

Patient participation in patient-reported outcome instrument development in systemic sclerosis

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ABSTRACT

Objective. *The patient perspective captured using Patient-Reported Outcome (PRO) instruments provide insight into the patient condition not always captured by physician-derived assessment tools. Target patient population involvement is an essential component of PRO instrument development. We have reviewed the level of patient involvement in the development of PRO instruments used in the assessment of systemic sclerosis (SSc).*

Methods. *A comprehensive literature review was undertaken to identify studies reporting PRO instruments in SSc. Studies were assessed to establish whether the PRO instruments had been developed specifically for SSc or adopted from other disease areas. Studies reporting PRO instruments specific for SSc were scrutinised for evidence of target patient population involvement in the development of the instrument.*

Results. *A total of 58 PRO instruments that have been used in SSc research were identified. Twelve (21%) of these were developed specifically for outcome assessment within SSc populations. Of these, 5 (42%) had not reported any patient involvement in the development phase of the instrument. Five SSc PRO instruments (42%) involved target patient population in the domain/item generation stage. Four (33%) of SSc PRO instruments had undertaken cognitive interviewing to ensure item wording adequately captured the intended conceptual framework.*

Conclusion. *The majority of PRO instruments used to assess SSc have not involved significant target patient involvement in their development. By involving patients in the development of novel PRO instruments in SSc, we can ensure such instruments adequately capture the experiences most relevant to our patients.*

Introduction

The patient perspective provides insight into the patient condition that is not always captured by physician-derived assessment tools. Patient-Reported Outcome (PRO) instruments provide information on “the status of a patient’s health condition that comes directly from the patient, without interpretation of the patient’s response by a clinician or anyone else” (1). The assessment of disease status, disease impact, internal organ manifestations and other relevant outcomes (e.g. quality of life) is particularly challenging in a multi-faceted disease like systemic sclerosis (SSc). Manifestations such as Raynaud’s phenomenon (RP) are episodic, characterised by inherently subjective symptoms and not easily assessed in the clinical setting. For this reason, great emphasis has been placed on PRO instruments which feature prominently in the Scleroderma Clinical Trials Consortium (SCTC) provisional core set of response measures for clinical trials of SSc (2). There is consensus that directly involving patients in the earliest stages of item generation and domain definition greatly enhances the overall “validity” of a PRO instrument (3, 4). Furthermore, regulatory agencies, such as the US Food and Drug Administration (FDA), seek evidence of patient input when reviewing existing, modified and newly created PRO instruments that form the basis of labelling claims for medical product development (1). The objective of this review was to evaluate and describe the level of SSc patient input in the development of PRO instruments currently used to assess SSc.

Methods

A comprehensive literature search to identify PROs used in the assessment of SSc was performed on PubMed (January 7th 2016) using the following

search strategy: (“Systemic Sclerosis” OR “Scleroderma”) AND (“Domain” OR “Outcome” OR “Assessment” OR “Validation”) AND (“Participation” OR “Composite Measure” OR “Hand Function” OR “Physical Function” OR “patient global” OR “pain” OR “health related quality of life” OR “Raynaud’s” OR “Gastrointestinal” OR “Dyspnoea” OR “Fatigue” OR “Digital Ulcers” OR “Physician Global” OR “Skin” OR “Renal” OR “Cardiac” OR “Pulmonary”). No restrictions were placed on language or year of publication. The title and abstracts of articles identified in the initial search were reviewed (JP), and the full manuscripts of those thought to be relevant to this topic were scrutinised by a minimum of 2 authors (JP, TF, RD and MH) to seek evidence of target patient population involvement in the development, modification or validation of the PROs used to assess health status in SSc. A further hand search of cited articles from within these manuscripts and additional recent comprehensive reviews of PRO instruments utilised in SSc was undertaken to identify additional relevant manuscripts not captured in the initial search. Articles reporting the development and use of SSc-specific PRO instruments were evaluated for evidence of patient involvement in conceptual framework development, domain/item generation, cognitive interviewing and respondent burden.

Results

The title and abstracts of 2105 citations were reviewed (JP), and a full text review of manuscripts thought to be relevant to this topic (n=57) was undertaken. The hand search identified a further 17 relevant manuscripts of interest. A total of 58 PRO instruments that have been evaluated in SSc were identified and reviewed (all but one publication in English). A French publication was reviewed by a co-author fluent in this language (MH) (5). Twelve SSc-specific PRO instruments (21% of total) were identified and scrutinised for target patient population involvement in instrument development. A summary of the contribution of SSc patients to the development of the 12 SSc-specific PRO

instruments is presented in Table I and shall now be described in further detail.

General measures of function, quality of life and disease burden

Disability and function

• *UK Scleroderma Functional Score*

Following occupational and physiotherapist assessment of functional impairment, a 28-item disability assessment schedule was devised by the expert panel (6). The authors reported an extensive consultation process involving patients and therapists but did not expand on the number of patients involved, their disease demographics or their specific contribution to this design process. Item reduction (to a self-administered 11-item 0-3 Likert scale questionnaire), was undertaken primarily by a panel of therapists, to remove redundant or ambiguous questions (6). The instrument underwent partial validation of instrument reproducibility and content validity (6).

• *Scleroderma Functional Index*

The 11-item Scleroderma Functional Index was a disease-specific instrument developed for assessing upper limb function in SSc (5). The instrument’s development was not reported and limited evaluation of content, criterion, construct and discriminant validity has restricted its widespread adoption (7).

• *Generic instruments*

The Health Assessment Questionnaire Disability Index (HAQ-DI) was developed to assess functional status in rheumatoid arthritis but has subsequently undergone extensive confirmatory studies of its validity and reliability in SSc populations in a large number of observational and clinical trial settings (8-11). A number of other functional PRO instruments have been adopted unmodified from other disease areas and subsequently evaluated in SSc, including the Cochin Hand Functional Disability Scale (12-14), the Disabilities of the Arm, Shoulder and Hand (15) and Michigan Hand Outcomes Questionnaire (16). Whilst not SSc-specific McMaster Toronto Arthritis Patient Preference Disability Questionnaire (MACTAR) allows users

to set their own patient priorities and therefore provides a highly individualised approach to assessing disability that may provide a more comprehensive assessment of disability than traditional fixed-item questionnaires. The relatively poor correlation between the MACTAR and the HAQ-DI (Spearman’s Rho 0.38) when applied to SSc highlights the importance of target patient population input in PRO design when assessing function and disability (17). Indeed, the majority of the 37 activities prioritised by SSc patients issued with the MACTAR are not assessed in the HAQ-DI (e.g. ability to participate in sport), highlighting the value of a disease-specific approach to disability (17).

Health-Related Quality Of Life

(HRQOL)

Similar to the aforementioned MACTAR, the Patient Generated Index (PGI) allows patients to prioritise and weight up to 5 individualised life area responses most relevant to their health and is the closest to a SSc-specific patient-derived PRO instrument for assessing HRQOL (18). A study evaluating the PGI in SSc identified 258 life area responses highlighting the variability in effects of disease on quality of life experienced by patients with SSc (18). A number of generic tools have been evaluated in SSc including the Short Form 36 (SF-36) (14, 19-27), Short Form-6 Dimensional (28, 29), EuroQol-5 Domain (24, 29, 30), Quality of Well-being Scale Self-Administered (31), WHO Disability Assessment Schedule II (27, 32, 33) and the National Institutes for Health (NIH) Patient-Reported Outcomes Measurement Information System 29-item Health Profile (PROMIS-29) (34).

Global assessment of health status in SSc

Global assessment of health status has been evaluated using a number of generic instruments in SSc including the health Rating Scale, Standard Gamble, Illness Perceptions Questionnaire-Revised and Time Trade-Off scale (25, 35). A number of SSc-specific tools have also been developed.

Table I. Summary table of patient involvement in development of SSc-specific PRO instruments.

Organ system	Conceptual Framework	Author, Year	Patient Reported Outcome	Patient involvement in:				
				Conceptual Framework	Domain generation	Item generation	Cognitive interviewing	Respondent Burden
Disability & function	Disability & Function in SSc	Steen and Medsger, 1997 (9)	Scleroderma HAQ subscales	No	No	No	Yes	No
	Disability and Function in SSc	Silman <i>et al.</i> , 1998 (6)	UK Scleroderma Functional Score	No	Yes (no details supplied)	Yes (no details supplied)	No	No
	Disability and Function in SSc	Guillevin and Ortonne, 1983 (5)	Scleroderma Functional Index	No	No	No	No	No
Global Assessment of Health Status	Global disease assessment	Suarez-Almazor, <i>et al.</i> , 2007 (40) & Kallen <i>et al.</i> , 2010 (41)	Symptom Burden Index	No	Yes	Yes	No	No
	Global disease assessment in SSc	Ruof <i>et al.</i> , 1999 (38)	Systemic Sclerosis Questionnaire	No	Yes	Yes	Yes	No
	Global disease assessment in SSc	Ostojic and Damjanov, 2006 (39)	Scleroderma Assessment Questionnaire	No	Yes	Yes	No	No
Skin	Skin thickening, tethering and thinness in SSc	Nagy <i>et al.</i> , 2009 (42)	Patient Skin Self Assessment Questionnaire	No	No	No	Yes	No
Body Image	Body Image in SSc	Jewett, 2015 (71)	BCSS	No	No	No	No	No
	Body Image in SSc	Jewett, 2010	Brief-SWAP	No	No	No	No	No
Peripheral Vascular	Raynaud's phenomenon in SSc	Wigley <i>et al.</i> , 1998 (44) & Black <i>et al.</i> , 1998 (43)	Raynaud's Condition Score Diary	No	No	No	No	No
Gastrointestinal	GI symptoms in SSc	Khanna <i>et al.</i> , 2007 (28) & Khanna <i>et al.</i> , 2009 (51)	SCTC GIT 1.0 and 2.0	No	Yes	Yes	Yes	No
	Mouth Handicap in SSc	Mouthon <i>et al.</i> , 2007 (56)	MHISS	Yes Postal survey	Yes Postal survey	Yes Postal survey	No	No

• *Patient Global Assessment*

A Patient Global Assessment is recommended in the core-set response measures for clinical trials of SSc (2). It is variously applied as a continuous 100mm VAS or 11-point numeric rating scale (36). Neither the conceptual framework, wording of the question or recall period has been standardised to ensure it captures the specific views and priorities of SSc patients. This may, in part, account for discordance between patient and physician global assessments in SSc (ICC 0.377) (37).

• *Systemic Sclerosis Questionnaire (SySQ)*

A combination of expert opinion and individual patient interviews (n=12 with a wide spectrum of diseases activity, severity and duration) were used to develop a preliminary 113 item ques-

tionnaire covering 4 major domains (general/cutaneous, musculoskeletal, cardiopulmonary and gastrointestinal) to assess general disease symptoms, organ-specific symptoms and functional limitation (38). Patient input guided the wording of the item questions (assessed using 0-3 Likert anchors) evaluating the ability to perform activities, intensity of symptoms or frequency of symptoms for each item respectively (38). Item reduction using a combination of factor analysis, tests of internal consistency and consideration of content/face validity led to the development of a 4-domain, 12-scale, 32-item questionnaire (seven of which were adopted directly from the SHAQ) (38).

• *Scleroderma Assessment Questionnaire (SAQ)*

The development of the SAQ followed

extensive consultation with SSc experts. Subsequent patient interviews were undertaken to generate additional potential items for the questionnaire, which also included items derived from the earlier SySQ (38, 39). An initial 86-item questionnaire was developed and subsequently reduced using expert opinion *e.g.* removal of duplicate items. There was no reported patient involvement in either questionnaire design or item reduction leading to the development of the final SAQ; a 23-item self administered questionnaire assessing both symptom severity and function across 4 organ domains (peripheral vascular, respiratory, gastrointestinal and musculoskeletal) (39).

• *The Symptom Burden Index (SBI)*

The development stage of the SBI included patient focus groups (14 pa-

tients) and individual patient interviews (5 patients) using scripted guiding questions based on a literature search and clinical experience to assess patients' assessment of disease and symptom burden in SSc (40). Purposive sampling was adopted to allow separate focus groups for early and late disease. Thematic analysis of transcribed interviews/focus groups was conducted to establish SSc-specific issues within *a priori* themes such as patient awareness, SSc-related problems, disease progression, symptoms, disease activity and expectations (40). The SBI instrument itself was primarily clinician-derived but sought to encompass several of the themes that emerged in the earlier qualitative work (41). The SBI includes 8 domains (skin, hand, calcinosis, shortness of breath, eating, bowel, sleep and pain); each of which are evaluated using 0-10 anchored response scales to evaluate the following 5 domain characteristics; "How much of a problems was...", "How often was... a problem", "How much did... interfere with daily activities", "How often did ... interfere with daily activities" and "How important a problem was..." (41). There was no reported patient involvement in item generation or questionnaire design. The authors identified different scoring patterns within each domain with "how much did...interfere" questions consistently yielding lower scores than "how often" or "how important" questions across each of the domains. There was low inter-item and item-total correlation for the skin domain. The variability in scoring items according to concept (how often vs. how much vs. how important) demonstrates the multifaceted nature of symptom burden in SSc. These findings also highlight the value of cognitive interviewing and linguistic evaluation to ensure the wording of the questions fully capture of the PRO instruments intended conceptual framework and how subtle differences in wording can influence outcomes.

Organ specific manifestations

The Scleroderma HAQ (S-HAQ) supplemented the original HAQ-DI (including pain VAS) with 5 additional patient-generated 15cm VAS scales

that capture the patient's perspective on the level of interference with normal activity over the last week caused by RP symptoms, digital ulcer disease, gastrointestinal symptoms, breathing problems and overall scleroderma disease severity (9). Having developed the supplementary items and associated VAS scales, the authors assessed the face validity of the chosen questions by asking 11 patients to describe their symptoms in response to the chosen items and reported that all patients used at least one of the same words or phrases in their responses (9).

Skin

• Patient Skin Self Assessment Questionnaire (Pt SSAQ)

The Pt SSAQ is the only PRO instrument for assessing skin involvement in SSc (42). There was no direct patient involvement in the instrument design which comprises patient reported assessment of overall skin thickness, tethering and thinness across the 17 anatomical regions assessed as part of the modified Rodnan Skin Score (mRSS). Like the mRSS, the assessments took the form of a 0-3 Likert Scale assessing global skin features (thickness, tethering and thinness) at each site, in addition to a transition VAS to describe change in skin feature over the last calendar month and a 10-region 0-3 Likert scale assessment of skin features (incorporating the major regions of the body assessed in the mRSS), from which a 17-region patient-reported composite score (0-51) was derived (analogous to the mRSS). Patients participating in the validation study were given the opportunity to comment on the wording, relevancy and comprehensiveness of the questions (upon completion of the questionnaire) and it was reported that the participants "found the questionnaire 100% understandable, relevant to their disease and feasible" (42). The 17-area skin thickness score appeared to perform best in relation to objective assessment, although the correlation with the mRSS remained modest (Spearman's rho 0.435), highlighting the challenges in modifying validated clinician assessment tools to develop a patient-reported equivalents in SSc (42).

Peripheral vascular manifestations

• The Raynaud's condition score (RCS) diary

The RCS diary collects daily information over a 2-week period on the frequency, duration and impact of RP attacks and was first used in 2 studies of oral iloprost in SSc (43, 44). It had evolved from a diary and Raynaud's severity score applied in an earlier clinical trial (45). Neither publication described the development of the tool, and there was no reported SSc patient involvement in item generation, instrument design or any assessment of respondent burden.

Gastrointestinal manifestations

Gastrointestinal (GI) involvement in SSc is common and patient questionnaires to test for GI involvement can be a useful screening method to guide further investigation and ensure relevant symptoms are not overlooked (46). The NIH PROMIS Gastrointestinal Symptoms Scales has recently been developed to capture the breadth and depth of physical symptoms associated with the GI tract, irrespective of diagnosis (47). Whilst not SSc-specific, the instrument was developed with the support of patients with SSc and provides a useful template of the valuable contribution patients can make to PRO instrument development. The generic Gastroesophageal reflux disease questionnaire (GERD-Q) has been evaluated in SSc populations and compared with objective assessment of GERD with gastroscopy and 24-hr pH monitoring. The majority (83%) of asymptomatic GERD patients were found to have abnormal pH monitoring despite the lack of symptoms, highlighting a pitfall in overreliance on self-report (48). More SSc-specific tools have also been developed.

• The SCTC GIT 1.0 and 2.0 questionnaires

The development of the SCTC GIT 1.0 questionnaire followed an extensive literature review and the assembly of an expert panel who derived a 69-item questionnaire with a 4-week recall period (49). Subsequent focus group meetings with SSc patients (n=16) were

undertaken to refine the questionnaire, identify missing domains/items, reduce item redundancy, and clarify wording of questions. This led to the emergence of a 75-item instrument across 11 domains with a modified recall period of 1 week. A subsequent cross-sectional validation study with multi-trait analysis was used to remove items with low item-to-hypothesised scale correlations ($n=19$) or poor discrimination across scales ($n=4$). The construct validity and reliability of the resulting 52-item GIT 1.0 questionnaire was assessed (49). A subsequent validation study in a UK-based cohort highlighted limitations including respondent burden and absence of an item by which to assess rectal incontinence (50). A revised 34-item GIT 2.0 questionnaire was developed, without specifically consulting SSc patients on content, following multi-trait analysis of the original instrument (including a novel item to assess rectal incontinence) within a second multicentre SSc cohort to remove superfluous items (*e.g.* subsets of items with high inter-item correlation) (51). The revised GIT 2.0 questionnaire has subsequently been validated in US and Canadian scleroderma cohorts (51, 52). The GIT 2.0 questionnaire has been translated into a number of languages using the “forward-backward method” with varying levels of cognitive debriefing of the translated versions with SSc patients to check comprehension, interpretation and cultural relevance within the target patient population (53-55).

• *Mouth Handicap in Systemic Sclerosis (MHISS) questionnaire*

The MHISS questionnaire was developed with the input of 74 SSc patients, in the form of a mail-based patient survey (56). The design and content of the survey was not reported in detail but patients were asked by mail to indicate the main situations of daily living (*e.g.* eating, speaking, relationship with relatives) that affected them because of mouth involvement. A provisional 34-item instrument to evaluate oral function in SSc was developed using the outcome of the survey, expert opinion and a detailed literature review. The

wording of the 34-item questionnaire did not have any SSc patient input but an initial cross-sectional study of 71 patients with SSc was used to achieve item reduction, resulting in the MHISS; a 12-item 0-4 ordinal scale with a composite score derived from the sum of item scores (56).

Cardiopulmonary disease

A number of PRO instruments assessing respiratory symptoms have been adopted from other disease areas (often COPD) and assessed in SSc populations including the St. George Respiratory Questionnaire (57, 58), the University of California San Diego Dyspnoea Questionnaire (59), Borg Dyspnoea Scale (60), modified Pulmonary Functional Status and Dyspnoea Questionnaire (27), the Functional Assessment of Chronic Illness Therapy-Dyspnoea short form (23, 34), The Cough Index (61) and Mahler Dyspnoea Scales (62). Recent work to identify patient-perspectives of living with CTD-ILD utilising mixed method approaches including focus group interviews and subsequent quantitative self-administered questionnaires has identified a number of values important to patients with CTD-interstitial lung disease (including SSc patients, $n=17$) not captured using legacy PRO instruments (63).

Body image perception

The Appearance Subscale of the State Self-Esteem Scale (ASE) and the 15-item Adapted Satisfaction With Appearance Scale (ASWAP) were originally developed for survivors of burn injuries but each tool has been adopted and assessed unmodified (other than replacing the word “burn” to “illness”) in SSc populations (64-67). SSc-specific PRO instruments for body image perception have also been devised (sometimes adapted from legacy instruments *e.g.* SWAP).

• *The Brief-Satisfaction With Appearance Scale (Brief-SWAP)*

The 6-item Brief-SWAP was devised specifically with the needs of SSc patients in mind to remove redundant items (from the original SWAP devised specifically for disfigurement follow-

ing burns injuries). The item-reduction exercise was clinician and data-derived, with items chosen on theoretical (*e.g.* body parts most commonly affected in SSc) and psychometric considerations (*e.g.* variance of item responses and item-total correlations) (68). There was no SSc patient input into item generation of the Brief-SWAP. The SWAP (adapted and unmodified) and Brief-SWAP have undergone subsequent assessment of convergent and divergent validity in SSc (68-70).

• *Body Concealment Scale for Scleroderma (BCSS)*

The BCSS has recently been developed to capture the unique body image concerns and body concealment behaviour of patients with SSc (71). A preliminary version of the BCSS was developed by a team comprising psychologists, experts in body image research, rheumatologists and a nurse specialist with expertise in SSc (but without specific target patient population involvement). The preliminary BCSS incorporated items from the Body Image Avoidance Questionnaire with the addition of new items thought to reflect SSc-specific body concealment behaviours. A development cohort ($n=93$) was used to undertake item reduction exercise in which 4 items were removed (without direct patient involvement). The finalised BCSS has been partially validated in a cross-sectional study of SSc. The authors acknowledge the lack of patient involvement in item generation as a limitation of the instrument’s development (71).

Pain

Sources of pain in SSc include tissue ischaemia, musculoskeletal dysfunction and GI disease (72). Single-item VAS instruments for pain and RP from the S-HAQ have been proposed for assessing pain associated with RP in SSc (2, 7), although the RP VAS item wording does not specifically mention pain (instead capturing interference with daily activity) and the item wording for the pain VAS does not specifically mention RP or other aetiological driver. Similarly, the wording of the SHAQ VAS item for digital ulcers (DU) makes no

reference to pain despite this being the major symptom of DU. As previously described, the wording of the SHAQ VAS items were developed without prior patient involvement (9). The generic Short-Form McGill Pain Questionnaire and an 11-point pain numeric rating scale have been partially validated in SSc (73).

Fatigue

Generic PRO instruments evaluating fatigue and sleep quality including the Functional Assessment of Chronic Illness Therapy-Fatigue (29, 74-76), Multidimensional Assessment of Fatigue (77, 78), Fatigue Severity Scale (79, 80), Medical Outcomes Study Sleep Scale (76), 9-item Sleep Problem Index (76) and the Pittsburgh Sleep Quality Index (20) have been evaluated in cross-sectional studies of SSc.

Sexual dysfunction

Sexual dysfunction and relationship problems contribute to impaired function and reduced quality of life in SSc (81). No disease-specific PRO instrument for assessing sexual dysfunction in SSc has been developed to date. Generic instruments such as the International Index of Erectile Function-5 questionnaire, Female Sexual Distress Scale, Female Sexual Function Index and sexual-relationships subscale of the Psychosocial Adjustment to Illness Scale-Self-Report have been adopted to evaluate the burden of sexual dysfunction in men and women with SSc (82-84). Analysis of the inter-relationship between multiple PRO instruments suggested that pain is a more important determinant of sexual dysfunction than body image dissatisfaction, although qualitative research methods might be better placed to explore such themes (84).

Psychological aspects of SSc

The Center for Epidemiologic Studies-Depression Scale (25, 65, 85-87), Illness Cognition Questionnaire (65), Beck Depression Inventory (19, 20, 88, 89), mood and tension subscales of the Arthritis Impact Measurement Scale 2 (44), Hospital Anxiety and Depression Scale (56, 67, 90, 91) and Patient

Health Questionnaire-9 (21, 87, 92) have each been evaluated in their unmodified form in SSc. The Illness Behavior Questionnaire has been studied in a large cross-sectional cohort of SSc and exploratory factor analysis applied to establish a SSc-specific factor structure with good convergent and divergent validity (80).

Development for Core Outcome Set (COS) for SSc Clinical Trials

Organisations such as COMET and OMERACT advocate the inclusion of patient representation in COS development to ensure the inclusion of outcome measures considered to be important by the target patient population (4, 93). The provisional COS for SSc clinical trials was developed using expert opinion garnered using Delphi and Nominal Group techniques, but did not include SSc patient involvement (2).

Discussion

The patient-perspective obtained by PRO instruments provides unique insight into severity, importance and impact of disease that physician-derived assessment tools sometimes fail to capture. Evidence of patient involvement in PRO development is required to satisfy regulatory bodies such as the FDA of the validity of labeling claims in medical product development (1). PRO instruments are a vital method of evaluating disease status in SSc due to the subjective and often episodic nature of disease manifestations such as Raynaud's. The majority of PROs utilised in SSc have been generic instruments developed for other disease areas and adopted (typically applied unmodified) in SSc populations. The adoption of generic PRO instruments avoids the need to develop a PRO instrument and has the advantage of facilitating comparison of disease and symptom burden across different disease populations. The major limitation of adopting generic PRO instruments is the varied extent to which the PRO items capture the experiences of patients within specific target populations. This can lead to the inclusion of redundant items and exclusion of items that SSc patients

might consider important. Few of the PRO instruments utilised in the assessment of SSc were developed specifically for patients with SSc and the majority of these did not meaningfully involve SSc patients in the development of the instrument. Despite being SSc-specific, the SySQ, SAQ and SBI were not included in the proposed core outcome set for SSc clinical trials (or identified as potential PRO instruments for future research) (2). Reasons for the apparent preference for generic PRO instruments over SSc-specific tools in Delphi and Nominal Group techniques involving SSc experts should be explored.

There is a growing body of qualitative research in SSc that is providing a deeper understanding of the patient experience of SSc (40, 49, 63, 67, 81, 94-96). This work has explored experiences of functioning and health in SSc (40, 81, 96), been used to develop a self-paced education program (95) and evaluated the impact of organ-specific SSc manifestations (63, 67, 94). The use of qualitative research methods to inform the design of novel PRO instruments in SSc has been relatively infrequent to date (41, 49). This might explain the limited extent to which existing PRO instruments used in SSc capture "personal factors" influencing health and function highlighted in recent work (81, 97). The UCLA SCTC GIT 2.0 questionnaire was highlighted as the SSc-specific PRO instrument that most successfully captured concepts pertaining to "personal factors"; possibly reflecting the extensive qualitative research work and patient involvement that underpinned the development of this instrument (97).

To ensure strong content and face validity, the development of novel PRO instruments for SSc should include patient representation at every stage of an iterative PRO development programme (1, 98). By drawing on qualitative research exploring the patient experience of SSc and involving patients in the development of novel PRO instruments in SSc, we can ensure that outcome measures used in the clinical and research settings adequately capture experiences most relevant to our patients.

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