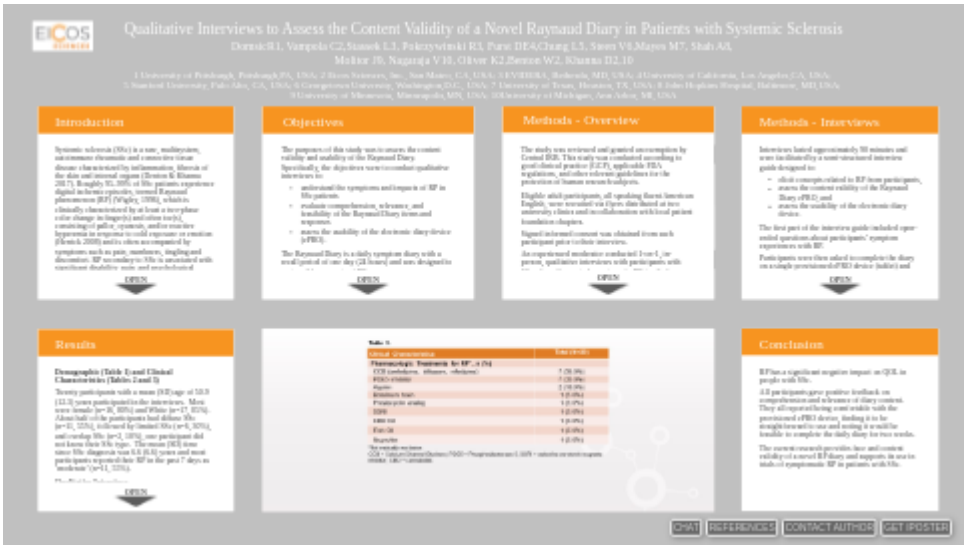
Qualitative Interviews to Assess the Content Validity of a Novel Raynaud Diary in Patients with Systemic Sclerosis



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INTRODUCTION

Systemic sclerosis (SSc) is a rare, multisystem, autoimmune rheumatic and connective tissue disease characterized by inflammation, fibrosis of the skin and internal organs (Denton & Khanna 2017). Roughly 95–99% of SSc patients experience digital ischemic episodes, termed Raynaud phenomenon (RP) (Wigley, 1996), which is clinically characterized by at least a two-phase color change in finger(s) and often toe(s), consisting of pallor, cyanosis, and/or reactive hyperemia in response to cold exposure or emotion (Herrick 2008) and is often accompanied by symptoms such as pain, numbness, tingling and discomfort. RP secondary to SSc is associated with significant disability, pain, and psychological impact that reduce quality of life (QOL) (Merkel et al., 2002). In addition to pain, annoyance, and functional disability caused by RP attacks, many patients with SSc report that they change their daily routine to accommodate their RP and may have significant anxiety associated with their disease, often expressing fears concerning digital ulcers and potential autoamputation (Merkel et al., 2002).

OBJECTIVES

The purposes of this study was to assess the content validity and usability of the Raynaud Diary. Specifically, the objectives were to conduct qualitative interviews to:

- understand the symptoms and impacts of RP in SSc patients
- evaluate comprehension, relevance, and feasibility of the Raynaud Diary items and responses
- assess the usability of the electronic diary device (ePRO).

The Raynaud Diary is a daily symptom diary with a recall period of one day (24 hours) and was designed to capture 3 key aspects of RP:

- attack frequency,
- duration and
- severity (assessment of disease severity as well as ratings for worst pain, numbness, tingling and discomfort in the fingers).

METHODS - OVERVIEW

The study was reviewed and granted an exemption by Central IRB. This study was conducted according to good clinical practice (GCP), applicable FDA regulations, and other relevant guidelines for the protection of human research subjects.

Eligible adult participants, all speaking fluent American English, were recruited via flyers distributed at two university clinics and in collaboration with local patient foundation chapters.

Signed informed consent was obtained from each participant prior to their interview.

An experienced moderator conducted 1-on-1, in-person, qualitative interviews with participants with SSc who self-reported symptomatic RP, i.e. 2-phase color change of the fingers (white, red, blue, and/or purple) and symptom experience (pain, numbness, discomfort, tingling).Interview transcripts were analyzed using ATLAS.ti version 8.3.17 with a coding dictionary initially developed based on the interview guide but adapted as new concepts emerged. Four trained coders completed coding, and 2 researchers reviewed all coding. A database for quantitative data collected during the interviews was developed, tested, and validated using the software package DataFax. Quantitative analyses were conducted on the final SAS-ready dataset. Descriptive statistics (mean, standard deviation, frequency) were used to characterize the sample in terms of sociodemographic and self-reported health characteristics.

METHODS - INTERVIEWS

Interviews lasted approximately 90 minutes and were facilitated by a semi-structured interview guide designed to:

- elicit concepts related to RP from participants,
- assess the content validity of the Raynaud Diary ePRO, and
- assess the usability of the electronic diary device.

The first part of the interview guide included open-ended questions about participants' symptom experiences with RP.

Participants were then asked to complete the diary on a single provisioned ePRO device (tablet) and were cognitively debriefed on the measure to assess understandability, relevance, and feasibility of the diary (instructions, items, recall period, and response scales).

Usability of the device was also discussed with participants. Specifically, this part of the guide was used to ensure that the layout and usability of the ePRO device were appropriate.

RESULTS

Demographic (Table 1) and Clinical Characteristics (Tables 2 and 3)

Twenty participants with a mean (SD) age of 50.9 (12.3) years participated in the interviews. Most were female (n=16, 80%) and White (n=17, 85%). About half of the participants had diffuse SSc (n=11, 55%), followed by limited SSc (n=6, 30%), and overlap SSc (n=2, 10%), one participant did not know their SSc type. The mean (SD) time since SSc diagnosis was 6.6 (6.6) years and most participants reported their RP in the past 7 days as 'moderate' (n=11, 55%).

Qualitative Interviews

Concept Elicitation

- Participants reported their experiences identifying an attack in terms of finger color changes (white, red, blue, and purple) and symptom experience (pain, numbness, discomfort, tingling; see Table 4 for symptoms experienced most frequently).
- Variability in attack triggers, duration and frequency was reported both within and among participants.
- Participants stated that RP impacted their daily life and functioning (Figure 1), including avoiding or limiting outdoor activities and having difficulty gripping items.

Cognitive interview (see Figure 1 for representative quotes)

- Broadly, the participants gave positive feedback about the content of the diary and no major issues in comprehension were identified. Participants reported differentiation between symptoms such as pain and discomfort, describing pain as "true pain" and discomfort as something a bit more bearable. Differentiation between numbness and tingling was also conveyed, with numbness being a loss of feeling and tingling as a sensation that was felt (e.g. tickling or "pins and needles").

ePRO Usability

- All participants reported having some experience with technology and all reported being comfortable with the device.
- Participants had positive overall impression of the ePRO device reporting that it was easy or straightforward to use.

Table 1.

Demographic Characteristics	Total (N=20)
Age (years)	
Mean (SD)	50.9 (12.3)
Gender, n (%)	
Female	16 (80.0%)
Male	4 (20.0%)
Ethnicity, n (%)	
Not Hispanic or Latino	19 (95.0%)
Hispanic or Latino	1 (5.0%)
Race, n (%)	
Asian	1 (5.0%)
Black or African American	2 (10.0%)
White	17 (85.0%)

SD = Standard Deviation.

Table 2.

Clinical Characteristics	Total (N=20)
Time Since SSc Diagnosis (years)	
Mean (SD)	6.6 (6.6)
Range	1.0-25.5
SSc Type, n (%)	
Limited Cutaneous	6 (30.0%)
Diffuse Cutaneous	11 (55.0%)
Overlap	2 (10.0%)
Don't know	1 (5.0%)
Time Since RP Diagnosis (years)	
Mean (SD)	7.7 (6.6)
Range	1.3-25.0
Severity of RP in Past 7 Days (self-reported) , n (%)	
Mild	4 (20.0%)
Moderate	11 (55.0%)
Severe	5 (25.0%)
Very Severe	0 (0.0%)
Digital Ulcers Within Past 6 Months, n (%)	
Yes	7 (35.0%)
No	13 (65.0%)

SD = Standard Deviation; RP = Raynaud's Phenomenon; SSc = Systemic Sclerosis.

Table 3.

Clinical Characteristics	Total (N=20)
Pharmacologic Treatments for RP* , n (%)	
CCB (amlodipine, diltiazem, nifedipine)	7 (35.0%)
PDE5 inhibitor	7 (35.0%)
Aspirin	2 (10.0%)
Botulinum toxin	1 (5.0%)
Prostacyclin analog	1 (5.0%)
SSRI	1 (5.0%)
CBD Oil	1 (5.0%)
Fish Oil	1 (5.0%)
Ibuprofen	1 (5.0%)

*Not mutually exclusive.
CCB = Calcium Channel Blockers; PDE5 = Phosphodiesterase 5; SSRI = selective serotonin reuptake inhibitor; CBD = cannabidiol.

Table 4.

Symptoms Experienced by Participant During Attack	Total Experiencing Symptom N=20 n (%)	Symptom Experienced Most Frequently N=20* n (%)
Numbness	19 (95%)	7 (35%)
Pain	19 (95%)	8 (40%)
Discomfort	18 (90%)	0 (0%)
Tingling	17 (85%)	2 (10%)

*Several participants selected more than one symptom as experienced most frequently. The numbers presented in this column therefore do not add up to 20. Two participants (10%) did not think they experienced any symptoms more frequently than others.

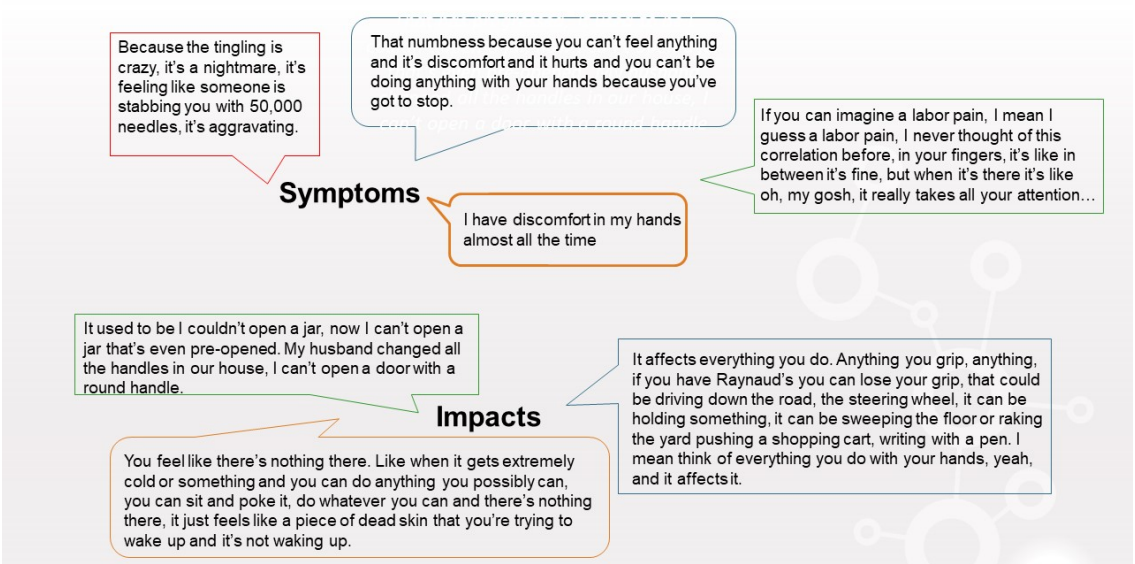

Figure 1. Quotes relating to symptoms and impacts of RP in people with SSc.

CONCLUSION

RP has a significant negative impact on QOL in people with SSc.

All participants gave positive feedback on comprehension and relevance of diary content. They all reported being comfortable with the provisioned ePRO device, finding it to be straightforward to use and noting it would be feasible to complete the daily diary for two weeks.

The current research provides face and content validity of a novel RP diary and supports its use in trials of symptomatic RP in patients with SSc.

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