc-RP lead to considerable emotional distress, and impaired ability to use the hands results in significant impact on daily life. Cold exposure is the major trigger for SSc-RP symptoms, although many participants also reported emotional stress as an exacerbating factor. People with SSc take considerable measures to avoid or ameliorate SSc-RP symptoms, but self-management approaches are seldom completely effective and can directly impact on functional capacity, social participation, and quality of life. Patients adapt over time, developing strategies that increase resilience and help them to carry on life despite SSc-RP, although for many, SSc-RP symptoms contribute to a

Table 5. Uncertainty and adaptation themes of the patient experience of systemic sclerosis–Raynaud's phenomenon (SSc-RP)

Theme and subtheme Q: location, subject*	Quotation
Uncertainty	
Consequences of SSc RP (especially ulcers)	
76: P1, S1	If I knew there was not going to be any ulcers it [SSc-RP] probably wouldn't bother me that much.
77: P1, S3	Because I do worry about getting ulcers, and that's the whole name of the game. If it [SSc-RP] was just inconvenience and not perhaps long-term damage, then I wouldn't probably care. I'd deal with it.
78: B2, S6	I just fear, when I've got them and they're coming very regularly, I just fear the ulcers, because I get ulcers.
79: B1, S5	I think I worry whether the Raynaud's is sort of connected with the general sort of aging process, which you know, we all have to accept as we get older.
Efficacy of treatment	
80: N1, S5	What other treatments can we get, if one don't work, what's next? I mean, I'm on so much medication. . .I'm just confused on what. . .what's working some days and what's not working.
Uncertainty around changes in usual activity	
81: P1, S3	It does concern me going on trips. If I get into a really cold room, and what's going to happen. I just want to be comfortable and be safe, that's all.
82: N3, S3	In my case I had a high level of anxiety, because I was driving someone else's car and the heater didn't work, and it was cold outside that day, and within such a short span of time with the heater not working my hands began to sort of numb up, and I said I'm not going to be able to drive that far. So then I began to get stressed, saying my car's in the shop and if this thing's cold I won't be able to drive this car, so that caused me stress.
Anxiety	
83: P1, S5	It's always. . .what kind of clothes? And who's going to be with me? So there's a lot of anxiety that comes with it, and maybe that's a lot of reasons I'm at home a lot, too. I don't have to worry about it.
84: N3, S1	I do believe that anxiety is associated with Raynaud's. You have to always be aware of something that may affect you. . .it's almost like packing for a newborn baby, you have to make sure you have everything you need with you, because you don't want to be caught some place you don't have what you need.
Adaptation	
Doing things differently	
85: N3, S2	I have bottle openers in my house. . .it opens bottles of different sizes. . .you learn, and you just, you just keep adapting.
Making tradeoffs	
86: B1, S1	I do save my washing up until I feel that I really do need to go and warm my hands up a bit.
87: N3, S2	I remember thinking "no buttons, no buckles, no shoestrings." Anything like that just had to go.
88: B1, S6	And I've had to change how I exercise, because I can't climb anymore. So I swim instead.
89: P1, S2	If it's cold I will go for a walk in the snow, I just probably won't roll around sleigh riding with my grandchildren. But I just can't let this control my life. I've got to keep going and doing what I enjoy.
Seeking help	
90: N3, S2	I need to do something like put air in my tires. . .I can't really do something like that if it's really cold and I have all these gloves on. If I can get somebody to help me with something like that, well then, I would.
Not letting it beat you/acceptance	
91: B1, S3	But I've just learned to get on and do things. It's painful, but I won't give in to it.
92: B2, S5	If I have an attack and I'm with somebody and they say, "Oh what's wrong?" I'll say, "Oh I've got my purple paws again." And put them in my pocket and I say, "Don't worry, you carry on, and I'll be alright in about quarter of an hour."
93: P1, S1	Any time somebody sees it for the first time, they get really freaked out, and it gets kind of old hearing, "Oh, you should get that looked at," or "That's not normal." And you're like, "I know, I've known that for a long time. I've had it looked at. It's not

(continued)

Table 5. *(Cont'd)*

Theme and subtheme Q: location, subject*	Quotation
94: N2, S7	necessarily under control, but I'm familiar with it." So that can get old after years and years of that, every time you meet somebody new. It's not that big of a deal. Even when my hands were real, real black, I never was embarrassed about, you know. I'm not that type of person that gets embarrassed about it. That's just a part of life. Everybody got something, you know.

* Q indicates the numbered quote cited in the text. P1 indicates Pittsburgh group 1; N1, N2, N3 indicate New Orleans groups 1, 2, and 3; B1, B2 indicate Bath groups 1 and 2; S number indicates the subject/participant within each focus group.

pervading uncertainty for the future progression of their disease and general well-being.

Our findings have implications for current approaches to assessing SSc-RP. The episodic nature of SSc-RP has resulted in a reliance on patient self-report. Early therapeutic studies of SSc-RP sought a categorical assessment of SSc-RP severity (typically as better, same, or worse) (13–16). These assessments were gradually superseded by linear psychometric scales, allowing quantification of specific components of SSc-RP symptoms, such as pain intensity and the severity of attacks (17–20). The most widely adopted scale is the Scleroderma Health Assessment Questionnaire RP visual analog subscale (SHAQ RP VAS), which asks patients to consider the extent to which their SSc-RP "problems interfered with your activities" during the preceding week (21). Diary cards have attempted to quantify the frequency and duration of RP attacks, often incorporating linear psychometric global assessments of RP severity (22–25). The Raynaud's Condition Score (RCS) diary was originally developed for 2 separate studies of oral iloprost (26,27). The RCS diary collects daily information over a 2-week period of the frequency and duration of RP attacks while also incorporating a single item, 11-point numeric rating scale (the actual RCS) that assesses the difficulty patients have experienced from their SSc-RP each day (26,27). When considering the RCS score, patients are asked to consider the difficulty they have experienced due to a range of domains, including the number of attacks, the duration of the attacks, symptoms such as pain/numbness, and the ability to use their hands (26,27). Item wording of the RCS differed between the original studies, with the impact of "painful sores" included in the response options for the RCS that underwent post hoc analysis of the validity, feasibility, and reliability of the tool using original clinical trial data (27,28). The RCS diary has subsequently been recommended (alongside the SHAQ RP VAS) for use in clinical trials of SSc-RP (29,30).

The present work has revealed limitations to current methods for assessing SSc-RP. First, our findings challenge the accepted paradigm of Raynaud's "attacks," as not all patients identify with this concept. For many, SSc-RP represents a more nebulous concept that encompasses experiences across several of the themes defined in this work. Moreover, diary monitoring of SSc-RP attack frequency and duration makes no allowance for the considerable measures patients take on a daily basis to prevent or ameliorate symptoms of SSc-RP (themes 4 and 6). In this regard, diary monitoring more accurately provides a combined assessment of peripheral microvascular compromise in conjunction with the effectiveness of self-management approaches adopted by patients to control their symptoms. The RCS, meanwhile, attempts to capture the complex multidomain construct of SSc-RP in a single-item global assessment. This approach risks missing clinically important improvements in individual domains (e.g., pain) as respondents are forced to consider the impact of other domains that might be more resistant to intervention. The item wording ("how much difficulty") might be influenced by habituation and adaptation (themes 4 and 6), whereas the inclusion of "painful sores" in the originally validated RCS might result in inadvertent assessment of digital ulcer disease.

These limitations might offer some explanation for the poor agreement between RCS diary returns and objective assessments of peripheral microvascular function in SSc (31). Similarly, the SHAQ RP VAS item wording ("interfered with your activities") might also be influenced by self-management and adaptation (themes 4 and 6). Existing PRO instruments do not capture frequently expressed physical symptoms of SSc-RP such as tingling and hypersensitivity of the fingertips or feeling cold, whereas other important physical symptoms such as pain and numbness might be better assessed in isolation. Emotional distress (theme 2) and the impact of SSc-RP on social participation, family life, and work (theme 5) are not captured using existing tools, despite such themes emerging prominently in this study. Additional concerns have been raised regarding existing methods for assessing SSc-RP (e.g., placebo effect and respondent burden), and there is consensus that novel approaches to assessing SSc-RP are required (32).

There was little patient participation in the development of existing PRO instruments for SSc-RP (33). Regulatory bodies now seek target patient population involvement in PRO instrument design when examining labeling claims in medical product development (7), and patient involvement ensures the capture of experiences relevant to the patient in a comprehensible and unambiguous manner (34). Work to develop a novel patient-derived PRO instrument for assessing the severity and impact of SSc-RP, comprising domains/items grounded in the patient experiences of SSc-RP identified in this work, is currently underway.

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. Pauling 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.

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Acquisition of data. Pauling, Domsic, Saketkoo, Almeida, Dures, Hewlett.

Analysis and interpretation of data. Pauling, Domsic, Saketkoo, Almeida, Withey, Jay, Frech, Ingegnoli, Dures, Robson, McHugh, Herrick, Matucci-Cerinic, Khanna, Hewlett.

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