Domains and outcome measures for the assessment of digital vasculopathy and Raynaud's phenomenon in adult and juvenile systemic sclerosis: a scoping literature review

V. Maniscalco[1], N. Vasquez-Canizares[2], J. Lemon[3], L. Stead[4], V. Leone[5], K. Clarke[4], F. Zulian[6], S.C. Li[7], M. Twilt[8], A. Adrovic[9], S. Appenzeller[10], E. Marrani[1], M. Çakan[11], E. Del Giudice[12], M. Cattalini[13], F. Tirelli[6], L.A. Robinson[14], S. Sampath[15], G. Mastrangelo[6], G. Simonini[1], C.E. Pain[4,16], on behalf of the International Juvenile Systemic Sclerosis Outcome Group (IJOG) initiative, and the Childhood Arthritis and Rheumatology Research Alliance (CARRA) Scleroderma Working Group

Affiliations: see page 1651.

*Valerio Maniscalco, MD**
*Natalia Vasquez-Canizares, MD, MS**
Jennifer Lemon, BM, MSc
Lucy Stead, MBChb
Valentina Leone, MD
Katherine Clarke, MBChB, MSc
Francesco Zulian, MD
Suzanne C. Li, MD, PhD
Marinka Twilt, MD, MScE, PhD
Amra Adrovic, MD
Simone Appenzeller, MD, PhD
Edoardo Marrani, MD
Mustafa Çakan, MD
Emanuela Del Giudice, MD, PhD
Marco Cattalini, MD
Francesca Tirelli, MD, PhD
Lauren A. Robinson, MD
Sunil Sampath, MD, PhD
Greta Mastrangelo, MD
*Gabriele Simonini, MD***
*Clare E. Pain, MD, BMBS, BMedSci, MS***

**Contributed equally as co-first authors*
***Contributed equally as co-senior authors*

Please address correspondence to:
Clare Pain
Department of Women's and Children's Health, Institute of Life Course and Medical Sciences, University of Liverpool, L69 7ZX Liverpool, UK.
E-mail: clare.pain@alderhey.nhs.uk

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ABSTRACT

Objective. *Juvenile systemic sclerosis (jSSc) is a rare but severe paediatric rheumatic disease associated with substantial morbidity. Digital vasculopathy is nearly universal and includes Raynaud's phenomenon (RP), digital ulcers (DU) and critical ischaemia. Despite advances in adult systemic sclerosis (SSc), progress in jSSc remains limited. This scoping review aimed to identify outcome measures used to assess digital vasculopathy in SSc and jSSc to support core outcome set development for jSSc.*

Methods. *A scoping review was conducted following PRISMA-ScR guidelines. Medline, Embase, Web of Science, and CENTRAL were searched (1994–2024) for prospective studies reporting outcomes in digital vasculopathy domains (DU, RP, microvascular involvement, telangiectasia).*

Results. *Of 46,002 records, 108 studies were included; 105 (97.2%) involved adults only. Fifty distinct outcome measures were identified, including 35 clinician-reported outcomes (ClinROs) and 15 patient-reported outcomes (PROs). In the DU domain, 12 ClinROs and 5 PROs were identified, with ClinROs most frequently used as primary trial endpoints. In RP, 1 ClinRO and 9 PROs were identified; PROs predominated as primary outcomes. The microvascular domain included 16 ClinROs and no PROs, with instrumental measures used as primary endpoints. In telangiectasia, 6 ClinROs and 1 PRO were identified, rarely used in trials. Only three studies included paediatric patients, and no outcome measures were validated in children.*

Conclusion. *Outcome measures for digital vasculopathy in SSc are heterogeneous and derived almost entirely from adult studies, with no paediatric-specific validation. Transferability of these measures to children requires formal evaluation. These findings support the need for standardised, validated outcomes for jSSc and inform core outcome set development.*

Introduction

Although rare in childhood, juvenile systemic sclerosis (jSSc) is among the most severe paediatric rheumatic diseases with significant morbidity, impaired quality of life, and mortality (1-4).

Digital vasculopathy is nearly universal and often the first manifestation, typically presenting as Raynaud's phenomenon (RP), reported in up to 70-90% of paediatric cases (1, 3-6). It encompasses RP, digital ulcers (DU), digital pitting scars, nailfold capillary changes and critical ischaemia, representing a major source of disease burden (1, 3-6). Recurrent DU cause severe pain, functional impairment, and reduced quality of life (6, 7). In severe cases, progression to digital gangrene and amputation can occur (6, 7). Despite advances in adult SSc, including targeted therapies for RP and DU, no such trials have been conducted in jSSc, partly due to the lack of validated paediatric outcome measures (7-13).

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(SHARE) initiative developed consensus-based recommendations for the management of jSSc based on a literature review from 2013, focusing exclusively on paediatric studies and excluding adult SSc data (14). A subsequent multidisciplinary effort defined 22 outcomes for use in jSSc trials through consensus meetings. However, these recommendations are based on literature that has not been updated through a recent systematic review (15).

To address these critical gaps, the International Juvenile Systemic Sclerosis Outcome Group (IJOG) was established in collaboration with the Childhood Arthritis and Rheumatology Research Alliance (CARRA) and the Paediatric Rheumatology European Society (PRES). The primary objective of IJOG is to develop consensus outcome measures that are feasible, meaningful, and applicable for evaluating treatment response in jSSc clinical trials across diverse geographic regions and patient populations. The overall study protocol has been published previously (16). Briefly, the initiative includes a scoping literature review to identify outcome measures used across six major disease domains in adult and jSSc, followed by international surveys and Delphi-based consensus processes to evaluate the feasibility, relevance, and prioritisation of candidate measures. The goal is to establish a standardised core set of outcome measures for use in future multinational jSSc clinical trials. In this manuscript, we present the results of the digital vasculopathy domain review, focusing on outcome measures used to assess digital vasculopathy and RP in adult and juvenile SSc.

Methods

Scoping review search strategy

The IJOG study protocol including the scoping review strategy has been previously published (16). In summary, we followed the Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) guidelines (17, 18). The Pubmed, Embase, Web of Science, and Cochrane Central Register of Controlled Trials (CENTRAL) databases were searched with the assistance of a librarian from the Albert Einstein College of Medicine. An initial search was conducted in June 2021 and covered the literature published in English, between 1994 and 2021. An updated search was completed from June 2021 to November 2024.

References were subsequently imported to Covidence. The screening process and identification of relevant studies was planned in four principal steps: 1) Initial title and abstract screening, 2) Title and abstract screening by disease domain, 3) Full text screening by disease domain, and 4) Inclusion for data extraction by disease domain. A team of paediatric rheumatologists completed these steps with two reviewers at each step and a third reviewer resolving any conflicts.

Eligibility criteria

Original peer-reviewed research related to adult and jSSc reporting outcomes within predefined disease domains were included (described in previous publication) (16). Both adult and juvenile SSc studies were included because jSSc is a rare disease with few paediatric clinical trials, making adult SSc literature a reasonable source of candidate outcome measures given the shared pathophysiology. Here we focus on digital vasculopathy and RP domains. Eligible studies were required to be English, published from 1994 onwards and have an available abstract. Both observational and interventional designs were included, with minimum sample size thresholds of 3 paediatric or 10 adult SSc cases. Studies also had to include with prospective assessment of an outcome measure at two or more time points. Eligibility was further restricted to studies reporting outcome measures related to DU, microvascular involvement, RP, or telangiectasia. Reviews, metanalyses, case reports, and conference abstracts were excluded. Outcome measures related to large vessel disease were also excluded due to this being extremely uncommon in jSSc.

Data extraction and analysis

Following guidelines outlined by the Joanna Briggs Institute (18), members of the advisory group developed data extraction forms for the vasculopathy domain group. An initial Excel spreadsheet was drafted, encompassing main variables that addressed the specific research questions of the scoping review. Subsequently, a virtual meeting was conducted with the remaining international collaborators to gather input on the forms and identify other pertinent variables. Forms were pilot tested in Covidence by two members of the group (VM, CP) to assess the appropriateness of the data being collected. Multiple rounds of beta testing were conducted to ensure the feasibility of the forms, considering the extensive number of studies to be collected. Refinements of the forms were undertaken, with adjustments to the variables to accurately reflect the scope of the study, vascular manifestations, and the overall level of evidence available.

Data were analysed descriptively to summarise study characteristics. Outcome measures were classified based on U.S. Food and Drug Administration (FDA) typologies (19): clinician-reported outcomes (ClinRO; clinical signs evaluated by a professional), performance outcomes (PerfOM; standardised tasks administered or performed independently), and patient-reported outcomes (PRO; self-reported health status). The quality of evidence for each included study was classified according to the Oxford Centre for Evidence-Based Medicine (OCEBM) Levels of Evidence framework.

Results

Search results

The study selection process is summarised in Figure 1. The initial search (1994–2021), previously published (16), and the updated search (2021–2024) 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 digital vasculopathy and RP domains, and 443 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 [Supplemental Table S1, cited throughout the text as (S1-S108)].

Study characteristics

The characteristics of the included studies are provided in Table I, with two thirds of studies being observational and one third randomised controlled trials (RCTs). Based on the OCEBM classification, 39 studies (36.1%) were level 1b/1b–, 44 (40.7%) were level 2b/2b–, and 25 (23.1%) were level 4. Most studies included patients with both diffuse cutaneous (dcSSc) and limited cutaneous (lcSSc) subtypes. One hundred and five (97.2%) studies included only adult patients, whereas 3 studies (2.8%) included both paediatric and adult patients (S36, S62, S63). The number of paediatric patients included was not extractable.

Identified domains

The four pre-defined domains of digital vasculopathy were DU, RP, microvascular, and telangiectasia. These domains were reported in 72 (66.6%), 51 (47.2%), 42 (38.8%), and 4 (3.7%) studies, respectively. Several studies included more than one domain. Overall, 50 distinct outcomes were identified, including 35 ClinROs and 15 PROs. Of the ClinROs, 12 related to DU, 1 to RP, 16 to microvascular, and 6 to telangiectasia. Among the PROs, 5 were related to DU, 9 to RP, and 1 to telangiectasia, while no PROs were identified for the microvascular domain.

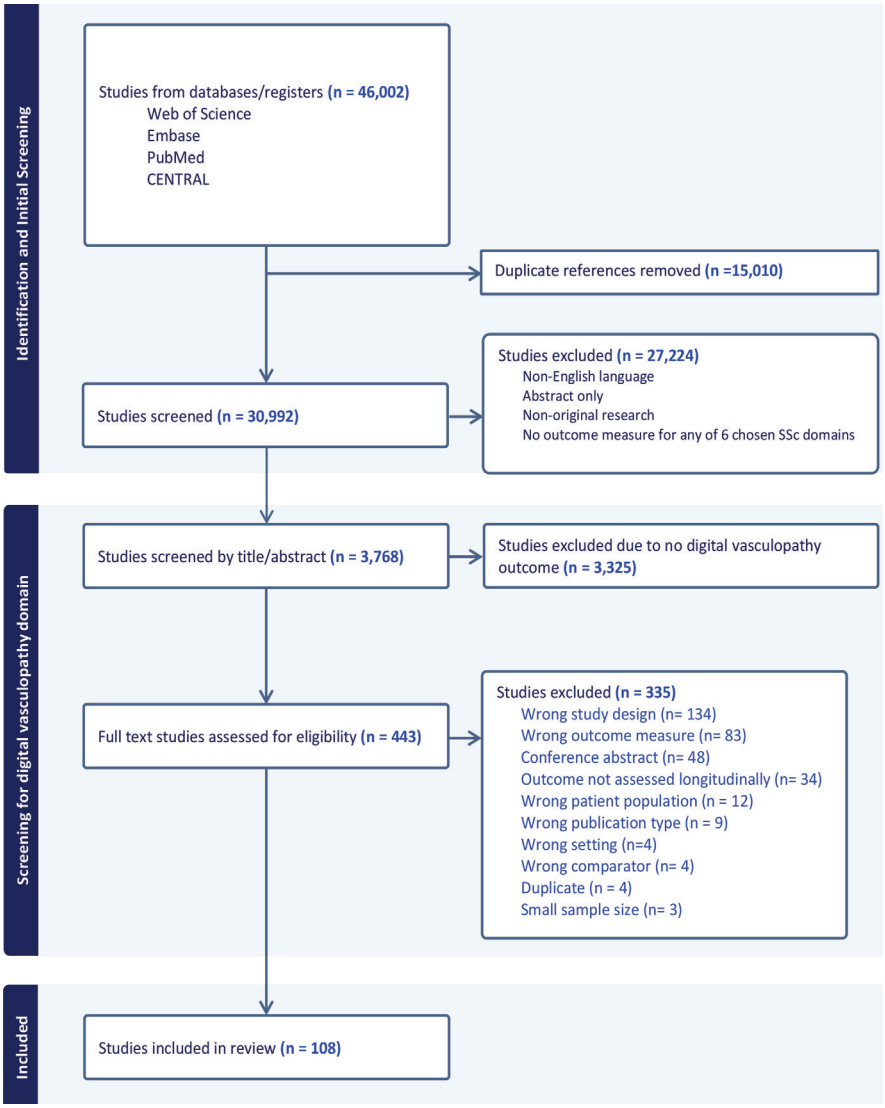

Fig. 1. PRISMA flow diagram.

Digital ulcers domain

Table II details the most frequently used outcome measures to assess the DU domain. DU were assessed in 72 studies, including 37 observational longitudinal studies, 28 RCTs, and 7 open-label or non-controlled interventional studies (S1, S4, S6-S8, S10, S12, S15, S16, S18-S23, S25, S26, S30-S38, S40-S46, S50-S54, S58, S60-S64, S66, S72-S74, S77-S94, S98, S99, S101, S104-S106). Overall, 7 outcome measures have been used as primary outcomes in interventional drug trials (17 RCTs, and 6 non-controlled interventional studies). Three studies included children (S36, S62, S63).

The number of new DU since the last visit, the number of active DU, and the presence of active DU were the most frequently used ClinRO measures. The number of new DU since the last visit was reported in 28 studies (38.8% of DU studies) and served as a primary outcome in 4 interventional trials. The number of active DU was assessed in 26 studies (36.1%), serving as a primary outcome in 6 trials. The presence of active DU was reported in 25 studies (34.7%) and also served as a primary endpoint.

Among PROs, DU pain VAS was reported in 20 studies and used as a primary endpoint in 2 clinical trials. The SHAQ-derived DU VAS appeared in 4 studies but was never adopted as a primary outcome. Notably, the Digital Ulcer Clinical Assessment Score (DUCAS), a composite ClinRO recommended for jSSc trials, was not identified in any included study.

Raynaud's phenomenon domain

The most frequently used outcome measures for the RP domain are detailed in Table III. RP-related outcomes were evaluated in 51 studies: 18 observational longitudinal studies, 28 RCTs, and 5 open-label or non-controlled interventional trials (S3, S9, S10, S14, S17-S19, S21, S26, S36, S38, S40-S42, S46-S48, S50-S52, S54, S55, S60, S61, S64, S65, S67, S68, S74, S75, S78, S82-S87, S89-S94, S100-S103, S105, S108). Overall, six outcome measures served as primary outcomes across these interventional trials (12 RCTs and 5 non-controlled studies), with one study specifically including children (S36). The leading PRO measures identified were the frequency/number of RP attacks, the dura-

Table I. Characteristics of the included studies (n=108).

Study type	Number of studies (%)
Observational longitudinal	61 (56.4%)
Randomised controlled trials	39 (36.1%)
Open label studies/non-randomised interventional	8 (7.4%)
Oxford level	
1b/1b-	39 (36.1%)
2b/2b-	44 (40.7%)
4	25 (23.1%)
Included populations	
Studies including dcSSc and lcSSc	102 (94.4%)
Studies including dcSSc only	1 (0.9%)
Studies including lcSSc only	5 (4.6%)
Children and adults	3 (2.7%)
Adults only	105 (97.2%)
Children only	0 (0%)
Single centre	72 (66.7%)
Multi-centre	36 (33.3%)

dcSSc: diffuse cutaneous systemic sclerosis; lcSSc: limited cutaneous systemic sclerosis.

tion of attacks, and the Raynaud's Condition Score. All three had been used as a primary outcome in an interventional trial. The frequency/number of RP attacks was reported in 32 studies (62.7% of RP studies), serving as a primary outcome in 9 interventional trials. Duration of RP attacks was assessed in 29 studies (56.9%), used as a primary endpoint in 7 trials. The Raynaud's Condition Score was reported in 25 studies (49.0%) and served as a primary outcome in 5 trials. The only ClinRo identified was the Physician Global Assessment of RP severity, which was reported in three studies including two controlled drug intervention trials (S46, S74, S84), but never utilised as a primary outcome.

Microvascular domain

Microvascular involvement was evaluated in 42 studies: 24 observational longitudinal studies, 14 RCTs, and four open-label or non-controlled interventional trials (S1, S2, S4, S6, S7, S9-S13, S16, S18, S22, S24, S25, S27, S29, S31, S39, S45, S49, S50, S56, S59, S66, S68-S71, S74, S77-S80, S90, S93, S95, S97, S101, S102, S104, S107). Table IV summarises the most frequently used outcome measures for the microvascular domain, including ClinRO measures of peripheral blood flow and capillaroscopic features. Four outcome measures were used as primary outcomes in eight interventional drug trials (six RCTs). One study included children (S63).

The most frequently used ClinRO measures of peripheral blood flow were Laser Doppler Imaging perfusion and cold challenge thermography, both of which served as primary outcomes in clinical trials. Laser Doppler Imaging perfusion was assessed in 15 studies (35.7% of microvascular studies) and served as a primary outcome in 4 trials. Cold challenge thermography was reported in 8 studies (19.0%), used as a primary endpoint in 1 trial. For capillaroscopic features, capillary density and change in scleroderma pattern were the most frequently assessed measures. Capillary density was evaluated in 10 studies (23.8%), including 7 drug intervention studies and four controlled studies, but was never used as a primary outcome. Change in scleroderma pattern was assessed in 6 studies; neither capillaroscopic measure was used as a primary outcome.

Table II. Outcome measures related to digital ulcer domain.

Outcome measure	Type of outcome measure	n. of studies (with children)	n. of studies with control group (comparison with control group)	n. of studies with intervention (response to intervention)	n. of trials using as primary outcome (RCT)
New DU since last visit	ClinRO	28 (2)	13 (13)	19 (19)	4 (3)
Number of active ulcers	ClinRO	26 (1)	12 (12)	22 (22)	6 (3)
Presence of active ulcer	ClinRO	25 (0)	8 (8)	17 (17)	1 (1)
Change in extent (area or depth) of ulcers	ClinRO	9 (0)	2 (2)	7 (7)	3 (0)
Time to healing ulcers	ClinRO	8 (0)	6 (6)	7 (7)	4 (3)
Healing ulcers	ClinRO	7 (0)	6 (6)	5 (5)	5 (5)
Number of healed ulcers	ClinRO	6 (1)	3 (3)	5 (5)	0 (0)
Change in DU appearance	ClinRO	2 (0)	0 (0)	2 (2)	0 (0)
Physicians VAS DU	ClinRO	2 (0)	2 (2)	2 (2)	0 (0)
Net ulcer burden	ClinRO	1 (0)	1 (1)	1 (1)	0 (0)
Acute digital ischaemia	ClinRO	2 (0)	1 (1)	2 (2)	0 (0)
Amputation	ClinRO	1 (0)	1 (1)	1 (1)	0 (0)
VAS DU pain	PRO	20 (0)	9 (9)	17 (17)	2 (1)
SHAQ-derived DU VAS	PRO	4 (1)	4 (4)	4 (4)	0 (0)
VAS DU global severity	PRO	2 (0)	0 (0)	0 (0)	0 (0)
Time to resolution of DU pain	PRO	1 (0)	1 (1)	1 (1)	0 (0)
Ulcer-healed ulcer VAS	PRO	1 (1)	0 (0)	1 (1)	0 (0)

ClinRO: clinician reported outcome; DU: digital ulcer; PRO: patient reported outcome; RCT: randomised controlled trial; SHAQ: Scleroderma Health Assessment Questionnaire; VAS: visual analogue scale.

Table III. Outcome measures related to Raynaud's phenomenon domain.

Outcome measure	Type of outcome measure	n. of studies (with children)	n. of studies with control group (comparison with control group)	n. of studies with intervention (response to intervention)	n. of trials using as primary outcome (RCT)
Frequency/number of RP attacks	PRO	32 (1)	18 (18)	25 (25)	9 (7)
Duration of RP attacks	PRO	29 (1)	17 (17)	23 (23)	7 (5)
Raynaud's condition score	PRO	25 (0)	17 (17)	20 (20)	5 (4)
VAS RP global severity	PRO	16 (1)	5 (5)	10 (10)	3 (2)
VAS RP attack pain	PRO	12 (0)	6 (6)	9 (9)	2 (1)
SHAQ-derived RP VAS	PRO	6 (1)	4 (4)	4 (4)	0 (0)
McCabe cold sensitivity score	PRO	2 (0)	1 (1)	1 (1)	0 (0)
Raynaud's condition score	PRO	2 (0)	0 (0)	2 (2)	2 (0)
Patient global opinion of RP symptoms	PRO	1 (0)	1 (1)	1 (1)	0 (0)
Physician global assessment of RP severity	ClinRO	3 (0)	2 (2)	2 (2)	0 (0)

ClinRO, clinician reported outcome; PRO, patient reported outcome; RCT, randomised controlled trial; RP, Raynaud's phenomenon; SHAQ, Scleroderma Health Assessment Questionnaire VAS, visual analogue scale.

Telangiectasia domain

Telangiectasia was assessed in four studies, including one observational longitudinal study, one RCT, and two non-controlled interventional studies (S5, S28, S96, S104). Table V summarises the most frequently used outcome measures to assess the telangiectasia domain. Overall, six ClinROs and one PRO were identified. Four outcome measures were used as primary outcomes in interventional drug trials (one RCT). The most frequently used ClinRO was observer opinion of telangiectasia, reported in 3 studies (75.0%), including 2 drug intervention studies, but it was never used as a primary outcome. Appearance assessment by clinical photography was assessed in 2 studies (50%) and served as primary outcome in 2 clinical trials. Laser Doppler imaging perfusion, thermography and telangiectasia count were each reported in 2 studies (50%) and each used as primary outcome in 1 study. Dermoscopy was evaluated in one study but was not used as primary outcome. Patient opinion was the only PRO measure identified, reported in two studies, both involving drug intervention, with one including a control group (S28, S96). It was assessed using subjective ratings of telangiectasia improvement, including a Likert-scale assessment in one study and a non-validated global assessment of perceived improvement and treatment preference in another (S28, S96). Patient opinion was not used as a primary outcome in interventional trials. No studies in this domain included paediatric patients.

Discussion

This scoping review provides a comprehensive overview of outcome measures used to assess digital vasculopathy and RP in adults and children with SSc. Across 108 included studies, 50 distinct outcome measures were identified spanning four domains: DU, RP, microvascular involvement, and telangiectasia. The most striking findings are the considerable heterogeneity of outcome measures across all domains and the notable paucity of data in the paediatric population. Despite the key role of vasculopathy in both adult and jSSc, currently available measures are largely derived from adult studies.

DU was the most frequently assessed domain (72 studies), with ClinROs predominating. The number of new DU since the last visit, the number of active DU, and the presence of active DU were the most commonly used measures and each served as primary endpoints in interventional trials. These findings are consistent with prior recommendations identifying active DU count as a key outcome measure for disease activity assessment in SSc clinical trials (21). PROs were widely reported but less often used as primary outcomes. DU pain VAS was the most frequently used and the only PRO adopted as a primary endpoint in interventional drug studies. In contrast, the SHAQ-derived VAS, despite being recommended by both the European Scleroderma Trials and Research group and the Hamburg consensus for jSSc trials (13, 15), was only rarely adopted in the literature. The DU-CAS, a composite ClinRO also recommended for jSSc trials, was not used in any of the included studies. This likely reflects both the recency of its preliminary validation in a cross-sectional design in 2019 (22) and the exclusion of studies without longitudinal assessment from our scoping review, underscoring the gap between consensus recommendations and actual adoption in clinical research. The World Scleroderma Foundation Digital Ulcer Ad Hoc Committee recently published points to consider for standardised DU reporting in interventional studies, identifying seven essential domains including uniform DU definitions, standardised outcome measures, and harmonised wound care protocols (23). Adoption of such frameworks may help reduce the heterogeneity identified in this review and improve cross-trial comparability.

In contrast to the DU domain, RP assessment relied predominantly on PRO measures. Frequency and duration of attacks, together with the Raynaud's Condition Score were the most used outcome measures and were frequently adopted as primary endpoints. This measure has established minimally important difference (MID) thresholds of 14-15 points on a 0–100 scale and a patient acceptable symptom state (PASS) of 34 points, providing anchors for interpreting treatment effects in clinical trials (24). However, RP global severity VAS, RP pain VAS, and the SHAQ-derived RP VAS were less commonly used, particularly as primary outcomes in clinical trials. Although SHAQ-de-

Table IV. Outcome measures related to microvascular domain.

Outcome measure	Type of outcome measure	n. of studies (with children)	n. of studies with control group (comparison with control group)	n. of studies with intervention (response to intervention)	n. of trials using as primary outcome (RCT)
Peripheral blood flow					
Laser Doppler Imaging perfusion	ClinRO	15 (0)	7 (7)	13 (13)	4 (3)
Cold challenge thermography	ClinRO	8 (0)	6 (6)	6 (6)	1 (1)
Finger temperature after cold challenge	ClinRO	5 (0)	4 (4)	5 (5)	2 (2)
Baseline Thermography	ClinRO	3 (0)	1 (1)	2 (2)	0 (0)
Flow mediated dilatation	ClinRO	2 (1)	0 (0)	1 (1)	0 (0)
^{99m}technetium tetrofosmin scintigraphy	ClinRO	1 (0)	1 (1)	1 (1)	0 (0)
Skin post-occlusive reactive hyperaemia test	ClinRO	1 (0)	1 (1)	1 (1)	1 (0)
Transcutaneous oxygen tension	ClinRO	1 (0)	1 (1)	1 (1)	0 (0)
Capillaroscopy					
Capillary density	ClinRO	10 (0)	4 (4)	7 (7)	0 (0)
Capillary dimension	ClinRO	4 (0)	2 (2)	3 (3)	0 (0)
Capillary morphology	ClinRO	5 (0)	2 (2)	3 (2)	0 (0)
Microhaemorrhages	ClinRO	5 (0)	2 (0)	2 (2)	0 (0)
Change of scleroderma pattern	ClinRO	6 (1)	1 (0)	1 (0)	0 (0)
Capillaroscopic skin ulcer risk index	ClinRO	3 (0)	0 (0)	0 (0)	0 (0)
Microangiopathy evolution score	ClinRO	2 (1)	0 (0)	0 (0)	0 (0)
NEMO score	ClinRO	1 (0)	0 (0)	0 (0)	0 (0)

ClinRO: clinician reported outcome; NEMO score: number of extravasated micro-haemorrhages and micro-thromboses; RCT: randomised controlled trial.

Table V. Outcome related to telangiectasia domain.

Outcome measure	Type of outcome measure	n. of studies (studies with children)	n. of studies with control group (comparison with control group)	n. of studies with intervention (response to intervention)	n. of trials using as primary outcome (RCT)
Observer opinion	ClinRO	3 (0)	1 (1)	2 (2)	0 (0)
Appearance assessment by clinical photography	ClinRO	2 (0)	1 (1)	2 (2)	2 (1)
Perfusion measured by laser Doppler imaging	ClinRO	2 (0)	1 (1)	2 (2)	1 (0)
Thermography	ClinRO	2 (0)	1 (1)	2 (2)	1 (0)
N° of telangiectasia	ClinRO	2 (0)	1 (1)	2 (2)	1 (0)
Dermoscopy	ClinRO	1 (0)	1 (1)	1 (1)	0 (0)
Patient opinion	PRO	2 (0)	1 (1)	2 (2)	0 (0)

ClinRO: clinician reported outcome; PRO: patient reported outcome; RCT: randomised controlled trial.

rived RP VAS has been validated as an outcome measure to assess digital vasculopathy and has been recommended for jSSc trials (10, 12), its limited adoption in the literature raises questions about its perceived utility among investigators. The OMERACT Vascular Disease in SSc Working Group has similarly identified broad variability in RP outcome domains across studies and is working to establish a core set of disease domains (21, 25). Additionally, the Assessment of Systemic Sclerosis-Associated Raynaud's Phenomenon (ASRAP) questionnaire, a recently developed PRO grounded in the lived patient experience of SSc-RP, has undergone psychometric calibration and may offer a more comprehensive assessment of RP burden than traditional diary-based approaches (26). Its potential applicability to the paediatric population warrants further investigation. The only ClinRO identified for RP was the Physician Global Assessment of RP severity, reported in three studies but never used as a primary outcome, highlighting the inherent challenge of clinician-based assessment of a symptom that is episodic and largely patient-experienced.

Microvascular involvement was mainly evaluated through objective techniques assessing peripheral blood flow and capillaroscopic features. Laser Doppler Imaging and cold challenge thermography were the most used measures of peripheral blood flow, and both served as primary outcomes in clinical trials. For capillaroscopic measures, capillary density was evaluated in 10 studies, including seven drug intervention studies, yet was never used as a primary endpoint. This relatively high frequency use despite non-adoption as a primary outcome suggests that the field recognises pathophysiological relevance of capillaroscopy measures but lacks sufficient validation to support their use as primary endpoints. This is consistent with current recommendations and likely reflects concerns regarding standardisation, feasibility, and operator dependency.

Telangiectasia was poorly represented, with only four studies and no standardised outcome measures, highlighting a largely neglected domain.

A major finding of this review is the heterogeneity of outcome measures across all domains. This variability may

contribute to inconsistent findings in clinical trials. An imbalance between outcome types was observed: DU measures were mainly clinician-reported, RP measures largely patient-reported, and microvascular involvement assessed using instrumental techniques. This limited integration across domains may hinder comprehensive evaluation of disease activity and treatment response.

The most critical finding of this review is the near-complete absence of paediatric data. Only three studies included children across 108 longitudinal and interventional records, and none reported paediatric-specific subgroup analyses. No outcome measures were specifically developed or validated for jSSc. This highlights a significant gap, as outcome measures derived from adult SSc are currently applied to children without adequate validation or adaptation, which may impact the design, feasibility, and interpretability of clinical trials in this rare population.

Despite this, several measures used in adult SSc may be transferable to children, although this assumption has not been formally tested. ClinROs commonly used for DU assessment, such as active DU count and new DU count, are based on clinical observation and may perform comparably in jSSc. Similarly, simple PROs such as VAS are widely accepted in paediatric rheumatology and have demonstrated feasibility in jSSc (4, 27). The Childhood Health Assessment Questionnaire (CHAQ), a validated paediatric tool, may also facilitate alignment with HAQ components of the SHAQ in studies spanning age groups. Performance of SHAQ-derived measures in jSSc warrants further evaluation and represents an important research priority.

Previous consensus efforts in jSSc have emphasised the importance of using standardised outcome measures where available (15). In this context, the DUCAS score has been proposed as a ClinRO for digital vasculopathy, alongside the SHAQ as a PRO. Notably, key components of DUCAS-such as the number of and new DU-were among the most frequently reported outcomes in this review. For RP, while the Raynaud's Condition Score has been considered, simpler measures such as the SHAQ-derived RP VAS may be preferable in children due to lower reporting burden, though their limited adoption in the adult literature warrants consideration.

Several limitations should be acknowledged. First, this scoping review was restricted to English-language publications, which may have excluded relevant studies published in other languages. Second, conference abstracts were excluded, potentially omitting emerging paediatric data that have not yet been published in full. Third, as a scoping review, the methodology prioritises breadth over depth and does not include formal risk-of-bias assessment or quality appraisal of individual studies, which limits the ability to draw conclusions about the comparative validity of specific outcome measures. Fourth, studies were required to report outcome measures assessed at two or more time points, as the primary aim was to identify measures capable of capturing disease progression or treatment response over time, a prerequisite for utility in clinical trials. This criterion may have excluded cross-sectional studies reporting potentially relevant outcome measures that have not yet been evaluated longitudinally. Finally, some outcome measures used in clinical practice may not appear in the published literature, meaning the findings described here may not fully reflect current clinical use, and the frequency with which measures were identified may instead reflect publication and reporting practices rather than their true validity, utility, or adoption in practice.

This work represents Phase 1 of the IJOG project. Subsequent phases will evaluate these outcomes through international surveys and Delphi-based consensus meetings, prioritising candidate measures based on feasibility, accessibility, and applicability across clinical settings rather than solely on whether a measure was used in paediatric-inclusive studies. The heterogeneity and inconsistent application of outcome measures for digital vasculopathy in SSc, particularly in children, underscore the urgent need for standardisation and validation. These findings provide a foundation for the development of a core outcome set within the IJOG initiative and highlight the critical importance of including paediatric-specific validation in future efforts.

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Affiliations

[1]Rheumatology Unit, ERN-ReCONNET Center, Meyer Children's Hospital IRCCS, Florence, Italy;
[2]Department of Pediatrics, Division of Pediatric Rheumatology, Children's Hospital at Montefiore/Albert Einstein College of Medicine, Bronx, NY, USA;
[3]Department of Development Paediatrics, Alder Hey Children's NHS Foundation Trust, Eaton Road, Liverpool, UK;
[4]Department of Rheumatology, Alder Hey Children's NHS Foundation Trust, Liverpool, UK;
[5]Department of Paediatrics, Istituto Mediterraneo per i Trapianti e Terapie ad Alta Specializzazione-IRCCS ISMETT, University of Pittsburgh Medical Centre (UPMC), Palermo, Italy;
[6]Division of Paediatric Rheumatology, Department of Women and Children Health, University of Padova, Italy;
[7]Hackensack Meridian School of Medicine, Joseph M. Sanzari Children's Hospital, Hackensack, NJ, USA;
[8]Department of Pediatrics, Alberta Children's Hospital, Cumming School of Medicine, University of Calgary, Alberta, Canada;
[9]Department of Paediatric Rheumatology, Marmara University Pendik Training and Research Hospital Istanbul, Turkey;
[10]Department of Orthopaedics, Rheumatology and Traumatology, Universidade Estadual de Campinas, Brazil;
[11]Zeynep Kamil Women and Children's Diseases Training and Research Hospital, Department of Paediatric Rheumatology, Istanbul, Turkey;

[12]Paediatrics and Neonatology Unit, Maternal-Child Department, Santa Maria Goretti Hospital, Sapienza University of Rome, Latina, Italy;
[13]Pediatrics Clinic University of Brescia and ASST Spedali Civili di Brescia, ERN-RITA Centre, Brescia, Italy;
[14]Division of Pediatric Rheumatology, Hospital for Special Surgery, New York, NY, USA;
[15]Department of Paediatric Rheumatology, Great North Children's Hospital, Newcastle upon Tyne NHS Foundation Trust, Newcastle-upon-Tyne, UK;
[16]Department of Women's and Children's Health, Institute of Life Course and Medical Sciences, University of Liverpool, UK.

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