Review

Outcome measures for cutaneous and musculoskeletal involvement in juvenile systemic sclerosis: a scoping literature review

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ABSTRACT

Objective. *Cutaneous and musculoskeletal involvement are major contributors to morbidity and disability in juvenile systemic sclerosis (jSSc). This scoping review aimed to identify outcome measures used to assess these domains in sclerosis (SSc) to support juvenile SSc clinical trials.*

Methods. *A scoping review was conducted following PRISMA-ScR guidelines. PubMed, Embase, Web of Science, and the Cochrane Central Register of Controlled Trials (CENTRAL) were searched (1994–2026) for longitudinal studies evaluating skin and musculoskeletal outcome measures in SSc.*

Results. *Of 46,002 records identified, 108 studies met the inclusion criteria; 106 (98.1%) included adults only, whereas two studies included only jSSc patients (n=13). Overall, 35 distinct outcome measures were identified, including 23 clinician-reported outcomes (of which 6 were imaging measures), 9 patient-reported outcomes, 2 performance outcomes, and 1 biomarker. Hand involvement was the most frequently evaluated domain (54 studies), followed by overall function (51), mouth (24), joints/bone/tendon (18), muscle (8), and skin (8). Grip strength was the most frequently reported hand outcome measure. The modified Rodnan Skin Score was the only skin clinician-reported outcome evaluated in paediatric studies. Mouth, joint, and muscle involvement were primarily assessed using interincisal distance, joint counts, and the 6-minute walk test, respectively.*

Conclusion. *Outcome measures for skin and musculoskeletal involvement in SSc are heterogeneous and derived almost exclusively from adult studies. These findings highlight the need for standardised and validated outcome measures for jSSc and support the ongoing International Juvenile Systemic Sclerosis Outcome Group initiative to develop a core outcome set.*

Introduction

Juvenile systemic sclerosis (jSSc) is a rare autoimmune disorder characterised by immune dysregulation, vasculopathy, and progressive fibrosis involving the skin and internal organs resulting in substantial morbidity, impaired quality of life, and increased mortality (1-3). Cutaneous and musculoskeletal involvement constitute major hallmarks of jSSc and contribute substantially to functional impairment and long-term disability (1, 2, 4, 5) Skin involvement in jSSc is characterised by progressive thickening and hardening of the skin, frequently associated with oedema, loss of elasticity, pigmentary changes and subcutaneous fibrosis (2, 4, 5). The extent and progression of skin disease are clinically relevant, as cutaneous fibrosis has traditionally been considered a surrogate marker of overall disease severity and internal organ involvement in SSc (2, 4, 5). Musculoskeletal manifestations are highly prevalent in jSSc and encompass arthritis, arthralgia, tendon involvement, muscle weakness, myositis, joint contractures, and impaired hand and mouth function, all of which may significantly interfere with growth,

physical development, and daily activities, particularly in children with early and severe disease (1, 2, 4-7). Similarly, studies in adult-onset SSc (aSSc) have shown that skin fibrosis and hand involvement are major determinants of disability and reduced health-related quality of life, highlighting the clinical importance of accurately assessing these disease domains across the disease spectrum (8, 9). Notably, jSSc and aSSc differ in the frequency and distribution of clinical manifestations. Compared with aSSc, jSSc is characterised by a higher prevalence of diffuse cutaneous disease, overlap syndromes, and musculoskeletal involvement, including skeletal muscle disease and inflammatory arthritis (10, 11). In the largest international jSSc inception cohort, 17% of patients had overlap features, which were associated with significantly higher musculoskeletal and pulmonary involvement (11). These phenotypic differences underscore the particular relevance of skin and musculoskeletal outcome measures in jSSc and highlight the need for disease domain-specific assessment tools that capture the distinct clinical profile of paediatric patients.

Despite recent advances in the understanding of SSc pathogenesis and the increasing development of targeted therapies, the assessment of disease activity and treatment response in SSc remains challenging because of the marked heterogeneity of clinical manifestations and disease trajectories (2, 6, 12). This challenge is particularly relevant for skin and musculoskeletal involvement, which encompass inflammatory, fibrotic, and functional components that may evolve differently over time and therefore require multidimensional assessment strategies (4, 5). Although numerous outcome measures have been developed for different disease domains, the lack of standardisation and the limited validation of many instruments have been recognised as major limitations in aSSc clinical research and have likely contributed to inconsistent findings across clinical trials (6, 13, 14). In aSSc, substantial efforts have been made to standardise disease assessment through the development of consensus domains, organ-specific measures, and composite outcome tools (13, 15).

However, outcome measures currently used for skin and musculoskeletal assessment in jSSc have been extrapolated from aSSc and have not undergone formal validation in paediatric populations (6, 12, 16). Several international initiatives have attempted to address this unmet need. The Single Hub and Access point for Pediatric Rheumatology in Europe (SHARE) initiative developed consensus-based recommendations for the management of jSSc, while more recent international expert consensus efforts proposed core outcome domains and response parameters for use in jSSc clinical trials (17, 18). Nevertheless, these recommendations were not supported by a recent systematic evaluation of the available literature, and significant uncertainty remains regarding the optimal assessment tools in jSSc (17, 18). Because clinical trials require outcome measures capable of detecting disease progression and treatment response over time, identifying outcome measures that have been evaluated longitudinally is an essential prerequisite for the development of future paediatric clinical trials. To address these gaps, the International Juvenile Systemic Sclerosis Outcome Group (IJOG), in collaboration with members of the Childhood Arthritis and Rheumatology Research Alliance (CARRA) and the Paediatric Rheumatology European Society (PReS), initiated a multistep project aimed at developing standardised outcome measures and assessment strategies for future jSSc treatment studies (19). As part of this initiative, a scoping literature review was conducted to identify outcome measures used to assess major disease domains in adult and jSSc, and to evaluate their potential relevance for paediatric clinical research (19).

In this paper, we present the results of the scoping literature review focused on outcome measures used to assess cutaneous and musculoskeletal involvement in adult and juvenile SSc.

Methods

Scoping review search strategy

The study protocol developed by the IJOG, including the methodology for the scoping review, has been published previously (19). Briefly, the review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) guidelines (20, 21). A comprehensive literature search was performed in PubMed, Embase, Web of Science, and the Cochrane Central Register of Controlled Trials (CENTRAL), with the support of a librarian from the Albert Einstein College of Medicine. The initial search included English-language studies published between 1994 and 2021 and was completed in June 2021. An updated search was subsequently performed to identify studies published from June 2021 through April 2026. All retrieved references were imported into Covidence for study management. Study selection was performed through four sequential phases: 1) initial title and abstract screening, 2) title and abstract screening by disease domain, 3) full-text review by disease domain, and 4) final selection of studies for data extraction within each disease domain. Each stage was independently conducted by two paediatric rheumatologists, with disagreements resolved by a third reviewer.

Eligibility criteria

The eligibility criteria have been described in detail in the published IJOG protocol (19). In brief, original peer-reviewed studies evaluating outcome measures in aSSc and jSSc within the prespecified disease domains were considered eligible. The present review focuses on cutaneous and musculoskeletal involvement. Both observational and interventional studies were eligible, provided they included at least 3 paediatric or 10 adult patients with SSc. These cut-off values were set by the IJOG advisory group who sought to balance the greater rarity of jSSc *versus* aSSc, importance of capturing rare paediatric data while limiting inclusion of isolated anecdotes, and feasibility of evaluating the much larger number of adult studies. For the skin and musculoskeletal domain, studies were required to report longitudinal assessment of one or more skin and/or musculoskeletal outcome

Table I. Characteristics of the included studies (n=108) and tissue/region of interest.

Type of study	Number of studies (%)	Total number of patients (number of jSSc)
Randomised controlled trial	*39 (36.1%)*	*2584 (0)*
Non-randomised experimental study	28 (25.9%)	810 (0)
Prospective cohort	30 (27.8%)	6008 (0)
Retrospective cohort	11 (10.2%)	339 (13)
Oxford level of evidence		
1b/1b-	35 (32.4%)	2418 (0)
2b/2b-	39 (36.1%)	6388 (0)
4	34 (31.5%)	935 (13)
n. of centres/countries		
Single centre	76 (70.4%)	3850 (13)
Multicentre	32 (29.6%)	5891 (0)
Single country	95 (88.0%)	7719 (13)
Multinational	13 (12.0%)	2022 (0)
Included population		
dcSSc	89 (82.4%)	4200 (0)
lcSSc	58 (53.7%)	3892 (0)
ssSSc	4 (3.7%)	106 (0)
Overlap	6 (5.6%)	140 (0)
NS	24 (22.2%)	1403 (13)
Tissue / region or overall function		
Hand	54 (50.0%)	4021 (0)
Overall function	51 (47.2%)	4935 (0)
Mouth	24 (22.2%)	1266 (0)
Joints/bone/tendon	18 (16.7%)	1033 (0)
Muscle	8 (7.4%)	380 (0)
Skin	8 (7.4%)	681 (13)

SSc: systemic sclerosis; jSSc: juvenile systemic sclerosis; dcSSc: diffuse cutaneous systemic sclerosis; lcSSc: limited cutaneous systemic sclerosis; ssSSc: systemic sclerosis sine scleroderma; overlap: systemic sclerosis overlap syndrome; NS: subtype not specified.

measures in at least two study visits. Detailed inclusion and exclusion criteria for the skin and musculoskeletal domain are provided in the Supplementary methods. Outcomes of interest encompassed skin, joint, bone, tendon, hand, mouth, and muscle. Skin outcomes included clinician-reported outcomes (ClinROs), biomarkers, and patient-reported outcomes (PROs). Skin imaging studies (elastography, Doppler assessment of cutaneous blood flow, and ultrasound (US) skin assessment) are a type of ClinRO, which we chose to list under the sub-header of "Imaging" rather than ClinRO in Table II, the mRSS was only considered in jSSc studies. Joint, tendon and bone outcomes included joint counts, composite disease activity measures, contracture assessments, and magnetic resonance imaging (MRI), or US evaluation of inflammatory arthritis, tenosynovitis, and tendon involvement. Hand outcomes included measures of mobility, strength, and function. Mouth outcomes comprised mouth aperture measurements and mouth-related functional assessments. Muscle outcomes included serum muscle enzyme levels, physical examination-based muscle strength assessments, functional performance tests, and MRI evaluation of muscle involvement.

Data extractions and data analysis

In accordance with the Joanna Briggs Institute methodology for scoping reviews (21), members of the IJOG advisory group (SL, MT, CP, FZ, NVC) developed standardised data extraction forms for each disease domain. For the skin and musculoskeletal domain, a preliminary Excel-based extraction form was created to capture the variables required to address the objectives of the review. The draft form was subsequently discussed during virtual meetings with the international collaborators, who provided feedback and suggested additional variables relevant to the domain.

The extraction forms were pilot-tested in Covidence by three reviewers (AR, MÇ, SL) to evaluate the completeness and appropriateness of the collected data. Several rounds of refinement were performed to optimise feasibility, considering the large number of eligible studies, and to ensure that the extracted variables adequately captured the spectrum of cutaneous and musculoskeletal manifestations as well as the available level of evidence.

Data were summarised using descriptive analyses to characterise the included studies and reported outcome measures. Outcome measures were categorised according to the U.S. Food and Drug Administration (FDA) framework as ClinRO, performance outcomes (PerfOM), and PRO (22). In addition, the quality of evidence of each included study was graded using the Oxford Centre for Evidence-Based Medicine (OCEBM) Levels of Evidence classification (23).

Results

Search results

The study selection process is summarised in Figure 1. The initial search (1994-2021), previously published (19), and the updated search (2021-2026) identified a combined total of 46,002 records. After removal of duplicates, 30,992 records underwent title and abstract screening. Of these, 3,768 records were screened for the skin and musculoskeletal domains, and 742 articles were assessed for full-text eligibility. Following full-text review, 108 studies met the inclusion criteria and were included in the final data extraction (9, Supplementary refs. S24-S130).

Study characteristics

The characteristics of the included studies are summarised in Table I. Most studies were randomised controlled trials (36.1%). About a quarter of the studies were non-randomised experimental studies (25.9%), another quarter prospective cohort studies (27.8%), and the remainder retrospective cohort studies (10.2%). According to the OCEBM classification, 35 studies (32.4%) were classified as level 1b/1b - (Grade A), 39 (36.1%) as level 2b/2b - (Grade B), and 34 (31.5%) as level 4 (Grade C). Most studies were conducted at a single centre (70.4%) and within a single country (88.0%). Diffuse cutaneous systemic sclerosis (dcSSc) was the most frequently re-

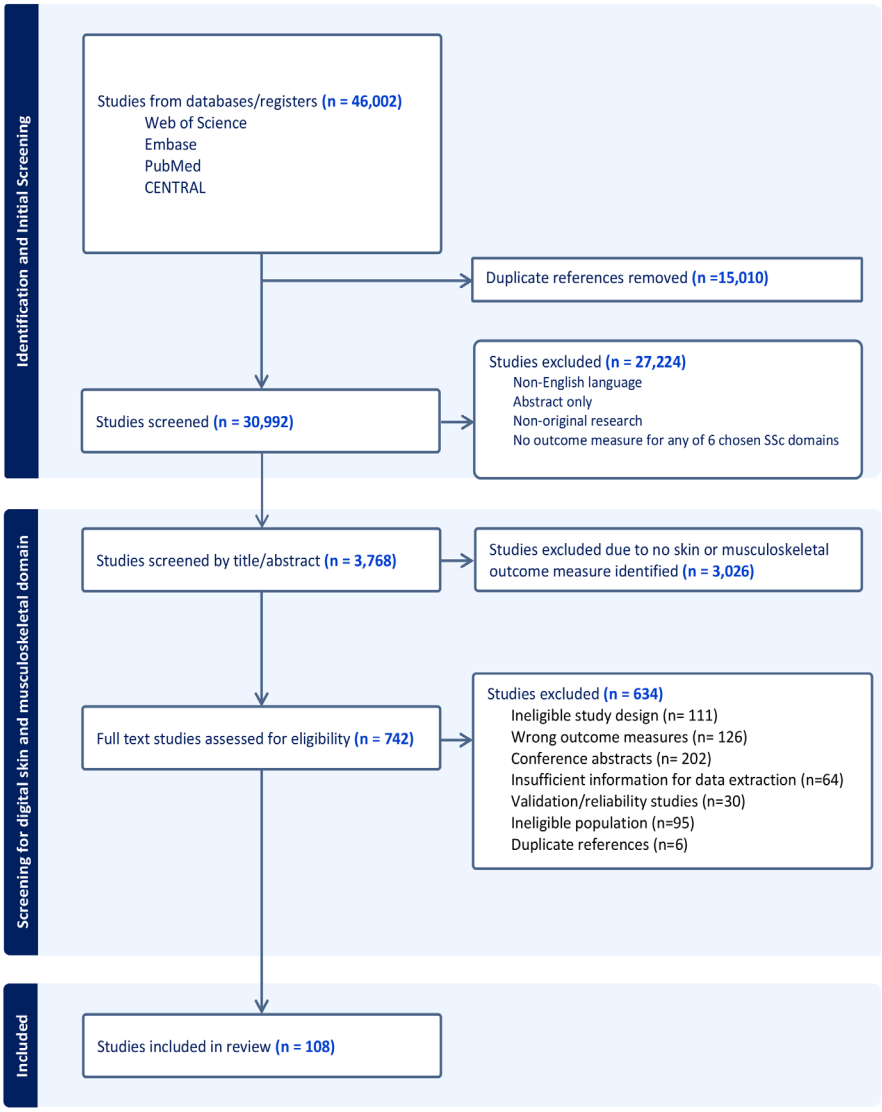

Fig. 1. PRISMA flow diagram.

ported subtype (82.4% of studies), followed by limited cutaneous systemic sclerosis (lcSSc) (53.7%). Overall, 106 studies (98.1%) included only adult patients, whereas two retrospective cohort studies (1.9%) included only jSSc patients (total of 13 patients with jSSc).

Identified domains

The predefined domains of cutaneous and musculoskeletal involvement included hand, mouth, skin, joints/bone/tendon, muscle and overall function. Supplementary Table S1 provides an overview of the outcome measures considered in this review, including those identified in the included studies as well as selected clinically relevant instruments not captured by the scoping review, with a summary of their assessment targets, known validity and reliability properties, and reported use in paediatric populations. Hand was the most frequently evaluated domain (50%; 54 studies), followed by overall function (47.2%; 51 studies), mouth (22.2%; 24 studies), joints/bone/tendon (16.7%; 18 studies), muscle (7.4%; 8 studies), and skin (7.4%; 8 studies). For joint and strength testing assessments of the hand, we listed them only under the hand domain. Overall, 35 distinct outcome measures were identified, including 23 ClinROs (including 6 imaging measures), 9 PROs, 2 PerfOMs, and 1 biomarker (Table I).

Hand domain

A total of 13 outcome measures were identified for the hand domain (Table II). Among ClinROs, grip strength was the most frequently reported outcome measure, followed by pinch strength and finger-to-palm distance. Grip and pinch strength showed significant improvement in more than half of the interventional studies in which they were evaluated. Among PROs, the most frequently reported outcome measures were the Cochin Hand Functional Scale/Duruöz Hand Index (CHFS/DHI), and the Hand Mobility in Scleroderma (HAMIS) scale. No studies were done using the CHFS-6. Both the CHFS/DHI and HAMIS demonstrated significant improvement in more than half of the interventional studies evaluating these measures. CHFS/DHI was assessed for correlation with clinical manifestations in a single study, where it was found to have a significant association.

Overall function

The PRO, the Health Assessment Questionnaire Disability Index (HAQ-DI), was the most commonly used PRO of all the PROs assessed for skin and musculoskeletal involvement and frequently used in intervention studies. In about a third of these studies, there was a significant change in HAQ-DI scores in response to the intervention. The HAQ-DI was assessed for correlation with clinical manifestations in a single study, where it was found to have a significantly association. The PROMIS Physical function was infrequently utilised.

Mouth domain

Three outcome measures were identified for the mouth domain (Table II), where oral involvement was primarily assessed using mouth aperture measurements. Among ClinROs, interincisal distance was the most frequently reported outcome measure, followed by interlabial distance. Both measures demonstrated significant improvement in the majority of interventional studies, with significant changes reported in 10 of 17 and 7 of 9 studies, respectively. The Mouth Handicap in Systemic Sclerosis Scale (MHISS) was the only identified PRO and was evaluated in eight studies, showing significant improvement in four of the eight interventional studies assessing this measure.

Table II. Outcome measures identified by region/tissue evaluated.

Type of outcome measure	n. of studies reporting the outcome measures, n (including jSSc, n)	n. of studies evaluating response to intervention (n. reporting significant change)	n. of longitudinal studies where measure was evaluated ≥2 timepoints, excluding intervention studies (n. reporting significant change)	n. of studies evaluating the measure in healthy controls vs. SSc patients (n. reporting a significant difference)	n. of studies evaluating correlations between skin/MSK symptoms and the outcome measure (n. reporting a significant correlation)
Hand					
ClinRO					
Wrist ROM	2 (0)	2 (2)	0 (0)	0 (0)	0 (0)
Finger to palm	14 (0)	12 (6)	2 (0)	0 (0)	0 (0)
Delta finger to palm	5 (0)	4 (3)	1 (1)	0 (0)	0 (0)
Hand anatomic index (HAI)	2 (0)	1 (0)	1 (0)	0 (0)	0 (0)
Hand span (Hand extension)	4 (0)	2 (0)	2 (0)	0 (0)	0 (0)
Kapandhi finger opposition test (Kapandji Score or Index)	2 (0)	2 (0)	0 (0)	0 (0)	0 (0)
Grip strength	43 (0)	40 (24)	3 (1)	0 (0)	0 (0)
Pinch strength	15 (0)	13 (8)	2 (2)	0 (0)	0 (0)
PRO					
HAMIS	14 (0)	12 (8)	2 (1)	0 (0)	0 (0)
Modified HAMIS	3 (0)	2 (2)	1 (1)	0 (0)	0 (0)
CHFS/DHI	27 (0)	22 (13)	5 (3)	0 (0)	1 (1)
CHFS-6	0				
DASH	5 (0)	4 (3)	1 (0)	0 (0)	0 (0)
QuickDASH	5 (0)	5 (2)	0 (0)	0 (0)	0 (0)
Function, overall					
PRO					
HAQ-DI	49 (0)	40 (15)	9 (2)	0 (0)	1 (1)
PROMIS	2 (0)	2 (1)	0 (0)	0 (0)	0 (0)
Mouth					
ClinRO					
Interincisal distance	18 (0)	17 (10)	1 (1)	0 (0)	0 (0)
Interlabial distance	11 (0)	9 (7)	2 (0)	0 (0)	0 (0)
PRO					
MHISS	8 (0)	8 (4)	0 (0)	0 (0)	0 (0)
Joint/bone/tendon					
ClinRO					
Limited joint ROM	3 (0)	2 (0)	1 (0)	0 (0)	0 (0)
n. of joints with swelling	10 (0)	9 (7)	1 (0)	0 (0)	0 (0)
n. of joints with pain	13 (0)	13 (10)	0 (0)	0 (0)	0 (0)
DAS28	6 (0)	6 (6)	0 (0)	0 (0)	0 (0)
Imaging					
US inflammatory arthritis/tenosynovitis	3 (0)	1 (1)	2 (0)	0 (0)	0 (0)
US erosions	2 (0)	0 (0)	2 (0)	0 (0)	0 (0)
Muscle					
ClinRO					
MMT	2 (0)	2 (1)	0 (0)	0 (0)	0 (0)
MRC	1 (0)	1 (1)	0 (0)	0 (0)	0 (0)
PerfOM					
Isokinetic muscle strength (biodex)	1 (0)	1 (0)	0 (0)	0 (0)	0 (0)
6MWT	7 (0)	7 (4)	0 (0)	0 (0)	0 (0)
Biomarker					
Muscle enzymes	4 (0)	3 (2)	1 (0)	0 (0)	0 (0)
Skin					
ClinRO					
mRSS (only jSSc studies)	2 (2)	2 (2)	0 (0)	0 (0)	0 (0)
Imaging					
Doppler US	1 (0)	1 (0)	0 (0)	0 (0)	0 (0)
HFUS skin thickness	5 (0)	3 (2)	2 (2)	1 (1)	0 (0)
HFUS skin echogenicity	2 (0)	0 (0)	2 (1)	1 (1)	0 (0)
Shear wave elastography	1 (0)	0 (0)	1 (1)	1 (1)	0 (0)
PRO					
DLQI	1 (0)	1 (0)	0 (0)	0 (0)	0 (0)

6MWT: 6-minute walk test; CHFS: Cochin Hand Function Scale; ClinRO: clinician-reported outcome; DASH: Disabilities of the Arm, Shoulder and Hand; DAS28: Disease Activity Score in 28 joints; DHI: Duruoz Hand Index; DLQI: Dermatology Life Quality Index; FDA: U.S. Food and Drug Administration; HAI: Hand Anatomic Index; HAQ-DI: Health Assessment Questionnaire Disability Index; HAMIS: Hand Mobility in Scleroderma; jSSc: juvenile systemic sclerosis; LROM: limited range of motion; MHISS: Mouth Handicap in Systemic Sclerosis Scale; MMT: Manual Muscle Testing; MRC: Medical Research Council muscle strength scale; mRSS: modified Rodnan Skin Score; PerfOM: performance outcome; PRO: patient-reported outcome; PROMIS: Patient-Reported Outcomes Measurement Information System; SSc: systemic sclerosis; US: ultrasound; HFUS: high-frequency ultrasound.

Joint, bone and tendon domain

A total of 6 outcome measures were identified for the joint, bone, and tendon domain (Table II). Joint, bone, and tendon involvement was primarily assessed using clinical joint counts and composite disease activity measures. The most frequently reported ClinROs were the number of painful joints, the number of swollen joints, and the Disease Activity Score in 28 joints (DAS28). Among these, DAS28 demonstrated the strongest evidence of responsiveness, with significant improvement reported in all six interventional studies evaluating this measure. Significant improvement was also observed in the majority of studies assessing the number of painful joints (10/13) and swollen joints (7/9). US was the principal imaging modality and was used to evaluate inflammatory arthritis, tenosynovitis, and erosive changes, although imaging outcomes were reported considerably less frequently than clinical assessments. No MRI studies fulfilled the eligibility criteria, as none evaluated patients with SSc longitudinally at two or more time points.

Muscle domain

A total of five outcome measures were identified for the muscle domain (Table II), spanning ClinROs, PerfOMs, and biomarkers. The 6-minute walk test (6MWT) was the predominant outcome measure and the principal performance outcome, demonstrating significant improvement in four of the seven interventional studies evaluating this measure. Among biomarkers, serum muscle enzymes were most frequently assessed, showing significant improvement in two of the three interventional studies where they were evaluated. Finally, ClinROs, including manual muscle testing (MMT) and the Medical Research Council (MRC) muscle strength scale, were infrequently utilised, appearing in only one or two studies each.

Skin domain

A total of six outcome measures were identified for the skin domain across 8 studies, including two exclusively involving children with jSSc (Table II). According to the predefined eligibility criteria, the mRSS was only evaluated in children and demonstrated significant improvement in both interventional jSSc studies. Most of the ClinRO were imaging measures, with high-frequency US (HFUS) assessment of skin thickness being the most frequently reported, followed by HFUS skin echogenicity, Doppler US, and shear-wave elastography. HFUS assessment of skin thickness was the only imaging outcome evaluated in both interventional and observational longitudinal studies, demonstrating a significant change in four of the five studies assessing this measure. The Dermatology Life Quality Index (DLQI) was the only identified PRO and was evaluated in a single interventional study, in which no significant change was observed.

Discussion

This scoping review provides, to our knowledge, the first comprehensive overview of outcome measures used to assess cutaneous and musculoskeletal involvement in both aSSc and jSSc. Across 108 longitudinal studies, we identified 35 distinct outcome measures spanning ClinROs, PROs, PerfOMs, and biomarkers. Although this broad range of instruments reflects the complexity and multisystem nature of SSc, it also highlights substantial heterogeneity in outcome selection and evaluation across studies. Importantly, despite the clinical relevance of skin and musculoskeletal manifestations in jSSc, only two studies, including 13 children, met the eligibility criteria, indicating that current paediatric assessment remains almost entirely based on outcome measures developed and evaluated in adult populations. Beyond cataloguing available instruments, our review systematically summarised their use in interventional and longitudinal studies, including reported changes over time and following intervention, and associations with clinical manifestations. These data provide an evidence base to inform the selection of outcome measures for future clinical studies and support the ongoing IJOG initiative to develop evidence-informed core outcome measures for future jSSc clinical trials.

Hand involvement emerged as the most extensively investigated anatomical region in our review, being evaluated in more than half of the included studies, whereas mouth, joint/bone/tendon, muscle and skin outcomes were assessed less frequently. This distribution likely reflects the major impact of hand dysfunction on daily activities and quality of life in patients with SSc (S108, S109). Accordingly, the literature has progressively expanded beyond simple clinical examination to include objective measurements of hand mobility, strength, disability, and more recently imaging techniques capable of capturing different components of tissue involvement (S109, S110). Among the identified hand outcome measures, grip strength and CHFS/DHI were the most frequently reported ClinRO and PRO, respectively, and both frequently showed significant change following therapeutic interventions. The HAQ-DI was the most commonly used PRO for skin and musculoskeletal involvement, used in almost half of the studies of our review, with most of the identified studies evaluating a therapeutic intervention.

Our findings are consistent with recent international initiatives, including the HANDSOME project, which advocate a multidimensional assessment integrating functional performance, patient-reported disability, clinical examination, and advanced imaging to comprehensively characterise hand involvement in SSc (S109). Previous literature identified HAQ-DI as the best validated PRO for functional disability in SSc clinical trials and CHFS as the preferred PRO for hand disability, while recognising HAMIS and finger-to-palm measurements as valuable complementary tools for hand assessment (14, S111, S112). Nevertheless, our review highlights the considerable heterogeneity in hand outcome assessment, with a wide variety of instruments being used across longitudinal studies. Although HAQ-DI was the most frequently reported PRO, several other recommended measures, including CHFS and HAMIS, were used less consistently.

Oral involvement was the second most frequently investigated anatomical region in our review, although substantially fewer outcome measures were

identified compared with hand involvement. Assessment was primarily based on measurements of mouth opening, particularly interincisal and interlabial distance, while the MHISS was the only PRO identified. Both ClinRO of mouth opening and MHISS scores frequently showed significant change over time or following intervention, suggesting that these measures may be useful for monitoring longitudinal changes in oral involvement. Microstomia is one of the most disabling oral manifestations of SSc, substantially affecting oral hygiene, nutrition, speech, appearance and quality of life (S118-S120). However, oral involvement extends beyond reduced mouth opening to include xerostomia, temporomandibular dysfunction, periodontal disease, and perioral fibrosis (S118-S120). Despite this complexity, our findings indicate that longitudinal assessment remains largely focused on mouth opening, whereas the MHISS, the only instrument specifically designed to capture the broader functional impact of oral involvement, was evaluated in relatively few longitudinal studies. Recent studies further suggest that oral handicap reflects not only the severity of oral manifestations but also psychosocial burden, including anxiety, social appearance concerns, and reduced health-related quality of life, supporting the value of incorporating PRO into the assessment of oral involvement (S121). Notably, current paediatric consensus recommendations do not identify validated oral-specific outcome measures for jSSc, further emphasising the need to validate instruments capable of capturing both objective impairment and patient-perceived oral disability in children (17, 18).

Joint, bone and tendon involvement has been evaluated in relatively few longitudinal studies despite representing an important contributor to pain, functional limitation, and disability in patients with SSc (S122). Assessment relied predominantly on conventional clinical measures, including tender and swollen joint counts, whereas imaging modalities such as US were investigated in only a limited number of studies. The recent Hamburg international consensus for jSSc similarly identified active joint count as the preferred clinical outcome for musculoskeletal assessment in future therapeutic trials (18). Recent studies suggest that imaging techniques, particularly US and MRI, can detect synovitis, tenosynovitis, tendon fibrosis, and other inflammatory or structural abnormalities that may not be fully appreciated by clinical examination alone (S77, S123). Nevertheless, current evidence remains insufficient to support their routine use as outcome measures in clinical trials because of limited longitudinal data, variability in acquisition protocols, and the lack of standardised scoring systems (S122). This is also reflected in current adult points-to-consider for SSc clinical trials, which recognise the need for further validation and standardisation of imaging-based outcome measures before their routine incorporation into multicentre studies (13).These limitations are even more pronounced in children with jSSc, for whom longitudinal data on joint and tendon assessment remain entirely lacking.

Relatively few longitudinal studies have evaluated skin-specific outcome measures in our review. This finding should be interpreted in the context of our eligibility criteria, which excluded studies assessing the mRSS exclusively in adults because of the extensive evidence already supporting its use in aSSc, while retaining paediatric studies in which mRSS was evaluated (14, S113). The mRSS is currently regarded as the gold standard outcome measure for skin assessment in aSSc clinical trials, with well-established validity, reliability, and responsiveness, and an established minimal clinically important difference (MCID) for diffuse cutaneous SSc (S113).In our scoping review, only two studies, which included 13 children, evaluated skin involvement in jSSc, both using mRSS as the primary clinical assessment tool, underscoring its role as the current standard for paediatric skin assessment despite the lack of formal validation in this population (18). Moreover, validation in children is particularly important because physiological changes in skin thickness during growth, together with differences related to body mass index, sex, and pubertal development, influence normative skin thickness values, making interpretation and standardisation of the mRSS more challenging than in adults (S114). Current paediatric expert consensus similarly recommend the mRSS for skin assessment in jSSc, reflecting the absence of validated paediatric-specific alternatives rather than robust paediatric validation (17, 18). Importantly, unlike aSSc, neither the measurement properties nor the MCID of the mRSS have been established in children with jSSc, supporting our decision to specifically retain paediatric mRSS studies in this review. As the mRSS is already the most extensively validated and widely adopted clinical measure of skin fibrosis in aSSc, the remaining adult literature primarily focused on emerging imaging techniques aimed at providing more objective and quantitative assessment of skin involvement (4). Among imaging modalities, HFUS was the most frequently investigated technique, particularly for the assessment of skin thickness, whereas HFUS skin echogenicity, Doppler US and shear-wave elastography were evaluated less often. Overall, studies assessing skin thickness by HFUS most frequently reported significant change over time or following intervention, supporting the growing interest in quantitative imaging as a complementary tool for monitoring skin fibrosis. These findings are consistent with recent reviews and international consensus documents, which recognise HFUS as the most mature imaging technique currently available for skin assessment in SSc because of its reproducibility and correlation with clinical skin involvement (4, S115-S117). At the same time, these reports emphasise that methodological heterogeneity and the limited availability of longitudinal validation studies currently preclude its widespread adoption as a replacement for conventional clinical assessment (4, 115-S117).

Muscle involvement was infrequently investigated in our review. Assessment was predominantly based on the 6MWT, followed by serum muscle enzymes, and manual muscle testing. However, the limited number of avail-

Table III. Outcome measures to consider for jSSc evaluation in future clinical trials.

Tissue assessed	Measure	Parameter assessed	Pros	Cons
Skin	mRSS	Skin thickness	Does not require special equipment. Validated for adults with SSc.	Requires training to improve reliability. Not validated for jSSc. Need to account for normal developmental differences in paediatric skin thickness
	Elastography	Skin stiffness	Can provide quantitative values for tracking change. Non-invasive. Has been used in paediatric localised scleroderma [S127]	Requires US machine with appropriate software. Standards not established for paediatric conditions or jSSc.
Joint/bone/tendon	Standard JIA Joint count	Number of joints with limited range of motion (ROM), painful ROM, and swelling	Does not require special equipment. Validated for JIA	Sensitivity to change has not been evaluated for jSSc
	Imaging: Ultrasound and/or Magnetic resonance imaging	Joint and tendon inflammation *vs*. fibrosis. Joint effusion or tendon swelling, synovial thickening and enhancement	More sensitive than clinical exam. Can help differentiate arthritis from tenosynovitis *vs*. other pathology.	Requires special equipment. Training required for acquiring US images. MRI is expensive and sedation may be needed for the younger child.
Muscle	Manual Muscle Testing in 8 muscles (MMT-8) or the Childhood Myositis Assessment Scale (CMAS)	Muscle strength	Does not require special equipment. Validated for juvenile dermatomyositis	Requires training. Sensitivity to change has not been evaluated for jSSc [S128]
	Muscle enzymes: aldolase, CK, LDH	Muscle inflammation and/or breakdown	Available as standard laboratory tests	Sensitivity to change has not been evaluated for jSSc
	Magnetic resonance imaging	Muscle oedema, fibrosis	Can provide global assessment of muscle inflammation	Expensive, requires sedation in younger child. Reserve for patients with severe muscle involvement.
Hand	Delta finger to palm	Hand mobility	Quick, easy to perform, minimal equipment needed	Not validated for jSSc. Sensitivity to change has not been evaluated for jSSc
	mHAMIS	Hand mobility	Quick (2-5 minutes) and assesses more aspects of hand mobility than delta finger to palm	Requires 3 standardised cylinders. Has not been studied in patients <18 years old. Not validated for jSSc.
	Grip strength	Hand strength	Quick (5 minutes), has been studied in children (4-15 years old).	Need a calibrated, clinician-grade hand dynamometer. Only limited study has been done in jSSc.
Mouth	Interincisal diff	Mouth opening	Standard assessment for evaluating the TMJ in JIA	Not validated for jSSc. Sensitivity to change has not been evaluated for jSSc
Function overall	6-Minute Walk Test	Measures exercise capacity that reflects musculoskeletal and cardiopulmonary function	Does not require special equipment. Validated in paediatric pulmonary hypertension and used in juvenile dermatomyositis studies.	Distances walked need to be interpreted in comparison to reference values from healthy children of the same age, height, weight, and sex [S129]. These reference values also differ between countries. Findings are not specific for any single organ system.
	Childhood Health Assessment Questionnaire (CHAQ)	A PRO that measures a child's physical function in 8 domains and their health status.	Validated for children with juvenile idiopathic arthritis from 1-19 years old and has also been validated for juvenile dermatomyositis and childhood systemic lupus erythematosus. Available in multiple languages [S130].	Ceiling effect. Not validated for jSSc.
	PROMIS Physical function	Mobility Upper extremity, and pain interference	Available in paediatric self-report and proxy-report item banks; validated for other paediatric rheumatic diseases, CAT (computer adaptive testing) can minimise respondent burden while maintaining measurement precision, t-scores allow comparison with healthy children and other chronic diseases, excellent psychometric properties, available in multiple languages	Not disease- or organ-specific, not yet validated in jSSc, possible ceiling effect with mild disease, possible limited responsiveness in fibrotic disease

CHAQ: Childhood Health Assessment Questionnaire; CK: Creatine Kinase; CMAS: Childhood Myositis Assessment Scale; JIA: Juvenile Idiopathic Arthritis; jSSc: Juvenile Systemic Sclerosis; LDH: Lactate Dehydrogenase; mHAMIS: Modified Hand Mobility in Scleroderma; MMT-8: Manual Muscle Testing of 8 Muscle Groups; MRI: Magnetic Resonance Imaging; mRSS: Modified Rodnan Skin Score; PRO: Patient-Reported Outcome; ROM: Range of Motion; SSc: Systemic Sclerosis; TMJ: Temporomandibular Joint; US: Ultrasound.

able studies precludes firm conclusions regarding the most appropriate outcome measures for monitoring muscle involvement. Recent evidence suggests that conventional clinical and laboratory assessments may underestimate the extent of muscle involvement in SSc (S124, S125). Consistent with current points-to-consider for SSc clinical trials, our findings support the use of a multimodal assessment integrating muscle strength, laboratory biomarkers, imaging findings, and PROs, rather than reliance on any single outcome measure (13). Advanced imaging techniques, particularly MRI, have demonstrated the ability to detect inflammatory and structural muscle abnormalities, including oedema, fatty replacement, and fasciitis, which may not be fully reflected by muscle enzyme levels or clinical examination (S124). Notably, no MRI studies of muscle involvement met our inclusion criteria, as none assessed patients at two or more time points. This does not imply that MRI has not been studied in this context; rather, the available evidence is limited to cross-sectional or single-assessment observational studies that did not meet the longitudinal design required for inclusion in this review. Nevertheless, as highlighted by our findings and similarly to other disease domains, the lack of standardised imaging protocols and longitudinal validation studies currently limits the incorporation of these techniques into routine clinical trials (S125, S126).

This review has several strengths. To our knowledge, it represents the first comprehensive synthesis of outcome measures used to assess skin and musculoskeletal involvement across both aSSc and jSSc. In addition to cataloguing available instruments, we systematically summarised their application in longitudinal and interventional studies. By focusing on longitudinal assessments, we identified outcome measures that have been used to monitor disease progression or treatment response over time, providing information directly relevant to the design of future clinical studies. Importantly, our review also highlighted the limited evidence linking outcome measures to patient symptoms, with such associations being evaluated almost exclusively for selected hand outcome measures.

Different limitations should also be considered when interpreting our findings. First, as a scoping review, our objective was to map the available literature rather than critically appraise the measurement properties of individual instruments or determine their comparative performance. Second, the substantial heterogeneity of study designs, interventions, follow-up duration, and outcome reporting limited direct comparisons across studies. Third, only English-language publications were included, and conference abstracts were excluded, which may have resulted in omission of relevant or emerging evidence. Fourth, only longitudinal studies reporting outcome measures at two or more time points were included. Consequently, outcome measures evaluated exclusively in cross-sectional or single time-point observational studies were not captured, despite potentially having relevance for disease assessment. Fifth, this review focused on measures that we considered potentially applicable to jSSc, so existing measures that did not seem feasible for paediatrics were excluded. Reasons for exclusion included time required for evaluation, need for a specialised assessor, and the topics covered by questionnaires. We also did not include skin assessments such as the durometer and cutometer, because they require specialised equipment and were not considered feasible for jSSc at this time. In addition, adult studies evaluating the mRSS as the sole skin outcome were intentionally excluded to focus on complementary skin assessment tools and paediatric evidence; therefore, the distribution of skin outcome measures reported here should not be interpreted as reflecting their overall use in aSSc. Finally, the frequency with which an outcome measure appeared in the literature should not be equated with its measurement quality or clinical usefulness, as publication practices and historical preferences likely influenced the observed distribution.

Our findings emphasise that the current challenge in SSc is no longer the lack of available outcome measures, but rather the identification of standardised, feasible, and clinically meaningful instruments for each disease domain. In Table III, we list measures we suggest merit further consideration as potential outcome measures for jSSc. Several have been studied in paediatrics but not jSSc, while others need to be evaluated in the paediatric population.

This work represents the first phase of the IJOG initiative. Subsequent phases will combine the evidence generated by this review with international expert consensus and stakeholder input to establish core outcome measures for skin and musculoskeletal involvement in jSSc. Such standardisation will be essential to improve the design of future observational studies and clinical trials, facilitate comparisons across studies, and ultimately strengthen the evidence base for the treatment of children with this rare disease.

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