Supplementary methods

Skin and musculoskeletal study group: inclusion and exclusion criteria.
Inclusion criteria

Study characteristics

Studies with at least two visits containing skin and/or musculoskeletal outcome measure data

Outcomes of interest

1. Skin outcomesModified Rodnan Skin Score (mRSS), included only for studies involving jSSc
   - Elastography
   - Two-dimensional blood flow mapping/Doppler assessment of cutaneous blood flow
   - Ultrasound (US) assessment of skin thickness and echogenicity
   - Skin biopsy
   - Patient-reported outcomes (PROs), including the Dermatology Life Quality Index (DLQI)
2. Joint, tendon, and bone outcomes
   - Joint counts, including number of limited, swollen, painful, or synovitic joints
   - Composite joint disease activity measures, including Disease Activity Score in 28 joints using C-reactive protein (DAS28-CRP) or erythrocyte sedimentation rate (DAS28-ESR)
   - Contracture assessments, including table-top sign, prayer sign, and Rosenbloom limited joint mobility score
   - Magnetic resonance imaging (MRI) assessment of inflammatory arthritis and tenosynovitis, including the Rheumatoid Arthritis Magnetic Resonance Imaging Score (RAMRIS)
   - US assessment of inflammatory arthritis and tenosynovitis, tendon fibrosis, joint effusion, synovial hypertrophy, and erosions
3. Hand outcomes
   - Hand Mobility in Scleroderma (HAMIS)
   - Modified HAMIS (mHAMIS)
   - Hand Anatomic Index (HAI)
   - Modified HAI (mHAI)
   - Hand span (hand extension)
   - Kapandji finger opposition test (*Kapandji Score or Index)*
   - Finger-to-palm distance
   - Delta finger-to-palm distance (delta FTP)
   - Grip strength measured by hand dynamometer
   - Pinch grip strength measured by pinch meter
   - Cochin Hand Functional Scale (CHFS)/ Duruöz Hand Index (DHI)
   - Cochin Hand Functional Scale-6 (CHFS-6)
   - Disabilities of the Arm, Shoulder and Hand questionnaire (DASH)
   - Quick Disabilities of the Arm, Shoulder and Hand questionnaire (QuickDASH)
   - Health Assessment Questionnaire Disability Index (HAQ-DI)
4. Oral outcomes
   - Mouth aperture/oral opening measurements
   - Mouth Handicap in Systemic Sclerosis Scale (MHISS)
5. Muscle outcomes
   - Serum muscle enzymes
   - Physical examination-based muscle strength assessments, including Manual Muscle Testing (MMT) and Childhood Myositis Assessment Scale (CMAS)
   - Functional assessments, including the 6-minute walk test (6MWT), 2-minute walk test (2MWT), and sit-to-stand test
   - Muscle MRI assessment
6. Overall function
   - Health Assessment Qestionnarire Disability Index (HAQ-DI)
   - Patient Reported Outcomes Measurement Information System (PROMIS) physical function

Exclusion criteria

Studies not meeting the inclusion criteria described above or reporting only the following outcomes were excluded:

- mRSS in studies including only adult patients
- Composite disease activity or severity indices not specific to skin or musculoskeletal assessment (e.g., European Scleroderma Study Group Activity Index [EScSG-AI])
- Durometer assessment
- Calcinosis
- Acro-osteolysis
- Tendon friction rubs
- Conventional radiography
- Dual-energy X-ray absorptiometry (DEXA)
- Muscle scintigraphy
- Arthritis Hand Function Test
- Keitel Function Test
- Jebsen-Taylor Hand Function Test
- Michigan Hand Questionnaire
- Brief Michigan Hand Outcomes Questionnaire
- Sequential Occupational Dexterity Assessment (SODA/Shortened SODA)
- McMaster-Toronto Arthritis Patient Preference Disability Questionnaire
- Dreiser's Index
- Hand Scleroderma Lived Experience (HAnDE) Scale
- UK Scleroderma Functional Score
- Canadian Occupational Performance Measure
- Cochin 17-item Scleroderma Functional Scale
- Short Form-36 Health Survey (SF-36)
- Histopathology of skin biopsy

Supplementary Table S1. Characteristics of the outcome measure extracted.

Tissue/region– type of outcome measure	Outcome measure	Parameter assessed	Psychometric properties	Studied in paediatrics
Skin - ClinRo	Modified Rodnan Skin Score (mRSS)	Skin thickness by palpation at 17 body sites. Each site scored 0-3 (0=normal to 3=severe). Range 0-51.	Validated in SSc. Good inter-rater reliability (ICC 0.81) and intra-rater reliability (ICC 0.94). Correlates with skin biopsy weight and histologic fibrosis. Skin improvement by mRSS parallels favourable changes in other organ systems. Sensitive to change in RCTs. Published MCID: 3-4 units overall, 5 units in dcSSc.	Endorsed by the 2024 Hamburg Symposium on jSSc as a key skin activity measure. However, not formally validated in jSSc [18, S131-S136]
Skin – PRO	Dermatology Life Quality Index (DLQI)	Generic skin PRO measure. 10 item questionnaire assessing impact on symptoms (itch/pain), daily activities, and relationships. Score 0-30 (higher = greater impairment).	Generic dermatology QOL instrument validated across multiple skin diseases, though not specifically validated in SSc. Strong internal consistency ($\alpha \geq 0.85$). Good test-retest reliability. MCID 3.3-4 points for inflammatory skin diseases. Does not capture SSc-specific skin symptoms such as tightness/ contractures.	The Children's DLQI (CDLQI) has been studied in juvenile localized scleroderma. Very limited data in jSSc [137-139]
Skin -ImagingRO	Ultrasound: doppler	Cutaneous blood flow assessed using colour or power doppler. A skin vascular score is derived from semi-quantitative grading of dermal blood flow signal at various body sites.	Dermal doppler signal reflects cutaneous microvascular perfusion, which is reduced in ssc due to vasculopathy and fibrosis. Not yet validated. No standardized scoring system. Data limited to a single pilot study for cutaneous application.	Not validated in jssc [S140, S141]
	Ultrasound- Skin Thickness	Dermal thickness measured in mm. Measured at sites corresponding to the 17 mRSS body sites.	Best validated US domain. Good correlation with histologic skin thickness (r=0.69). Weaker correlation with local mRSS (r=0.59). Excellent intra-rater reliability (0.95-0.98). Good to excellent inter-rater reliability (ICC 0.65-0.97). No evidence for sensitivity to change or MCID.	Not validated in jSSc [S140-142]
	Ultrasound-Skin Echogenicity	Qualitative/semiquantitative grading of dermal echogenicity (iso/hypo/hyperechoic) compared to controls	Echogenicity changes (iso→ hypo→ hyperechoic) correlate with higher mRSS. Moderate to good intra-rater reliability (ICC 0.65-0.87). Limited evidence for validity against histological findings. No evidence for sensitivity to change or MCID.	Not validated in jSSc [140,143,144]
	Ultrasound-Skin Stiffness by Shear Wave Elastography (SWE) or Acoustic Radiation Force Impulse (ARFI)	Skin stiffness measured as elastic modulus (kPa) using SWE or ARFI	Strong correlation with mRSS (r=0.83 across 17 sites) and dermal collagen (r=0.71). Distinguishes SSc from controls with high accuracy (AUC 0.95-0.97). Excellent intra-rater reliability (ICC 0.95-0.97) and inter-rater reliability (ICC 0.82-0.99). No evidence for sensitivity to change or MCID.	Not validated in jSSc [142,144].
Joint, bone, tendon-ClinRO	Joint Contracture, Limited Range of Motion	Presence of contracture assessed using either a binary (yes/no) or continuous measure such as goniometry (ROM <75% of normal).	Contracture count correlates with inflammatory markers, mRSS, and HAQ-DI. Total >10 contractures or >4 unilateral hand contractures are associated with poor outcome over 6 years and are independent predictors of disease progression. Skin fibrosis can confound whether ROM limitation is articular vs. cutaneous in origin.	Not validated in jSSc. Core component of the JIA-ACR response criteria [S111, 145-147]
	Swollen Joint Count	Number of tender joints on palpation or motion.	Excellent inter-rater reliability (ICC 0.97) and intra-rater reliability (ICC 0.99) in dcSSc. Does not correlate well with ultrasound findings of inflammatory synovitis in adults with SSc (osteophytosis major contributor). Correlates with HAQ-DI.	Not validated in jSSc. Core component of JIA-ACR response criteria (active joint count) and JDAS. [S132, 146, S148, 149]
	Tender Joint Count	Number of joints with clinically detectable swelling.	Poor inter-rater reliability (ICC 0.24) in dcSSc, though acceptable intra-rater reliability (ICC 0.71). Confounded by skin fibrosis and subcutaneous oedema, reducing sensitivity to 14.6% compared to ultrasound.	Not validated in jSSc. Core component of JIA-ACR response criteria (active joint count) and JDAS.
	Disease Activity Score 28 (DAS28)	Compositive index incorporating the tender and swollen joint counts of 28 joints, ESR or CRP, and patient global VAS.	Initially developed for RA. Validated for assessing arthritis in SSc. Correlates with HAQ-DI, Cochin Hand Function Scale, and SF-36 physical component. Discriminates SSc from RA and healthy controls. DAS28-ESR has the best performance for reliability and construct validity. Good inter- and intra-rater reliability. Sensitive to change when tender/swollen joints are present at baseline.	Not validated in jSSc. The paediatric correlate, JDAS, has been validated in JIA, used in JIA RCTs, and is endorsed by the ACR [150,151]

Tissue/region– type of outcome measure	Outcome measure	Parameter assessed	Psychometric properties	Studied in paediatrics
Joint, bone tendon – ImagingRO	Ultrasound: Inflammatory Arthritis, Tenosynovitis	B-mode and Doppler assessment of synovial hypertrophy, joint effusion, and tenosynovitis using OMERACT definitions. Typically assessed at hands, wrists, and feet.	Significantly more sensitive than clinical exam for detecting synovitis (52% vs. 25%) and tenosynovitis (16% vs. 4%). Can differentiate between inflammatory and sclerosing synovitis. Can detect subclinical involvement. No standardised scoring system specific to SSc (OMERACT RA applied). No MCID or sensitivity to change data available in SSc.	Not validated in jSSc. Extensively studied in JIA [S152-S154].
	Ultrasound: Erosions	B-mode detection of cortical bone erosions at joint margins. Typically assessed at hands and wrists.	Very low prevalence in SSc. Only 0.7% of SSc patients had US-detectable erosions in the largest cohort study (n=145 joints). Uses RA-OMERACT definitions without SSc-specific validation. No MCID or sensitivity to change data.	Not validated in jSSc. [S155]
Muscle - ClinRo	Manual Muscle Test (MMT)-8	Isometric strength of 8 proximal and axial muscle groups. Each scored 0-10 on the Kendall scale. Total score 0-80 (unilateral) or 0-150 (bilateral).	Validated for idiopathic inflammatory myopathies (IIMs) and adopted for SSc-myopathy assessment. Can be affected by skin fibrosis, joint contracture, and cardiopulmonary involvement.	Not validated in jSSc. Used in juvenile dermatomyositis trials as part of the IMACS/ PRINTO core set [156,157]
	Medical Research Council (MRC) for Muscle Strength	Ordinal grading of muscle strength per muscle group (0-5 scale; 0 = no contraction; 5 = normal strength). Can be summed across multiple groups.	Well-established clinical grading system. Known ceiling effect—cannot distinguish subtle weakness within grade 4-5. Limited sensitivity to change. No SSc-specific reliability or MCID data.	Used for routine clinical paediatric neuromuscular assessment. MMT-8 and CMAS preferred for JDM trials.
	Isokinetic Muscle Strength Testing	Quantitative measurement of muscle torque (Nm) and work (J) during dynamic contraction at controlled angular velocities using an isokinetic dynamometer. Can also measure agonist/antagonist ratios and muscle endurance.	Provides continues, objective data superior to ordinal MMT. Correlate with handgrip strength and HAQ-DI. No SSc-specific validation. Requires specialized equipment and trained personnel, limiting feasibility.	Not validated in jSSc. Has been studied in JDM.
Muscle- PerfRo	6-Minute Walk Test	Distance walked in 6 minutes (meters) on a flat corridor. Also captures HR, BP, SpO2, and Borg dyspnoea score. Exercise capacity that reflects integrated musculoskeletal, cardiopulmonary, and neurologic function.	Not validated as an MSK-specific outcome measure in SSc. Excellent reproducibility (ICC 0.99). Muscle disability score is independently associated with lower 6MWD. Significantly reduced in SSc patients with proximal muscle weakness. Quadriceps strength was the strongest independent predictor of 6MWD in women with SSc-ILD. A cross-sectional study demonstrated that muscle involvement and joint involvement were not independently associated with 6MWD after adjusting for PH and other factors. Global functional capacity measure that is influenced by, but not specific to, musculoskeletal disease. Used as an endpoint for SSc-PH trials.	Not validated in jSSc. Validated in paediatric PH and used in JDM exercise studies.
Muscle-Biomarker	Muscle Enzymes	Biomarkers of muscle damage, inflammation.	Aldolase has superior predictive value for subsequent myopathy occurrence (AUC 0.80 vs. CK 0.75). Aldolase > 9 U/L confers HR 10.3 for developing SSc-myopathy within 3 years. CK> 3x ULN recommended as an enrolment criterion for SSc myopathy trials to prevent floor effect. Can be normal in fibrotic/chronic myopathy.	Not validated in jSSc. Endorsed by the 2024 Hamberg Symposium as part of myositis assessment in jSSc. CK is a core set measure in JDM trials as part of the IMACS/PRINTO core set [S158]
Hand – ClinROs	*Wrist range of motion (ROM)*	Measure the degree of mobility in four directions: flexion, extension, radial deviation, and ulnar deviation. Assessed with a goniometer.	Valid, reliable, sensitive measure when used by trained examiners. Standard assessment for rheumatoid arthritis.	Routinely used in juvenile idiopathic arthritis assessment. Not validated in jSSc
	Finger to palm	3rd finger flexion to palm: summation of flexion of MCP, PIP and DIP	Valid, reliable, sensitive to change, and feasible. But does not account for contractures, so can misclassify some patients with severe contractures as minimally affected [S112].	Not validated in jSSc [S112]
	Delta finger to palm	3rd finger extension and flexion to palm	Valid, reliable, sensitive to change, and feasible. Better face validity than finger to palm because it accounts for the patient's contractures. Strong correlation with finger range of motion measured by goniometry and HAMIS, and more reliable than goniometry. Not yet evaluated in a clinical trial. [S112, S159]	Not validated in jSSc [S112]
	Hand span (hand extension)	Measures from tips of thumb to 5th fingers when hand is maximally opened. Evaluated in both hands	Has been used in clinical trials as secondary outcome measure. Found associated with overall functional status. But values depend upon the patient's sex and body size [14, S160].	Not validated in jSSc

Tissue/region– type of outcome measure	Outcome measure	Parameter assessed	Psychometric properties	Studied in paediatrics
	Hand anatomic index (HAI)	Measures the open hand span minus the closed hand span and divides this by the lateral height of the hand to correct for patient size differences.	Adjusts for differences due to body size, sex. Found reliable, correlates with grip strength and global functional impairment [S161].	Not validated in jSSc
	Kapandhi finger opposition test (Kapandji Score or Index)	Assesses thumb mobility around the hand. The patient is asked to touch the tip of their thumb to 14 sites on the hand including along the fingers and to the distal palmar crease.	Valid, reliable, feasible test widely used by hand therapists and orthopaedists. Found valid and responsive for rheumatoid arthritis. Limited study in SSc [S162].	Not validated in jSSc
	Hand Mobility in Scleroderma (HAMIS)	Assess hand mobility; 9 items assessing finger, thumb, and wrist movements. Each item graded from 0, normal function, to 3, severe immobility. Total summed	Validated for use in SSc clinical trials. Moderate correlation with mRSS in early disease, joint range of motion and moderate to strong positive correlations with CHFS and HAQ-DI [14, S19, S163]	Not validated in jSSc
	Modified Hand Mobility in Scleroderma (mHAMIS)	4 items: finger flexion, finger extension, finger abduction, dorsal extension. Simpler to administer than HAMIS, so skills needed for administration are easier to acquire.	Simpler to perform than HAMIS and found to have high correlation with HAMIS. Highly reliable, correlates with mRSS, discriminates mild vs severe impairment. Correlates moderate to strongly with CHFS, HAQ [S164].	Not validated in jSSc
	Grip strength	JAMAR Hand Dynamometer typically used, need standardization in how performed	Found to have excellent reliability. And moderate to strong validity. May be performed as average of 3 measurements, or as highest score of two measurements from each hand. Should follow standard recommended testing positions.	Has been evaluated in children down to age 3 years old. Only limited study in jSSc [S165, S166]
	Pinch strength	Pinch meter device; may check tip of thumb to tip of 2nd finger pinch, squeezing pad of thumb against pads of both 2nd and 3rd finger, and lateral pinch, squeezing thumb against side of 2nd finger.	Found to have excellent reliability. And moderate to strong validity. May be performed as average of 3 measurements, or as highest score of two measurements from each hand. Should follow standard recommended testing positions.	Has been evaluated in children down to age 3 years old. Not validated in jSSc [S167].
Hand – PRO	Cochin Hand Function Scale (CHFS); also known as the Duruöz Hand Index	18 item questionnaire asks if patient feels limited in daily activities for specific tasks	Validated for use in SSc clinical trials. Highly reliability, feasible to use for both diffuse and limited SSc, and available in multiple languages. [14, S111, S168]	Not validated in jSSc. Some questions involve tasks that are not developmentally appropriate for younger children.
	Cochin Hand Function Scale -6 (CHFS-6)	Shortened version of CHFS, with only 6 of the original 18 questions	Excellent correlation with CHFS. Strong validity, excellent reliability, excellent sensitivity to change. [S168]	Not validated in jSSc. Some questions involve tasks that are not developmentally appropriate for younger children.
	Disabilities of the Arm, Shoulder, and Hand (*DASH)*	30 item questionnaire that assesses upper limb function, symptoms, and impact of upper limb problems on social activities.	Valid, reliable, and responsive measure used to assess musculoskeletal disorders of the upper limb, including in patients with SSc. Strong correlation with Scleroderma Health Assessment Questionnaire (SHAQ) and HAQ-DI . Takes 5-30 minutes to complete, and has been translated into 55 languages [S169, S170]	Not validated in jSSc. May miss some finger and thumb limitations
	Quick Disabilities of the Arm, Shoulder, and Hand (Quick*DASH)*	Shortened version of DASH with only 11 of the original questions.	Excellent correlation with DASH, with high validity, reliability, and sensitivity to change [S164, S171]	Validated in children 5-18 years old with upper extremity fractures. Not validated in jSSc. May miss some finger and thumb limitations [172].
Mouth – ClinRO	Interincisal Distance, Interlabial Distance	Maximum mouth opening measured in mm with a ruler or calipers.	Validated in SSc. Discriminates SSc from healthy controls. Correlates with disease severity. Maximal opening < 30 mm associated with worse 30-year survival and risk of PH. Excellent inter-rater reliability (kappa> 0.85). Among the most reproducible clinical measures in SSc; less variability than mRSS and global assessments.	Not validated in jSSc. Well-validated in JIA (TMJ arthritis). However, maximum mouth opening in jSSc also reflects perioral skin fibrosis and microstomia.
Mouth – PRO	Mouth Handicap in Systemic Sclerosis Scale (MHISS)	SSc-specific PRO measure mouth-related disability. 12 item questionnaire, each scored 0-4. Range 0-48 (high = greater impairment). Three domains = handicap from reduced mouth opening, sicca/xerostomia, aesthetic concerns.	Validated in SSc. Excellent test-retest reliability (ICC 0.96). Good internal consistency (Cronbach's $\alpha = 0.86$). Correlates with mRSS. Discriminates dsSSc from lcSSc (28.2 ± 11.3 vs 11.4 ± 8.7). No published MCID.	Not validated in jSSc. No paediatric adaptation exits.

Tissue/region– type of outcome measure	Outcome measure	Parameter assessed	Psychometric properties	Studied in paediatrics
Global function - PRO	Health Assessment Questionnaire Disability Index (*HAQ-DI)*	20 item questionnaire that is used to track how well the patient can perform daily tasks in 8 domains over the past 7 days. Both upper and lower extremity function are assessed. The highest item scores in each domain are summed, then divided by eight to get a score ranging from 0 (no disability) to 3 (severe disability). Developed to assess function in patients with arthritis.	Validated for use in SSc clinical trials as a primary outcome measure. Excellent reliability, sensitive to change, with minimally important difference estimates identified. Strong correlation with DASH questionnaire [S111, S173, 174]	Not validated in jSSc. Adult-centric so many questions are developmentally inappropriate for v
	PROMIS Physical Function	Questionnaire assessing physical function, available in different lengths depending upon if focused on specific domains, and if long or short versions. Items span upper extremity tasks (gripping/carrying), lower extremity tasks (walking/climbing), and central tasks (getting in/out of bed).	Validated in SSc. Strong convergent validity with HAQ-DI and SF-36 PCS. SSc patients score ~2/3 SD below the general population. Joint contracture, GI involvement, PH, ILD, digital ulcers, and diffuse subtype are all independently associated with worse PROMIS PF scores. Good internal consistency and test-retest reliability. Longer PROMIS short forms recommended to improve responsiveness.	Not validated or studies in jSSc. PROMIS paediatric measures exist and are validated in JIA and other paediatric rheumatic diseases [S175-177]

CDLQI: Children's Dermatology Life Quality Index; CHAQ: Children's Health Assessment Questionnaire; CHFS: Cochin Hand Function Scale; CHFS-6: Cochin Hand Function Scale-6; ClinRO: Clinician-Reported Outcome; DASH: Disabilities of the Arm, Shoulder and Hand; DLQI: Dermatology Life Quality Index; HAI: Hand Anatomic Index; HAMIS: Hand Mobility in Scleroderma; HAQ-DI: Health Assessment Questionnaire Disability Index; mHAMIS: Modified Hand Mobility in Scleroderma; MHISS: Mouth Handicap in Systemic Sclerosis Scale; QuickDASH: Quick Disabilities of the Arm, Shoulder and Hand; PRO: Patient-Reported Outcome; ROM: Range of Motion; ImagingRO: imaging-reported outcome.

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