Review

Outcome measures used to assess gastrointestinal tract involvement in adults and children with systemic sclerosis: a scoping review

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ABSTRACT

Objective. *The gastrointestinal (GI) tract is commonly affected in children and adults with systemic sclerosis (SSc) leading to substantial morbidity including malnutrition, growth failure, and poorer quality of life. We aimed to identify the GI measures used in SSc, describe their performance characteristics, and assess their applicability for use in juvenile-onset SSc (jSSc) trials.*

Methods. *We performed a scoping review of GI outcome measures in SSc studies from 1994-2024. Studies with at least one GI outcome measure were included, and test performance details were extracted.*

Results. *From the 159 studies identified, there were 25 outcome measures that assessed the oropharyngeal, oesophageal, gastric, small intestinal, colorectal, nutritional and/or patient-reported GI domains. The vast majority (150/159) were observational studies. The oesophagus was the most-studied segment of the GI tract (97/159). Oesophageal manometry was the most commonly reported measure (56 studies). While manometry consistently differentiated SSc from healthy controls, findings inconsistently correlated with GI symptoms. The University of California Los Angeles Scleroderma Clinical Trials Consortium Gastrointestinal Tract 2.0 questionnaire (UCLA GIT 2.0) was the most frequently reported patient-reported outcome (PRO) (34 studies). Very few measures were performed longitudinally or used to assess response to intervention, and only two studies had paediatric-specific outcome data.*

Conclusion. *We identified a wide array of outcome measures used to assess GI tract involvement in SSc with a paucity of longitudinal and paediatric data. Objective measures of GI tract function correlated poorly with symptoms and PROs, underscoring the need for both to be included in future trials.*

Introduction

Systemic sclerosis (SSc) is a complex autoimmune disease characterised by immune cell activation, vasculopathy, and fibroblast dysfunction impacting the skin and multiple internal organ systems (1). The gastrointestinal (GI) tract is the most frequently involved internal organ system, affecting up to 90% of adults with SSc and contributing to both the morbidity and mortality associated with this disease (2-4). Gastro-oesophageal involvement was recently found to be nearly ubiquitous in a French adult SSc cohort, and associated with poorer pulmonary function parameters, while a study of an Australian cohort identified gastroesophageal reflux and abdominal distension to be associated with poorer quality of life and depression (5). Juvenile-onset SSc (jSSc) represents a rare and serious paediatric rheumatic disease, with notable similarities and differences from adult-onset SSc. Although many jSSc features mirror those found in adults, major differences include auto-antibody profiles and disease subtype patterns, with a higher prevalence of diffuse cutaneous disease and overlap syndromes seen in children (6, 7). Furthermore, the study and care of patients with jSSc requires unique consideration regarding

the impact of disease on normal growth and development. In jSSc, GI tract involvement has been shown to have the strongest impact on poorer quality of life (QoL) of any organ system, and it is likely that GI involvement is directly related to the high incidence of severe malnutrition in this population (6). To date, there have been no treatments identified that modify GI disease progression in patients with SSc, and this remains an understudied and unmet need for both adults and children (3, 4, 8, 9).

Measurement of GI outcomes in SSc is challenging owing both to the widespread and heterogenous manifestations of the GI involvement, which spans from mouth to anus and is characterised by mucosal and structural changes, neuromuscular compromise and dysmotility, dysbiosis, and malnutrition (2, 10). To capture disease-related outcomes, a variety of radiographic, endoscopic and manometric modalities may be required in each GI segment. Adding to the challenges inherent to assessing GI involvement in SSc is the well-established discordance between symptoms and GI pathology (11, 12). Assessment of GI involvement in paediatric patients is further complicated by the lack of paediatric validation and age-appropriate norms for many established measures, as well as the heightened risks presented by the need for repeated sedations and cumulative radiation exposure in this population (13-15).

As part of a larger effort to develop consensus outcome measures for use in future jSSc international clinical trials, the International Juvenile Systemic Sclerosis Outcome Group (IJOG) was formed in collaboration with members of the Childhood Arthritis and Rheumatology Research Alliance (CARRA) and the Paediatric Rheumatology European Society (PRES) (15). In this paper we report on the findings of the GI scoping literature review of outcome measures used in SSc. We assess the performance of outcome measures used in SSc broadly with particular attention to the available evidence in children. We also determine the feasibility and appropriateness of these measures for paediatric use to inform consensus outcome development for use in future clinical trial design.

Methods

Scoping review search strategy

The initial phase of this scoping review sought to identify the extent of available data on outcome measures across 6 domains of SSc, and the methods for the multisystem portion of this scoping review have been published elsewhere (16). Briefly, in accordance with the Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) guidelines, 4 databases (PubMed, Embase, Web of Science, and Cochrane Central Register of Controlled Trials) were searched for the relevant literature published in English between 1994 and 2024, using both general and specific search terms. For this analysis, we focused on outcome measures specific to the GI tract.

The specific research questions for the scoping review were:

1. What outcome measures or instruments have been used to assess the GI tract in SSc?
2. How many of these measures/instruments have been used to evaluate the GI tract in jSSc?
3. If used in jSSc, how many of these measures/instruments have established age-appropriate definitions of normality?
4. What is the level of evidence for the outcome measures studied?
5. What is the level of change or sensitivity to change of the outcome measures?
6. How reliably do the outcome measures differentiate SSc from healthy controls (HC)?
7. How many of these measures/instruments have findings that correlate with GI symptoms in SSc?

Scoping review screening strategy

Identified references were imported into Covidence software for managing and tracking of the literature review process. Duplicate studies were identified and removed. After an initial title and abstract screening for relevance to SSc in all 6 domains by the larger multidisciplinary team, a second title and abstract screening was undertaken by the authors to identify studies reporting on outcome measures related to the GI tract. Finally, full text review was completed to determine inclusion for data extraction. The team involved in the GI-specific scoping review included 5 paediatric rheumatologists as well as a paediatric gastroenterologist and motility specialist. All steps of screening required two independent reviewers, with conflicts adjudicated by a third reviewer. Percent agreement for the title and abstract screening was 96.3% with a pooled Cohen's kappa of 0.78. Percent agreement for the full text screening was 94.8% with a pooled Cohen's kappa of 0.83.

Study inclusion criteria were English language, published between January 1994 and October 2024, included patients with SSc (minimum of 10 adult or 3 paediatric patients), and reported data for at least one outcome measure relating to the GI tract. Outcome measures were included if they met one of the following criteria: (a) routinely used in secondary and tertiary clinical settings for evaluation of GI tract structure and function; or (b) validated patient reported outcomes (PROs) specific to GI manifestations of SSc. Purely experimental or research modalities were excluded. A list of all excluded GI outcome measures with rationale for exclusion can be found in Supplementary Table S1. The following types of studies were allowed: observational cross-sectional or longitudinal studies, case-control studies, prospective cohort studies, randomised control trials (RCTs), non-RCTs, pragmatic treatment studies, and pre- and post (treatment) observational studies. Exclusion criteria were case series with fewer than the minimum number of SSc patients, non-human or non-clinical (basic science) studies, and those mainly focused on SSc-associated complications such as malignancy, cardiovascular risk, infection, osteoporosis, or sexual dysfunction.

Data extraction

A GI tract-specific data extraction form was developed following guidelines outlined by the Joanna Briggs Institute

(17). Multiple rounds of beta testing were conducted on the pilot form to ensure feasibility and reliability for capturing the relevant information. Data was extracted from each article into the extraction form in Covidence software by a primary reviewer, and the extracted data was subsequently checked for accuracy and completeness by a secondary reviewer. Multiple measures were extracted from each article where applicable.

For each outcome measure extracted, the following details were recorded and collated: whether the measure was used to assess response to intervention (*e.g.* treatment), evaluated longitudinally, compared between SSc and HC, or statistically correlated with GI symptoms. If the outcome measure was performed pre- and post- intervention or longitudinally, the change was considered significant if $p<0.05$ or if an established minimal clinically important difference for the test was achieved. Studies were considered longitudinal if the outcome measured was performed and recorded at least two different time points and did not include an intervention. If the outcome measure results for SSc were compared to those for HC or to GI symptoms, significance was defined as $p<0.05$. If significance was not reported, the comparison was assumed not to have reached significance.

Studies were assessed for potential cohort overlap using the following criteria: explicit naming of a shared registry or trial or cohort and/or identification of an institutional cohort with an overlapping enrolment period.

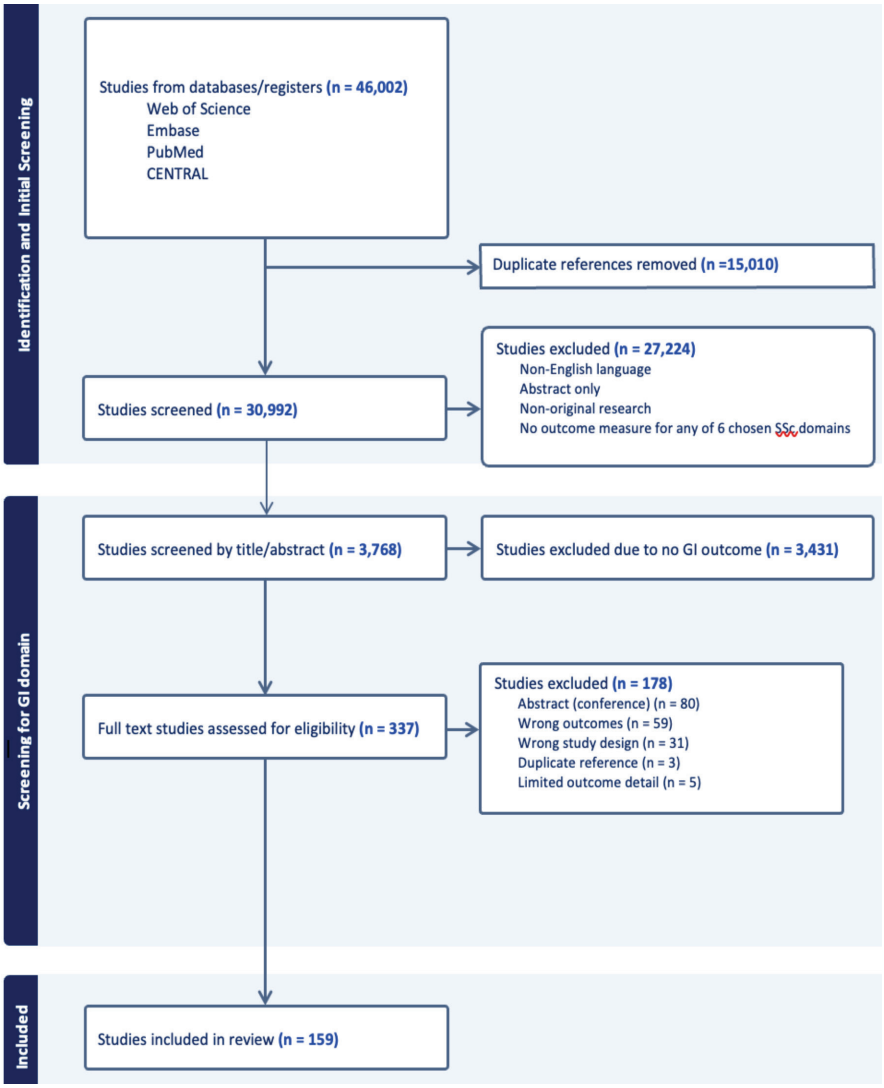

Fig. 1. PRISMA flowchart.

Results

Literature search

A total of 46,002 studies were screened, yielding 337 studies with GI outcome measures identified by title and abstract, of which 159 met inclusion criteria on full-text review and were extracted (Fig. 1). A list of all included studies can be found in Supplementary Table S2. According to the Oxford level of evidence system, of the 159 included studies, 2 (1.3%) were level 1, 61 (38.4%) were level 2, 31 (19.5%) were level 3, and 65 (40.9%) were level 4.

Of the 159 included studies, 72 were identified as potentially drawing patients from 23 overlapping cohorts, and therefore the studies included represent an estimated 110 independent patient populations. A list of all studies reporting on potentially overlapping cohorts can be found in Supplementary Table S3.

Study characteristics

Of the 159 included studies, the majority were observational (94.4%), and 4 (2.5%) were RCTs. The most commonly studied GI region was the oesophagus in 61.0% of the studies, followed by the stomach (18.9%) and colorectum (12.6%). Over one fifth (21.4%) of studies included the University of California Los Angeles Scleroderma Clinical Trials Consortium gastrointestinal tract 2.0 questionnaire (UCLA GIT 2.0) as an outcome. Very few studies (5.0%), included patients with jSSc, and notably only 2 (1.3%) were dedicated jSSc studies with paediatric-specific outcome data (Table I).

Oropharyngeal measures

The oropharynx was the least commonly assessed section of the GI tract, and none of the studies reporting on these measures included paediatric patients. Furthermore, none of the measures were studied longitudinally or in response to an intervention. Barium swallow was the only oropharyngeal measure for which a correlation with GI symptoms was assessed, and no studies demonstrated a significant correlation between this outcome measure and symptoms (Table II). Of note, measures assessing mouth opening

Table I. Characteristics of SSc studies on GI outcome measures from scoping review.

Study type	n. of studies (%)
Randomised controlled trials	4 (2.5%)
Non-randomised/controlled interventional studies	1 (0.6%)
Observational (total)	150 (94.3%)
- Case series	6
- Cohort	107
- Case-control	28
- Cross-sectional	9
Diagnostic test accuracy	4 (2.5%)
GI region/topic studied	**n (%)**
Oropharynx	4 (2.5%)
Oesophagus	97 (61.0%)
Stomach	30 (18.9%)
Small intestine	15 (9.4%)
Colorectum	20 (12.6%)
Nutrition	17 (10.7%)
GIT/QoL	34 (21.4%)
Inclusion of juvenile SSc Subjects	**n (%)**
Yes	8 (5.0%)
No	151 (95.0%)

*many studies included more than one GI region/topic, percentages will total >100%.
GIT: UCLA Scleroderma Clinical Trials Consortium Gastrointestinal Tract Instrument; QoL: quality of life.

were considered to reflect skin disease; they were therefore included under the skin domain of SSc and are not reported here.

Oesophageal measures

The most prevalent oesophageal measure used was oesophageal manometry (56 studies), followed by endoscopy (26 studies), and oesophageal scintigraphy (18 studies). Oesophageal manometry reliably differentiated SSc from HC, and in 2 of 4 interventional studies demonstrated statistically significant changes following treatment. Manometry findings demonstrated inconsistent correlation with symptoms (6 of 16 studies, 37.5%) (Table II).

Of the remaining oesophageal measures, scintigraphy, endoscopic evaluation of the oesophagus, and pH probe/pH impedance also demonstrated fairly consistent ability to differentiate between SSc and HC, whereas correlation of test findings with symptoms was poor. Very few oesophageal measures were studied over time or in response to intervention (Table II).

The oesophageal measures with paediatric-specific data were chest computed tomography (CT) (oesophageal diameter), oesophagram, and pH probe. Neither study with paediatric-specific data assessed these outcomes in response to intervention or longitudinally.

Gastric measures

Endoscopic evaluation of the stomach (11 studies) and gastric scintigraphy (9 studies) were the most frequently studied gastric measures in SSc, followed by antroduodenal manometry (7 studies). Very few studies assessed response to an intervention, and none reported longitudinal data. Antroduodenal manometry and gastric scintigraphy generally differentiated between SSc and HC; however, these outcomes demonstrated inconsistent correlations between test findings and GI symptoms. Very few studies reported on the ^{13}C Octanoic Acid and ^{13}C Acetate Breath Tests for gastric emptying. No studies reporting gastric outcome measures included paediatric patients (Table II).

Small intestinal measures

The lactulose breath test was used to assess orocecal transit time (OCTT) and/or small intestinal bacterial overgrowth (SIBO). In both contexts, though the total number of studies was low, the outcome successfully differentiated SSc from HC. However, these tests showed an inconsistent or absent correlation with symptoms. Glucose breath testing, used to evaluate for SIBO, notably failed to demonstrate a response to intervention in any of the three interventional studies, while also showing an inconsistent correlation with GI symptoms (Table II).

Colorectal measures

The most frequently reported colorectal outcome was anorectal manometry (14 studies), followed by colonic scintigraphy (3 studies). Both measures demonstrated ability to differentiate SSc from HC as well as significant correlation of the test findings with symptoms. No colorectal measures were assessed in response to intervention or longitudinally (Table II).

Nutritional measures

Body mass index (BMI) was the most commonly reported nutritional measure (24 studies) followed by the Malnutrition Universal Screening Tool (MUST) (8 studies), with very few studies reporting on weight or weight loss as an outcome measure. The MUST was not assessed in response to an intervention or longitudinally. No nutritional outcome measure demonstrated consistent ability to differentiate SSc from HC or consistent correlation with GI symptoms. Although rarely assessed, neither BMI nor weight demonstrated a response to an intervention or a significant change longitudinally. Finally, no studies evaluating nutritional outcomes included paediatric patients (Table II).

Patient-reported outcome

The UCLA GIT 2.0 was a commonly used measure (34 studies) and was the measure most often assessed in response to intervention and/or longitudinally. All studies that assessed responsiveness to intervention of the GIT 2.0 demonstrated significant change, and many demonstrated sensitivity to change over time (Table II). At the time of completion of this scoping review, the UCLA GIT 2.0 had not been validated in children, and no studies assessing this as an outcome measure included paediatric patients.

Table II. Use and performance of GI outcome measures in SSc.

Outcome measure	Studies (jSSc)	Intervention (change post intervention)	Longitudinal (change over time)	Control group (patient *vs*. control difference)	Symptom assessment* (correlation with symptoms)
Oropharyngeal					
Barium swallow	2 (0)	0	0	0	2 (0)
Videofluoroscopy (VFG)	3 (0)	0	0	1 (0)	0
Rhinolaryngoscopy/ laryngoscopy	2 (0)	0	0	0	0
Bedside swallow evaluation	1 (0)	0	0	0	0
Oesophageal					
Oesophageal manometry	56 (3)	4 (2)	0	11 (11)	16 (6)
Endoscopy (oesophagus)	26 (0)	2 (0)	0	4 (3)	9 (5)
Oesophageal scintigraphy	18 (3)	2 (0)	2 (2)	7 (6)	7 (3)
pH and/or pH impedance	13 (1)	1 (0)	0	3 (3)	1 (1)
HR Chest CT	15 (1)	2 (1†)	1 (1)	0	1 (0)
Fluoroscopic Oesophagram (UGI) or barium swallow	9 (1)	0	0	0	4 (1)
Functional lumen imaging probe (FLIP)	4 (0)	0	0	1 (1)	1(0)
Gastric					
Antroduodenal manometry	7 (0)	0	0	3 (3)	2 (0)
Endoscopy (stomach)	12 (0)	1 (0)	0	1 (1)	1 (0)
Gastric scintigraphy (gastric emptying study using scintigraphy)	9 (0)	1 (1)	0	2 (2)	5 (3)
^{13}C octanoic acid breath test	2 (0)	0	0	2 (1)	1 (1)
^{13}C acetate breath test	1 (0)	1 (1)	0	0	1 (0)
Small intestine					
Endoscopy (duodenum)	2 (0)	0	0	1 (1)	1 (0)
Lactulose breath test (SIBO)	3 (0)	0	0	1 (1)	1 (0)
Lactulose breath test (OCTT)	5 (0)	0	0	2 (2)	2 (1)
Glucose breath test	6 (0)	3 (0)	0	1 (1)	6 (3)
Colorectal					
Anorectal manometry	14 (1)	0	0	5 (5)	4 (4)
Colonic scintigraphy	3 (0)	0	0	1 (1)	2 (2)
Sitz marker study	1 (0)	0	0	0	1 (0)
Nutritional, BMI					
BMI	24 (0)	1 (0)	1 (0)	6 (2)	5 (3)
Weight	1 (0)	1 (0)	0	1 (0)	0
Weight loss	2 (0)	0	1 (0)	0	2 (1)
MUST	8 (0)	0	0	0	3 (1)
PRO					
UCLA GIT 2.0	34 (0)	8 (8)	9 (5)	0	NA

*sx comparison includes comparison to UCLA GIT 2.0.
† oesophageal diameter increased after intervention over several years, which may represent disease progression.
SIBO: small intestinal bacterial overgrowth; OCTT: orocecal transit time; BMI: body mass index; MUST: malnutritional universal screening tool; UCLA GIT 2.0: University of California Los Angeles Scleroderma Clinical Trials Consortium Gastrointestinal Tract 2.0 questionnaire.

GI outcome measures proposed for future clinical trials in SSc: characteristics and paediatric feasibility

Table III provides a comprehensive overview of 13 clinically available GI outcome measures we propose for use in future SSc clinical trials, organised by GI segment. For each measure, the clinical outcome assessment category, assessed symptom or pathology, tools required, advantages, disadvantages, and feasibility for use in children are summarised. Oropharyngeal measures were excluded given the paucity of evidence for their use in SSc. All outcomes are recommended for use in both adult and paediatric SSc trials with the exception of the MUST and colonic scintigraphy. BMI and weight are favoured as nutritional outcomes over the MUST in children due to its lack of validation in paediatrics and its inability to capture poor weight gain. Although BMI may not be sensitive for malnutrition in adults with SSc, it has been found to be predictive of severe lower segment GI disease and hospitalisation, and therefore likely remains a valuable metric (18, 19). Given the generally lower burden of colonic dysmotility in jSSc, the additional radiation exposure of colonic scintigraphy may not justify its use in this population.

Discussion

In this scoping review, we identified a broad array of outcome measures used to assess GI tract involvement in SSc. We categorised 25 measures by GI segment/domain, summarised their use and performance in SSc studies over the last two decades, and proposed GI outcome measures for use in future adult and paediatric SSc trials.

Table III. GI outcome measures proposed for use in future SSc trials.

GI region assessed	Outcome measure	Pathology assessed	Pros	Cons	Feasibility in children
Oesophagus	Fluoroscopic oesophagram	Oesophageal anatomy May assess oesophageal peristalsis and bolus clearance	No anaesthesia Non-invasive	Radiation exposure	Very feasible in children of all ages Paediatric-specific SSc data
Oesophagus	Functional Lumen Imaging Probe (FLIP)	Oesophageal function - Oesophageal contractility and distensibility, esophagogastric junction (EGJ) opening dynamics	Performed at time of EGD (one anaesthesia)	General Anaesthesia Instrumental	Feasible in children; easier to tolerate than manometry. Lack of standardised protocol and normative values in children
Oesophagus	High Resolution Oesophageal Manometry	Oesophageal function - evaluate for oesophageal motor disorder (*i.e.* oesophageal dysmotility)	Awake ± sedation/anaesthesia No radiation Standard for diagnosis of oesophageal motor disorder Metrics defined by the Chicago Classification, validated in adults Most studied GI measure in SSc	Instrumental Limited to centres with capability to perform oesophageal manometry	Feasible in children, but may be challenging in younger and more anxious patients Chicago Classification criteria widely adopted in children but not validated
Oesophagus	pH probe and pH-Impedance	Gastroesophageal reflux	Awake ± sedation/anaesthesia Symptom correlation with reflux events No radiation	Instrumental Requires catheter to stay for 24-hour ambulatory measurement	Feasible in children, but may not be tolerated by some children who are anxious or sensitive to intra-nasal catheter
Oesophagus/stomach/ small bowel	Oesophagogastroduodenoscopy (EGD, Endoscopy)	Anatomy (strictures, stenosis, hiatal hernia, etc.) and mucosa (infection, inflammation, allergy)	No radiation Can assess anatomy and mucosa of oesophagus, stomach and small intestine	Anaesthesia Instrumental	Feasible in children of all age groups Widely used modality in children to diagnose mucosal disease (esophagitis, gastritis, duodenitis, etc.) and do therapeutic interventions
Stomach	Gastric emptying scintigraphy	Gastric emptying	No anaesthesia Non-invasive	Heterogeneous protocols Radiation exposure	Feasible in children
Stomach	^{13}C spirulina, ^{13}C octanoic Acid, ^{13}C acetate breath tests	Gastric emptying	No anaesthesia Non-invasive	Confounded by lung disease	Very feasible for children Spirulina is FDA approved for children with normative data available for children 7-18 years of age
Small bowel	Glucose breath test, Lactulose breath test	Small intestinal bacterial overgrowth (SIBO)	No anaesthesia Non-instrumental Non-invasive	Confounded by lung disease, compliance to protocol prior to test, gastroparesis and delayed OCTT (false negative result) and rapid OCTT (false positive result) Decreased accuracy compared to endoscopic jejunal aspirate and culture (gold standard)	Feasible in children
Colorectal	Anorectal manometry	Anorectal function (including voluntary and involuntary properties)	Awake ± sedation/anaesthesia No radiation	Results dependent on patient cooperation Operator dependent Limited centres with availability	Feasible and validated in children
Colorectal	Colonic scintigraphy	Total and segmental colonic transit	No anaesthesia Non-invasive	Heterogenous protocols Radiation exposure	Feasible for children but limited availability Lack of normative values in paediatrics
Nutritional	MUST	Underweight and malnourished states, risk for development of malnutrition	Quick, simple tool, uses routinely collected clinical information Scores >=2 associated with higher mortality risk	Scores do not reflect specific part of GI tract Misses early malabsorption	Poor weight gain rather than weight loss likely a more relevant manifestation in children
Nutritional	Weight/BMI	Weight loss, underweight status, growth failure	Obtained in routine clinical practice	Limited sensitivity of BMI for malnutrition in adults with SSc	Feasible for children Obtained in routine clinical practice Well established age-specific z-scores
PRO	UCLA GIT 2.0	GI-specific symptom burden, impact on QoL	Extensively studied in SSc Validated in many languages and settings Sensitive to change	Poor correlation with pathology floor/ceiling effects	Highly feasible for jSSc Preliminary validation in a paediatric cohort

OCCT: orocecal transit time; BMI: body mass index; MUST: malnutritional universal screening tool; PRO: patient reported outcome; UCLA GIT 2.0: University of California Los Angeles Scleroderma Clinical Trials Consortium Gastrointestinal Tract 2.0 questionnaire.
Shaded rows indicate measures proposed for use in adult SSc trials only.

The oesophagus was the most represented GI segment, in keeping with the known high prevalence of oesophageal involvement in SSc (3, 9). Oesophageal manometry was by far the most frequently reported measure, though it was very rarely assessed in response to intervention or longitudinally, potentially due to the invasive nature of the test. The most validated instrument for use in SSc was the UCLA GIT 2.0, a 34-item questionnaire assessing the severity and impact of GI symptoms in patients with SSc over the preceding 7 days (20).

For all measures except the UCLA GIT 2.0, response to intervention was rarely assessed and infrequently demonstrated. It is important to note that lack of response of GI outcomes to an intervention may reflect a lack of treatment efficacy rather than the inability of the test to capture response. The vast majority of GI measures, with the exception of those specific to the colorectum, demonstrated inconsistent or poor correlation between test findings and GI symptoms. This suggests that relying on GI symptoms alone to guide diagnostic investigation or to serve as a therapeutic trial outcome is likely to miss significant pathology. Longitudinal assessment of many of these measures in SSc, particularly oesophageal manometry, is prudent to determine the natural history of GI disease and subsequently guide selection of appropriate trial targets. Our study highlights the need for interventional and longitudinal studies of the GI tract in SSc, especially those evaluating GI function rather than the UCLA GIT 2.0 alone given the poor correlation between symptoms and test findings.

Our findings additionally highlight the need for studies assessing GI outcomes in jSSc. Only two studies that met our inclusion criteria (Weber *et al*. 2000; Ambartsumyan et al 2019) had paediatric-specific data on three total measures (chest CT, oesophagram and pH probe), none of which were assessed longitudinally or in response to an intervention (21, 22). Utilising many of these identified GI measures in jSSc presents unique challenges, specifically regarding risk and tolerability/feasibility for invasive procedures like manometry, endoscopy, and pH probe testing. Scintigraphy represents a feasible option for measuring whole gut and segmental motility in paediatric patients; however, age-specific data and validation are lacking. Although the UCLA GIT 2.0 was created for use in adults and not assessed in children in the studies published during our search period, a recent study by Stefanic *et al*. validated this tool in a cohort of children with jSSc, finding acceptable validity and sensitivity to change (23). Thus, the UCLA GIT 2.0 may serve as an appropriate PRO measure in jSSc trials. Finally, because no studies assessing nutrition or growth in jSSc were identified, we highlight this as an urgent unmet need given the high prevalence of malnutrition in this patient population (6). As nutritional status uniquely impacts the growing child, it is imperative to study this aspect of disease in children and incorporate it robustly into future trial designs.

A key strength of this study is its comprehensive search strategy and rigorous screening and extraction process, representing the first formal review of the literature on GI outcomes for use in SSc. This approach ensured a broad capture of outcome measures across all GI segments, domains, and categories. Additionally, our multispecialty review group, comprising paediatric rheumatologists and a paediatric gastroenterologist, provided the expertise necessary to appraise these measures for relevance in jSSc and their feasibility for use in children. As a result, this review provides a practical, paediatric-specific framework to guide outcome selection for future jSSc trials.

A primary limitation of this review was the marked heterogeneity across included studies, which varied widely regarding patient characteristics, study designs, and the definitions and protocols used for each outcome measure. This heterogeneity limited our ability to directly compare individual measures and assess their performance. A further limitation was the paucity of paediatric-specific data, which hindered our ability to make evidence-based conclusions regarding outcome performance in jSSc. Additionally, while focusing on widely available clinical measures allowed us to target near-term trial design, this approach may have excluded emerging biomarkers or novel imaging techniques that could have relevance for future SSc research. Another limitation, typical of scoping reviews, is the lack of a critical appraisal of the studies or assessment of the risk of bias. Finally, cohort overlap analysis identified several centres with a high number of publications on overlapping cohorts, which leads to overrepresentation of certain patient populations and potential inflation of the volume of evidence for certain GI outcomes. Given these limitations, the conclusions of our study should be interpreted cautiously.

In summary, this scoping review identified a range of measures used to evaluate GI involvement in SSc. Although several of these outcome measures demonstrate pathology and differentiate SSc from HC, very few have been studied longitudinally or in response to an intervention, while most demonstrate poor correlation between GI symptoms and objective pathology. Given this discrepancy between symptoms and GI tract function, future SSc trials should include objective measures to adequately assess GI outcomes. This need is particularly urgent in jSSc where malnutrition is highly prevalent and uniquely impacts growth. Consequently, incorporating feasible, objective GI and nutritional measures into future jSSc trials is imperative.

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