CLINICAL SCIENCE

Development and validation of a patient-reported outcome measure for systemic sclerosis: the EULAR Systemic Sclerosis Impact of Disease (ScleroID) questionnaire

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Handling editor Josef S Smolen

► Additional supplemental material is published online only. To view, please visit the journal online (http://dx.doi.org/10.1136/annrheumdis-2021-220702).

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For 'Presented at statement' see end of article.

Received 5 May 2021
Accepted 9 November 2021
Published Online First
25 November 2021

To cite: Becker MO, Dobrota R, Garaiman A, *et al*. *Ann Rheum Dis* 2022;**81**:507–515.

ABSTRACT

Objectives Patient-reported outcome measures (PROMs) are important for clinical practice and research. Given the high unmet need, our aim was to develop a comprehensive PROM for systemic sclerosis (SSc), jointly with patient experts.

Methods This European Alliance of Associations for Rheumatology (EULAR)-endorsed project involved 11 European SSc centres. Relevant health dimensions were chosen and prioritised by patients. The resulting Systemic Sclerosis Impact of Disease (ScleroID) questionnaire was subsequently weighted and validated by Outcome Measures in Rheumatology criteria in an observational cohort study, cross-sectionally and longitudinally. As comparators, SSc-Health Assessment Questionnaire (HAQ), EuroQol Five Dimensional (EQ-5D), Short Form-36 (SF-36) were included.

Results Initially, 17 health dimensions were selected and prioritised. The top 10 health dimensions were selected for the ScleroID questionnaire. Importantly, Raynaud's phenomenon, impaired hand function, pain and fatigue had the highest patient-reported disease impact. The validation cohort study included 472 patients with a baseline visit, from which 109 had a test–retest reliability visit and 113 had a follow-up visit (85% female, 38% diffuse SSc, mean age 58 years, mean disease duration 9 years). The total ScleroID score showed strong Pearson correlation coefficients with comparators (SSc-HAQ, 0.73; Patient's global assessment, Visual Analogue Scale 0.77; HAQ-Disability Index, 0.62; SF-36 physical score, −0.62; each $p<0.001$). The internal consistency was strong: Cronbach's alpha was 0.87, similar to SSc-HAQ (0.88) and higher than EQ-5D (0.77). The ScleroID had excellent reliability and good sensitivity to change, superior to all comparators (intraclass correlation coefficient 0.84; standardised response mean 0.57).

Conclusions We have developed and validated the EULAR ScleroID, which is a novel, brief, disease-specific, patient-derived, disease impact PROM, suitable for research and clinical use in SSc.

Key messages

What is already known about this subject?
- Patient-reported outcome measures (PROMs) are important to integrate the patient's view into routine care.
- They are an integral part of clinical trials and required for registration of novel treatments.
- A brief and specific validated PROM for overall systemic sclerosis (SSc) is lacking.

What does this study add?
- It develops and validates the Systemic Sclerosis Impact of Disease (ScleroID), a disease-specific PROM that captures patient experience and SSc complexity in an easy to apply format for clinical care and clinical trials.

How might this impact on clinical practice or future developments?
- ScleroID can be used to integrate patient experience to improve decision making in clinical practice.
- Further studies are needed to validate ScleroID as a potential PROM for future clinical trials in SSc.

INTRODUCTION

Systemic sclerosis (SSc) is characterised by a chronic and frequently progressive course and by a high patient-to-patient variability.[1] SSc has one of the highest morbidities and case-specific mortalities among the connective tissue diseases.[2 3] Overall, general health (as measured by the Short Form-36 (SF-36) and EuroQol Five Dimensional (EQ-5D) questionnaires), as well as quality of life and functional abilities (as measured by the Health Assessment Questionnaire Disability Index, HAQ-DI) are significantly reduced in SSc.[4–6]

A disease-specific, patient-reported outcome measure (PROM) for use in clinical trials and in

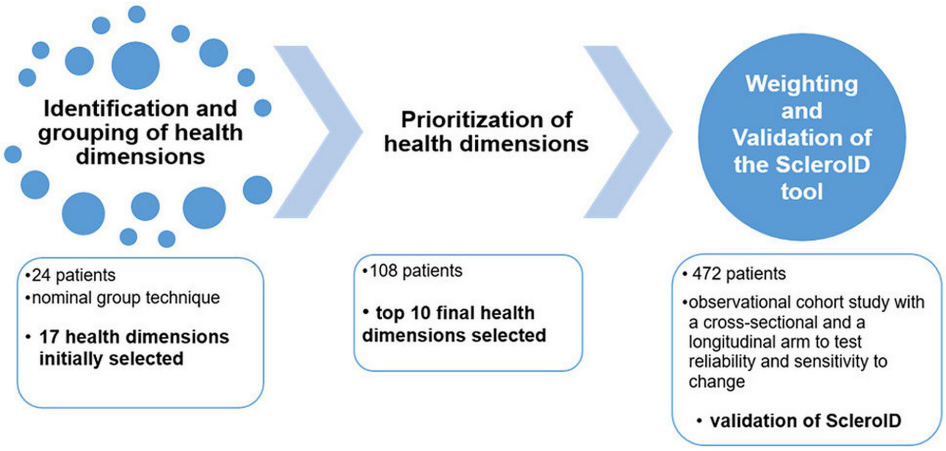

Figure 1 General ScleroID project workflow and procedure. ScleroID, Systemic Sclerosis Impact of Disease.

clinical practice in SSc that covers the different disease features of this multiorgan autoimmune disease is lacking.[7] The European Medicines Agency recommends that sufficient evidence needs to be provided on the patient benefit by PROMs before granting approval of a new therapeutic agent,[8] and PROMs need to be included as outcome measures in therapeutic randomised controlled trials (RCTs). Thus, the lack of sensitive, disease-specific PROMs covering the overall disease is currently one of the greatest challenges for drug development in this devastating disease. In addition, published data show that systematic use of PROMs in clinical practice improves patient-physician communication and decision making, as well as patients' satisfaction.[9]

Research in the field of other autoimmune diseases provides the basis for the successful development of disease-specific PROMs. For rheumatoid arthritis, the Rheumatoid Arthritis Impact of Disease (RAID) questionnaire,[10 11] and for psoriatic arthritis, the Psoriatic Arthritis Impact of Disease (PsAID) questionnaire,[12] were designed to capture the burden of disease that is most important to patients. Furthermore, the RAID has been successfully used to identify thresholds for symptom states acceptable for patients, as well as evaluating onset of response to medication.[13 14]

In this study, we aimed to develop a novel, patient-derived PROM for SSc that is able to cover the global disease burden—the EULAR Systemic Sclerosis Impact of Disease (ScleroID). Furthermore, we validated the ScleroID by the Outcome Measures in Rheumatology (OMERACT) filter in a large, multicentric, clinical cohort study.[15]

METHODS

The development of the European Alliance of Associations for Rheumatology (EULAR) ScleroID follows approaches used in the EULAR-endorsed RAID and PsAID questionnaires,

Table 1 Initially selected candidate health dimensions and their prioritisation ranking by importance

No	Health dimensions*	Mean rank	Median rank	Order by median rank	% patients giving rank 1 to the dimension	% patients giving rank 1–3 to the dimension	% patients giving rank 1–10 to the dimension
1	Raynaud	5.8	5	1	19.4	36.1	84.3
2	Hand function	6.7	5	1	8.3	25.0	78.7
3	Upper GI symptoms	7.2	6	2	7.4	24.1	73.1
4	Pain	6.9	6	2	10.2	25.9	75.9
5	Fatigue	6.7	6	2	9.3	26.9	78.7
6	Lower GI symptoms	7.8	7	3	10.2	24.1	69.4
7	Limitation of life choices and activities	8.3	8	4	4.6	20.4	66.7
8	Body mobility	8.7	8,5	5	2.8	11.0	65.7
9	Breathlessness	8.6	9	6	12.0	27.8	52.8
10	Digital ulcers	9.5	10	7	1.9	17.6	54.6
11	Anxiety	10.2	10	7	2.8	9.3	50.9
12	Dryness	10.1	10	7	1.9	9.3	54.6
13	Appearance	10.3	11	8	3.7	9.3	49.1
14	Concentration difficulties	10.9	12	9	1.9	9.3	39.8
15	Cough	11.3	13	10	1.9	10.2	38.9
16	Depression	11.6	13	10	0.9	7.4	35.2
17	Calcinosis	12.5	14	11	0.9	6.5	31.5

*Patients from the prioritisation cohort were asked to rank the dimensions in order of their importance by giving a rank from 1 (most important) to 17 (least important). Each rank could only be used once. The top 10 dimensions with the lowest median rank (highest importance) were selected for the questionnaire. The 10–12th dimension had an equal median rank but the 10th dimension had a higher role for more patients (% giving top rank, last two columns) and was consequently chosen in favour of dimensions 11 and 12. Dimensions included in the final ScleroID questionnaire are bolded.
GI, gastrointestinal; No, number; ScleroID, Systemic Sclerosis Impact of Disease.

Table 2 The ScleroID questionnaire

The EULAR ScleroID												
How much have the different aspects of systemic sclerosis affected you during the last week?												
Please mark your responses on the scale by choosing the appropriate no for each of the following dimensions:												
Raynaud's phenomenon:												
Circle the no that best describes the severity of your Raynaud's phenomenon during the last week:												
None	0	1	2	3	4	5	6	7	8	9	10	Extreme
Hand function:												
Circle the no that best describes your hand function limitations due to your systemic sclerosis during the last week:												
No limitation	0	1	2	3	4	5	6	7	8	9	10	Extreme limitation
Upper gastrointestinal tract symptoms (eg, swallowing difficulties, reflux, vomiting):												
Circle the no that best describes the severity of your upper gastrointestinal tract symptoms due to your systemic sclerosis during the last week:												
None	0	1	2	3	4	5	6	7	8	9	10	Extreme
Pain:												
Circle the no that best describes the pain you felt due to your systemic sclerosis during the last week:												
None	0	1	2	3	4	5	6	7	8	9	10	Extreme
Fatigue:												
Circle the no that best describes the impact of overall fatigue due to your systemic sclerosis during the last week:												
None	0	1	2	3	4	5	6	7	8	9	10	Extreme
Lower gastrointestinal tract symptoms (eg, bloating, diarrhoea, constipation, anal incontinence):												
Circle the no that best describes the severity of lower gastrointestinal tract symptoms during the last week:												
None	0	1	2	3	4	5	6	7	8	9	10	Extreme
Limitations of life choices and activities (eg, social life, personal care, work):												
Circle the no that best describes how severe the limitations of life choices and activities due to your systemic sclerosis were during the last week:												
No	0	1	2	3	4	5	6	7	8	9	10	Extreme
Body mobility:												
Circle the no that best describes how much your body mobility was affected due to your systemic sclerosis during the last week:												
Not affected	0	1	2	3	4	5	6	7	8	9	10	Extremely affected
Breathlessness:												
Circle the no that best describes how severe your breathlessness due to systemic sclerosis was during the last week:												
None	0	1	2	3	4	5	6	7	8	9	10	Extreme
Digital ulcers:												
Circle the no that best describes how much your digital ulcers affected you overall during the last week:												
None	0	1	2	3	4	5	6	7	8	9	10	Extreme

ScleroID, Systemic Sclerosis Impact of Disease.

as well as in the Pancreatic Cancer Disease Impact Score (PACADI),[10–12 16 17] with some modification given the differences between these diseases and SSc. Validation of the EULAR ScleroID follows the internationally recommended methodology of the OMERACT filter[15] (online supplemental file). This is a longitudinal, multicentric project, involving 11 European expert SSc centres and patient research partners. The project workflow and process are presented in figure 1.

Patient and public involvement

Patient research partners were involved in all the stages of the ScleroID project, starting with project design (KF and ATK), to the identification of the relevant health dimensions, and development and validation of the ScleroID including item reduction by weighting. These steps are detailed in the sections below. Furthermore, the dissemination of the study has been supported by the patient organisation Federation of European Scleroderma Associations (FESCA) by invited presentations of the preliminary results at patient congresses.

Part 1: development of the ScleroID questionnaire

Identification, prioritisation and selection of the health dimensions for the ScleroID

Initially, 24 patients with SSc participated in a nominal group technique exercise and selected candidate health dimensions with the highest impact on their disease status. First, the expert investigators (RD, MB and TH) presented a review of the literature on PROMs used in SSc. The patient representatives thereafter suggested health dimensions on which the disease has an important impact, according to their personal perception. On day one, 66 health dimensions were collected. On the second day, these were discussed and grouped by the patients according to the main concept that they are referring to, under moderation by TH. Finally, 17 candidate dimensions were unanimously selected (further details in online supplemental annex 2).

Subsequently, the identified health dimensions were evaluated by a larger group of SSc patients from all 11 participating centres. The objective of this exercise was to optimise face validity and to prioritise the dimensions. The health dimensions were translated by the investigators and patient research partners into each language (online supplemental file). Patients were presented with the list of candidate health dimensions in a random order and asked to rank them according to a decreasing order of importance. The top 10 dimensions based on median ranking were selected by the steering committee (MB, RD, KF, ATK, TH and OD) for the final ScleroID. The limitation to 10 dimensions was chosen based on ranking and aiming for a better feasibility of the final questionnaire and focussing on the most relevant health dimensions reported by the SSc patient research partners.

Development of the ScleroID questionnaire

The experts (MB, RD, TH and OD) developed one question with Numeric Rating Scales (NRS) to assess each of the selected top 10 health dimensions. The ScleroID questionnaire was subsequently translated into all applicable languages following the protocol detailed in online supplemental file.

Part 2: weighting of the dimensions and validation of ScleroID

Study design

A cross-sectional international observational cohort study with longitudinal reliability and sensitivity to change arms was performed. Patients above 18 years of age fulfilling the American College of Rheumatology/European Alliance of Associations for Rheumatology (ACR/EULAR) 2013 classification criteria for SSc were prospectively included.[18] Patients with severe comorbidities not related to SSc were excluded (eg, concomitant inflammatory disease, organ failure, recent acute cerebrovascular event, serious psychiatric or neurological disease). All patients signed written informed consent.

The sample target for the cohort study was 500 patients for the cross-sectional arm and 100/150 patients for reliability/sensitivity to change longitudinal arms, respectively, based on previous experiences with RAID and PsAID. As comparator questionnaires for the ScleroID, the most frequently used global PROMs applied in SSc were selected (online supplemental file).

Data collection

Clinical and demographic data were collected according to the European Scleroderma Trials and Research group (EUSTAR) standards[19] (online supplemental file). In addition, patients completed the ScleroID questionnaire, the selected comparators (SSc-HAQ, EQ-5D, SF-36), patient's global assessment on a Visual Analogue Scale (VAS), specific questions on the state of disease and a minimal clinically important difference question (online supplemental table S1) at all visits (online supplemental file).[20–25] For the weighting procedure, in order to assess the relative impact of the health dimensions, patients were asked to distribute 100 points between the 10 dimensions of the ScleroID according to the perceived impact on their health (online supplemental file). This was the basis for calculation of the ScleroID score (see statistical methods). Patients considered to be in a stable state by the physician and with no foreseeable change in treatment or medical intervention in the next 10 days following the baseline visit were included into the reliability arm, and asked to complete the reliability questionnaire at 7±3 days after the baseline visit (online supplemental annex). Patients considered to have active disease by the treating physician were included into the sensitivity to change arm and completed the respective questionnaire at the 12 months visit and/or at the 6 months visit, if available (online supplemental annex).

Statistical analysis

The calculation of the ScleroID score was based on the ranking of the weights, as performed in RAID, PsAID and PACADI.[10–12 16 17] Mean and median weights were calculated for each health dimension, after which mean and median ranks were computed for the whole cohort. These represent the basis for calculating the final weight, which is multiplied by the value on the NRS for each dimension/item and summed up for the final ScleroID score, which is then divided by 100.

The validation of ScleroID psychometric properties was performed according to the OMERACT filter, which assesses three main features: feasibility, truth and discrimination.[15] Feasibility addresses the applicability of the ScleroID questionnaire. Truth encompasses face validity (does the measure make sense), and content validity (eg, distribution of the score, floor/ceiling effect). As other measures of truth, internal consistency using Cronbach's alpha and construct validity (concurrent validity) with Pearson correlations to other scores (SSc-HAQ, SF-36, EQ-5D) were calculated. Construct validity was also investigated using a confirmatory factor analysis (online supplemental file). In addition, we assessed reliability and sensitivity to change. In the reliability arm, patients, who reported themselves as 'stable', were included in the test–retest reliability (reproducibility) analysis by assessing the intraclass correlation coefficient and agreement by Bland-Altman plot. In the sensitivity to change arm, patients reporting themselves as 'not stable' were included in the sensitivity to change (responsiveness) analysis by the standardised response mean (SRM, which is the difference in the baseline and follow-up mean values divided by the SD of the change scores). CIs were obtained by bootstrapping.

RESULTS

Part 1: development of the ScleroID questionnaire

Identification and prioritisation of health dimensions for the ScleroID

In the initial nominal group exercise, 24 patient research partners selected 17 health dimensions reflecting the impact of SSc (table 1). An additional cohort of 108 patients (online supplemental table S2) subsequently prioritised these health dimensions. The selected health dimensions and their prioritisation are summarised in table 1.

Selection of health dimensions and development of the ScleroID questionnaire

The steering committee agreed unanimously to include the ten health dimensions rated with the highest priority into the ScleroID questionnaire. One question with appropriate anchors to assess each of the selected ten health dimensions was developed by the steering committee (MB, RD, KF, ATK, TH and OD). These questions formed the ScleroID questionnaire (table 2), which was also agreed on by the patient research partners.

Part 2: weighting and validation of the ScleroID questionnaire

Cohort study

In total, 472 SSc patients from nine countries (France, Italy, Hungary, Poland, Romania, Spain, Sweden, Switzerland, UK) were included in the cross-sectional cohort study.

Most patients were female (84.8%), more than one-third had diffuse cutaneous SSc (dcSSc, 37.5%) and the median age was 57 years. The various disease manifestations, including lung fibrosis (42.6%), pulmonary arterial hypertension (7%), gastrointestinal (GI) involvement (>60% of patients with oesophageal symptoms), articular involvement (4.4% with synovitis) and digital ulcers (24.0% with previous ulcers, 13.0% with current ulcers) were well represented, reflecting a typical SSc population (table 3).

Weighting of the health dimensions and calculation of the ScleroID score

Overall, valid data on weighting was provided by 446 (94%) patients, and 462 (98%) patients provided complete data on the ScleroID questionnaire.

The health dimensions which were assigned the highest weights (and thus highest impact) by the patients were Raynaud's phenomenon, fatigue, hand function and pain, followed by

Table 3 Characteristics of the patients with SSc included in the weighting and validation cohort study

Characteristics	Overall	% of missingness
Age, years, median (IQR)	57 (48–65)	1.1
Female gender (n, %)	396 (84.8)	1.1
Time since RP onset, years, median (IQR)	11 (5.8–20)	26.3
Time since first non-RP manifestations, years, median (IQR)	9 (4.7–15)	5.5
Diffuse cutaneous SSc (n, %)	152 (37.5)	14.2
Limited cutaneous SSc (n, %)	253 (62.5)	14.2
mRSS, median (IQR)	4 (0–8)	26.5
Presence of Raynaud's phenomenon (n, %)	332 (94.6)	25.6
Digital ulcers (n, %)	47 (13)	23.5
Joint contractures (n, %)	124 (35.7)	26.5
Joint synovitis (n, %)	15 (4.4)	28.4
Oesophageal symptoms (dysphagia, reflux) (n, %)	232 (60.3)	18.4
Stomach symptoms (early satiety, vomiting) (n, %)	61 (17.6)	26.5
Intestinal symptoms (diarrhoea, bloating, constipation) (n, %)	135 (33.8)	15.5
Malabsorption syndrome (n, %)	18 (7.4)	48.7
Dyspnoea, NYHA stages III and IV (n, %)	27 (9.6)	40.7
FVC, % predicted, median (IQR)	95 (82–108)	40.5
FVC <80% predicted (n, %)	58 (20.6)	40.5
DLCO/SB, % predicted, median (IQR)	69 (55–81)	44.9
DLCO/SB, <70% predicted (n, %)	133 (51.2)	44.9
Lung fibrosis detected by HRCT (n, %)	78 (42.6)	61.2
Pulmonary hypertension (n, %)	19 (6.6)	39.4
PAPsys, mm Hg, median (IQR)	28 (24–32)	54.4
LVEF, %, median (IQR)	60 (55–65)	35.4
ANA positive (n, %)	319 (96.7)	30.1
ACA positive (n, %)	118 (36.5)	31.6
Anti-Scl-70 AB positive (n, %)	112 (35.2)	32.6
Anti-RNA Polymerase III AB positive (n, %)	21 (7.6)	41.1
ESR, mm/h, median (IQR)	17 (10–30)	25.2
CRP, mg/L, median (IQR)	2 (0.9–5)	35
Immunosuppression (n, %)	59 (21.2)	41.1

Definitions of organ manifestations according to EUSTAR.[19]
ACA, anticentromere antibodies; ANA, antinuclear antibodies; CRP, C reactive protein; DLCO/SB, diffusing capacity of the lung for carbon monoxide/single breath; ESR, erythrocyte sedimentation rate; EUSTAR, European Scleroderma Trials And Research; FVC, forced vital capacity; HRCT, high resolution CT; LVEF, left ventricular ejection fraction; mRSS, modified Rodnan Skin Score; NYHA, New York Heart Association; RP, Raynaud's phenomenon; Scl70, anti-Scl70 antibodies, anti-topoisomerase I antibodies; SSc, systemic sclerosis.

upper and lower GI symptoms (table 4), confirming the results from the prioritisation.

The mean ranks given in table 4 were rescaled to sum up to 1 for the final weights. The ScleroID was calculated as a composite score of the selected 10 dimensions. For each dimension, the NRS score was multiplied by the specific weight for this item and the weighted scores were summed up (see example in table 5).

Performance of ScleroID by the OMERACT filter

Feasibility

The ScleroID showed feasibility in the application, given the low proportion of missing data: ten patients (2.1%) had missing items, compared with 36 and 37 patients with missing data for SF-36 physical/mental component summary (PCS), 8 for EQ-5D, 12 for HAQ-DI and 16 for SSc-HAQ (online supplemental table S3). The majority of participants (462 or 98%) had complete data on the ScleroID questionnaire. Missing data were evenly distributed among the ScleroID items (no item had significantly higher missing values).

In daily practice, single items of questionnaires are frequently missing. We therefore assessed how imputation of single items affects the overall ScleroID score. When one missing item of the ScleroID score was imputed by the mean of the remaining cohort for this item, the error was minimal (up to 0.29/10 or <10%, (online supplemental table S4)).

Truth

Face validity was ensured by the involvement of patient research partners in all steps of the ScleroID development.[26]

The ScleroID score range is 0–10, the actual median and IQR in our patients was 3.2 (1.9–4.7) at baseline. The median and IQ for lcSSc patients was 3.3 (2.0–4.7) and for difusse cutaneous SSc (dcSSc) patients 3.3 (1.7–4.8; online supplemental figure S2). In total, eight patients recorded a ScleroID score of 0, while the highest observed value was 9.4. There was no relevant floor or ceiling effect, which would be assumed if >15% of patients scored either the minimum or maximum value ([27] online supplemental figure S2). The ScleroID questionnaire showed a good construct validity when correlated with the comparators (SSc-HAQ r=0.73; EQ-5D r=−0.48; Patient's global assessment, VAS r=0.77; HAQ-DI r=0.62; SF-36 PCS r=−0.62; each p<0.001, table 6).

The internal consistency as another measure of construct validity was also strong: Cronbach's alpha for the ScleroID was 0.87, similar to the SSc-HAQ (0.88) and higher than for the EQ-5D (0.77, online supplemental table S2). We also performed a confirmatory factor analysis which suggested a bifactor model (one general factor with additional two or three factors) with good model fit indices (online supplemental table S6 and figure S2). The omega indices, which are thought to

Table 4 Weighting of the health dimensions according to their perceived impact by the patients participating in the cross-sectional cohort study (n=472)

Dimension	Weight mean (SD)	Rank mean (SD)	Top ranked	Upper 25%	Bottom 25%	Lowest ranked
Raynaud	20.9 (18.9)	7.8 (2.6)	39.0	65.9	28.0	16.7
Fatigue	12.9 (10.6)	7.6 (2.0)	23.7	58.5	25.6	18.2
Hand function	12.1 (10.4)	7.3 (2.3)	19.5	55.9	36.2	21.2
Pain	10.4 (8.7)	7.0 (2.3)	16.7	46.0	42.2	23.5
Upper.GI symptoms	8.0 (8.2)	6.4 (2.4)	12.3	37.3	50.6	36.0
Life choices	7.9 (8.2)	6.6 (2.3)	12.1	35.8	52.1	37.9
Lower GI symptoms	7.6 (9.1)	6.2 (2.5)	11.4	36	56.1	42.8
Body mobility	7.0 (6.7)	6.4 (2.3)	8.1	38.6	54.0	39.2
Dyspnoea	6.8 (8.8)	6.1 (2.4)	9.3	33.7	64.4	46.2
Digital ulcers	5.9 (9.8)	5.6 (3.0)	17.2	32.2	68.6	61.4

Column 'weight' gives the mean (SD) of the weight given to each dimension, column "Rank" gives the mean (SD) ranking of each dimension according to the patient distributed weights. The remaining four columns give the percentage of times the dimension was ranked as most important (top ranked), the percentage of times it was ranked as least important (lowest ranked), as well as in the upper and lower quartiles of importance.
GI, gastrointestinal.;

Table 5 Computation of the ScleroID score

Element	Raynaud	Fatigue	Hand function	Pain	Life choices	Upper GI symptoms	Body mobility	Lower GI symptoms	Dyspnoea	Digital ulcers
ScleroID weights	0.117	0.114	0.109	0.104	0.098	0.096	0.095	0.093	0.091	0.083
Example NRS scores	9	3	4	0	7	2	6	4	0	3
weights(x)scores	0.117×9	0.114×3	0.109×4	0.104×0	0.098×7	0.096×2	0.095×6	0.093×4	0.091×0	0.083×3
=	1.053	0.342	0.436	0	0.686	0.192	0.57	0.372	0	0.249
ScleroID =	3.9									

Example of computation of the ScleroID score for a given patient. The final score is computed using a weighted sum over the NRS (0–10) scores given to each dimension by the patient. The weights sum to 1, and are proportional to the mean ranks given to each dimension.
GI, gastrointestinal tract; NRS, Numeric Rating Scale; ScleroID, Systemic Sclerosis Impact of Disease.

be superior to Cronbach's alpha,[28 29] suggested not only good model fit for the bifactor models (online supplemental table S7), but also supported our claim for sufficient unidimensionality to justify the use of a sum score (see also online supplemental file).

Test–retest reliability

In total, 109 patients were included in the longitudinal reliability arm and completed a second visit at 7±3 days after baseline. The ScleroID had a very good test–retest reliability, with an intraclass correlation coefficient of 0.84 (ranging 0.61–0.79 for the individual items), superior to all comparators (online supplemental table S8); see also Bland-Altman plot for agreement in online supplemental figure S5).

Sensitivity to change

A total of 113 patients were included and had a median follow-up visit at 12.2 (IQR 11.5–13.1) months. The sensitivity to change for the ScleroID was estimated using the SRM between baseline and follow-up, using only those patients (n=37) reporting disease status as not-stable (table 7). The SRM is computed for all patients regardless of whether they report improved/worsened disease state, and then separately for those with improved and worsened state (table 7). The ScleroID performed better than all other comparator PROMs in indicating overall change. This performance was even better in patients who experienced improvement (table 7).

Table 6 Construct validity analysis by correlation between ScleroID and other established PROMs

Variable	Pearson correlation coefficient*
Physician's Global Assessment	0.28 (0.05)
Patient's Global Assessment	0.77 (0.03)
SF-36 Physical Component Score	−0.62 (0.03)
SF-36 Mental Component Score	−0.47 (0.03)
HAQ-DI	0.62 (0.03)
SSc-HAQ	0.73 (0.02)
EQ-5D (UK-weighted)	−0.48 (0.04)
VAS-GIT	0.38 (0.05)
VAS-Dyspnoea	0.38 (0.04)
VAS-Raynaud	0.42 (0.04)
VAS-Ulcers	0.37 (0.05)

*Bootstrap standard errors (SEs) of estimated correlation given in brackets.
EQ-5D, EuroQol Five Dimensional Questionnaire; GIT, gastrointestinal tract; HAQ-DI, Health Assessment Questionnaire Disability Index; PROMs, patient-reported outcome measures; ScleroID, Systemic Sclerosis Impact of Disease; SF-36, Short Form (36) Health Survey; SSc, systemic sclerosis; VAS, Visual Analogue Scale.

DISCUSSION

PROMs are being developed to capture the patient's aspects of a disease, that is, the specific patient experience beyond the disease manifestations that are in the physician's focus, which are typically lethal or associated with high morbidity. Especially in SSc, which has a high morbidity and mortality as well as a high work disability, there is a discordance between the patient's experience and the physician's assessment, exemplified by differences in the patient's and physician's global assessment.[30–32] This was also observed in this study, underlining the need to implement PROMs in the clinical assessment and shared decision making. Most PROMs used in SSc are legacy questionnaires adapted from other diseases and not SSc-specific instruments.

Hence, specific PROMs are needed, although some have tried to incorporate the patient's view.[7 33]

We have developed and validated the ScleroID questionnaire as a global measurement tool to assess the disease burden in SSc patients. The questionnaire is simple and easy to apply, has high internal consistency and shows good correlation with the patient global assessment and the SSc-HAQ. Although weighting reflects patient experience, it does not significantly change the overall score. It is planned to develop a calculator (or app) to provide final scores. The ScleroID health dimensions have a high face validity due to the inclusion of SSc patient research partners throughout the development and validation process. Notably, main dimensions of the ScleroID questionnaire such as dyspnoea, pain, digital ulcers, GI symptoms or fatigue were also associated with a high self-reported disability and high disease burden in other reports from the literature.[5 34]

The ScleroID questionnaire has a very good retest reliability, which is even better than comparators and has better sensitivity to change than the comparators used. This is especially important as a high percentage of patients are relatively stable, but progression of the disease drives mortality and morbidity.[35] In addition, other frequently used major outcomes of SSc studies, such as the mRSS, show a relatively low sensitivity to change, which might partially explain the many randomised clinical trials with borderline significance using the mRSS as a primary outcome.[36]

Comparison to other PROMs

In contrast to other validated PROMs that have not been developed specifically for SSc (such as Patient-Reported Outcomes Measurement Information System-29; PROMIS-29)[37–39] or have only been adapted to SSc (such as the Scleroderma Health Assessment Questionnaire (SHAQ))[39 40], the ScleroID questionnaire was specifically developed, with involvement of SSc patient research partners. Although other specific PROMs for SSc have been developed, the Symptom Burden Index and the Systemic Sclerosis Questionnaire (SySQ) did not involve the target

Table 7 Sensitivity to change of the ScleroID compared with other PROMs

Variable	SRM (all)	95% CI (all)	SRM (improved)	95% CI (improved)	SRM (worsened)	95% CI (worsened)
ScleroID	0.57 (36)	0.31 to 0.86	0.76 (20)	0.42 to 1.23	−2.31 (4)	−25.14 to −1.35
Raynaud	0.08 (37)	−0.26 to 0.4	0.21 (20)	−0.25 to 0.68	−1.50 (4)	– to −1.17
Hand function	−0.20 (36)	−0.57 to 0.11	−0.22 (20)	−0.77 to 0.22	−0.78 (4)	−3.5 to −0.5
Pain	0.01 (37)	−0.23 to 0.45	0.04 (20)	−0.39 to 0.51	0.00 (4)	−1.5 to 1.5
Fatigue	0.24 (37)	−0.08 to 0.54	0.40 (20)	0 to 0.79	−1.306 (4)	– to −0.5
Upper GI symptoms	0.56 (37)	0.33 to 0.81	0.58 (20)	0.25 to 0.99	– (4)	–
Lower GI symptoms	0.44 (37)	0.09 to 0.82	0.43 (20)	−0.03 to 1.07	– (4)	–
Life Choices	0.53 (37)	0.25 to 0.87	0.77 (20)	0.33 to 1.51	0.50 (4)	0.5 to 1.5
Body mobility	0.35 (37)	0.03 to 0.63	0.54 (20)	0.14 to 1	0.00 (4)	−1.5 to 1.5
Dyspnoea	0.50 (37)	0.2 to 0.85	0.65 (20)	0.25 to 1.24	0.00 (4)	−1.5 to 1.5
Digital ulcers	−0.09 (36)	−0.43 to 0.23	0.00 (20)	−0.62 to 0.39	−0.5 (4)	−1.5 to −0.5
Patient's Global Assessment	0.29 (36)	−0.04 to 0.66	0.57 (20)	0.22 to 1.02	−0.20 (4)	−1.5 to 1.5
Physician's Global Assessment	0.09 (29)	−0.26 to 0.47	0.31 (17)	−0.18 to 0.9	−0.5 (4)	−1.5 to −0.5
SF-36 Physical Component Score	−0.2 (37)	−0.53 to 0.08	−0.45 (20)	−0.85 to −0.07	10.96 (4)	9.25 to 128.35
SF-36 Mental Component Score	−0.08 (37)	−0.4 to 0.26	−0.18 (20)	−0.64 to 0.31	−0.24 (4)	−1.22 to 2.65
HAQ-DI	−0.01 (36)	−0.39 to 0.32	0.10 (19)	−0.34 to 0.61	−0.78 (4)	−2.6 to −0.5
SSc HAQ	0.15 (34)	−0.23 to 0.45	0.24 (18)	−0.26 to 0.69	−0.46 (4)	−5.5 to 0.5
EQ-5D	0.41 (37)	0.09 to 0.74	0.33 (20)	−0.09 to 0.74	1.42 (4)	1.25 to 9.94

EQ-5D, EuroQol Five Dimensional; GI, gastrointestinal; HAQ-DI, Health Assessment Questionnaire Disability Index; PROMs, patient-reported outcome measures; ScleroID, Systemic Sclerosis Impact of Disease; SF-36, Short Form (36) Health Survey; SRM, standardised response mean; SSc, systemic sclerosis.

population for dimension/item generation. The Scleroderma Assessment Questionnaire (SAQ), which is based on the SysQ, had only partial involvement of patients.[41 42] However, these questionnaires have only been partially validated, mostly lacking a discriminant validity analysis, and are partly not validated in English (SysQ and SAQ). The recently published PROM Cochin Scleroderma Functional scale 17, a 17-item PROM that focused on mobility and general task aspects of SSc, was also developed with involvement of SSc patients.[43] It has been evaluated in a smaller cohort than the ScleroID and in French only, with data on discriminant validity (sensitivity to change) still missing.

Limitations of the study

Although patients with diverse disease manifestations participated in the nominal group exercise, disease-related or demographic data were not prospectively collected at this early stage. Patients included in the cross-sectional analysis had to fulfil the ACR/EULAR 2013 classification criteria for SSc but there were no recommendations concerning disease subtype or organ involvement. The final selection of participants by the centres has an impact on the weighting of the ScleroID dimensions and the cross-sectional part included mainly patients with long-standing disease. However, our cohort reflects other observational cohorts such as the EUSTAR registry, etc, indicating that it is a representative SSc population. Although SSc patients often acquire expert knowledge about their disease and are aware that the questionnaire evaluates SSc-related burden, it might be difficult at times to distinguish symptoms related to SSc from common, unrelated symptoms, for example, as in the case of GI problems. This is however common to all PROMs.

Another potential limitation is the relative paucity of patients who experience change of their disease status, who then enter the sensitivity to change analysis. As this change was anchored by the patients themselves, there were no prior data to guide selection of these patients.

The ScleroID was designed as an overall measure of disease impact. It was derived from patients under routine clinical care and as such, it is still to be validated in clinical trials aiming at overall disease modification. If the ScleroID questionnaire can also be used for clinical trials focusing on organ-specific disease progression is subject to further analysis.

In summary, the ScleroID questionnaire is a unique, easy to apply, SSc-specific PROM that has been successfully validated in a large European clinical cohort using multiple translations. It should be further validated for clinical trials and in large registries and has the potential to measure disease impact that will be more meaningful for patients and health authorities than currently used approaches.

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Presented at
Part of this work has previously been presented, as follows: Presentations: The EULAR Systemic Sclerosis Impact of Disease score – a new patient-reported outcome measure under development, 4th Scleroderma World Congress, Patient Congress, Lisbon, Feb 18th – 20th, 2016, Poster EULAR 2016, Poster ACR 2016, Abstract book EULAR 2017, Poster ACR 2017, Poster Patients' Congress SWC 02/2018 Bordeaux,

Abstract book EULAR 2018. Meetings: Working group patients and PIs inkl. teleconference – Rome, 06/2015, Task force meetings, EULAR 06/2016 London, ACR 11/2016 Washington, EULAR 06/2017 Madrid, EULAR 2020 Online E-Congress.

Acknowledgements We sincerely thank the patients' representatives who contributed to the study, without whom this project would not have been possible: Ann Kennedy, Kim Fligelstone, Heleen Lever, Yanne Perriault, Anna Vegh, Susanne Tuppeck, Silvia-Daniela Sandulescu, Mervat Gaafar, Barbara Zappitello, Rachida Amrouch, Grazia Tassini, Helene Kambourakis, Elisabeth Scheel, Stephan Houbertz, Beata Garay Toth, Ana Marcela Badea, Stefana Dumitru, Alicia García Oliva, Begoña María Gorricho Corta, Johanna Berglind, Natalie Perruchoud, Alice Martins Correia, Richard Dodds, Nicola Whitehill. Our thoughts go to Mr. Richard Dodds, who unfortunately is no longer with us.

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Funding The development and validation of the ScleroID was in part supported by a grant from EULAR.

Competing interests MB personal fees from Amgen and Bayer, outside the submitted work. RDo reports grants from Articulum Fellowship, sponsored by Pfizer (2013-2014), grants from Actelion, personal fees from Actelion and Boehringer-Ingelheim, outside the submitted work. AG none with respect to the study. RDe none with respect to the study.KF none with respect to the study. ATK none with respect to the study. AR none with respect to the study. YA reports grants and personal fees from Bayer, Boehringer-Ingelheim, Bristol Myers Squibb, Curzion, Inventiva, Roche and Sanofi during the conduct of the study. PEC reports consultancy relationship and/or research grants from: Abbvie, Actelion, Bayer, Boehringer Ingelheim, Corbus Pharma, Emerald Health Pharmaceuticals, Galapagos, Gesynta Pharma, Inventiva, iQvia, Mitsubishi Tanabe Pharma, MSD, Roche and Sanofi Genzyme. LC none with respect to the study. CPD reports grants and personal fees from GSK, Mitsubishi Tanabe Pharma, Boehringer-Ingelheim, Servier, Arxx Therapeutics, Bayer, Inventiva, Galapagos, Horizon, Roche, CSL Behring, Sanofi during the conduct of the study.RH reports personal lecture fees from Actelion Pharmaceuticals Sweden AB, Boehringer-Ingelheim Sweden AB, and Roche Sweden AB, and has been co-investigator in clinical trials for United Therapeutics and Actelion Pharmaceuticals Sweden AB, and has been involved in research advisory boards for Actelion Pharmaceuticals Sweden AB and Boehringer-Ingelheim Sweden AB. GS none with respect to the study. OK-B reports personal fees and/or congress support from Bayer, Boehringer Ingelheim, CSL Behring, Gilead, Inventiva, Medac, MSD, Novartis, Pfizer, Roche, Sandoz, outside the submitted work. CB reports personal fees from Actelion, personal fees from Boehringer-Ingelheim, personal fees from Eli Lilly, grants from Gruppo Italiano Lotta alla Sclerodermia (GILS), grants from New Horizon Fellowship, grants from European Scleroderma Trials and Research (EUSTAR), grants from Foundation for Research in Rheumatology (FOREUM), grants from Fondazione Italiana per la Ricerca sull'Artrite (FIRA), outside the submitted work. MM-C reports grants and personal fees from Actelion, personal fees from Biogen, personal fees from Bayer, personal fees from Boehringer Ingelheim, personal fees from CSL Behring, personal fees from Eli-Lilly, outside the submitted work. CM reports personal fees from Boehringer Ingelheim, Eli-Lilly, Mepha, MEDTalks Switzerland and congress support from Actelion and Roche, outside the submitted work. AMG reports consultancy fees from Boehringer-Ingelheim and congress support from Abbvie and Novartis, outside the submitted work. UM-L none with respect to the study. JS none with respect to the study. TKK none with respect to the study. TH reports no conflicts of interest.OD has/had consultancy relationship and/or has received research funding in the area of potential treatments of scleroderma and its complications from (last three years): Abbvie, Acceleron Pharma, Alexion, Amgen, AnaMar, Arxx Therapeutics, Baecon Discovery, Bayer, Boehringer Ingelheim, Catenion, Drug Development International, CSL Behring, ChemomAb, GSK, Horizon (Curzion) Pharmaceuticals, Inventiva, Italfarmaco, iQvia, Lilly, Medac, Medscape, Mitsubishi Tanabe Pharma, MSD, Novartis, Pfizer, Roche, Sanofi, Serodapharm, Target Bio Science and UCB In addition, he has a patent mir-29 for the treatment of systemic sclerosis issued (US8247389, EP2331143).

Patient consent for publication Not applicable.

Ethics approval The project was approved by the ethics committee in each participating centre.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available on reasonable request. On request, and subject to review by the steering committee, access can be granted to the anonymised raw data and the R code. Deidentified data will be made available via secure data transfer. Data requests may be sent to the ScleroID steering committee, represented by OD, Department of Rheumatology, University Hospital Zurich, University of Zurich, Switzerland. Email oliver.distler@usz.ch.

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Supplementary material

Development and validation of a patient reported outcome measure for systemic sclerosis: the EULAR Systemic sclerosis Impact of Disease (ScleroID) questionnaire

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1. SUPPLEMENTARY METHODS

Main concept:

The ScleroID aims to specifically capture the global burden of disease of systemic sclerosis (SSc) as perceived by the patients themselves. In other words, it aims to provide an integrated and standardized overall assessment of the multiple health dimensions affected by SSc that are most important to patients. Hence, it aims to function similarly to the already successfully developed RAID and PsAID tools for rheumatoid arthritis and psoriatic arthritis, respectively [1-4].

ScleroID aims to meet an unmet need in the current assessment of the patients' disease experience in SSc. The current medical practice consists of using several existing PROM tools, which are either generic (e.g. SF-36) or somewhat adapted for SSc (e.g. SHAQ), or specifically focussing on one aspect of the disease (e.g. UCLA GIT for gastrointestinal involvement). This is in general important to detail certain aspects of the disease, but may burden the patients with lengthy and time-consuming questionnaires which however fail to capture the complexity of SSc. A specific, brief but also comprehensive questionnaire could considerably improve the inclusion of the patient perspective in clinical practice and clinical research in SSc.

We have validated the ScleroID questionnaire following the Outcome Measures in Rheumatology (OMERACT) filter, a widely acknowledged framework for development

of PROMs in Rheumatology [5]. By the OMERACT filter, a candidate outcome measure is evaluated according to three main pillars which are represented by *truth*, *discrimination* and *feasibility* [6]. *Truth* essentially means that the PROM measures what it is intended to, hereby including content validity, face validity and construct validity, which we investigated for ScleroID (as detailed in the main manuscript). Further, *discrimination* refers to whether the instrument can differentiate between situations of interest (either different states at one time or states at different times).[6] For this, we tested ScleroID for test/retest reliability and sensitivity to change in a clinical setting. Lastly, the feasibility of applying ScleroID in practice has been addressed in terms of translation, practicability, concision and easiness of use.

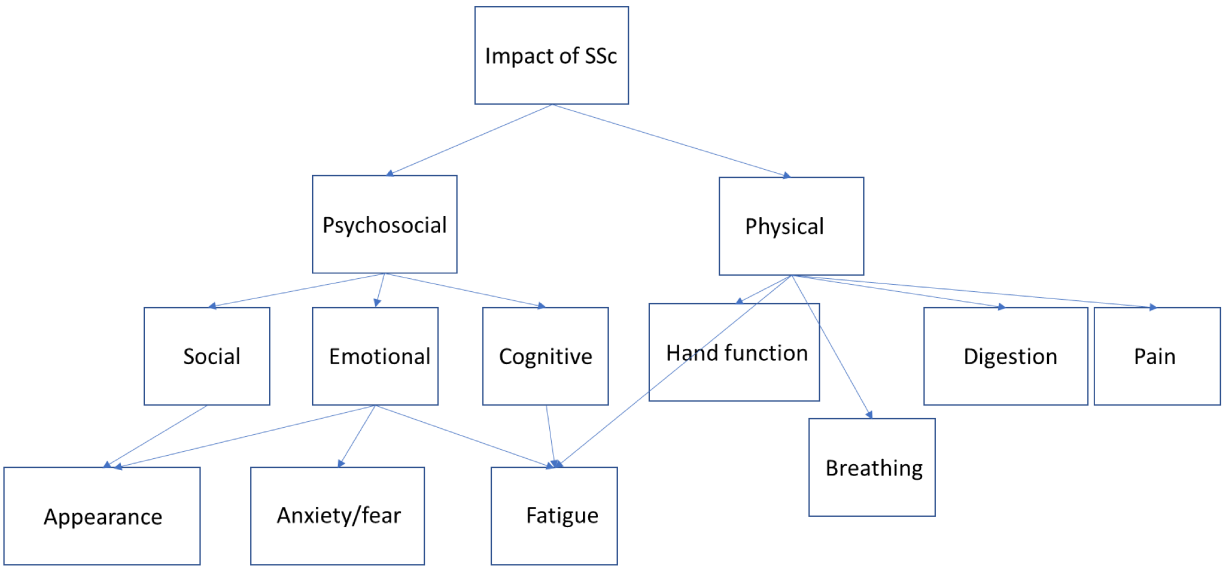
The clinical data were collected following generally accepted EUSTAR (European Scleroderma Trials and Research group) standards. Accordingly, detailed clinical, laboratory and imaging data from the patients' regular visits at the participating expert SSc centres are collected following a standardized protocol and datasheet. This includes yearly assessments with screening for organ involvement as well as potentiallly additional follow-up visits, according to the treating physician [7]. The data are systematically uploaded in a joint electronic database which undergoes periodic quality checks.

Development of the ScleroID questionnaire

Expert investigators from each centre, representing 11 European countries, invited one to three English-speaking patients, each with complementary disease features, as to cover the different aspects of the disease. Only one patient per centre was required on site, whereas the 1-2 additional patients joined via webinar/telephone conference. Given the heterogeneity of SSc, the availability of patient research partners for this first step was essential. Although there is no definitive need to calculate sample size in qualitative approaches, the principle of saturation, i.e. to reveal the full range of important perceptions, is regarded as an indicator.

The meeting took place on two days during the EULAR congress in Rome in June 2015. Eleven patients joined on site and 13 through a telephone conference. On the first day, the expert investigators (RD, MB, TH) presented a review of the literature on PROMs used in SSc to the patient research partners. The best-established and well-known questionnaires, the SHAQ and SF-36, were used as examples. The patient representatives thereafter suggested health dimensions on which the disease has an important impact, according to their personal perception, using the nominal group technique [8]. Only neutral moderating from the experts was permitted at this stage. On day one, 66 health dimensions were collected. On the second day, these were discussed, grouped and finally reduced to 17 candidate dimensions, which were approved unanimously by whole group. An example: patients initially freely reported areas in which they felt themselves affected by their SSc. The first brainstorming exercise brought up (among others) musculoskeletal aspects like “body stiffness” and “muscular weakness” as main issues for the patients. After a subsequent discussion with the group, the patients felt that these would best be captured under the term “body mobility”, understood as the general subjective perception of impaired body movement comprising both flexibility and strength aspects. A visualization of a conceptual model for a ScleroID PROM is given below.

Figure S1: A conceptual model for the ScleroID PROM



Development of study materials and translation protocol

All study materials intended for patients (prioritization sheet, ScleroID questionnaire, cohort study case report forms, CRFs) have been developed in English (RD, MB, TH, OD). For the development of the ScleroID questionnaire, the questions and NRS scales were constructed by the steering committee, including patient research partners (RD, MB, TH, OD, ATK) and agreed upon by the patient representatives who participated in the nominal group exercise in Rome (see main methods).

All study materials intended for patients (ScleroID, CRFs) were translated from English into the local language by each centre under the supervision of the local PI. The standardized translation protocol, which was recommended, required that two bilingual persons (one preferably a patient) separately translated from English into the target language, then met and reached consensus. A third person subsequently did the back translation from the local language to English. Finally, they all met to agree for a final version. The PI was advised to at least participate at this last meeting with the translation team.

The study CRFs are provided as Annex 1.

A standardized excel template for data collection was provided to the centres. All data were after completion sent to the lead centre. Where appropriate, queries were sent by the steering committee (MB, RD) to the PIs.

Selection of other PROMs as comparators for ScleroID

After literature review and discussion within the steering committee (MB, RD, OD, TH), the following questionnaires were initially selected as potential validation instruments for ScleroID and its constituting dimensions: SF-36, SSc-HAQ, EQ-5D, EUSTAR activity index, Cochin Hand Function Scale, ULCA GIT 2.0, FACIT, Raynaud's Condition Score.

Consistent with the experiences from the earlier successful EULAR projects on patient reported outcomes (RAID, PsAID) [1-3], PIs then agreed that single dimensions of the ScleroID questionnaire were not to be tested for concurrent validity. Instead, it was decided that the whole ScleroID questionnaire will be validated by comparison to other overall scores, i.e. questionnaires that evaluate the disease status of SSc patients more broadly. These were chosen to be the SF-36, the SSc-HAQ, the EQ-5D and the EUSTAR SSc activity index, based on the available data from the literature validating

their use in SSc. Translations for the comparator PROMs were retrieved from the literature, as available.

Table S1. Weighting exercise, as presented to patients

(extract from patient's baseline CRF, see Annex 1)

We want you to indicate how much your systemic sclerosis (scleroderma) impacts your health in the following selected health dimensions, shown below.

Please distribute 100 points between the dimensions according to their impact; the sum should be 100.

Please read all dimensions before starting to distribute your points.

You can spend your points in sets of 5. Give more points to dimensions which have important impact and less to dimensions that are not so important. You do not have to spend points in every area. You cannot spend more than 100 points.

Please take into account your whole disease history, not only how you feel today, when distributing the points.

In this table, you have to distribute your 100 points between 10 domains of health:

Domain/dimension	POINTS
Raynaud's Phenomenon	I__I__I
Hand function	I__I__I
Pain	I__I__I
Fatigue *(being tired physically, but also mental fatigue, lack of energy)*	I__I__I
Upper gastrointestinal tract symptoms *(e.g. swallowing difficulties, reflux, vomiting)*	I__I__I
Lower gastrointestinal tract symptoms *(e.g. bloating, diarrhea, constipation, anal incontinence)*	I__I__I
Limitations of life choices and activities *(e.g. social life, personal care, work)*	I__I__I
Body mobility	I__I__I
Breathlessness	I__I__I
Digital ulcers	I__I__I
TOTAL POINTS: Remember must add up to 100 points	100

2. Sample size considerations

For the initial group of patients who selected the main candidate health dimensions there was no formal sample size calculation, based upon the rationale that there is no definitive need to calculate sample size in qualitative approaches. Nonetheless, the principle of saturation, i.e. to reveal the full range of important dimensions is regarded as an indicator. A critical review from Yamazaki et al. identified a median sample size of 36 (range 9-383) in 80 qualitative studies published in the 5 most influential medical journals [9]. We also took into consideration that SSc has a wide range of clinical phenotypes, which requires diverse patient representation. As a result, the experts recruited SSc patients with a wide range of disease phenotypes and demographic characteristics, and a total of 24 took part to the nominal group exercise in Rome in 2015. For comparison, the number of participants in the initial phase of the RAID and PsAID studies for identification of candidate dimensions were 10 and 12, respectively [1, 2]. Focus groups were reported to usually contain 6 -12 participants [10]. Hence, we considered 24 SSc patients for the focus group to be sufficient.

For the prioritisation and weighting exercises, and for the validity study, formal power calculations were not performed. The literature suggested that a patient population of around 500 or more was estimated to be sufficient and we used the studies behind PsAID and RAID as models [10]. Numbers are very similar across the three studies [1-3].

Becker MO, *et al. Ann Rheum Dis* 2021;0:1–9. doi: 10.1136/annrheumdis-2021-220702

2. SUPPLEMENTARY RESULTS

Table S2. Clinical and demographic characteristics of the patients who performed the prioritization step (N=108)

Variable	Frequency
Age (years, median (IQR))	53 (17)
Gender (n, %)	
Female	82 (76%)
Male	25 (24%)
Disease duration* (years, median (IQR))	10 (10)
Disease subset according to Le Roy (n, %)	
Limited skin involvement	53 (49.5%)
Diffuse skin involvement	54 (50.5%)
Distribution per country (alphabetically, n)	
France	9
Germany	10
Hungary	9
Italy	10
Netherlands	10
Poland	10
Romania	11
Spain	10
Sweden	7
Switzerland	12
UK	10
*time since onset of the first non-Raynaud symptom of the disease Abbreviations: IQR, interquartile range; UK, United Kingdom.	

Performance of ScleroID by the OMERACT filter – additional results

Table S3. Number and percentage of missing values for scores in the cross-sectional study.

Questionnaire	Patients with missing items, n(%)	Mean of missing items (SD)
ScleroID	10 (2.1)	3.3 (3.0)
Physician Global Assessment	23 (4.9)	1.0 (0.00)
Patient Global Assessment	3 (0.6)	1.0 (0.00)
SF-36 Physical component score	36 (7.6)	3.0 (3.7)
SF-36 Mental component score	37 (7.8)	3. 9 (3.7)
EQ-5D	8 (1.7)	1.8 (0.5)
HAQ-DI	12 (2.5)	8.0 (0.00)
SSc-HAQ	16 (3.4)	3.8 (0.8)

Abbreviations: n, number; SD, standard deviation; SF-36, 36-Item Short Form Survey; HAQ-DI, Health Assessment Questionnaire Disability Index; SSc-HAQ, Systemic Sclerosis Health Assessment Questionnaire Disability Index;

The table illustrates the number (and percentage) of patients who had at least one missing item per questionnaire and the mean number of missing items per questionnaire in those patients.

Imputation of missing ScleroID items

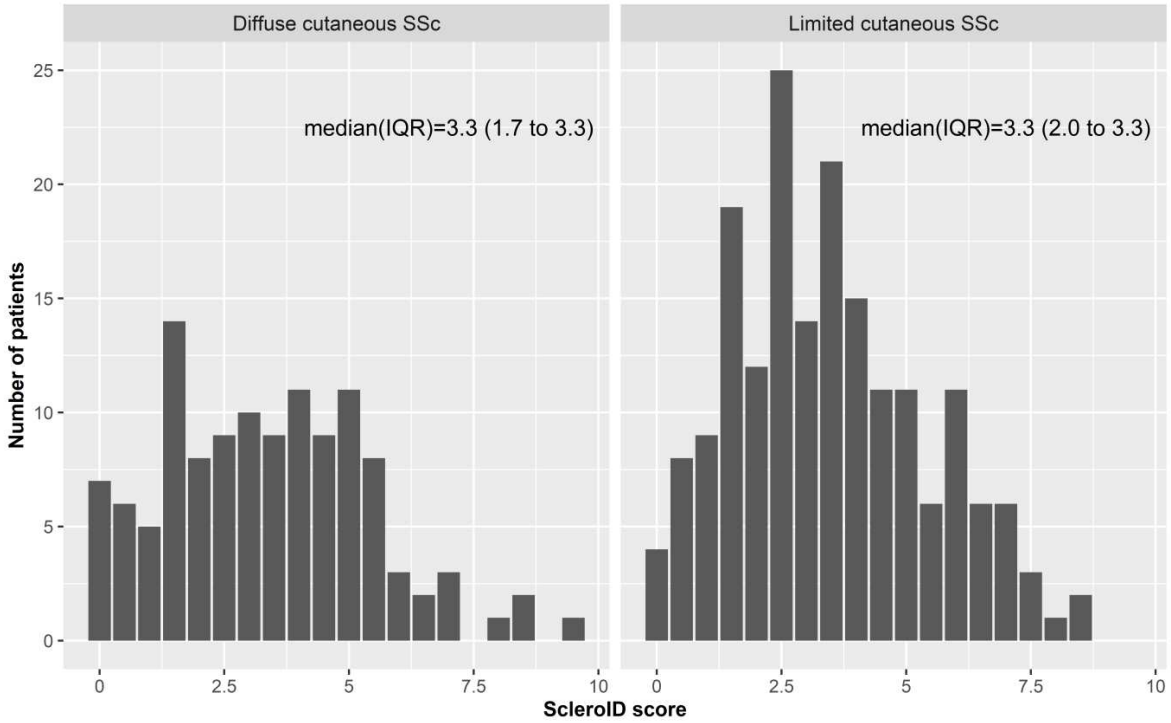
Two approaches to imputing a single missing component of ScleroID were investigated. The first is the approach that was used for PsAID, where the missing item of the ScleroID score is replaced by the average of the other components of the ScleroID score of the same patient ('PsAID Imputation'). The second method imputes the missing ScleroID item in one patient using the average value for this item across all patients, ('Mean Imputation'). Both methods were compared by setting one item as missing and using both methods to impute the missing item. Results were compared to the “true” ScleroID score. The difference between the imputed and true ScleroID is measured using the mean absolute error. The table below suggests that both approaches seem to work adequately, with the PsAID Imputation yielding slightly lower mean absolute errors.

Supplementary Table S4: Imputation of single ScleroID component. Mean absolute error.

ScleroID component	Mean absolute error (PsAID Imputation)	Mean absolute error (Mean Imputation)
Raynaud`s phenomenon	0.27	0.29
Hand function	0.19	0.26
Pain	0.17	0.26
Fatigue	0.21	0.28
Upper gastrointestinal symptoms	0.17	0.21
Lower gastrointestinal symptoms	0.19	0.23
Life choices	0.16	0.24
Body mobility	0.14	0.21
Dyspnoea	0.17	0.20
Digital ulcers	0.23	0.18
Abbvreviations: PsAID, Psoriatic Arthritis Impact of Disease		

The table illustrates the mean absolute error when any ScleroID component is imputed by the PsAID or Mean Imputation method (see above). Given the ScleroID score range from 0 to 10 and the median and interquartile range (IQR) of 3.2 (1.9-4.7), the errors vary from 0.14 (4.3%) to 0.29 (9.1%).

Figure S2. Distribution of ScleroID scores across 472 patients at baseline.



The graphs show the distribution of final ScleroID scores amongst dcSSc (left) and lcSSc (right) patients with the respective median and IQR.

Table S5. Internal consistency of ScleroID analysed by Cronbach's alpha.

Health dimension	**Value***
Raynaud	0.87
Hand function	0.85
Pain	0.84
Fatigue	0.85
Upper GI symptoms	0.85
Lower GI symptoms	0.86
Life choices	0.84
Body mobility	0.84
Dyspnea	0.85
Digital ulcers	0.87
Cronbach's alpha	**0.87**

*Table gives Cronbach's alpha (last row) of components of ScleroID, and the value of Cronbach's alpha with individual dimension removed. For comparison, Cronbach's alpha for SSc-HAQ was 0.88, for HAQ 0.92, and for EQ5D 0.77.
Abbreviations: GI, gastrointestinal.

For Cronbach's alpha, a cut-off of 0.7-0.8 usually is regarded as satisfactory, and we interpreted values > 0.8 as strong[11, 12]. However, acceptable levels might be different and even lower depending on the actual study. Similarly, cut-off levels have been provided for correlation coefficients such as Pearson's r: "0-0.19 is regarded as very weak, 0.2-0.39 as weak, 0.40-0.59 as moderate, 0.6-0.79 as strong and 0.8-1 as very strong correlation"[13].

Further instruments to assess construct validity are methods that measure the relationship between a latent trait to be measured and the items of a questionnaire, such as principal component analysis, factor analysis or a Rasch model. We decided to implement a confirmatory factor analysis (CFA) as we a) had assumptions

concerning the possible internal structure of the questionnaire and b) thought it likely that preconditions for a Rasch model would be violated (e.g. the a priori assumption that all items measure the same latent trait and that correlations of items with the latent trait are equally distributed). With missings of no more than 3% we did a complete case analysis. The Kaiser-Maier-Olkin Measure of Sampling Adequacy was close to 1 with 0.89, Bartlett`s test suggested the variables were not completely uncorrelated ($p < 0.001$) and the determinant of the data regarded as a matrix was 0.019, all of which supported a confirmatory factor analysis. Because we hypothesised that a common latent trait might be important for all items, we tested a one factor structure as well as a bifactor/2 factors and a bifactor/3 factors structure. For comparison, structures with 2 and 3 factors were also evaluated. The model fit indices indicated slightly mixed results that in general favoured a bifactor model with either 2 or 3 factors (2 factors: hand – encompassing Raynaud`s, hand function, pain and ulcers, systemic: the remaining items; 3 factors: hand – as for the bifactor/2 factors model, GIT – lower and upper GI symptoms, life – the remaining items; see Supplementary Table S6 and Supplementary Figure S3).

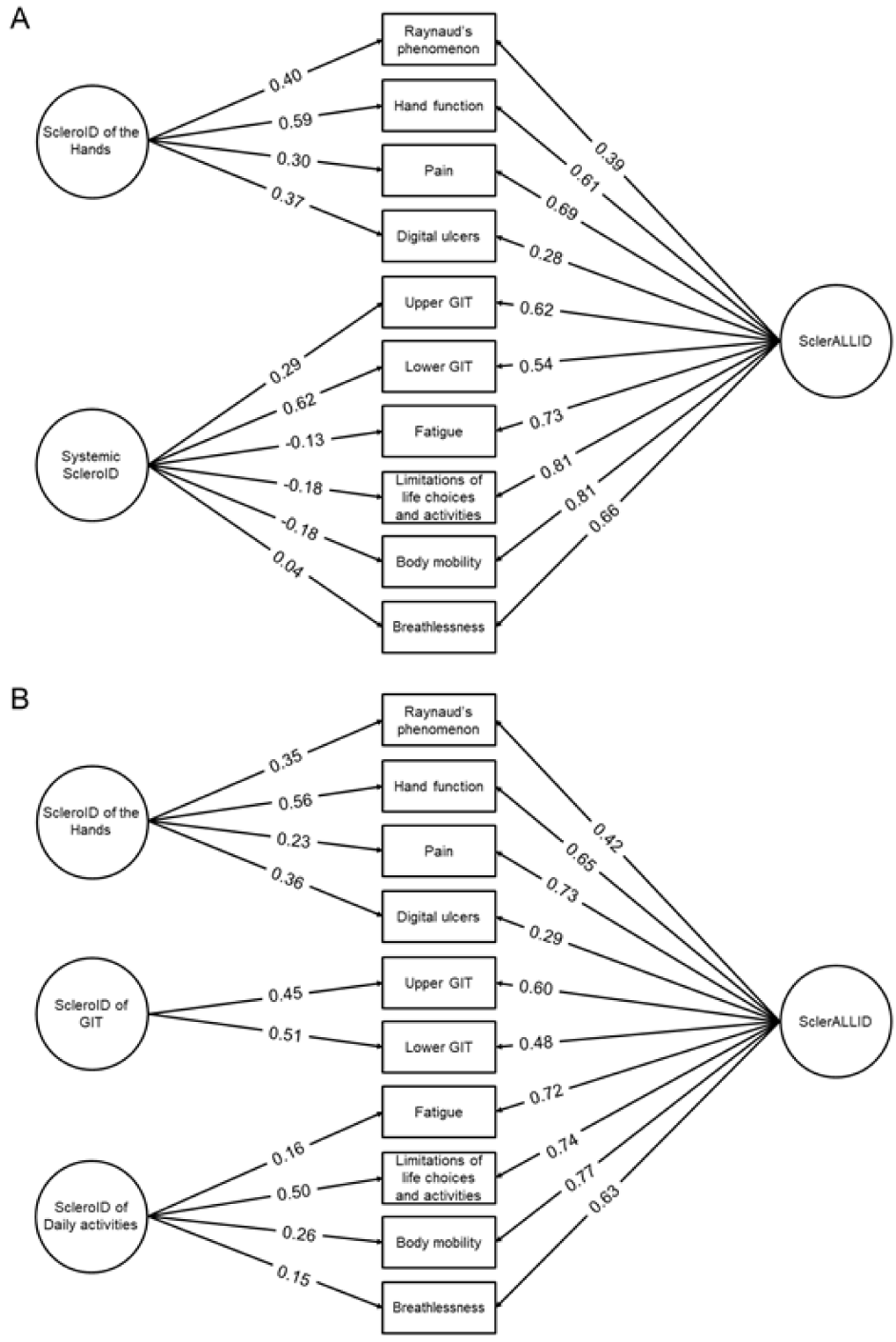
Table S6. Model fit indices of the confirmatory factor analysis models.

Model	Chisq	DF	Chisq/DF	CFI	RMSEA	SRMR	AIC	TLI
1 factor	236.38	35	6.8	0.89	0.11 (0.10-0.13)*	0.06	21112.05	0.86
2 factors	153.91	34	4.5	0.93	0.09 (0.07 – 0.10)*	0.05	21031.58	0.91
bifactor, 2 factors	50.78	25	2.0	0.99	0.05 (0.03 - 0.07)	0.02	20946.44	0.97
3 factors	92.74	32	2.9	0.97	0.06 (0.05 – 0.08)	0.04	20974.41	0.95
bifactor, 3 factors	62.95	25	2.5	0.98	0.06 (0.04 – 0.08)	0.03	20958.61	0.96

Chisq - chi-square statistic (all $p < 0.05$); DF – degrees of freedom; CFI - comparative fit index; RMSEA - root mean square error of approximation; SRMR - standardized root mean square residual; AIC - Akaike information criterion, TLI - Tucker Lewis. * indicates RMSEA p values < 0.05.

There are rules of thumb in the literature to assess model fit with indices: large sample sizes will almost always give significant chi-square statistics by default, therefore the ratio of the chi-square test statistic to the degrees of freedom is calculated, where a model fit is indicated by values smaller than 3 [14]. CFI should be > 0.9, better > 0.95 [15, 16]. RMSEA should be ≤ 0.6 [16], the SRMR ≤ 0.5 or at least ≤ 0.8 [16, 17]. AIC should be as low as possible with lower values indicating better fit (no absolute cut-offs). TLI should be ≥ 0.95 [16].The two bifactor models also showed the lowest local misfit in the variance-covariance matrix of standardised residuals (bifactor/2 factors: -0.474 to 0.542; bifactor/3 factors -0.474 to 0.640; compared to 1 factor: -0.652 to 1.805; 2 factors: -0.697 to 1.825; 3 factors: -0.677 to 0.800), see data in Annex 3.

Figure S3. Factor structure of ScleroID: A. Bifactor/2 factors model, B. Bifactor/3 factors model.



Standardized parameter estimates for the factor structure of the ScleroID. GIT: gastro-intestinal tract;

Factor loadings on the general factor for both models were meaningful for all items but digital ulcers (with loadings > 0.32 being meaningful according to Tabachnick and Fidell [18]; see Annex 4. However, as model fit measures alone are suggested to be insufficient to assess the validity of a model (see [19]) and bifactor models were suggested, we calculated additional indices, namely omegaH, omega and the reliable variance (i.e. not due to error) of the scores attributable to a general factor (i.e. possible SSc impact; calculated as omegaH divided by omega; see also [20]). Omega estimates are thought to be superior to Cronbach`s alpha, especially in the face of some multidimensionality as in bifactor models [21-25]. Although the superiority of the bifactor models speaks for (at least some) multidimensionality, we agree with Dunn et al. [26] that "an important question that the bifactor model can help the researcher to answer is: "Is this test unidimensional enough to be reported on a single scale, and relatedly, does it make sense to also report domain sub-scores?" In some respects, the bifactor model fleshes out the insight gained from the unidimensional model in cases where the researcher knows that there are likely to be dependencies between sub-groups of items within the test. Researchers in other disciplines suggest that this factor structure can, in fact, lead to greater conceptual clarity than alternative CFA model structures (e.g., Chen et al., 2012 [27]) and are particularly valuable for evaluating the plausibility of subscales (Reise et al., 2010, 2018: [28, 29]). The omega indices are given in supplemental Table S7. **With omegaH > 0.8, PUC <0.8 and ECV > 0.6, we conclude in analogy to Pretorius [21] despite some evidence of multidimensionality, there is largely reasonable evidence to claim unidimensionality and compute a single summary scale, because the large majority of variance in scores can be attributed to a general factor and 89% (bifactor/3 factors model) or 93% (bifactor/2 factors model) of the reliable variance can be accounted for by this general factor** (see also [20, 30]).

Table S7: Omega estimates of the explained variance from the two bifactor models.

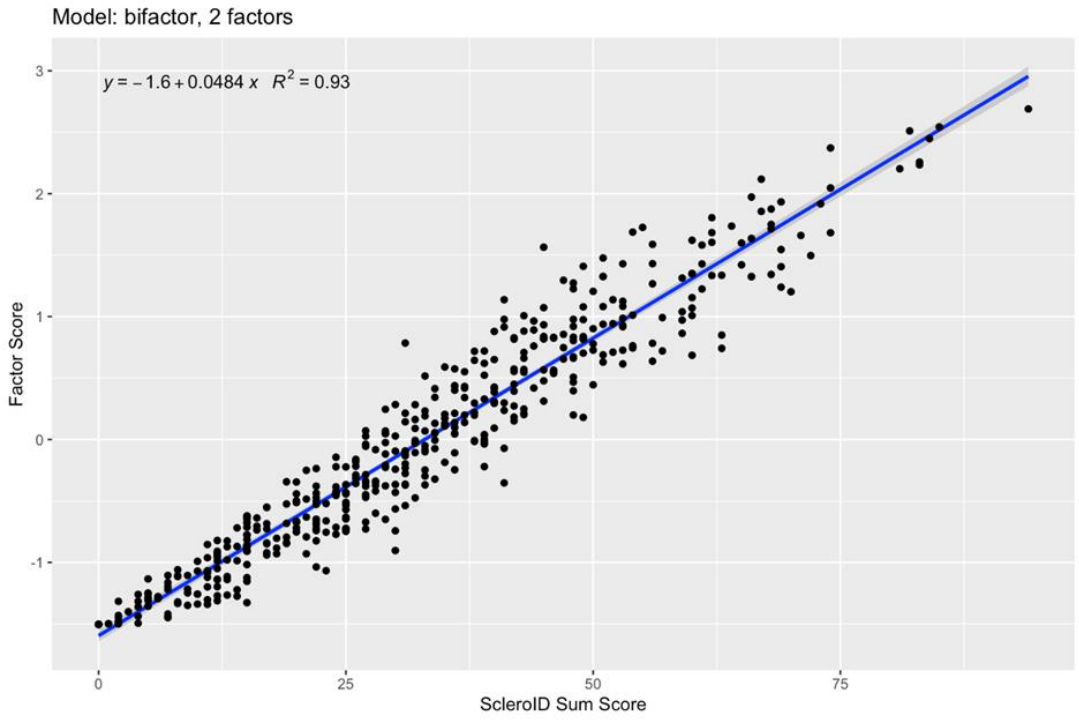
Model	Omega	OmegaH	OmegaH/Omega	ECV	PUC
Bifactor/2 factors	0.896	0.830	0.927	0.758	0.533
Bifactor/3 factors	0.895	0.800	0.894	0.727	0.711

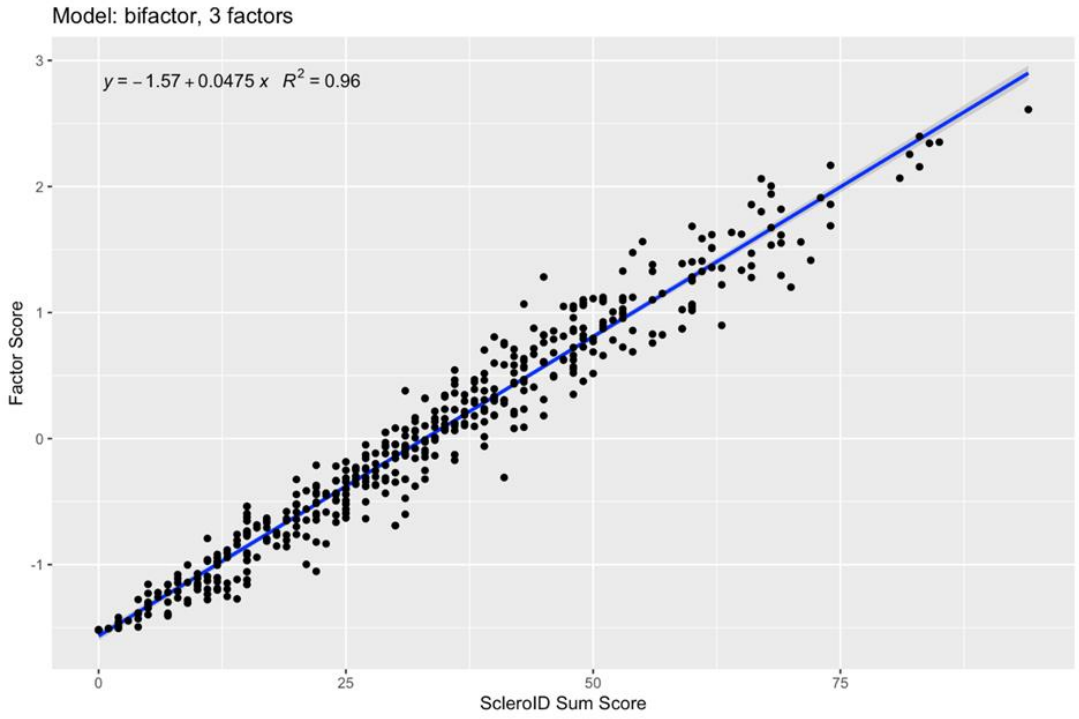
Omega - McDonald's omega: a model-based estimate of reliability; OmegaH – omega hierarchical; ECV - explained common variance; PUC - percentage of uncontaminated correlations.

If we assume that a summary score is justified, it remains to be clarified how to calculate the summary score that ideally represents the SSc impact on the life of patients as the latent trait measured by the questionnaire. Several methods exist to determine weights from a factor analysis and even using "unweighted" items (or unit-based weighting) for a sum score would have to be justified by the model [31]. One model-driven approach is for example, to use factor scores of the factor analysis model as weights for a sum score [32].

Our chosen patient-centred approach calculated weights by assigning item importance as reported by the patients and calculated a summary score. When we correlated the ScleroID sum scores with the calculated factor scores of the bifactor/2 factors model and the bifactor/3 factors model, the correlation was very high ($R^2 = 0.93$ and $R^2 = 0.96$, respectively; see Supplemental Figure S4) indicating only small differences between our weighted ScleroID sum scores and weights based on factor scores.

Figure S4: Correlation of Factor Scores with ScleroID sum scores for the two bifactor models (bifactor/2 factors above, bifactor/3 factors below).





Reliability – additional results

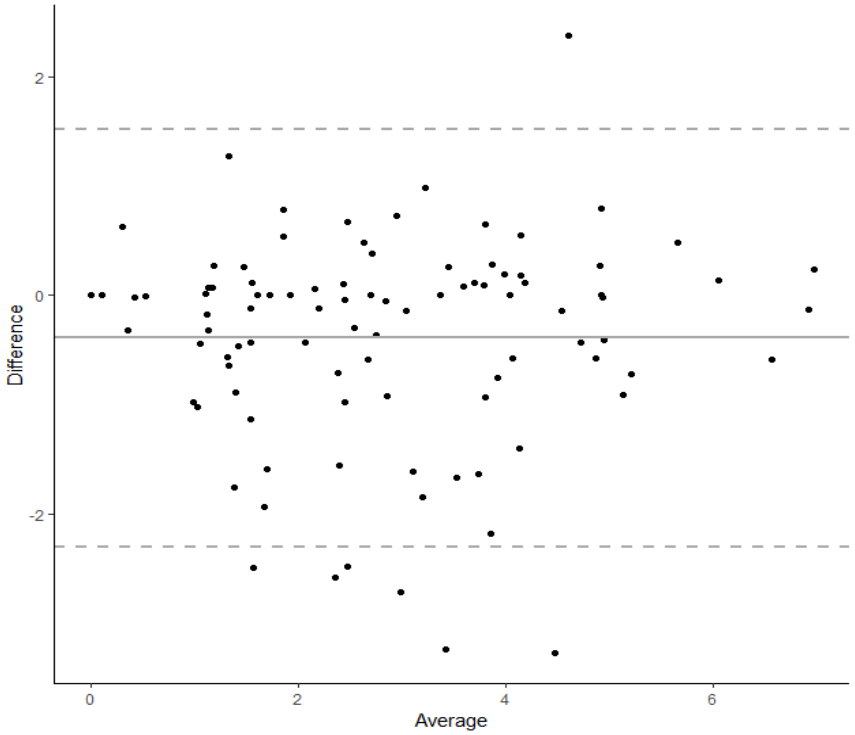
Patients' distribution per centre was: France (none), Italy (n=10), Hungary (n=20), Poland (n=3), Romania (n=10), Spain (none), Sweden (n=16), Switzerland (n=42), United Kingdom (n=8). All patients reporting a stable disease status were analysed (Table S8).

Table S8. Test-retest reliability of ScleroID compared to other PROM

Variable	**Intra-class correlation** [no. of valid cases]	**95% Confidence interval**
ScleroID	0.84 [98]	(0.77,0.89)
Raynaud	0.78 [100]	(0.68,0.84)
Hand function	0.79 [100]	(0.70,0.85)
Pain	0.67 [100]	(0.55,0.77)
Fatigue	0.66 [100]	(0.53,0.76)
Upper GI symptoms	0.67 [100]	(0.55,0.77)
Lower GI symptoms	0.61 [100]	(0.47,0.72)
Life Choices	0.72 [99]	(0.61,0.81)
Body Mobility	0.67 [101]	(0.54,0.76)
Dyspnoea	0.63 [100]	(0.50,0.74)
Digital ulcers	0.65 [101]	(0.52,0.75)
Patient's Global Assessment	0.78 [101]	(0.69,0.85)
SF-36 Physical component score	0.76 [100]	(0.66,0.83)
SF-36 Mental component score	0.69 [100]	(0.57,0.78)
HAQ-DI	0.72 [95]	(0.61,0.8)
SSc HAQ	0.72 [93]	(0.60,0.8)
EQ-5D	0.43 [97]	(0.25,0.58)

Abbreviations: SF-36: the short form (36) health survey; HAQ-DI: health assessment questionnaire disability index; SSc HAQ: systemic sclerosis health assessment questionnaire; EQ-5D: EuroQol five dimensional questionnaire. UK: United Kingdom; VAS: visual analogue scale.

Figure S5. Bland-Altman plot for agreement regarding test-retest reliability of ScleroID.



The Bland-Altman plot shows on the y-axis the mean difference between every pair of two tests (test and re-test, solid line) and the upper and lower levels of agreement (+/- 1.96 standard deviation of the difference). The x-axis depicts the average ScleroID score of the two tests (test and re-test).

Sensitivity to change – responsiveness statistics

The formula for SRM includes in the nominator the difference of the mean score at the follow up and mean scores at the baseline (so the change mean), while the denominator is represented by the standard deviation of this difference between follow up scores and baseline scores.[33] It can also be defined as a function of the paired t-test (or vice versa). Since there is no standard error of the mean in the denomination, the SRM remove the dependence on the sample size, which represents a big asset.[34] Moreover, the denominator is represented by the standard deviation of this difference and, and therefore it reflects the standard deviation of the change which

makes SRM to be more attractive than other effect size measures which are capable to reflect only the standard deviation of the baseline scores only and not the variability of the change scores. [35] Often, cut off values of 0.2, 0.5, 0.8 or greater have been proposed to distinguish small, moderate and large responsiveness, respectively.

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ANNEX 1 (see .pdf file):

1) **Baseline patient CRF**
2) **Baseline physician CRF**
3) **Reliability patient CRF**
4) **Reliability physician CRF**
5) **Sensitivity to change patient CRF**
6) **Sensitivity to change physician CRF**

Annex 2: Item mapping of the health dimensions selected for ScleroID

Initial candidate health dimensions as freely reported by the patient research partners in the first step of the nominal group exercise:

1. Digestion - bloating
2. Oesophagus – difficulty swallowing and pain
3. Limitation of hand function – pain, loss of mobility, shortened fingers
4. Disability - change of face, hands and all physical aspects
5. Quality of life
6. Social and governmental support
7. Cold and aching fingers - due to Raynaud
8. Breathlessness
9. Fear of losing my job
10. Fatigue - Shortness of breath
11. Depression
12. Body stiffness
13. Hand limitation*
14. Fatigue
15. Anxiety
16. Fatigue
17. Fear of uncertainty
18. Hand disability
19. Vomiting
20. Cold fingers with loss of sensibility – due to Raynaud
21. Muscular weakness
22. Pain due to calcinosis
23. Painful feet – due to loss of tissue in the soles
24. Anal incontinence
25. Digestion problems - acidity, constipation
26. Hand function
27. Appearance
28. Exhaustion
29. Focusing attention
30. Managing changing symptoms
31. Uncertainty
32. Shortness of breath
33. Need to explain to others
34. Appearance - hands, face
35. Limitations of choice in everyday life
36. Anxiety (uncertainty)
37. Digestion problems – reflux, vomiting, anal incontinence, incl. social aspects
38. Fatigue – exhaustion after small efforts
39. Dryness of eyes and mouth
40. Forgetfulness
41. Cold and stiff fingers
42. Loss of time – due to the disease
43. Appearance
44. Limitation of hand and feet function due to ulcers
45. Digestion – reflux, cough
46. Loss of hand mobility and strength
47. Loss of weight
48. Eating problems – because of small mouth
49. Suffocation (shortness of breath), cough
50. Pain in bowels and anal incontinence
51. Frequent infections
52. Frequent infections
53. Fatigue, lack of energy - work impairment
54. Constipation
55. Coughing constantly
56. Short breath
57. Burden of taking medicines – esp. attention to risk of infection as a side effect
58. Oesophageal (GI) reflux
59. Painful and cold hands –due to Raynaud
60. Fear – of transplant rejection
61. Fear – of comorbidity e.g. cancer
62. Breathlessness – due to heart problems
63. Limitations of everyday life - due to reduced body mobility, incontinence
64. GI difficulty - with reflux, swallowing and digestion (as a whole)
65. Painful digital ulcers and calcinosis
66. Fatigue – due to musculoskeletal pain

Exercise to group the initial health dimensions according to their common concept:

GI:
1. Digestion - bloating
2. Esophagus – difficulty swallowing and pain
3. Vomiting
4. Anal incontinence
5. Digestion problems - acidity, constipation
6. Digestion problems – reflux, vomiting, anal incontinence, incl. social aspects
7. Digestion – reflux, cough
8. Loss of weight
9. Eating problems – because of small mouth
10. Pain in bowels and anal incontinence
11. Constipation
12. Esophageal (GI) reflux
13. GI difficulty - with reflux, swallowing and digestion (as a whole)

Hands and feet function:
14. Limitation of hand function – pain, loss of mobility, shortened fingers
15. Hand limitation
16. Hand disability
17. Hand function
18. Limitation of hand and feet function due to ulcers
19. Loss of hand mobility and strength

Mixed:
20. Disability - change of face, hands and all physical aspects
21. Quality of life
22. Fatigue - Shortness of breath
23. Limitations of choice in everyday life

Social:
24. Social and governmental support
25. Fear of losing my job
26. Appearance
27. Need to explain to others
28. Appearance - hands, face
29. Loss of time – due to the disease
30. Appearance
31. Limitations of everyday life - due to reduced body mobility, incontinence

Peripheral vascular:
32. Cold and aching fingers - due to Raynaud
33. Cold fingers with loss of sensibility – due to Raynaud
34. Cold and stiff fingers
35. Painful and cold hands –due to Raynaud

Breathlessness:
36. Breathlessness
37. Shortness of breath
38. Suffocation (shortness of breath), cough
39. Short breath
40. Breathlessness – due to heart problems

Fatigue:
41. Fatigue
42. Fatigue
43. Exhaustion
44. Fatigue – exhaustion after small efforts
45. Fatigue, lack of energy - work impairment
46. Fatigue – due to musculoskeletal pain

Mental:
47. Depression
48. Anxiety
49. Fear of uncertainty
50. Focusing attention
51. Managing changing symptoms
52. Uncertainty
53. Anxiety (uncertainty)
54. Forgetfulness
55. Fear – of transplant rejection
56. Fear – of comorbidity e.g. cancer

Musculoskeletal:
57. Body stiffness
58. Muscular weakness

Pain:
59. Pain due to calcinosis
60. Painful feet – due to loss of tissue in the soles
61. Painful digital ulcers and calcinosis

62. Dryness of eyes and mouth
63. Coughing constantly

Side effects of therapy:
64. Frequent infections
65. Frequent infections
66. Burden of taking medicines – esp. attention to risk of infection as a side effect

Selected 17 candidate health dimensions for the following prioritisation exercise:

1. Upper gastrointestinal tract symptoms (e.g. swallowing difficulties, reflux, vomiting)
2. Lower gastrointestinal tract symptoms (e.g. bloating, diarrhea, constipation, anal incontinence)
3. Pain
4. Raynaud
5. Hand function
6. Body mobility
7. Ulcers
8. Calcinosis
9. Appearance
10. Limitations of life choices and activities (e.g. social life, personal care, work)
11. Breathlessness
12. Cough
13. Fatigue
14. Depression
15. Anxiety (unpredictable course of disease, or infection as a side effect of therapy)
16. Concentration ability
17. Dryness (eyes, mouth, skin)

Final top 10 health dimensions to be included in ScleroID as a result of the prioritisation exercise:

1. Raynaud
2. Hand function
3. Upper GI symptoms
4. Pain
5. Fatigue
6. Lower GI symptoms
7. Limitation of life choices and activities

8. Body mobility
9. Breathlessness
10. Digital ulcers

Annex 3 - Local misfit diagnostics with the variance-covariance matrix of standardised residuals

```
$`1 factor`
##          qraynd qhandf qpain  qulcrs qfatig qlifec qbodym qdyspn qlowrg
qupprg
## qraynaud  0.000
## qhandf    1.345  0.000
## qpain     0.708  0.716  0.000
## qulcers   0.321  1.296  0.489  0.000
## qfatigue  0.134 -0.327  0.029 -0.690  0.000
## qlifec   -0.444 -0.360 -0.508 -0.215  0.262  0.000
## qbodym   -0.536 -0.004 -0.173 -0.104  0.071  0.489  0.000
## qdyspnea -0.652 -0.641 -0.279 -0.488  0.302  0.278 -0.005  0.000
## qlowergi -0.203 -0.423  0.586 -0.472 -0.362 -0.447 -0.430  0.622  0.000
## quppergi -0.104 -0.145 -0.120 -0.029 -0.278 -0.025 -0.268  0.433  1.805
0.000
## $`2 factors`
##          qraynd qhandf qpain  qulcrs qfatig qlifec qbodym qdyspn qlowrg
qupprg
## qraynaud  0.000
## qhandf    0.462  0.000
## qpain    -0.059 -0.237  0.000
## qulcers  -0.216  0.591 -0.136  0.000
## qfatigue  0.210 -0.074  0.531 -0.697  0.000
## qlifec   -0.429 -0.179 -0.058 -0.272  0.063  0.000
## qbodym   -0.479  0.224  0.307 -0.125 -0.040  0.251  0.000
## qdyspnea -0.635 -0.500  0.059 -0.525  0.164  0.034 -0.170  0.000
## qlowergi -0.118 -0.205  0.970 -0.451 -0.354 -0.513 -0.442  0.580  0.000
## quppergi -0.034  0.065  0.279 -0.025 -0.316 -0.153 -0.331  0.346  1.825
0.000
## $`bifactor, 2 factors`
##          qraynd qhandf qpain  qulcrs qfatig qlifec qbodym qdyspn qlowrg
qupprg
## qraynaud  0.000
## qhandf    0.021  0.000
## qpain     0.266 -0.087  0.000
## qulcers  -0.462  0.096  0.080  0.000
```

```
## qfatigue  0.542  0.097  0.305 -0.327  0.000
## qlifec   -0.066 -0.003 -0.327  0.136 -0.041  0.000
## qbodym   -0.156  0.374  0.049  0.242 -0.155  0.065  0.000
## qdyspnea -0.393 -0.408 -0.180 -0.242  0.237  0.110 -0.110  0.000
## qlowergi -0.146 -0.474  0.388 -0.376 -0.039 -0.025  0.026 -0.005  0.000
## quppergi  0.122  0.046 -0.060  0.190 -0.118  0.117 -0.082  0.125 -0.016
0.000
## $`3 factors`
##          qraynd qhandf qpain  qulcrs qfatig qlifec qbodym qdyspn qlowrg
qupprg
## qraynaud  0.000
## qhandf    0.461  0.000
## qpain    -0.059 -0.235  0.000
## qulcers  -0.219  0.587 -0.140  0.000
## qfatigue  0.241 -0.028  0.580 -0.677  0.000
## qlifec   -0.416 -0.159 -0.035 -0.266 -0.032  0.000
## qbodym   -0.465  0.246  0.329 -0.117 -0.123  0.120  0.000
## qdyspnea -0.578 -0.417  0.146 -0.485  0.178  0.019 -0.181  0.000
## qlowergi -0.201 -0.322  0.849 -0.514 -0.126 -0.279 -0.229  0.800  0.000
## quppergi -0.169 -0.126  0.082 -0.126 -0.108  0.054 -0.141  0.555  0.000
0.000
$`bifactor, 3 factors`
##          qraynd qhandf qpain  qulcrs qfatig qlifec qbodym qdyspn qlowrg
qupprg
## qraynaud  0.000
## qhandf    0.030  0.000
## qpain     0.260 -0.089  0.000
## qulcers  -0.429  0.068  0.131  0.000
## qfatigue  0.365 -0.071  0.118 -0.403  0.000
## qlifec   -0.043  0.148 -0.150  0.199 -0.022  0.000
## qbodym   -0.232  0.364  0.041  0.234  0.001  0.010  0.000
## qdyspnea -0.474 -0.446 -0.221 -0.261  0.204  0.001 -0.090  0.000
## qlowergi -0.078 -0.295  0.597 -0.300 -0.330 -0.237 -0.313  0.640  0.000
## quppergi  0.042  0.006 -0.102  0.170 -0.235  0.221 -0.130  0.457  0.000
0.000
```

Annex 4 – Item loadings for the bifactor models

```
bifactor/2 factors
Latent Variables:
##                   Estimate  Std.Err  z-value  P(>|z|)   Std.lv  Std.all
##   hand =~
##     qraynaud         1.142    0.190    6.006    0.000    1.142    0.399
##     qhandf           1.669    0.214    7.791    0.000    1.669    0.592
##     qpain            0.858    0.171    5.011    0.000    0.858    0.298
##     qulcers          1.003    0.173    5.807    0.000    1.003    0.367
##   systemic =~
##     qfatigue        -0.389    0.176   -2.215    0.027   -0.389   -0.134
##     qlifec          -0.517    0.239   -2.165    0.030   -0.517   -0.177
##     qbodym          -0.489    0.184   -2.661    0.008   -0.489   -0.183
##     qdyspnea         0.118    0.226    0.523    0.601    0.118    0.044
##     qlowergi         1.829    0.473    3.867    0.000    1.829    0.620
##     quppergi         0.770    0.324    2.377    0.017    0.770    0.286
##   all =~
##     qraynaud         1.107    0.138    8.028    0.000    1.107    0.386
##     qhandf           1.730    0.122   14.160    0.000    1.730    0.613
##     qpain            1.982    0.115   17.233    0.000    1.982    0.687
##     qulcers          0.753    0.150    5.009    0.000    0.753    0.275
##     qfatigue         2.108    0.110   19.078    0.000    2.108    0.727
##     qlifec           2.369    0.100   23.616    0.000    2.369    0.813
##     qbodym           2.158    0.108   19.899    0.000    2.158    0.809
##     qdyspnea         1.757    0.117   15.059    0.000    1.757    0.656
##     qlowergi         1.588    0.210    7.572    0.000    1.588    0.538
##     quppergi         1.673    0.135   12.412    0.000    1.673    0.621


Bifactor/3 factors
Latent Variables:
##                   Estimate  Std.Err  z-value  P(>|z|)   Std.lv  Std.all
##   hand =~
##     qraynaud         1.013    0.236    4.302    0.000    1.013    0.354
##     qhandf           1.589    0.249    6.392    0.000    1.589    0.563
```

```
##     qpain            0.650    0.241    2.699    0.007    0.650    0.225
##     qulcers          0.974    0.203    4.788    0.000    0.974    0.356
##   life =~
##     qfatigue         0.461    0.467    0.988    0.323    0.461    0.159
##     qlifec           1.466    0.543    2.701    0.007    1.466    0.503
##     qbodym           0.685    0.417    1.642    0.101    0.685    0.257
##     qdyspnea         0.395    0.369    1.071    0.284    0.395    0.148
##   git =~
##     qlowergi         1.488    0.107   13.929    0.000    1.488    0.505
##     quppergi         1.207    0.180    6.710    0.000    1.207    0.448
##   all =~
##     qraynaud         1.204    0.153    7.867    0.000    1.204    0.420
##     qhandf           1.829    0.128   14.310    0.000    1.829    0.649
##     qpain            2.094    0.141   14.889    0.000    2.094    0.726
##     qulcers          0.798    0.158    5.047    0.000    0.798    0.292
##     qfatigue         2.085    0.157   13.311    0.000    2.085    0.719
##     qlifec           2.158    0.140   15.438    0.000    2.158    0.741
##     qbodym           2.046    0.136   15.068    0.000    2.046    0.767
##     qdyspnea         1.683    0.157   10.707    0.000    1.683    0.628
##     qlowergi         1.403    0.170    8.240    0.000    1.403    0.476
##     quppergi         1.604    0.131   12.222    0.000    1.604    0.595
```

Annex 5 : Model CRF for the collection of EUSTAR clinical data (see pdf)

Validation of ScleroID

COUNTRY_____ **Patient number /__/__/**

BASELINE – PATIENT CRF

Today's Date: Day /__/__/ Month /__/__/ Year 20/__/__/

B1. Impact and weighting of disease

We want you to indicate how much your systemic sclerosis (scleroderma) impacts your health in the following selected health dimensions, shown below.

Please distribute 100 points between the dimensions according to their impact; the sum should be 100.
Please read all dimensions before starting to distribute your points.

You can spend your points in sets of 5. Give more points to dimensions which have important impact and less to dimensions that are not so important. You do not have to spend points in every area. You cannot spend more than 100 points.
Please take into account your whole disease history, not only how you feel today, when distributing the points.

In this table, you have to distribute your 100 points between 10 domains of health:.

Domain/dimension	POINTS
Raynaud's Phenomenon	I__I__I
Hand function	I__I__I
Pain	I__I__I
Fatigue *(being tired physically, but also mental fatigue, lack of energy)*	I__I__I
Upper gastrointestinal tract symptoms *(e.g. swallowing difficulties, reflux, vomiting)*	I__I__I
Lower gastrointestinal tract symptoms *(e.g. bloating, diarrhea, constipation, anal incontinence)*	I__I__I
Limitations of life choices and activities *(e.g. social life, personal care, work)*	I__I__I
Body mobility	I__I__I
Breathlessness	I__I__I
Digital ulcers	I__I__I
TOTAL POINTS: Remember must add up to 100 points	100

Validation of ScleroID

COUNTRY_____ **Patient number /__/__/**

B2. The EULAR Scleroderma Impact of Disease Score (ScleroID)

How much have the different aspects of systemic sclerosis affected you during the last week? Please mark your responses on the scale by choosing the appropriate number for each of the following dimensions:

Raynaud's phenomenon:

Circle the number that best describes the severity of your Raynaud's phenomenon during the last week:

None	0	1	2	3	4	5	6	7	8	9	10	Extreme

Hand function:

Circle the number that best describes your hand function limitations due to your systemic sclerosis during the last week:

No limitation	0	1	2	3	4	5	6	7	8	9	10	Extreme limitation

Upper gastrointestinal tract symptoms (e.g. swallowing difficulties, reflux, vomiting):

Circle the number that best describes the severity of your upper gastrointestinal tract symptoms due to your systemic sclerosis during the last week:

None	0	1	2	3	4	5	6	7	8	9	10	Extreme

Pain:

Circle the number that best describes the pain you felt due to your systemic sclerosis during the last week:

None	0	1	2	3	4	5	6	7	8	9	10	Extreme

Fatigue:

Circle the number that best describes the impact of overall fatigue due to your systemic sclerosis during the last week:

None	0	1	2	3	4	5	6	7	8	9	10	Extreme

Lower gastrointestinal tract symptoms (e.g. bloating, diarrhea, constipation, anal incontinence):

Circle the number that best describes the severity of lower gastrointestinal tract symptoms during the last week:

None	0	1	2	3	4	5	6	7	8	9	10	Extreme

Limitations of life choices and activities (e.g. social life, personal care, work):

Circle the number that best describes how severe the limitations of life choices and activities due to your systemic sclerosis were during the last week:

No	0	1	2	3	4	5	6	7	8	9	10	Extreme

Validation of ScleroID

COUNTRY_____ **Patient number /__/__/**

Body mobility:

Circle the number that best describes how much your body mobility was affected due to your systemic sclerosis during the last week:

Not affected	0	1	2	3	4	5	6	7	8	9	10	Extremely affected

Breathlessness:

Circle the number that best describes how severe your breathlessness due to systemic sclerosis was during the last week:

None	0	1	2	3	4	5	6	7	8	9	10	Extreme

Digital ulcers:

Circle the number that best describes how much your digital ulcers affected you overall during the last week:

None	0	1	2	3	4	5	6	7	8	9	10	Extreme

B3. Are you currently …. ?

- Working full-time of part-time (employed for wages) ☐
- A student ☐
- Retired ☐
- Unable to work/disabled ☐

B4. What is the highest level of education you completed so far?

- No schooling ☐
- Elementary/primary school ☐
- High school/middle school **without** university entrance qualification ☐
- High school/middle school **with** university entrance qualification ☐
- College/university **without** degree ☐
- College/university **with** degree – Bachelor (or equivalent) ☐
- College/university **with** degree – Master (or equivalent) ☐
- Doctorate degree ☐
- Trade/technical/vocational training ☐

Validation of ScleroID

COUNTRY_____ **Patient number /__/__/**

B5. Think about all the ways in which the systemic sclerosis has affected you during the last week, how would you consider this state? (Mark "**X**" in only one box below)

❑ Very good

❑ Good

❑ Acceptable

❑ Bad

❑ Very bad

B6. Think about all the ways your systemic sclerosis has affected you during the last week.

Compared to 1 week ago, how has the overall state of your disease been during the last week? (Mark "**X**" in only one box below)

☐ Much improved

☐ Moderately improved

☐ Stable (mostly unchanged)

☐ Moderately worsened

☐ Much worsened

B7. Global assessment

Considering **all the ways your systemic sclerosis** has affected you during the last week, circle the number that best describes how you have been doing:

Very good	0	1	2	3	4	5	6	7	8	9	10	Very bad

Validation of ScleroID

COUNTRY_____ **Patient number /__/__/**

B8. We are interested in learning how your illness affects your ability to function in daily life. Please check (X) the one best answer which best describes your usual abilities OVER THE PAST WEEK:

	Without ANY Difficulty(0)	With SOME Difficulty(1)	With MUCH Difficulty(2)	UNABLE To Do(3)
DRESSING & GROOMING				
Are you able to:				
- Dress yourself, including tying shoelaces and doing buttons?	_____	_____	_____	_____
- Shampoo your hair?	_____	_____	_____	_____
ARISING				
Are you able to:				
- Stand up from a straight chair?	_____	_____	_____	_____
- Get in and out of bed?	_____	_____	_____	_____
EATING				
Are you able to:				
- Cut your meat?	_____	_____	_____	_____
- Lift a full cup or glass to your mouth?	_____	_____	_____	_____
- Open a new milk carton?	_____	_____	_____	_____
WALKING				
Are you able to:				
- Walk outdoors on flat ground?	_____	_____	_____	_____
- Climb up five steps?	_____	_____	_____	_____

Please check any AIDS OR DEVICES that you usually use for any of these activities:

_____ Cane
_____ Walker
_____ Crutches
_____ Wheelchair
_____ Devices used for dressing (button hook, zipper pull, long-handled shoe horn, etc.)
_____ Built up or special utensils
_____ Special or built up chair
_____ Other (Specify: _____)

Please check any categories for which you usually need HELP FROM ANOTHER PERSON:

_____ Dressing and Grooming
_____ Arising
_____ Eating
_____ Walking

Validation of ScleroID

COUNTRY_____ **Patient number /__/__/**

Please check the response which best describes your usual abilities OVER THE PAST WEEK:

	Without ANY Difficulty(0)	With SOME Difficulty(1)	With MUCH Difficulty(2)	UNABLE To Do(3)
HYGIENE				
Are you able to:				
- Wash and dry your body?	_____	_____	_____	_____
- Take a tub bath?	_____	_____	_____	_____
- Get on and off the toilet?	_____	_____	_____	_____
REACH				
Are you able to:				
- Reach and get down a 5 pound object (such as a bag of sugar) from just above your head?	_____	_____	_____	_____
- Bend down to pick up clothing from the floor?	_____	_____	_____	_____
GRIP				
Are you able to:				
- Open car doors?	_____	_____	_____	_____
- Open jars which have previously been opened?	_____	_____	_____	_____
- Turn faucets on and off?	_____	_____	_____	_____
ACTIVITIES				
Are you able to:				
- Run errands and shop?	_____	_____	_____	_____
- Get in and out of a car?	_____	_____	_____	_____
- Do chores such as vacuuming or yard work?	_____	_____	_____	_____

Please check any AIDS OR DEVICES that you usually use for any of these activities:

_____ Raised toilet seat
_____ Bathtub seat
_____ Jar opener (for jars previously opened)
_____ Other (Specify: _____)
_____ Bathtub bar
_____ Long-handled appliances for reach
_____ Long-handled appliances in bathroom

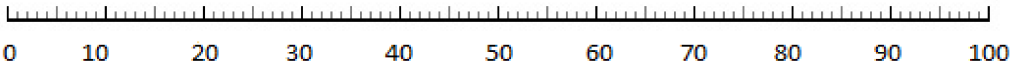
Please check any categories for which you usually need HELP FROM ANOTHER PERSON:

_____ Hygiene
_____ Reach
_____ Gripping and opening things
_____ Errands and chores

IN THE PAST WEEK, how much have your intestinal problems interfered with your daily activities?

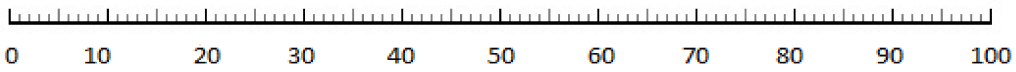
Validation of SclerolD

COUNTRY_____ **Patient number /__/__/**



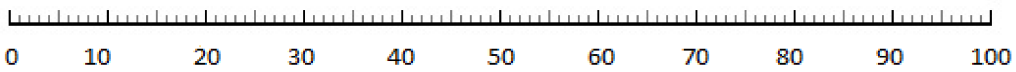
Does not interfere Very severe limitation

IN THE PAST WEEK, how much have your breathing problems interfered with your daily activities?



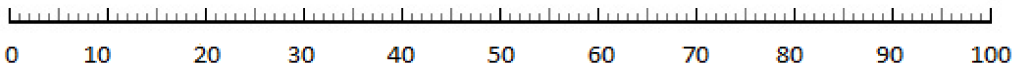
Do
es not interfere Very severe limitation

IN THE PAST WEEK, how much has Raynaud's interfered with your daily activities?



Does not interfere Very severe limitation

IN THE PAST WEEK, how much have your finger ulcers interfered with your daily activities?



Does not interfere Very severe limitation

B9. EQ-5D

By placing a tick in each group below, please indicate which statements best describe your own health state today.

Mobility

I have no problems in walking about ❒
I have some problems in walking about ❒
I am confined to bed ❒

Self-care

I have no problems with self-care ❒
I have some problems washing or dressing myself ❒
I am unable to wash or dress myself ❒

Usual activities (eg work, study, housework, family or leisure activities

Validation of ScleroID

COUNTRY_____ **Patient number /__/__/**

I have no problems with performing my usual activities ❒
I have some problems with performing my usual activities ❒
I am unable to perform my usual activities ❒

Pain / discomfort
I have no pain or discomfort ❒
I have moderate pain or discomfort ❒
I have extreme pain or discomfort ❒

Anxiety / depression
I am not anxious or depressed ❒
I am moderately anxious or depressed ❒
I am extremely anxious or depressed ❒

B10. Overall assessment of health status (SF-36)

1. In general, would you say your health is:	
Excellent	1
Very good	2
Good	3
Fair	4
Poor	5
2. **Compared to one year ago**, how would your rate your health in general **now**?	
Much better now than one year ago	1
Somewhat better now than one year ago	2
About the same	3
Somewhat worse now than one year ago	4
Much worse now than one year ago	5

The following items are about activities you might do during a typical day. Does **your health now limit you** in these activities? If so, how much?

(Circle One Number on Each Line)

	Yes, Limited a Lot	Yes, Limited a Little	No, Not limited at All

Validation of ScleroID

COUNTRY_____ **Patient number /__/__/**

3. **Vigorous activities**, such as running, lifting heavy objects, participating in strenuous sports	[1]	[2]	[3]
4. **Moderate activities**, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf	[1]	[2]	[3]
5. Lifting or carrying groceries	[1]	[2]	[3]
6. Climbing **several** flights of stairs	[1]	[2]	[3]
7. Climbing **one** flight of stairs	[1]	[2]	[3]
8. Bending, kneeling, or stooping	[1]	[2]	[3]
9. Walking **more than a mile**	[1]	[2]	[3]
10. Walking **several blocks**	[1]	[2]	[3]
11. Walking **one block**	[1]	[2]	[3]
12. Bathing or dressing yourself	[1]	[2]	[3]

During the **past 4 weeks**, have you had any of the following problems with your work or other regular daily activities **as a result of your physical health**?

(Circle One Number on Each Line)

	Yes	No
13. Cut down the amount of time you spent on work or other activities	1	2
14. **Accomplished less** than you would like	1	2
15. Were limited in the **kind** of work or other activities	1	2
16. Had **difficulty** performing the work or other activities (for example, it took extra effort)	1	2

During the **past 4 weeks,** have you had any of the following problems with your work or other regular daily activities **as a result of any emotional problems**(such as feeling depressed or anxious)? **(Circle One Number on Each Line)**

	Yes	No

Validation of ScleroID

COUNTRY_____ **Patient number /__/__/**

17. Cut down the **amount of time** you spent on work or other activities	1	2
18. **Accomplished less** than you would like	1	2
19. Didn't do work or other activities as **carefully** as usual	1	2

20. During the **past 4 weeks,** to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbors, or groups? **(Circle One Number)**

Not at all	1
Slightly	2
Moderately	3
Quite a bit	4
Extremely	5

21. How much **bodily** pain have you had during the **past 4 weeks**?

(Circle One Number)

None	1
Very mild	2
Mild	3
Moderate	4
Severe	5
Very severe	6

22. During the **past 4 weeks,** how much did **pain** interfere with your normal work (including both work outside the home and housework)? **(Circle One Number)**

Not at all	1
A little bit	2
Moderately	3

Validation of SclerolD

COUNTRY_____ **Patient number /__/__/**

Quite a bit 4

Extremely 5

These questions are about how you feel and how things have been with you **during the past 4 weeks**. For each question, please give the one answer that comes closest to the way you have been feeling. **(Circle One Number on Each Line)**

How much of the time during the **past 4 weeks** . . .

	All of the Time	Most of the Time	A Good Bit of the Time	Some of the Time	A Little of the Time	None of the Time
23. Did you feel full of pep?	1	2	3	4	5	6
24. Have you been a very nervous person?	1	2	3	4	5	6
25. Have you felt so down in the dumps that nothing could cheer you up?	1	2	3	4	5	6
26. Have you felt calm and peaceful?	1	2	3	4	5	6
27. Did you have a lot of energy?	1	2	3	4	5	6
28. Have you felt downhearted and blue?	1	2	3	4	5	6
29. Did you feel worn out?	1	2	3	4	5	6
30. Have you been a happy person?	1	2	3	4	5	6
31. Did you feel tired?	1	2	3	4	5	6

32. During the **past 4 weeks,** how much of the time has your **physical health or emotional problems** interfered with your social activities (like visiting with friends, relatives, etc.)? **(Circle One Number)**

All of the time 1

Validation of ScleroID

COUNTRY_____ **Patient number /__/__/**

Most of the time	2
Some of the time	3
A little of the time	4
None of the time	5

How TRUE or FALSE is each of the following statements for you.

(Circle One Number on Each Line)

	Definitely True	Mostly True	Don't Know	Mostly False	Definitely False
33. I seem to get sick a little easier than other people	1	2	3	4	5
34. I am as healthy as anybody I know	1	2	3	4	5
35. I expect my health to get worse	1	2	3	4	5
36. My health is excellent	1	2	3	4	5

Thank you for filling in this questionnaire

Validation of ScleroID

COUNTRY_____ **Patient number /__/__/**

Baseline physician CRF

G1. Today's Date: Day /__/__/ Month /__/__/ Year 20/__/__/

G2. Do you confirm the main inclusion and exclusion criteria?

	Yes	No
G2.1. Age ≥ 18 years	❑	❑
G2.2. Able to understand the objectives of the study and the different questionnaires	❑	❑
G2.3. Written informed consent obtained	❑	❑
G2.4. Patient fulfilling the ACR/EULAR 2013 criteria for SSc	❑	❑
G2.5. No severe comorbidity NOT related to SSc (e.g. concomitant acute infectious disease, organ failure, recent acute cerebrovascular event, serious psychiatric or neurological disease)	❑	❑

Any negative answer results in the non-inclusion of the patient in the study.

G3. SSc characteristics

Please make sure that all necessary items of the EUSTAR dataset are evaluated and filled into the system (date of birth and diagnosis, clinical features, laboratory values, therapies etc.) AND that the patient fills in the necessary questionnaires/CRF.

Validation of ScleroID

COUNTRY_____ **Patient number /__/__/**

G4. Physician's assessment of SSc

G4.1. Physician's global assessment of SSc

Considering all the ways systemic sclerosis has affected your patient during the last week, circle the number that best describes how he/she has been doing:

Very good	0	1	2	3	4	5	6	7	8	9	10	Very bad

At the end of this visit, please check:

1. Is the patient eligible for the RELIABILITY ARM?

Eligibility criteria for the reliability arm:

- willingness to fill in the Reliability CRF after 7 +/- 3 days from the baseline visit (this can be sent per post, e-mail, or handed to the patient, as suitable)
- no major health change/intervention is medically forseeable/planed during the next 10 days

If the above conditions are fulfilled, please include the patient in the Reliability arm (see Reliability study - Physician CRF and Reliability Study – Patient CRF).

2. Is the patient eligible for the SENSITIVITY TO CHANGE ARM?

Eligibility criteria for the sensitivity to change arm:

- patients with active disease as defined by the physician
- feasible follow-up visits at 6 and 12 months (or at least one complete follow-up visit at 12 months), as medically required

If the above conditions are fulfilled, please include the patient in the Sensitivity to change arm.

3. IN ANY CASE, PLEASE CHECK PATIENT CRF and EUSTAR dataset FOR COMPLETENESS and fill in patient number!

THANK YOU!

Validation of SclerolD

COUNTRY_____ **Patient number /__/__/**

Validation of ScleroID

COUNTRY_____ **Patient number /__/__/**

RELIABILITY STUDY – PATIENT CRF

Please fill in this questionnaire 7+/-3 days after your last visit.

Today's Date: Day /__/__/ Month /__/__/ Year 20/__/__/

Please cross the correct answer:

S1. Since you last filled in this questionnaire, do you consider your systemic sclerosis to be stable? ..... yes ❑ no ❑

S2. Since you last filled in this questionnaire, has your treatment for your systemic sclerosis been changed? .... yes ❑ no ❑

S3. **Think about all the ways in which the systemic sclerosis has affected you during the last week, how would you consider this state?** (Mark "**X**" in only one box below)

❑ Very good
❑ Good
❑ Acceptable
❑ Bad
❑ Very bad

S4. Think about all the ways your systemic sclerosis has affected you during the last week.
Compared to 1 week ago, how has the overall state of your disease been during the last week? (Mark "**X**" in only one box below)

☐ Much improved
☐ Moderately improved
☐ Stable (mostly unchanged)
☐ Moderately worsened
☐ Much worsened

Validation of ScleroID

COUNTRY_____ **Patient number /__/__/**

S5. The EULAR Scleroderma Impact of Disease Score (ScleroID)

How much have the different aspects of systemic sclerosis affected you during the last week? Please mark your responses on the scale by choosing the appropriate number for each of the following dimensions:

Raynaud's phenomenon:

Circle the number that best describes the severity of your Raynaud's phenomenon during the last week:

None	0	1	2	3	4	5	6	7	8	9	10	Extreme

Hand function:

Circle the number that best describes your hand function limitations due to your systemic sclerosis during the last week:

No limitation	0	1	2	3	4	5	6	7	8	9	10	Extreme limitation

Upper gastrointestinal tract symptoms (e.g. swallowing difficulties, reflux, vomiting):

Circle the number that best describes the severity of your upper gastrointestinal tract symptoms due to your systemic sclerosis during the last week:

None	0	1	2	3	4	5	6	7	8	9	10	Extreme

Pain:

Circle the number that best describes the pain you felt due to your systemic sclerosis during the last week:

None	0	1	2	3	4	5	6	7	8	9	10	Extreme

Fatigue:

Circle the number that best describes the impact of overall fatigue due to your systemic sclerosis during the last week:

None	0	1	2	3	4	5	6	7	8	9	10	Extreme

Lower gastrointestinal tract symptoms (e.g. bloating, diarrhea, constipation, anal incontinence):

Circle the number that best describes the severity of lower gastrointestinal tract symptoms during the last week:

None	0	1	2	3	4	5	6	7	8	9	10	Extreme

Limitations of life choices and activities (e.g. social life, personal care, work):

Circle the number that best describes how severe the limitations of life choices and activities due to your systemic sclerosis were during the last week:

No	0	1	2	3	4	5	6	7	8	9	10	Extreme

Validation of ScleroID

COUNTRY_____ **Patient number /__/__/**

Body mobility:

Circle the number that best describes how much your body mobility was affected due to your systemic sclerosis during the last week:

Not affected	0	1	2	3	4	5	6	7	8	9	10	Extremely affected

Breathlessness:

Circle the number that best describes how severe your breathlessness due to systemic sclerosis was during the last week:

None	0	1	2	3	4	5	6	7	8	9	10	Extreme

Digital ulcers:

Circle the number that best describes how much your digital ulcers affected you overall during the last week:

None	0	1	2	3	4	5	6	7	8	9	10	Extreme

S6. Global assessment

Considering **all the ways your systemic sclerosis** has affected you during the last week, circle the number that best describes how you have been doing:

Very good	0	1	2	3	4	5	6	7	8	9	10	Very bad

Validation of ScleroID

COUNTRY_____ **Patient number /__/__/**

S7. We are interested in learning how your illness affects your ability to function in daily life. Please check (X) the one best answer which best describes your usual abilities OVER THE PAST WEEK:

	Without ANY Difficulty(0)	With SOME Difficulty(1)	With MUCH Difficulty(2)	UNABLE To Do(3)
DRESSING & GROOMING				
Are you able to:				
- Dress yourself, including tying shoelaces and doing buttons?	_____	_____	_____	_____
- Shampoo your hair?	_____	_____	_____	_____
ARISING				
Are you able to:				
- Stand up from a straight chair?	_____	_____	_____	_____
- Get in and out of bed?	_____	_____	_____	_____
EATING				
Are you able to:				
- Cut your meat?	_____	_____	_____	_____
- Lift a full cup or glass to your mouth?	_____	_____	_____	_____
- Open a new milk carton?	_____	_____	_____	_____
WALKING				
Are you able to:				
- Walk outdoors on flat ground?	_____	_____	_____	_____
- Climb up five steps?	_____	_____	_____	_____

Please check any AIDS OR DEVICES that you usually use for any of these activities:

_____ Cane
_____ Walker
_____ Crutches
_____ Wheelchair
_____ Devices used for dressing (button hook, zipper pull, long-handled shoe horn, etc.)
_____ Built up or special utensils
_____ Special or built up chair
_____ Other (Specify: _____)

Please check any categories for which you usually need HELP FROM ANOTHER PERSON:

_____ Dressing and Grooming
_____ Arising
_____ Eating
_____ Walking

Validation of ScleroID

COUNTRY_____ **Patient number /__/__/**

Please check the response which best describes your usual abilities OVER THE PAST WEEK:

	Without ANY Difficulty(0)	With SOME Difficulty(1)	With MUCH Difficulty(2)	UNABLE To Do(3)
HYGIENE				
Are you able to:				
- Wash and dry your body?	_____	_____	_____	_____
- Take a tub bath?	_____	_____	_____	_____
- Get on and off the toilet?	_____	_____	_____	_____
REACH				
Are you able to:				
- Reach and get down a 5 pound object (such as a bag of sugar) from just above your head?	_____	_____	_____	_____
- Bend down to pick up clothing from the floor?	_____	_____	_____	_____
GRIP				
Are you able to:				
- Open car doors?	_____	_____	_____	_____
- Open jars which have previously been opened?	_____	_____	_____	_____
- Turn faucets on and off?	_____	_____	_____	_____
ACTIVITIES				
Are you able to:				
- Run errands and shop?	_____	_____	_____	_____
- Get in and out of a car?	_____	_____	_____	_____
- Do chores such as vacuuming or yard work?	_____	_____	_____	_____

Please check any AIDS OR DEVICES that you usually use for any of these activities:

_____ Raised toilet seat
_____ Bathtub seat
_____ Jar opener (for jars previously opened)
_____ Other (Specify: _____)
_____ Bathtub bar
_____ Long-handled appliances for reach
_____ Long-handled appliances in bathroom

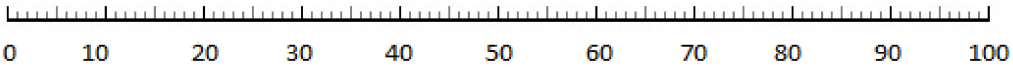
Please check any categories for which you usually need HELP FROM ANOTHER PERSON:

_____ Hygiene
_____ Reach
_____ Gripping and opening things
_____ Errands and chores

IN THE PAST WEEK, how much have your intestinal problems interfered with your daily activities?

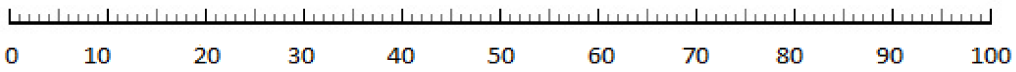
Validation of ScleroID

COUNTRY_____ **Patient number /__/__/**



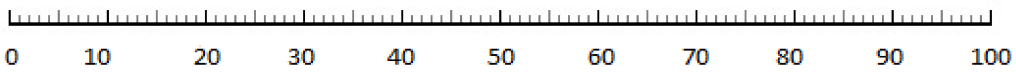
Does not interfere Very severe limitation

IN THE PAST WEEK, how much have your breathing problems interfered with your daily activities?



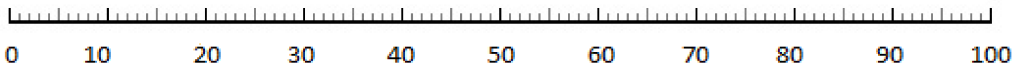
Do
es not interfere Very severe limitation

IN THE PAST WEEK, how much has Raynaud's interfered with your daily activities?



Does not interfere Very severe limitation

IN THE PAST WEEK, how much have your finger ulcers interfered with your daily activities?



Does not interfere Very severe limitation

S8. EQ-5D

By placing a tick in each group below, please indicate which statements best describe your own health state today.

Mobility

I have no problems in walking about ❒
I have some problems in walking about ❒
I am confined to bed ❒

Self-care

I have no problems with self-care ❒
I have some problems washing or dressing myself ❒
I am unable to wash or dress myself ❒

Usual activities (eg work, study, housework, family or leisure activities

Validation of ScleroID

COUNTRY_____ **Patient number /__/__/**

I have no problems with performing my usual activities ❒
I have some problems with performing my usual activities ❒
I am unable to perform my usual activities ❒

Pain / discomfort
I have no pain or discomfort ❒
I have moderate pain or discomfort ❒
I have extreme pain or discomfort ❒

Anxiety / depression
I am not anxious or depressed ❒
I am moderately anxious or depressed ❒
I am extremely anxious or depressed ❒

P10. Overall assessment of health status (SF-36)

1. In general, would you say your health is:	
Excellent	1
Very good	2
Good	3
Fair	4
Poor	5
2. **Compared to one year ago**, how would your rate your health in general **now**?	
Much better now than one year ago	1
Somewhat better now than one year ago	2
About the same	3
Somewhat worse now than one year ago	4
Much worse now than one year ago	5

The following items are about activities you might do during a typical day. Does **your health now limit you** in these activities? If so, how much?

(Circle One Number on Each Line)

	Yes, Limited a Lot	Yes, Limited a Little	No, Not limited at All

Validation of ScleroID

COUNTRY_____ **Patient number /__/__/**

3. **Vigorous activities**, such as running, lifting heavy objects, participating in strenuous sports	[1]	[2]	[3]
4. **Moderate activities**, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf	[1]	[2]	[3]
5. Lifting or carrying groceries	[1]	[2]	[3]
6. Climbing **several** flights of stairs	[1]	[2]	[3]
7. Climbing **one** flight of stairs	[1]	[2]	[3]
8. Bending, kneeling, or stooping	[1]	[2]	[3]
9. Walking **more than a mile**	[1]	[2]	[3]
10. Walking **several blocks**	[1]	[2]	[3]
11. Walking **one block**	[1]	[2]	[3]
12. Bathing or dressing yourself	[1]	[2]	[3]

During the **past 4 weeks**, have you had any of the following problems with your work or other regular daily activities **as a result of your physical health**?

(Circle One Number on Each Line)

	Yes	No
13. Cut down the amount of time you spent on work or other activities	1	2
14. **Accomplished less** than you would like	1	2
15. Were limited in the **kind** of work or other activities	1	2
16. Had **difficulty** performing the work or other activities (for example, it took extra effort)	1	2

During the **past 4 weeks,** have you had any of the following problems with your work or other regular daily activities **as a result of any emotional problems**(such as feeling depressed or anxious)? **(Circle One Number on Each Line)**

	Yes	No

Validation of ScleroID

COUNTRY_____ **Patient number /__/__/**

17. Cut down the **amount of time** you spent on work or other activities	1	2
18. **Accomplished less** than you would like	1	2
19. Didn't do work or other activities as **carefully** as usual	1	2

20. During the **past 4 weeks,** to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbors, or groups? **(Circle One Number)**

Not at all	1
Slightly	2
Moderately	3
Quite a bit	4
Extremely	5

21. How much **bodily** pain have you had during the **past 4 weeks**?

(Circle One Number)

None	1
Very mild	2
Mild	3
Moderate	4
Severe	5
Very severe	6

22. During the **past 4 weeks,** how much did **pain** interfere with your normal work (including both work outside the home and housework)? **(Circle One Number)**

Not at all	1
A little bit	2
Moderately	3

Validation of SclerolD

COUNTRY_____ **Patient number /__/__/**

Quite a bit 4

Extremely 5

These questions are about how you feel and how things have been with you **during the past 4 weeks**. For each question, please give the one answer that comes closest to the way you have been feeling. **(Circle One Number on Each Line)**

How much of the time during the **past 4 weeks** . . .

	All of the Time	Most of the Time	A Good Bit of the Time	Some of the Time	A Little of the Time	None of the Time
23. Did you feel full of pep?	1	2	3	4	5	6
24. Have you been a very nervous person?	1	2	3	4	5	6
25. Have you felt so down in the dumps that nothing could cheer you up?	1	2	3	4	5	6
26. Have you felt calm and peaceful?	1	2	3	4	5	6
27. Did you have a lot of energy?	1	2	3	4	5	6
28. Have you felt downhearted and blue?	1	2	3	4	5	6
29. Did you feel worn out?	1	2	3	4	5	6
30. Have you been a happy person?	1	2	3	4	5	6
31. Did you feel tired?	1	2	3	4	5	6

32. During the **past 4 weeks,** how much of the time has your **physical health or emotional problems** interfered with your social activities (like visiting with friends, relatives, etc.)? **(Circle One Number)**

All of the time 1

Validation of ScleroID

COUNTRY_____ **Patient number /__/__/**

Most of the time	2
Some of the time	3
A little of the time	4
None of the time	5

How TRUE or FALSE is each of the following statements for you.

(Circle One Number on Each Line)

	Definitely True	Mostly True	Don't Know	Mostly False	Definitely False
33. I seem to get sick a little easier than other people	1	2	3	4	5
34. I am as healthy as anybody I know	1	2	3	4	5
35. I expect my health to get worse	1	2	3	4	5
36. My health is excellent	1	2	3	4	5

Thank you for filling in this questionnaire

Validation of SclerolD

COUNTRY_____ **Patient number /__/__/**

RELIABILITY STUDY – PHYSICIAN CRF

(to be filled in 7+/-3 days after the baseline visit)

R1. Date of the visit */__/__/ /__/__/ 20__*
day month year

should be 7 days after the baseline visit (±3 days)

R2. **Do you confirm the main inclusion criteria?**

	Yes	No
R2.1. willingness to fill in the Reliability CRF after 7 +/- 3 days	❑	❑
R2.2. no major health change/medical intervention is forseeable/planed during the next 10 days.....	❑	❑

A negative answer to question 2.1 or 2.2 results in the non-inclusion of the patient in the reliability study.

Validation of ScleroID

COUNTRY_____ **Patient number /__/__/**

SENSITIVITY TO CHANGE STUDY – PATIENT CRF

Today's Date: Day /__/__/ Month /__/__/ Year 20/__/__/

Please cross the correct answer:

S1. Since you last filled in this questionnaire, do you consider your systemic sclerosis to be stable? ..... yes ❑ no ❑

S2. Since you last filled in this questionnaire, has your treatment for your systemic sclerosis been changed? ..... yes ❑ no ❑

S3. **Think about all the ways in which the systemic sclerosis has affected you during the last week, how would you consider this state?** (Mark "**X**" in only one box below)

❑ Very good
❑ Good
❑ Acceptable
❑ Bad
❑ Very bad

S4. Think about all the ways your systemic sclerosis has affected you during the last week. **Compared to 6 months ago, how has the overall state of your disease been during the last week?** (Mark "**X**" in only one box below)

☐ Much improved
☐ Moderately improved
☐ Stable (mostly unchanged)
☐ Moderately worsened
☐ Much worsened

Validation of ScleroID

COUNTRY_____ **Patient number /__/__/**

S5. The EULAR Scleroderma Impact of Disease Score (ScleroID)

How much have the different aspects of systemic sclerosis affected you during the last week? Please mark your responses on the scale by choosing the appropriate number for each of the following dimensions:

Raynaud's phenomenon:

Circle the number that best describes the severity of your Raynaud's phenomenon during the last week:

None	0	1	2	3	4	5	6	7	8	9	10	Extreme

Hand function:

Circle the number that best describes your hand function limitations due to your systemic sclerosis during the last week:

No limitation	0	1	2	3	4	5	6	7	8	9	10	Extreme limitation

Upper gastrointestinal tract symptoms (e.g. swallowing difficulties, reflux, vomiting):

Circle the number that best describes the severity of your upper gastrointestinal tract symptoms due to your systemic sclerosis during the last week:

None	0	1	2	3	4	5	6	7	8	9	10	Extreme

Pain:

Circle the number that best describes the pain you felt due to your systemic sclerosis during the last week:

None	0	1	2	3	4	5	6	7	8	9	10	Extreme

Fatigue:

Circle the number that best describes the impact of overall fatigue due to your systemic sclerosis during the last week:

None	0	1	2	3	4	5	6	7	8	9	10	Extreme

Lower gastrointestinal tract symptoms (e.g. bloating, diarrhea, constipation, anal incontinence):

Circle the number that best describes the severity of lower gastrointestinal tract symptoms during the last week:

None	0	1	2	3	4	5	6	7	8	9	10	Extreme

Limitations of life choices and activities (e.g. social life, personal care, work):

Circle the number that best describes how severe the limitations of life choices and activities due to your systemic sclerosis were during the last week:

No	0	1	2	3	4	5	6	7	8	9	10	Extreme

Validation of ScleroID

COUNTRY_____ **Patient number /__/__/**

Body mobility:

Circle the number that best describes how much your body mobility was affected due to your systemic sclerosis during the last week:

Not affected	0	1	2	3	4	5	6	7	8	9	10	Extremely affected

Breathlessness:

Circle the number that best describes how severe your breathlessness due to systemic sclerosis was during the last week:

None	0	1	2	3	4	5	6	7	8	9	10	Extreme

Digital ulcers:

Circle the number that best describes how much your digital ulcers affected you overall during the last week:

None	0	1	2	3	4	5	6	7	8	9	10	Extreme

S6. Global assessment

Considering **all the ways your systemic sclerosis** has affected you during the last week, circle the number that best describes how you have been doing:

Very good	0	1	2	3	4	5	6	7	8	9	10	Very bad

Validation of ScleroID

COUNTRY_____ **Patient number /__/__/**

S7. We are interested in learning how your illness affects your ability to function in daily life. Please check (X) the one best answer which best describes your usual abilities OVER THE PAST WEEK:

	Without ANY Difficulty(0)	With SOME Difficulty(1)	With MUCH Difficulty(2)	UNABLE To Do(3)
DRESSING & GROOMING				
Are you able to:				
- Dress yourself, including tying shoelaces and doing buttons?	_____	_____	_____	_____
- Shampoo your hair?	_____	_____	_____	_____
ARISING				
Are you able to:				
- Stand up from a straight chair?	_____	_____	_____	_____
- Get in and out of bed?	_____	_____	_____	_____
EATING				
Are you able to:				
- Cut your meat?	_____	_____	_____	_____
- Lift a full cup or glass to your mouth?	_____	_____	_____	_____
- Open a new milk carton?	_____	_____	_____	_____
WALKING				
Are you able to:				
- Walk outdoors on flat ground?	_____	_____	_____	_____
- Climb up five steps?	_____	_____	_____	_____

Please check any AIDS OR DEVICES that you usually use for any of these activities:

_____ Cane
_____ Walker
_____ Crutches
_____ Wheelchair
_____ Devices used for dressing (button hook, zipper pull, long-handled shoe horn, etc.)
_____ Built up or special utensils
_____ Special or built up chair
_____ Other (Specify: _____)

Please check any categories for which you usually need HELP FROM ANOTHER PERSON:

_____ Dressing and Grooming
_____ Arising
_____ Eating
_____ Walking

Validation of ScleroID

COUNTRY_____ **Patient number /__/__/**

Please check the response which best describes your usual abilities OVER THE PAST WEEK:

	Without ANY Difficulty(0)	With SOME Difficulty(1)	With MUCH Difficulty(2)	UNABLE To Do(3)
HYGIENE				
Are you able to:				
- Wash and dry your body?	_____	_____	_____	_____
- Take a tub bath?	_____	_____	_____	_____
- Get on and off the toilet?	_____	_____	_____	_____
REACH				
Are you able to:				
- Reach and get down a 5 pound object (such as a bag of sugar) from just above your head?	_____	_____	_____	_____
- Bend down to pick up clothing from the floor?	_____	_____	_____	_____
GRIP				
Are you able to:				
- Open car doors?	_____	_____	_____	_____
- Open jars which have previously been opened?	_____	_____	_____	_____
- Turn faucets on and off?	_____	_____	_____	_____
ACTIVITIES				
Are you able to:				
- Run errands and shop?	_____	_____	_____	_____
- Get in and out of a car?	_____	_____	_____	_____
- Do chores such as vacuuming or yard work?	_____	_____	_____	_____

Please check any AIDS OR DEVICES that you usually use for any of these activities:

_____ Raised toilet seat
_____ Bathtub seat
_____ Jar opener (for jars previously opened)
_____ Other (Specify: _____)
_____ Bathtub bar
_____ Long-handled appliances for reach
_____ Long-handled appliances in bathroom

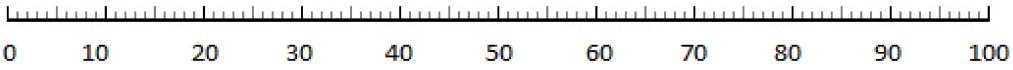
Please check any categories for which you usually need HELP FROM ANOTHER PERSON:

_____ Hygiene
_____ Reach
_____ Gripping and opening things
_____ Errands and chores

IN THE PAST WEEK, how much have your intestinal problems interfered with your daily activities?

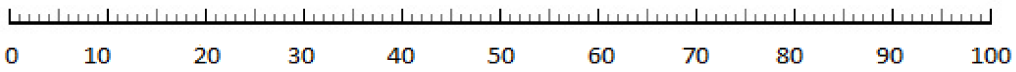
Validation of ScleroID

COUNTRY_____ **Patient number /__/__/**



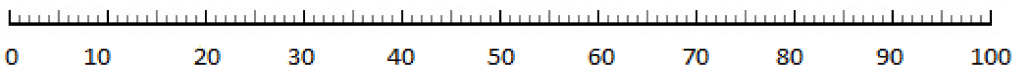
Does not interfere Very severe limitation

IN THE PAST WEEK, how much have your breathing problems interfered with your daily activities?



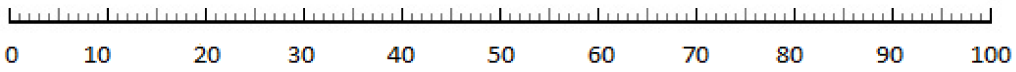
Do
es not interfere Very severe limitation

IN THE PAST WEEK, how much has Raynaud's interfered with your daily activities?



Does not interfere Very severe limitation

IN THE PAST WEEK, how much have your finger ulcers interfered with your daily activities?



Does not interfere Very severe limitation

S8. EQ-5D

By placing a tick in each group below, please indicate which statements best describe your own health state today.

Mobility

I have no problems in walking about ❒
I have some problems in walking about ❒
I am confined to bed ❒

Self-care

I have no problems with self-care ❒
I have some problems washing or dressing myself ❒
I am unable to wash or dress myself ❒

Usual activities (eg work, study, housework, family or leisure activities

Validation of ScleroID

COUNTRY_____ **Patient number /__/__/**

I have no problems with performing my usual activities ❒
I have some problems with performing my usual activities ❒
I am unable to perform my usual activities ❒

Pain / discomfort
I have no pain or discomfort ❒
I have moderate pain or discomfort ❒
I have extreme pain or discomfort ❒

Anxiety / depression
I am not anxious or depressed ❒
I am moderately anxious or depressed ❒
I am extremely anxious or depressed ❒

P10. Overall assessment of health status (SF-36)

1. In general, would you say your health is:	
Excellent	1
Very good	2
Good	3
Fair	4
Poor	5
2. **Compared to one year ago**, how would your rate your health in general **now**?	
Much better now than one year ago	1
Somewhat better now than one year ago	2
About the same	3
Somewhat worse now than one year ago	4
Much worse now than one year ago	5

The following items are about activities you might do during a typical day. Does **your health now limit you** in these activities? If so, how much?

(Circle One Number on Each Line)

	Yes, Limited a Lot	Yes, Limited a Little	No, Not limited at All

Validation of ScleroID

COUNTRY_____ **Patient number /__/__/**

3. **Vigorous activities**, such as running, lifting heavy objects, participating in strenuous sports	[1]	[2]	[3]
4. **Moderate activities**, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf	[1]	[2]	[3]
5. Lifting or carrying groceries	[1]	[2]	[3]
6. Climbing **several** flights of stairs	[1]	[2]	[3]
7. Climbing **one** flight of stairs	[1]	[2]	[3]
8. Bending, kneeling, or stooping	[1]	[2]	[3]
9. Walking **more than a mile**	[1]	[2]	[3]
10. Walking **several blocks**	[1]	[2]	[3]
11. Walking **one block**	[1]	[2]	[3]
12. Bathing or dressing yourself	[1]	[2]	[3]

During the **past 4 weeks**, have you had any of the following problems with your work or other regular daily activities **as a result of your physical health**?

(Circle One Number on Each Line)

	Yes	No
13. Cut down the amount of time you spent on work or other activities	1	2
14. **Accomplished less** than you would like	1	2
15. Were limited in the **kind** of work or other activities	1	2
16. Had **difficulty** performing the work or other activities (for example, it took extra effort)	1	2

During the **past 4 weeks,** have you had any of the following problems with your work or other regular daily activities **as a result of any emotional problems**(such as feeling depressed or anxious)? **(Circle One Number on Each Line)**

	Yes	No

Validation of ScleroID

COUNTRY_____ **Patient number /__/__/**

17. Cut down the **amount of time** you spent on work or other activities	1	2
18. **Accomplished less** than you would like	1	2
19. Didn't do work or other activities as **carefully** as usual	1	2

20. During the **past 4 weeks,** to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbors, or groups? **(Circle One Number)**

Not at all	1
Slightly	2
Moderately	3
Quite a bit	4
Extremely	5

21. How much **bodily** pain have you had during the **past 4 weeks**?

(Circle One Number)

None	1
Very mild	2
Mild	3
Moderate	4
Severe	5
Very severe	6

22. During the **past 4 weeks,** how much did **pain** interfere with your normal work (including both work outside the home and housework)? **(Circle One Number)**

Not at all	1
A little bit	2
Moderately	3

Validation of SclerolD

COUNTRY_____ **Patient number /__/__/**

Quite a bit 4

Extremely 5

These questions are about how you feel and how things have been with you **during the past 4 weeks**. For each question, please give the one answer that comes closest to the way you have been feeling. **(Circle One Number on Each Line)**

How much of the time during the **past 4 weeks** . . .

	All of the Time	Most of the Time	A Good Bit of the Time	Some of the Time	A Little of the Time	None of the Time
23. Did you feel full of pep?	1	2	3	4	5	6
24. Have you been a very nervous person?	1	2	3	4	5	6
25. Have you felt so down in the dumps that nothing could cheer you up?	1	2	3	4	5	6
26. Have you felt calm and peaceful?	1	2	3	4	5	6
27. Did you have a lot of energy?	1	2	3	4	5	6
28. Have you felt downhearted and blue?	1	2	3	4	5	6
29. Did you feel worn out?	1	2	3	4	5	6
30. Have you been a happy person?	1	2	3	4	5	6
31. Did you feel tired?	1	2	3	4	5	6

32. During the **past 4 weeks,** how much of the time has your **physical health or emotional problems** interfered with your social activities (like visiting with friends, relatives, etc.)? **(Circle One Number)**

All of the time 1

Validation of ScleroID

COUNTRY_____ **Patient number /__/__/**

Most of the time	2
Some of the time	3
A little of the time	4
None of the time	5

How TRUE or FALSE is each of the following statements for you.

(Circle One Number on Each Line)

	Definitely True	Mostly True	Don't Know	Mostly False	Definitely False
33. I seem to get sick a little easier than other people	1	2	3	4	5
34. I am as healthy as anybody I know	1	2	3	4	5
35. I expect my health to get worse	1	2	3	4	5
36. My health is excellent	1	2	3	4	5

Thank you for filling in this questionnaire

Validation of ScleroID

COUNTRY_____ **Patient number /__/__/**

SENSITIVITY TO CHANGE STUDY- PHYSICIAN CRF

(to be filled at visits occurring 6, respectively 12 months after the baseline visit)

S1. Date of the visit */__/__/ /__/__/ 20__*
day month year

S2. Do you confirm the main inclusion criteria?

	Yes	No
S2.1. Patient had active disease AT BASELINE as defined by the physician	❑	❑
S2.2. A follow-up visit at 6 and 12 months or at least at 12 months after baseline is feasible	❑	❑

A negative answer results in the non-inclusion of the patient in the sensitivity to change study.

S3. SSc characteristics

Please make sure that all necessary items of the corresponding EUSTAR dataset are evaluated and filled into the system (clinical features, laboratory values etc.) AND the patient fills in the necessary questionnaires/CRF.

S4. Physician's global assessment of SSc

Considering all the ways systemic sclerosis has affected your patient during the last week, circle the number that best describes how he/she has been doing:

Very good	0	1	2	3	4	5	6	7	8	9	10	Very bad

Systemic sclerosis - Assessment

Visit Date:

Name/Signature (MD):

PATIENT
Name:
Date of birth:
Sex: ○ Female ○ Male

If known: Unique patient number: ( ) EUSTAR ( ) VEDOSS

ACR-Criteria for Systemic Sclerosis

NEW CRITERIA for systemic sclerosis fulfilled ○ Yes ○ No

Add the maximum weight (score) in each category to calculate the total score.

Items	Sub-items	Weight/Score
Skin thickening of the fingers of both hands extending proximal to the metacarpophalangeal joints		9
Skin thickening of the fingers *(only count the highest score)*	Puffy fingers Whole Finger, distal to MCP	2 4
Finger tip lesions *(only count the highest score)*	Digital Tip Ulcers Pitting Scars	2 3
Telangiectasia		2
Abnormal nailfold capillaries		2
Pulmonary arterial hypertension and/or Interstitial lung Disease		2
Raynaud's phenomenon		3
Scleroderma related antibodies (any of anti-centromere, anti-topoisomerase I [anti-ScL 70], anti-RNA polymerase III)		3
	TOTAL SCORE:	

Patients having a total score of 9 or more are being classified as having definite systemic sclerosis.

SSc - Assessment

SSc-Ass: ACR/EULAR-criteria fulfilled

This page for NEW patients only

Height (cm)

Raynaud's present — Yes | No | unknown

Onset of Raynaud's disease

Onset of first non-Raynaud's of the disease

- Race
  - White
    - Hispanic
    - Any other white
  - Asian
    - Chinese
    - East- or South-East Asians
    - South Asians
    - Any other Asians
  - Black
    - Black Africans
    - Black Caribbeans
    - Black Americans
    - Any other Blacks
  - Other / Non defineable
    - Non-white Hispanic
    - Middle-eastern Person
    - Maghrebis
    - Any other
  - Unknown

Subset of SSc according to LeRoy (1988):

Limited cutaneous SSc | Diffuse cutaneous SSc | Unknown

Consent

Informed written consent to EUSTAR data Entry *

Myopathy substudy

Patient is included into Myopathy substudy — Yes, patient is included

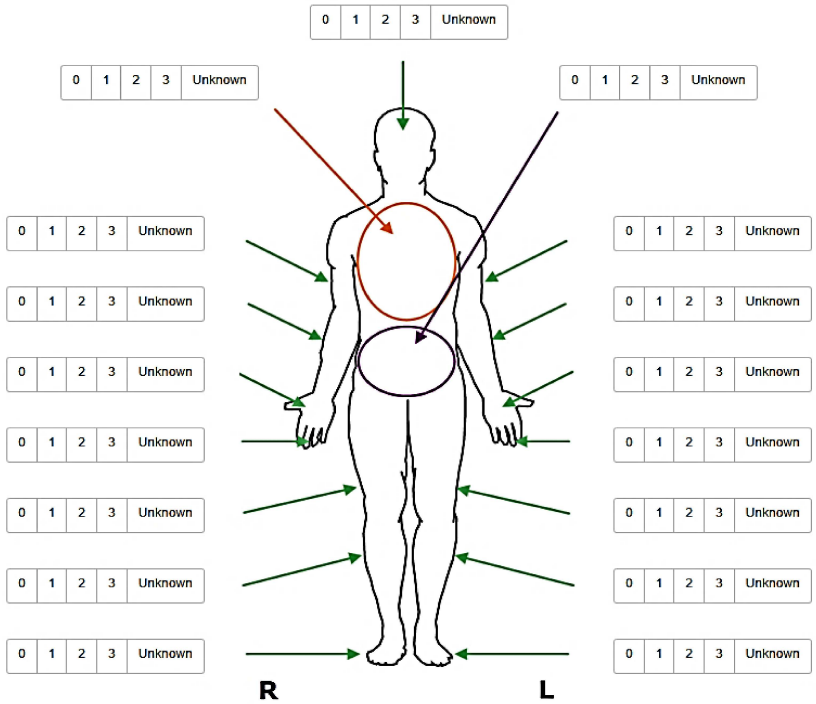
Inclusion details

SSc - Assessment

HISTORY

Cigarette smoking ever	Yes / No / unknown
Current cigarette smoker	Yes / No / unknown
Cigarette pack years	
Esophageal symptoms (dysphagia or reflux)	Yes / No / unknown
Stomach symptoms (early satiety, vomiting)	Yes / No / unknown
Intestinal symptoms (diarrhea, bloating, constipation)	Yes / No / unknown
Systemic Arterial hypertension	Yes / No / unknown
Renal crisis	Yes / No / unknown
Worsening of cardiopulmonary manifestations within the last month	Yes / No / unknown
Palpitations	Yes / No / unknown
Raynaud VAS mm	☐ Unknown

PHYSICAL EXAMINATION



Modified rodnan skin score | calculate

ACR/EULAR criteria for systemic sclerosis (2013) fulfilled at any time: Yes / No

SSc - Assessment

Skin thickening of the fingers of both hands extending proximal to the MCP joints ⓘ
Previously | Current | Never | Unknown

Scleredema (puffy fingers) ⓘ
Yes | No | unknown

Body weight (kg) ⓘ
☐ Unknown

Mouth inter-incisive distance (cm) ⓘ
☐ Unknown

Pitting scars on finger tips ⓘ
- Previously
- Current
- Never
- Unknown

Gangrene ⓘ
- Previously
- Current
- Never
- Unknown

Digital ulcer ⓘ
- Previously
- Current
- Never
- Unknown

Telangiectasia (any) ⓘ
Yes | No | unknown

Joint synovitis (at least one) ⓘ
Yes | No | unknown

Joint polyarthritis (more than 3 synovitis)
Yes | No | unknown

Tender joints (any)
Yes | No | unknown

Number of tenderJoints

Swollen joints (Any)
Yes | No | unknown

Number of swollen joints

Muscle weakness (any)
Yes | No | unknown

SSc - Assessment

Proximal muscle weakness not explainable by other causes	Yes / No / unknown
Myalgia	Yes / No / unknown
Muscle atrophy	Yes / No / unknown
Subcutaneous calcinosis (any) ⓘ	Yes / No / unknown
How active was your arthritis during the past week? ⓘ	
Patients global assessment of disease activity VAS ⓘ	
Physicians global assessment of disease activity VAS ⓘ	
DAS 28 (ESR, calculated) ⓘ	
DAS 28 (CRP, calculated) ⓘ	

LABORATORY

ANA positive ⓘ	Yes / No / unknown
ACA positive ⓘ	Yes / No / unknown
SCL-70 positive ⓘ	Yes / No / unknown
RNA Polymerase III positive ⓘ	Yes / No / unknown
U1RNP positive ⓘ	Yes / No / unknown
AntiSS-A ⓘ	Yes / No / unknown
AntiSS-B ⓘ	Yes / No / unknown
ACPA ⓘ	Yes / No / unknown
Rheumatoid factor ⓘ	Yes / No / unknown
CRP (mg/dl)	☐ Unknown

SSc - Assessment

Erythrocyte sedimentation rate ⓘ		☐ Unknown
HB (g/dl)		☐ Unknown
CK value in serum		☐ Unknown
Serum creatinine (mg/dl)		☐ Unknown
NT-proBNP (pg/ml)		☐ Unknown
BNP (pg/ml)		☐ Unknown
Uric Acid (mg/dl)		☐ Unknown
Proteinuria (> 300mg/d) ⓘ	Yes / No / unknown	

TEST/FUNCTIONS

Conduction blocks ⓘ	Yes / No / unknown	
Conduction block grade	I / II-III	
Arrhythmias requiring therapy ⓘ	Yes / No / unknown	
Pericardial effusion on echo	Yes / No / unknown	

and measured during the end-diastolic period

Small (localized or <10mm)	Moderate (10-20 mm)	Large (>20mm)

PAPsys (on echo) (mmHg) ⓘ		☐ Unknown
diastolic function abnormal (on echo, E/a < 10cm/sec):	Yes / No / unknown	
Left ventricular ejection fraction (%) ⓘ		☐ Unknown
Dyspnea stage	I / II / III / IV	

SSc - Assessment

HR-CT lung fibrosis	Yes / No / NotDone
Lung fibrosis % involvement	<20% / Indeterminate / >20% / Unknown
Any ground glass opacification	Yes / No / unknown
Any honey combing	Yes / No / unknown
Any reticular changes	Yes / No / unknown
Any tractions	Yes / No / unknown
Any bullae	Yes / No / unknown
Any lymph node enlargement	Yes / No / unknown
DLCO/SB (% predicted)	☐ Unknown
DLCO/VA (% predicted)	☐ Unknown
Forced Vital Capacity (FVC - % predicted)	☐ Unknown
Total lung capacity (TLC) predicted in %	☐ Unknown

NAILFOLD CAPILLAROSCOPY

Capillaroscopy scleroderma pattern	Yes / No / unknown
if scleroderma pattern present, tick when present	Early / Active / Late / Unknown
Giant capillaries	None / Rare / Moderate / Extensive / Unknown
Hemorrhages	None / Rare / Moderate / Extensive / Unknown
Capillary loss	None / Rare / Moderate / Extensive / Unknown
Ramified bushy capillaries	None / Rare / Moderate / Extensive / Unknown

CARDIAC

ECG

Right bundle branch block	Yes / No / unknown

SSc - Assessment

Right axis deviation	Yes	No	unknown
Right ventricular hypertrophy	Yes	No	unknown
Ventricular arrhythmias ⓘ	Yes	No	unknown
Auricular arrhythmias ⓘ	Yes	No	unknown

Echo

Tricuspid regurgitation velocity (m/sec)		☐ Unknown
RV/LV ratio		☐ Unknown
Right atrium area (cm^2)		☐ Unknown
Right ventricular area (cm^2)		☐ Unknown
Tricuspid annular plane systolic excursion (cm)		☐ Unknown

Cath

Right ventricular systolic pressure (mmHg) ⓘ		☐ Unknown
Right ventricular tele diastolic pressure (mmHg)		☐ Unknown
PAP mean (mmHg) ⓘ		☐ Unknown
Pulmonary resistance (dyn*s/cm^5) ⓘ		☐ Unknown
Pulmonary wedge pressure (mmHg) ⓘ		☐ Unknown
Wedge pressure after fluid challenge (mmHg)		☐ Unknown
Cardiac index (l/min/m^2) ⓘ		☐ Unknown
Cardiac output (l/min)		☐ Unknown

6 Minute walk test

Distance in m		☐ Unknown
O2-saturation at rest (%) ⓘ		☐ Unknown
Worst O2-saturation at exercise (%) ⓘ		☐ Unknown
Worst modified Borg dyspnea score during the test (from 0 to 10) ⓘ		☐ Unknown

SSc - Assessment

MYOPATHY

PM-SCL positive ⓘ	Yes	No	unknown
Aldolase elevation ⓘ	Yes	No	unknown

1-2 fold increase	2-5 fold increase	5-10 fold increase	Unknown

THERAPY

Only changes in medications since last visit should be recorded. You do not need to fill in the grey fields.

General	Start Date	Stop Date	Dose
Prednisone ( ) yes ( ) no ( ) unknown			In prednisone equivalent mg/day ( ) <=10 ( ) 11-20 ( ) >20 ( ) unknown
NSAID ( ) yes ( ) no ( ) unknown			
Cyclophosphamide ( ) yes ( ) no ( ) unknown route of administration: ( ) intravenous ( ) oral			
Methotrexate ( ) yes ( ) no ( ) unknown			Dose in mg/wk
Azathioprine ( ) yes ( ) no ( ) unknown			Dose in mg/d
Mycophenolate mofetil ( ) yes ( ) no ( ) unknown			( ) 1 g/d ( ) 2 g/d ( ) 3 g/d
Rituximab ( ) yes ( ) no ( ) unknown		date of last course	
TNF alpha antagonist ( ) yes ( ) no ( ) unknown Ongoing drug: ( ) Etanercept ( ) Adalimumab ( ) Infliximab ( ) Certolizumab ( ) Golimumab			
Autologous stem cell transplantation ( ) yes ( ) no ( ) unknown	Date of transplantation		
Immunoglobulins - i.v. or s.c. ( ) yes ( ) no ( ) unknown			
Tocilizumab - i.v. or s.c. ( ) yes ( ) no ( ) unknown			

SSc - Assessment

Abatacept - i.v. or s.c. ( ) yes ( ) no ( ) unknown			
JAK kinase inhibitors ( ) yes ( ) no ( ) unknown			

Endothelin receptor antagonists	**Start Date**	**Stop Date**	
Bosentan ( ) yes ( ) no ( ) unknown			
Ambrisentan ( ) yes ( ) no ( ) unknown			
Macitentan ( ) yes ( ) no ( ) unknown			

Nitric Oxide Modulators	**Start Date**	**Stop Date**	
Sildenafil ( ) yes ( ) no ( ) unknown			
Vardenafil ( ) yes ( ) no ( ) unknown			
Tadalafil ( ) yes ( ) no ( ) unknown			
Riociguat ( ) yes ( ) no ( ) unknown			

Prostanoids	**Start Date**	**Stop Date**	
Prostanoids ( ) yes ( ) no ( ) unknown ( ) Branded drug ( ) Biosimilar Route of administration ( ) inhaled ( ) intravenous ( ) oral ( ) sub-cutaneous			

Calcium channel blockers	**Start Date**	**Stop Date**	
Dihydropyridine (nifedipine, nicardipine, amlopidine, felopidine) ( ) yes ( ) no ( ) unknown			

SSc - Assessment

Dilitiazem ( ) yes ( ) no ( ) unknown			
ACE inhibitors ( ) yes ( ) no ( ) unknown			
Angiotensin receptor blocker ( ) yes ( ) no ( ) unknown			

Miscellaneous	**Start Date**	**Stop Date**			
Proton pump inhibitor ( ) yes ( ) no ( ) unknown					
Prokinetics ( ) yes ( ) no ( ) unknown					
Diuretics ( ) yes ( ) no ( ) unknown					
Antiplatelet agent ( ) yes ( ) no ( ) unknown					
Oral anti-coagulants ( ) yes ( ) no ( ) unknown					

Anti-fibrotic	**Start Date**	**Stop Date**	
Pirfenidone ( ) yes ( ) no ( ) unknown			
Nintedanib ( ) yes ( ) no ( ) unknown			

	Start Date	**Stop Date**	
Oxygen supply ( ) yes ( ) no ( ) unknown			

NEXT STEPS

Nächste Verlaufskontrolle

□ **reguläres Jahresassessment** (in ca. 1 Jahr)
Standard: LuFu/6MWD, CT Thorax, Echokardiografie, Kapillarmikroskopie, Ruhe-EKG + E60.

□ stationär
□ ambulant

Allfällige Abweichungen:

- zusätzlich
  - □ Ergotherapie
  - □ MMT-8/FI-2 (Physiotherapie)
  - □ MRI Herz
  - □ Sonstiges:_____
- ohne: _____

Zusätzlich Verlaufskontrolle in: □ 3 Monaten □ 6 Monaten □ sonst: _____

mit:
□ LuFu
□ 6 MWD
□ CT Thorax
□ Echokardiografie
□ Kapillarmikroskopie
□ Ergotherapie
□ MMT-8/FI-2 (Physiotherapie)
□ EKG
□ MRI Herz
□ Sonstiges:_____

+

□ K30 (30 Min.)
□ E60 (60 Min.)
bei (Arzt):_____

Inclusion in the myopathy sub-study
○ **Yes** (→ ***Myopathy visit)***
○ No
○ Unknown

Inclusion criteria (any one of the criteria is sufficient for inclusion):

- Elevated levels of the serum muscle enzymes CK or aldolase above upper limit of normal according to local laboratory without obvious explanation (e.g. extensive exercise, intramuscular injections, muscle injury)
- Proximal muscle weakness on physical examination as judged by the physician not explainable by other causes (e.g. neuropathogenic, genetic, metabolic, endocrinologic, infectious disorders, drug-induced, cachexia)
- Muscle atrophy on physical examination as judged by the physician not explainable by other causes (e.g. neuropathy, genetic disorders, cachexia)
- Positive myositis-associated autoantibodies (Jo-1, PM-Scl, U1-RNP, Ku, Mi-2, SRP, PL-7, PL-12, OJ, EJ, p155/140, MDA5, NXP2)