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Multicenter Qualitative Study Exploring the Patient Experience of Digital Ulcers in Systemic Sclerosis

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Objective. Digital ulcers (DUs) are a major cause of disease-related morbidity and are a difficult-to-treat vascular complication of systemic sclerosis (SSc). Demonstrating treatment efficacy has traditionally focused on clinician assessment of DUs alone. No existing patient-reported outcome (PRO) instrument captures the multifaceted impact of SSc-DU. We report the findings of a multicenter qualitative research study exploring the patient experience of SSc-DU.

Methods. Patient focus groups were conducted across 3 scleroderma units, following a topic guide devised by SSc patients, experts, and experienced qualitative researchers. A purposive sampling framework ensured that the experiences of a diverse group of patients were captured. Focus groups were audio recorded, and information was transcribed, anonymized, and analyzed using inductive thematic analysis. We continued focus groups until thematic saturation was achieved.

Results. Twenty-nine SSc patients with a history of DU disease participated in 4 focus groups across the UK (Bath, Manchester, and London). Five major interrelated themes (and subthemes) were identified that encompass the patient experience of SSc-DU: disabling pain and hypersensitivity; deep and broad-ranging emotional impact; impairment of physical and social activity; factors aggravating occurrence, duration, and impact; and mitigating, managing, and adapting.

Conclusion. The patient experience of SSc-DU is multifaceted and comprises a complex interplay of experiences associated with significant pain and morbidity. Patient experiences of SSc-DU are not captured using existing SSc-DU outcomes. Our findings will inform the development of a novel PRO instrument to assess the severity and impact of SSc-DU for use in future SSc-DU clinical trials.

INTRODUCTION

Digital ulcers (DUs) are a major cause of pain and disability in patients living with systemic sclerosis (SSc) (1). DUs are common, with approximately half of patients reporting a history of ulceration, and 5–10% of patients with SSc at any time have a current ulcer (2,3). DUs have a major impact on the quality of life and hand function, including occupation (4). Although we have a number of treatments available to both prevent and heal SSc-DU (5–8), a third of patients are affected by refractory DU disease (9).

In general, demonstrating treatment efficacy in previous clinical trials has been based on clinician assessment of ulcer healing and/or new ulcer occurrence alone (1). However, the agreement among SSc experts to classify SSc-DU is poor to moderate at

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SIGNIFICANCE & INNOVATIONS

- Existing systemic sclerosis (SSc)–digital ulcer (DU) outcome measures do not capture the complete patient experience of SSc-DU.
- The patient experience of SSc-DU comprises interrelated factors that contribute to the significant morbidity of SSc-DU.
- Five major interrelated themes were identified: disabling pain and hypersensitivity; deep and broad-ranging emotional impact; impairment of physical and social activity; factors aggravating occurrence, duration, and impact; and mitigating, managing, and adapting.
- The interplay between the themes suggests that the presence of SSc-DU can have a considerable impact on patients' physical and psychological wellbeing, impairing physical and social activities, and that patients expend great effort in remaining vigilant and managing their condition, often in innovative ways.
- Our findings can be used to inform the development of a novel patient-reported outcome instrument to assess the severity and impact of SSc-DU.

best (10–12). Interrater agreement is not improved with the provision of clinical (real-world) contextual information (e.g., the severity of pain and duration of the lesion) (11). Recent negative clinical trials of promising therapies for SSc-DU (13,14) have led to calls for a fresh approach to establishing treatment efficacy in SSc-DU (15–17).

No studies have specifically explored the patient experience of SSc-DU, although studies examining broader symptom burden in scleroderma have identified the major impact that SSc-DU can have for patients, as the following quotation attests: "The pain that you felt in your fingers as they were dying was so excruciating that you almost begged to say please cut it off" (reproduced from [18]).

Previous attempts to quantify the impact of SSc-DU have used legacy patient-reported outcome (PRO) instruments to assess broader aspects of SSc disease severity and function (19,20). There was limited or no SSc patient participation in the development of many of these instruments (21). The patient perspective captured by PRO instruments provides insight into the patient experience of disease that can not be assessed using clinician-reported instruments (22). Regulatory bodies, such as the Federal Drug Administration, seek target patient population involvement in PRO instrument development to ensure that instruments fully capture the way patients feel and function (23). A thorough understanding of the patient experience of SSc-DU is necessary to ensure that a future PRO instrument captures the multifaceted impact of DUs. Against this background, the aim of the current study was to comprehensively explore the experiences, attitudes, and perspectives of patients with SSc-DU. A further aim was to inform the development of a future SSc-DU PRO instrument.

PATIENTS AND METHODS

Study management. The development and conduct of the study were overseen by a dedicated steering committee that comprised SSc experts (MH, JDP, CPD, RTD, TMF, ALH, DK, MM-C, LAS), 2 patient research partners, and a team of experienced qualitative methodologists. The study was approved by the East Midlands–Nottingham 1 Research Ethics Committee (18/EM/0018), and all participants provided written informed consent.

Study design. A multicenter qualitative research study comprising patient focus groups was undertaken at scleroderma centers across the UK (Bath, Manchester, and London). Patient focus groups create an open environment in which a broad range of experiences can be expressed and explored and can often enable some (but not necessarily all) sensitive issues to be discussed more freely than in a one-to-one interview setting (24).

Participants. Adult SSc patients (ages >18 years) with a history of SSc-DU, fulfilling the 2013 American College of Rheumatology/European League Against Rheumatism classification criteria for SSc (25), and with sufficient language skills to participate in a focus group discussion were enrolled. A purposive sampling framework ensured the enrollment of a diverse cohort comprising a 60:40 split between limited and diffuse cutaneous SSc (26), early and established disease (≤3 and >3 years since first non-Raynaud's phenomenon symptom, respectively), a spectrum of historical DU disease, sex (aiming for 5:1 female predominance), and ethnicity (e.g., with Caucasian and Black British). The focus groups sought to include 6–10 participants to enable

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open discussion, while ensuring that each participant had the opportunity to express their personal experiences, interact, and offer alternative opinions should they wish. A minimum of 2 to 3 focus groups was expected to be necessary to achieve thematic saturation, but the intention was to continue enrollment until there was consensus that no meaningful new experiences were being shared by participants or that warranted further exploration by the investigators (27).

Data collection. Each focus group lasted approximately 1 hour and all were facilitated by MH, with the first focus group also facilitated by JDP and AM to ensure that there were no issues including a need to revise the topic guide (which was not the case). Focus groups were facilitated by rheumatologists (MH and JDP) with experience in the clinical heterogeneity and management of patients with SSc. Focus groups were held within hospitals but outside of clinical areas, in a quiet ambient environment without external distraction. The focus group lead facilitator (MH) is a rheumatologist with an interest in SSc and was not directly involved in the clinical care of the participants. JDP is a rheumatologist with an interest in SSc, and AM is an experienced qualitative researcher/methodologist. A relaxed environment in which each participant's views were sought, valued, and respected enabled individuals to share experiences of SSc-DU, and that setting allowed others to express similar or opposing views. The focus groups were audio recorded, and information was subsequently transcribed verbatim, with all the context anonymized. A topic guide was developed with input from the study steering committee (see Supplementary Appendix A, available on the *Arthritis Care & Research* web site at http://onlinelibrary.wiley.com/doi/10.1002/acr.24127/abstract). Each focus group started with broad open questions asking participants to describe their experience of their disease and DU history. Focus groups adopted an adaptive study design enabling incompletely explored or newly emerging themes to be investigated to ensure that thematic saturation was achieved.

Data analysis. Qualitative analysis was conducted by JJ and AM, both experienced qualitative methodologists, with further input from the wider team (MH, JDP, RG-H, and patient partners). NVivo 11 software was used to manage and interrogate the data. Transcribed data were analyzed using thematic analysis (27). First, JJ read and reread transcripts to ensure familiarity with the content. Information relevant to patients' experience and understanding of DUs was then coded using descriptive labels. Codes that occurred repeatedly, or that shared conceptual similarities, were then grouped together to form initial categories. The

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

Demographics/clinical phenotype	Bath	Manchester	London (1)	London (2)	Overall
Participants	8	7	6	8	29
Age, mean ± SD years	66.1 ± 12.6	61.6 ± 12.2	50.4 ± 12.4	59.5 ± 12.8	59.9 ± 13.3
Sex F:M ratio	7:1	7:0	3:3	3:5	20:9
Disease subtype					
LcSSc	8	6	2	4	20
DcSSc	0	1	4	4	9
RP duration, mean ± SD years	20.7 ± 19.9	17.9 ± 15.9	23.1 ± 22.1	13.6 ± 9.5	18.5 ± 16.6
Disease duration, mean ± SD years†	14.3 ± 11.2	10.9 ± 7.3	13.9 ± 12.6	13.2 ± 12.2	12.8 ± 9.7
Early vs. established disease‡					
Early	0	1	1	0	2
Established	8	6	5	8	27
History of DU					
1 previous	1	1	0	1	3
2–4 previous	3	3	2	1	9
≥5 previous	4	3	4	6	17
Ethnicity					
White/Caucasian	7	6	5	5	23
Black British	0	1	1	2	4
Asian	1	0	0	1	2
Vasodilator medication used§					
None	1	2	1	2	6
Calcium channel blocker	5	2	1	2	10
Phosphodiesterase type-5 inhibitor	5	4	4	5	18
Endothelin receptor antagonist	3	2	2	2	9

* Values are the number unless indicated otherwise. LcSSc = limited cutaneous systemic sclerosis; DcSSc = diffuse cutaneous systemic sclerosis; RP = Raynaud's phenomenon; DU = digital ulcer.
† Since first non-RP symptom.
‡ Early and established disease (≤3 and >3 years since first non-RP symptom, respectively).
§ Indication not specified and includes SSc-RP, SSc-DU, SSc-pulmonary artery hypertension, and/or systemic hypertension/cardiovascular risk.

initial set of codes and categories was then discussed with the wider team (MH, JDP, RG-H, and AM) to ensure they captured all elements from the focus group. The coding framework was then applied to subsequent transcripts, and any newly identified codes were added as appropriate. The focus group facilitators decided when data saturation had been reached (28). Codes were collated and grouped into themes and subthemes. Coded data within each theme were checked to ensure internal coherence (fit within the pattern of the theme) and external representativeness (fit within the whole data set). JJ and AM regularly discussed the conceptual development of the themes and subthemes and an analysis debriefing meeting was convened involving JJ, JDP, RG-H, and AM to discuss the final theme groupings and the conceptual map describing the interrelationship of the respective themes.

Our approach was both deductive, in the sense that the research team examined preconceived considerations on the impact of DUs (derived from an earlier comprehensive literature review (20) and how participants understood and managed them, for the purposes of developing a PRO instrument, and inductive, in the sense that there was no preexisting coding frame and the developing codes were derived from and grounded in the data themselves (29).

RESULTS

Twenty-nine patients with SSc participated in 4 focus groups conducted in Bath (n = 8), Manchester (n = 7), and 2 focus groups in London (n = 6 and n = 8). Our a priori purposive sampling framework ensured that we studied a broad population of patients with SSc and DU disease (Table 1). Thematic saturation was felt to have been achieved after 4 focus groups.

Five major themes emerged that together constitute the patient experience of SSc-DU: 1) disabling pain and hypersensitivity, 2) deep and broad-ranging emotional impact, 3) impairment of physical and social activity, 4) factors aggravating occurrence, duration, and impact, and 5) mitigating, managing, and adapting to ulcers. The 5 constituent themes (and subthemes) can be arranged within a conceptual map of the patient experience of SSc-DU (Figure 1).

Theme 1: disabling pain and hypersensitivity. Our study found that pain is a cardinal symptom of SSc-DU and is often very severe (question [Q]1–4) (Table 2). Participants used a wide range of words and phrases to describe the severity of pain such as: "excruciating," "pain that could reduce you to tears," "agonizing," and "unbearable." Participants often described the pain as pulsatile or throbbing in nature (Q5, Q6), including a pressure-like effect (Q7). Not all participants used the word "pain" to describe the physical discomfort of SSc-DU; other expressions included "soreness," "tenderness," or "discomfort." The level of reported pain was often considered as being disproportionate to the size of the DU (Q8). DU pain can radiate to the other digits and proximally (Q9, Q10). Coexistent infection of the ulcer increases DU pain (Q11), and some participants reported that changes in temperature can worsen DU pain (Q12, Q13). Many participants described pain in the areas where previous ulcers had occurred, whereas others said the area was tender, sore, or sensitive and could be aggravated by touch or exposure to cold (Q13–15). Other sensations in areas of previous ulcers included tingling nerve-like sensations and partial or complete numbness (Q16, Q17). One participant said, "It's never the same again" (participant 6, Manchester group) when talking about the area where previous ulceration had occurred. Due to the severity of DU pain, some participants suggested that invasive procedures (including digital amputation) may be both necessary and appropriate to relieve symptoms (Q1, Q4, Q5, Q7, Q18, Q24). Across all the focus groups, participants

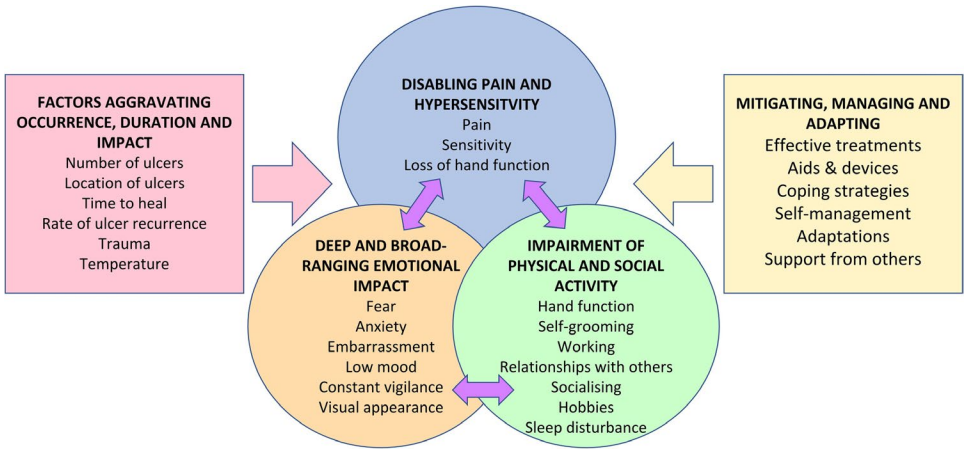

Figure 1. A conceptual map comprising the 5 major interrelated themes that constitute the patient experience of digital ulcers and systemic sclerosis.. The manifestation of pain that is often unbearable affects both the day-to-day functioning of the individual and their psychological well-being. For example, an inability to physically manipulate the world through their hands can lead to avoidance of activities or social interaction and subsequently cause low mood. This impairment can be supported through the use of aids and devices, such as gloves, or with help from other people.

Table 2. Quotes supporting the "disabling pain and hypersensitivity" theme of the patient experience of SSc-DU*

Subtheme: Q (subject and group)	Quotation
Pain:	
1 (P1 M1)	The pain is just unbearable, in fact you just want to chop your finger off, don't you? You think, well, I'd rather have my finger chopped off than have that pain. I've got to the point where I think just take it off. I can't stand it.
2 (P8 B1)	When the pain is really bad you, you just rock back and forward like this.
3 (P1 M1)	The pain, I just wanted to sit on the floor and cry…the pain is the worst thing I've had.
4 (P6 M1)	I just want it off. It needs to go, it gets that bad. You think, sorry, you feel like you want to bang your head to refer the pain somewhere else, just to relieve it.
Pulsatile/throbbing:	
5 (P7 L2)	You just want to take your finger off, that's how bad it is. The pulsating pain…
6 (P7 L2)	Like someone's getting a nail and hammering a nail right through the tip…And keep going and going, because it just keeps going through the finger.
Pressure: 7 (P2 B1)	If I could have taken my nail off just to release the pressure I would have done.
Pain disproportionate to ulcer size: 8 (P5 M1)	It's quite incongruous the amount of pain from the minimal amount of disruption to your thumb.
Radiation:	
9 (P2 B1)	The pain started actually in the finger bed, and I could feel it tracking along the finger and it dipped down into the first joint, so I could actually feel the pain in between the 2 joints.
10 (P7 B1)	So the ulcer is in the middle but I'll still get pain in the index and ring finger, which is equivalent to the ulcer pain but there's nothing there.
Infection: 11 (P5 L1)	I try not to get mine infected because then the pain level goes up.
Temperature:	
12 (P2 L1)	It's almost impossible to go in, in the summer when they've got the air conditioning on, it's not just the frozen aisles, it's the whole supermarket…if you've got an ulcer, the change in temperature will make the ulcer sensitive like a nerve, you can really feel it.
13 (P1 B1)	I don't go near the freezer for that reason, but even a cold bottle of milk in the winter, if you take it out of the fridge that's enough to set things off…where I've had the ulcers, particularly that one it, it becomes painful.
14 (P3 M1)	It's really tender if I just catch me finger now, but luckily I haven't had any more since then, it just left a lot of tenderness on, on the tips of me fingers… it's just the pain where I had the ulcer that's where it's straight away, the cold, as soon as I go out.
Pain/sensitivity at sites of past ulcers:	
15 (P1 L1)	It's the very end of the fingers, it's extremely sensitive, and it doesn't matter if it looks like an ulcer sort of wound, or it might be completely healed up, it can still be extremely sensitive to touch.
16 (P3 B1)	Just a slight tingly nerve sensation now, no pain.
Numbness at sites of past ulcers: 17 (P1 B1)	It's a bit numb.
Considered need for invasive procedures: 18 (P7 M1)	It's just so painful that the idea of cutting my finger open to take it out seems better than having that pain all the time.
Need to validate pain:	
19 (P4 B1)	Going back to what you said just now about people seeing it, sometimes you almost want to show, because you can't explain the pain you get with them, you almost want to show people this is what it's causing. My family's seen them obviously but I couldn't get it across.
20 (P1 B1)	Seems a bit feeble ringing and saying I can't come to work 'cause my finger's hurting, doesn't it?
21 (P2 L1)	Some people don't understand the pain we're going through.
22 (P1 M1)	But you could cry with them, it is, you could sit down and cry, and you can't explain to anyone in your family how bad the pain is.
Description of severity:	
23 (P5 L1)	It was very difficult to be an electrician. I think the difficulty is the severity of the winter, as you get the ulcer appear during the winter and then it's the amount of time after the winter they take to heal up.
24 (P5 B1)	I've had the 2 digital ulcers, touch wood that's healed up. I thought I was going to lose this finger at 1 stage.

* Q refers to the numbered quote cited in the text. SSc = systemic sclerosis; DU = digital ulcer; P = participant; B1 = Bath group; M1 = Manchester group; L1, L2 = London groups.

talked about the need to validate the pain they experienced with friends, family, and colleagues (Q19–22). Participants described the severity of their ulcers in different ways. These included the need for hospitalization, the time to heal, changes in their life (e.g., giving up work or hobbies) due to ulcers, and previous/risk of amputation (Q23, Q24). There was a wide variety in the reported location (fingertips, over the small joints, under the nails, and on the sides of the fingers) of DUs among participants. Some experienced ulcers in different locations on the hands, whereas others tended to only get ulcers in 1 area.

Theme 2: deep and broad-ranging emotional impact. Related to the severity of pain, most participants shared a constant fear of the development of new DUs (Q25), and many considered the development of further lesions inevitable (Q26, Q27) (Table 3). Participants experienced anxiety/uncertainty regarding how severe

Table 3. Quotes supporting the "deep and broad-ranging emotional impact" theme of the patient experience of SSc-DU*

Subtheme: Q (subject and group)	Quotation
Fear: 25 (P1 M1)	I don't particularly want to go out when I've got one because I'm so frightened of getting in the car and banging or, you know, picking my keys up and banging it.
Unavoidable recurrence of DUs:	
26 (P5 L1)	I don't know if it's a good or bad thing but I've got used to having them, so it becomes a way of life…when I used to maybe have 1 a year, I used to think it was quite a big deal but then since getting 5 or 6 a year, it doesn't become a big deal any more, you just get used to it.
27 (P4 L2)	Because you can probably guarantee you are going to get another one sometimes…I don't see how you can prevent it, if it's going to happen, it's going to happen. I don't see how it could be.
Anxiety/uncertainty: 28 (P7 M1)	I'm still learning about the whole thing so it changes every day. I call it the Hunger Games, when something starts to get better something else happens and you don't know what is happening, so the answer is I don't know what brings them, I don't know what I do wrong or not wrong…it's one of the worst things about the disease because it makes you scared and it makes you nervous, irritable.
Depression/anger/uncertainty about the future:	
29 (P2 L2)	It affected me quite a bit, yes…it really depressed me at that time.
30 (P1 M1)	It's like a black cloud, isn't it? It doesn't tend to go away, does it? Some days you just think, well, I'm not thinking about it and then other days it gets you down a bit, don't it?"
31 (P7 M1)	Just angry all the time, because you have to be conscious and you can't relax.
32 (P6 L2)	It really, it ruins the day, it changes your life.
Constant vigilance:	
33 (P3 M1)	You do feel very cautious, if you, if you do have a bang then you're more aware that you're not to do things for the next few days in case it goes really bad.
34 (P1 M1)	Well I've got to be particularly careful now if me nails grow, especially at the side I've got to try and cut them…and then of course you're worried when you cut them that you're not going to do any damage as well, so it's a bit difficult really.
Anger: 35 (P7 M1)	Just angry all the time because you have to be conscious and you can't relax… And it affects you, yes, it affects you and it affects the kids, it affects everything around you. You have to tell yourself all the time, you've got this, you have to, you have to remember your hand all the time.
Embarrassment/hiding/protecting ulcers:	
36 (P8 B1)	I used to hide mine under the table cloth at a function…Embarrassment, probably.
37 (P4 B1)	You don't want other people to be distressed at seeing them, also it's protection against infection.
38 (P2 B1)	So I kept them covered up and I've got photographs in my bag that I took for my own record really, you know, and my son said last time "don't you let me see those, I don't want to see them," but even the doctors never looked at my fingers when I had the ulcers.
39 (P7 L2)	Sometimes it looks awful, all the skin peeled back and it's all exposed, yeah, you just hide it…I just don't want people to look at it as well, I feel conscious sometimes.
40 (P4 B1)	If I was going out to a social function or meeting friends or something I would put plasters on, because it's better for someone to see plasters than, you know, and your friends get used to the fact of, how's your hands, you know.

* Q refers to the numbered quote cited in the text. SSc = systemic sclerosis; DU = digital ulcer; P = participant; B1 = Bath group; M1 = Manchester group; L1, L2 = London groups.

each ulcer would be, whether they were treating the ulcer correctly, and how long it would take the ulcer to heal (Q28). Although most participants did not explicitly say that ulcers caused them depression (Q29), they mentioned many associated emotions (in addition to anxiety and embarrassment), including uncertainty/fear for the future and anger (Q29–32). Participants described the need for a constant level of vigilance to prevent the development of new DUs and infection of intercurrent ulcers (Q33, Q34). Participants described many different emotions associated with the ulcers, from panic, anxiety, fear, and irritability to anger (Q35). Participants did not forget about the past impact of the ulcers, and some described frightening times (with current ulcers) when they were perhaps unsure whether they would need to have part of their finger amputated (Q24). Patients also experienced embarrassment and distress due to the physical appearance of SSc-DU and took a range of actions to hide DUs from others (Q36–40).

Theme 3: impairment of physical and social activity. The physical and psychological impact of SSc-DU was closely related to impact on physical and social functioning (Table 4). Patients' interactions with the world and other people were characterized by an avoidance of pain and a constant vigilance during physical and social interaction. Participants reported how DUs impacted their ability to use their hands during activities of daily living (Q41–46), including self-care/grooming (Q38, Q47, Q48), hobbies (Q49), and domestic activities (e.g., cooking and household chores) (Q13, Q50, Q51). Activities of daily living that were taken for granted became foregrounded, such as the ability to reach their hands into pockets, a bag, or a purse (Q45, Q52, Q53), difficulty driving (Q30, Q54), sleeping (Q55), and challenges when shopping (Q12, Q56, Q57). The impact of DUs on work varied among the participants. For some participants, ulcers had not severely impacted their work, whereas others had to change

Table 4. Quotes supporting the "impairment of physical and social activity" theme of the patient experience of SSc-DU*

Subtheme: Q (subject and group)	Quotation
Hand function and activities of daily living:	
41 (P1 L1)	Just trying to handle things with your fingers, you just have to careful you don't drop a tea cup, your dexterity goes.
42 (P5 L1)	Where the ulcers were, sort of like stop the movement in your hands so I wasn't able to do these things that I needed to do.
43 (P4 L2)	To actually bend the fingers where your ulcers are actually on top of the knuckles is practically impossible.
44 (P4 B1)	That's the thing, that's what I say, I can get things done, but I cannot do it at the speed that I used to before.
45 (P5 L1)	Putting things in bags, lifting stuff, you can't actually grip stuff so I just feel really clumsy.
46 (P6 M1)	It's like opening a bag of crisps if you're out for a drink, I can't open the crisps.
Self-care/grooming:	
47 (P1 M1)	I'm frightened of catching it. You don't want to get dressed in case you've got to zip something up and you catch it.
48 (P5 L1)	Even just going and brushing our teeth…it's painful when our hands are sore and ulcerated.
Hobbies: 49 (P2 B1)	I've had to stop doing things like knitting… Because they flare up straight away and open and it doesn't matter whether I use natural fibers, it's just the irritation of my skin so I had to give up knitting… I have to be very careful gardening.
Domestic activities:	
50 (P6 L1)	Two years ago I can do nothing really, so I needed help, my daughter, husband, everyone doing something at home. I could do nothing, cooking.
51 (P8 L2)	It's impossible to make the bed, I can't put my hand, I can't put the sheet under.
Putting hands in pockets/bags/purse:	
52 (P4 M1)	When it starts to crust over that, that's when I can't go in me bag, you know, and you just tip everything out to find what you want and then scoop everything back up.
53 (P1 L1)	Putting your hand in your pocket can be horrendous if you hit a key or something like that.
Difficulty driving: 54 (P4 B1)	Things to try and protect it, 'cause you're guaranteed knocks on every single day, you carefully put the ignition key in the car, you still knock this one on the steering wheel and things like that.
Sleep disturbance: 55 (P1 M1)	It's like somebody's sticking a needle in your finger when you're trying to go to sleep, you could hold your hand in the air.
Shopping:	
56 (P4 L1)	Going to supermarkets I can't go up and down the fridge aisle. I have to stand there and wait and think about do I need anything down there, but even just going into a supermarket, it's just too cold… Because you have to balance your bags so that you can carry them, if they're rushing you, you're just dropping everything in and it's all falling out and it just becomes a disaster.
57 (P3 L1)	There's always that doubt in the checkouts, you know, not only are they not hassling me, but I'm sort of thinking I'm holding the queue up and I suddenly hear this voice behind me saying, "you don't have to rush you know." People are nice I find.
Change in working/occupation:	
58 (P3 L1)	Well I was a programmer, so it wasn't a difficult job to carry on doing.
59 (P7 B1)	Obviously it's affected a lot of the work that I do as well. There's only 50% of the work that I used to do that I can continue to do now, with the digital ulcers, but it's just knowing what you can and can't get away with anymore.
Financial concerns: 60 (P7 B1)	Most people have said you need to change your job, but once you're set up and you're established and you've got a wife, kids, a mortgage and bills to pay, it's impossible to go back and start as tea boy again somewhere else, so you carry on but you've got to try and adjust what you do to maintain your income, that's the biggest difficulty I've had so far.
Concealing ulcers:	
61 (P4 B1)	You don't want other people to be distressed at seeing them, also it's protection against infection and also, you know, if you're going out to any social function I will bandage… I did go to my daughter's wedding, which was in all of this, and so I did wear my black gloves all through the wedding.
62 (P5 L1)	I don't know if it's them or myself thinking, oh are they thinking I'm contagious or that kind of thing, because they look horrible when they're at their worst, but now I'll try to keep them, I'll keep them covered if they're… I wouldn't go out anywhere without them being covered, but still when you're covered in a million plasters, that doesn't look nice either.
Change in caring roles within the family: 63 (P7 B1)	It changes the way you have to think of it, everything that you do. I mean the wife says to me, do you want to take the kids down the fair, and the first thing I have to do is check the temperature outside, you know. If it's 20° or less, I'll bail out, I wouldn't bother going, but it's not nice because you miss out on a lot of life experiences with your family.

* Q refers to the numbered quote cited in the text. SSc = systemic sclerosis; DU = digital ulcer; P = participant; B1 = Bath group; M1 = Manchester group; L1, L2 = London groups.

Table 5. Quotes supporting the "factors aggravating occurrence, duration, and impact" and "mitigating, managing, and adapting" themes of the patient experience of SSc-DU*

Subtheme: Q (subject and group)	Quotation
Factors aggravating occurrence, duration, and impact	
Number of ulcers:	
64 (P3 M1)	I have only had 1 ulcer, which was really quite bad. And it, I was put on a drip in hospital with, is it epoprostenol, twice to see if that would help, but it didn't and they ended up going to theatre to have it cleaned out, and that's the only ulcer I've ever had.
65 (P4 B1)	I was diagnosed with limited scleroderma approximately 28 years ago, which started with an ulcer in 1 finger and just gradually got worse over the years, with anything up to 4 or 5 ulcers every winter, which sometimes cleared up in the summer, yeah, so on-going.
66 (P2 L1)	When I was first diagnosed, ulcers weren't really a problem. I might have 1 a year, but as the scleroderma has progressed, I have had up to 10 ulcers at a time on my hands, in different degrees of severity.
Ulcers heal slower in the winter:	
67 (P4 M1)	They get easier in the summer, they heal better.
68 (P4 L1)	They just would erupt through the whole winter, and then I've got to wait till the middle to the end of the summer, then I get a short respite.
Mitigating, managing, and adapting	
Indication that treatment is effective:	
69 (P1 B1)	Being able to sleep during the night with the bearable pain would be an absolutely added bonus.
70 (P7 B1)	Well, within 5 days that finger healed up more than it did in 3 months, so the minute I came in on the iloprost…certainly the 5 days I spent here last week, I wouldn't be as healed up as I am now, and able to work again.
71 (P7 L2)	If the pain stops.
72 (P4 L2)	It helps it, calm it down, to stop being hurting.
73 (P5 L1)	I just find it keeps them at bay. I worry that if I was to lengthen it again it would just be worse, so yeah, it sort of helped the aggression that you say, the inflammation and things.
Burden of treatments:	
74 (P4 B1)	I think I would definitely say it's helped a lot and it's kept me out of hospital. I've managed, the ulcers are still taking several weeks, if not months to heal, but they do heal without the need to intervene with iloprost on top and a stay in hospital, presumably that's an extra cost to the NHS and it's better for me 'cause I'm not in hospital.
75 (P3 L1)	It takes forever to get them on and get them off and then you realize that the reason they're hurting more than usual is you made a complete mess of putting on last time and you've got to start again.
Coping strategies/aids and devices:	
76 (P8 B1)	I keep a pair of gloves up on top of the fridge freezer to do just that, you know, to take anything out from the freezer.
77 (P4 L1)	I've got things that help me grip jars.
78 (P1 L2)	I also wear gloves, 'cause every time you hit it on something it flares more, that is a big problem I've got no matter, if you touch it, or anything you touch, once you hit it, it flares up again.
79 (P8 L2)	The other thing that I've done for the last 18 months, I never, ever, wet them, as least as possible to get them wet, so in the shower I've got rubber gloves.
Support from others:	
80 (P4 L1)	They've adapted, my children have, I mean they're grown up now, but they know I'll just call, they walk in, open a bottle, if I'm cooking and if I look, they know which one, which saucepan to get out, they just know, like in and out of cars, and they just know now, and so do my friends. They just know.
81 (P7 M1)	I have 3 children, and I live alone and it's not easy because you have to do everything, so you have to cook, you have to touch water and that is something that terrifies you… It is very difficult but the way to cope about it, I think it is just to explain to them…and they will know that they have to step up to do something of the things so they understand that part, but the other part that you have to live, you have to do it, you have to bath them, you have to do everything else, and you know that you'll be in pain for that time, all the time. You know it's going to happen whether you like it or not.
Adaptations/self-management:	
82 (P1 L2)	It's really good, the pumice stone really helps peel it down.
83 (P7 L2)	I think the hardest thing is trying to treat it, and put bandages on it because it's such awkward positions, you can't keep the bandage on there and do other things.
84 (P2 L1)	It's just a lot of care that I have to take, and just move very, very slowly, be very aware of your space around you, with my ulcers.
85 (P3 M1)	You do feel very cautious, if you do have a bang then you're more aware that you're not to do things for the next few days in case it, it goes really bad.
86 (P1 B1)	When you put it in hot water or cold water, moving from one room to another it would just set the pain off again.

* Q refers to the numbered quote cited in the text. SSc = systemic sclerosis; DU = digital ulcer; P = participant; B1 = Bath group; M1 = Manchester group; L1, L2 = London groups.

roles in the organization or even change jobs completely (Q58, Q59). Some participants described financial concerns from the impact of DUs on their work (Q60). DUs have an impact on social participation, and participants reported taking measures to conceal ulcers with bandages or gloves, both to avoid others seeing them and to reduce the risk of infection (Q61, Q62). A number of participants described difficulties undertaking caring roles within the family, for example, avoiding taking their children outside to play due to the cold weather (Q63), because the cold both exacerbated the pain and aggravated the healing of ulcers or provoked their onset.

Theme 4: factors aggravating occurrence, duration, and impact. There were a number of factors that aggravated the occurrence and duration and impact of ulcers (Table 5). There was variation in the number of ulcers experienced by participants, ranging from experiences of solitary DUs to recurrent episodes of refractory digital ulceration (Q24, Q26, Q64–66). There was variation among participants on the time to DU healing (weeks, months, or even years). The length of time to heal was often related to the season and treatment. Most participants reported that over the winter ulcers took longer to heal (Q67), or they did not heal at all until the summer (Q68). Most participants seemed to be able to identify where previous ulcers had occurred, either based on how they looked or how they felt or both (Q13–16).

Theme 5: mitigating, managing, and adapting to ulcers. Participants used a variety of ways to describe whether a treatment had been effective or not (Table 5). This variety included whether and how quickly the ulcer had healed, whether there had been a reduced rate of recurrence of the ulcer, how the appearance of the ulcer had changed, whether the level of pain was reduced, the positive impact on other activities such as sleeping, whether the participant thought circulation had improved, whether the wound dressing had been effective in protecting the ulcer, and whether the risk of amputation was reduced (Q69–73). As well as the effectiveness of treatment, participants also alluded to the burden of treatment. This burden could mean the need for hospitalization or the burden of medication, the duration (time) of receiving treatments, or the severity of associated side effects, and the time and ease of putting on bandages (Q74, Q75). Participants discussed a range of coping strategies to manage DUs, including different ways in which they had adapted or used support to cope with their ulcers. This adaptation included using a device or aid to help manage ulcers (Q76, Q77), strategies to avoid causing pain or prevent a new ulcer developing (Q78, Q79), and getting help or support (paid or unpaid) from others (Q80). Several participants talked about how their children have adapted to the condition and help the patient cope with limited function (Q80). However, some participants noted that avoiding all activities that may aggravate the ulcer was not possible, especially if they have young children (Q81). Participants described a variety of techniques they used to manage their ulcers, from the earliest stages of development to when the ulcer is visible and active. These techniques included using "home remedies" and alternative treatments (Q82), wound care (Q83), the vigilance associated with self-management (Q84, Q85), and avoiding behaviors (e.g., cold exposure) that the patients consider can cause ulcers (Q86).

DISCUSSION

The current study is the first, to the best of our knowledge, to specifically explore the multifaceted patient experience of SSc-DU. We have identified 5 major interrelated themes (and subthemes) that constitute the patient experience of SSc-DU that we have organized within a conceptual map of SSc-DU. The major themes comprised disabling pain and hypersensitivity; deep and broad-ranging emotional impact; impairment of physical and social activity; factors aggravating occurrence, duration, and impact; and mitigating, managing, and adapting to SSc-DU.

The multicenter study design and purposive sampling framework ensured that we captured the experiences from a broad cohort of SSc patients and the spectrum of SSc-DU disease (from solitary DUs to recurrent refractory disease). Thematic analysis of the focus group transcripts was conducted by experienced qualitative researchers without direct experience in the management of SSc-DU, avoiding the potential bias that preconceptions held by scleroderma clinicians might have introduced. The study benefited from a broad international steering committee of SSc experts, qualitative researchers, and patient research partners.

Painful physical symptoms and signs were the most important experiences of SSc-DU. Pain is the cardinal symptom of SSc-DU and is often very severe. Patients often consider the severity of pain disproportionate to the physical size of DUs. Infection and changes in temperature can worsen DU pain. The physical symptoms of DUs result in considerable psychological distress, and impaired hand function impacts all the activities of daily living, including occupation and social interactions. Many patients describe a constant state of vigilance both during and between episodes of ulceration. There are a number of aggravating factors, including the number and severity of DUs. Of interest, participants reported that the ulcers took longer to heal during the winter and residual symptoms at sites of previous DUs. In particular, dysesthesias and paresthesias could suggest persistent nerve damage. Patients with SSc make considerable efforts to both prevent and manage DUs (e.g., avoiding trauma and preventing infection) and describe a wide range of coping strategies and adaptations. The patient experience of DUs mirrors that of Raynaud's phenomenon, in which patients report the need for constant vigilance and self-management (30). Overall, our themes show similarities to those reported by Nakayama et al (30), who conducted a systematic review and thematic analysis of 26 studies with 463 patients to explore patients' perspectives and experiences living with SSc. The 6 key themes were distressing appearance transformation,

palpable physical limitations, social impairment, navigating uncertainty, alone and understood, and gradual acceptance and relative optimism (30). Furthermore, DUs (along with Raynaud's phenomenon and calcinosis) were described as "being intensely painful by some patients," were "emotionally distressing," and "limited patients' ability to work, go outdoors," "or even walk" (30).

As previously described, in earlier clinical trials of SSc-DU, primary assessment of treatment efficacy has focused on clinician assessment of DU presence alone (occurrence and persistence) and has largely overlooked the patient experience of SSc-DU. Legacy PRO instruments assessing function and interference capture patient experiences relevant to SSc-DU, but those instruments are limited by the inclusion of redundant items that are less relevant to SSc-DU (e.g., the inclusion of nonhand domains of the Health Assessment Questionnaire disability index). The recent development of an SSc-specific PRO instrument, the Hand Disability in SSc DUs, was developed through modification of the Cochin Hand Function Scale, including qualitative patient interviews to assess the impact of DUs on hand function in patients with SSc (31). However, to date, other important experiences of SSc-DU (e.g., psychological impacts and social participation) have been comparatively overlooked. The development of a novel PRO instrument that captures the broader patient experience of SSc-DU (e.g., relationships and body image dissatisfaction) would be valuable for assessing interventions in clinical trials but also in clinical practice, where there is a dearth of practice-based evidence examining the comparative efficacy of different pharmacologic, surgical, and wound-care protocols. Furthermore, even after ulcer healing, patients can still suffer from significant residual pain and anxiety of future DUs. Therefore, effective ulcer treatments (and PRO instruments) should also modify future patient (negative) experiences of DU disease even after ulcer healing.

Our analysis has not addressed potential differences in experiences relating to DUs occurring at different locations on the hands (e.g., fingertip versus extensor). The etiopathogenesis (and patient experience) of different types of DU may differ, although all types of DU are generally accepted to have an ischemic contribution (32,33). Therefore, future efforts to develop a dedicated PRO instrument for assessing SSc-DU should explore different experiences (including treatment effects) at different ulcer locations. We also highlight the fact that we only recruited a relatively small number of patients with early disease. This situation is likely due to the need in our study to include a large majority of patients with a significant burden (history) of digital vascular disease, which usually takes time (years) to accrue. There were differences observed in the clinical and demographic characteristics (e.g., age and sex) of participants who participated in the 4 focus groups. For example, the majority of patients in Bath and Manchester had the limited subset of the disease, whereas approximately equal numbers of patients had diffuse disease in the 2 London focus groups.

We did not entirely achieve our intended purposive sampling framework, but we were satisfied that we had captured the experiences of a broad spectrum of patients and did not feel this gap was a barrier to achieving the study's aims. Due to the rarity and heterogeneity of the disease, identifying and enrolling patients with specific phenotypes to studies of this nature is not always possible. We also excluded participants who could not speak English. Although our focus groups were conducted only in the UK, previous studies (including multinational recruiting clinical trials) have demonstrated no important differences in DU disease between countries. In our study, we captured limited information on the impact of SSc-DU on intimate relationships (19). If the data had been collected during one-to-one interviews, then comments on the impact of DUs on intimate relationships likely would have arisen and should be considered in the design of future research. We will explore such themes in a 1:1 setting during future cognitive debriefing of a provisional item-bank for the proposed DU PRO instrument.

It should be highlighted that treating clinicians (MH and JDP) facilitated the focus groups, which could have impacted the reflexivity of the research and introduced potential bias, for example, by shaping the discussion and/or limiting patients' willingness to discuss certain aspects of their experience. However, mitigating factors include the study topic guide that was developed with support from patient insight partners and was used to inform the structure of the focus groups. Patients were only known to 1 individual clinician at 1 geographic location. Furthermore, while background clinical knowledge of SSc was essential to successfully facilitate the focus groups, the analysis of data was led by 2 independent researchers (JJ and AM), to mitigate this potential source of bias.

In conclusion, ours is the first study to examine the multifaceted patient experience of SSc-DU. Traditional clinical trial end points are not currently designed to capture the patient experience of SSc-DU, which should be a key priority for demonstrating meaningful treatment benefit. The resultant themes and subthemes from our study provide a unique insight into the patient experience of SSc-DU. This work could form the basis of a novel PRO instrument to assess the impact and severity of SSc-DU to support much needed new treatment approaches for SSc-DU.

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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. Hughes 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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