Pediatric Rheumatology

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Developing consensus outcome measures in juvenile systemic sclerosis: a global survey of pediatric rheumatologists and literature review

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Abstract

Background Juvenile systemic sclerosis (JSSc) is a rare multisystemic disease with high morbidity and mortality rates. Treatment options remain limited, and there is a significant unmet need for effective therapies. This study aims to address this gap by investigating current JSSc management practices and identifying key outcome measures that can be used to inform the development of standardized assessment tools for future clinical trials.

Methods A web-based survey was distributed to pediatric rheumatologists to assess cardiopulmonary assessment standard of care practices and immunosuppressive treatment use in JSSc. Respondents were categorized by region (North America, Europe, Latin America, and Asia/Africa), and country income level. A scoping literature review was conducted using the PRISMA-SCR framework to identify outcome measures for six domains in SSc.

Results One hundred forty-one pediatric rheumatologists from 26 countries completed the survey. Significant variations in JSSc cardiopulmonary assessment practices across regions and income levels were noted. Respondents in North America and Europe reported using pulmonary function tests (PFTs) with diffusing capacity of the lungs for carbon monoxide (DLCO) more frequently than those in Latin America, or Asia/Africa ($p < 0.001$). The 6-min walk test (6MWT) was used less frequently by respondents in North America than other regions ($p = 0.004$). Use of oral corticosteroid and cyclophosphamide for treatment of JSSc varies significantly based on country income level, with higher usage in low- and middle-income nations. The scoping review identified 848 relevant articles for data extraction (ranging from 36 to 156 per domain) from a pool of 31,825 records, which were screened in multiple stages by 39 investigators.

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Conclusion We found significant variability in JSSc assessment and treatment preferences, influenced by geography and income. This highlights the urgent need for international collaboration and standardized approaches in JSSc care.

Keywords Juvenile systemic sclerosis, Juvenile scleroderma, Systemic sclerosis, Scleroderma, Assessment, Scoping review, Outcome measure, Survey, Consensus, Treatment

Background

Juvenile systemic sclerosis (JSSc) is a rare multisystemic disease characterized by vasculopathy, autoimmunity, and fibrosis. Care for patients with systemic sclerosis (SSc) is challenging given the multi-organ nature of the disease, paucity of options for treating fibrosis, and difficulty in finding effective treatments. For JSSc, disability occurs in over a third of affected individuals, and 5-year mortality rates range from 5–16% [1–6]. Adult SSc clinical management, contrasting JSSc care, has seen welcomed advances in evidence-based care owing to improved understanding of pathogenesis and advancements from clinical trials [7–13]. For JSSc, there is a notable scarcity of high-quality data, clinical trials, and a dearth of international consensus tools for assessment and management. Due to significant differences in clinical manifestations between JSSc and adult SSc, including disease subtype pattern and predominance, antibody profile, and mortality risk, as well as the need to consider the impact on normal growth and development [5, 6, 14], optimal care for JSSc requires tailored treatment trials. Therefore, standardization of outcome measures is paramount. Efforts to address this need have included the recently published proposed response parameters for a 12-month trial in JSSc from the Hamburg International Consensus Meetings [15]. While this is a critical step towards harmonizing research, the need remains for validation and broader application of these parameters in diverse clinical settings.

In 2021, the Single Hub and Access point for Pediatric Rheumatology in Europe (SHARE) initiative formulated consensus-based recommendations for the assessment and treatment of JSSc [16]. However, these recommendations were formulated by a consensus panel primarily representing countries in Europe and relied on a literature review (LR) that ended in 2014, overlooking more recent evidence. The LR was limited in that it focused on evidence of a few organ systems and was centered exclusively on outcome measures and treatments pertinent to JSSc. Omitting studies in adult SSc, where more robust scientific evidence exists, resulted in identifying articles that generally had a low level of evidence. This potentially limits our ability to formulate more comprehensive recommendations regarding outcome measures in JSSc to be applied in future treatment trials. While the 2022 Best Clinical Practice in the treatment of JSSc provides updated recommendations from the SHARE guidelines [17], it is still mainly derived from expert opinion underscoring the need for more robust, data-driven recommendations. Similarly, the panel was predominantly composed of experts from Europe and the U.S, potentially limiting the generalizability of the recommendations to other contexts.

In response to these critical gaps, the international juvenile systemic sclerosis outcome group (IJOG) in collaboration with members of the Childhood Arthritis and Rheumatology Alliance (CARRA) and the Pediatric Rheumatology European Society (PRES), was created to work towards the development of consensus outcome measures and standards for assessment of JSSc to be used in future treatment studies. The IJOG study aims to ensure the usability and feasibility of these measures across diverse geographic and demographic populations. The IJOG study is led by a core advisory group of 3 CARRA and 2 PRES members with expertise in JSSc and has 4 phases (Fig. 1). The first phase is a scoping LR to identify outcome measures used to assess six disease domains (skin/musculoskeletal [MSK], pulmonary, cardiac, digital vasculopathy (including digital ulcers and Raynaud's phenomenon), gastrointestinal [GI], and health related quality of life [HRQoL]) in adult and JSSc, and the scores or change in scores considered to signal a significant change. The second and third phases will focus on assessing the usability and feasibility of the identified measures for each of the six domains through country-specific surveys about these measures. In the fourth phase, consensus meetings will be held to review the data from the scoping LR and surveys. Delphi method will be used to generate a core set of consensus outcome measures and standards for the six disease domains.

To further inform the initial stages of the IJOG study and to gain a preliminary understanding of current practices, the advisory group conducted a preliminary survey focused on current JSSc cardiopulmonary assessment and immunosuppressive treatment practices among pediatric rheumatologists worldwide. This survey aimed to identify potential participants for the IJOG study and gather preliminary data to support the development of consensus outcome measures intended to be feasible for assessing JSSc in treatment trials across diverse geographic and demographic populations. This manuscript presents the preliminary survey results, examining

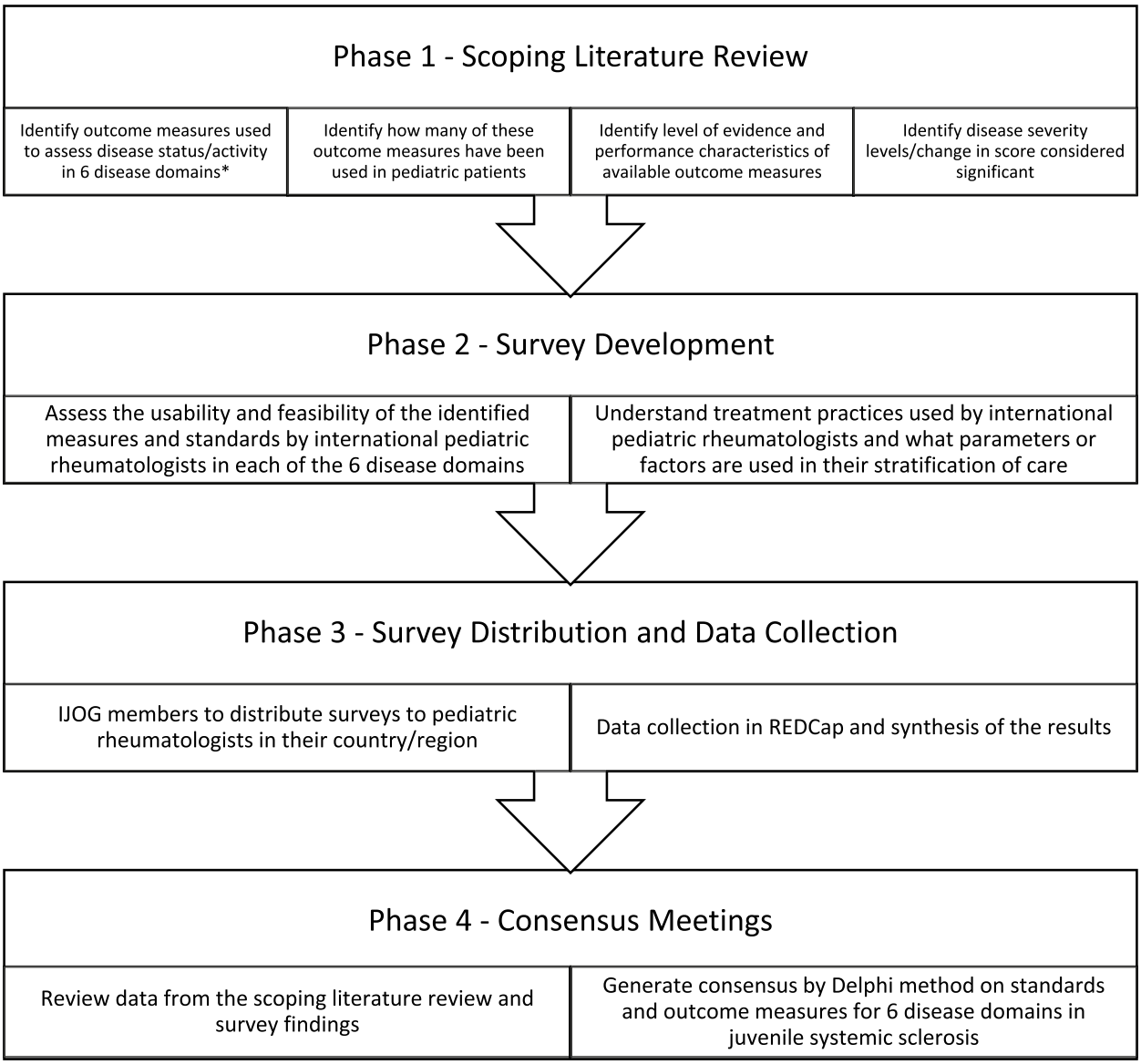

Fig. 1 Overview of the study protocol. *Skin/musculoskeletal, pulmonary, cardiac, digital vasculopathy (including digital ulcers and Raynaud's phenomenon), gastrointestinal, and health-related quality of life. Abbreviations: REDCap = Research Electronic Data Capture

factors associated with practice variation that will further support the IJOG initiative, and the protocol for the scoping literature review (phase 1).

Methods

Preliminary survey

In May 2021, Pediatric rheumatologists from CARRA ($n=348$) and PRES ($n=156$) were invited to participate in a web-based questionnaire (Survey Monkey) aimed to evaluate preferences for cardiopulmonary disease assessment and immunosuppressive treatments in JSSc, and to identify members interested in collaborating on the IJOG study.

Survey questions included consent to participate in the survey, respondent demographics, number of JSSc patients followed, proportion of JSSc patients with lung and cardiac involvement, tools used for cardiopulmonary assessment, and usual immunosuppressive treatment strategies (Additional file 1). Among a list of cardiopulmonary tools, respondents were asked to rank their importance on a 1–5 scale (1 = most important), and how frequently they used each of these tools for patient evaluation: always = 80–100% of the time,

often = 50–79%, sometimes = 20–49%, rarely = 1–19%, or never/not available. Different items could be given the same ranking value. Respondents were similarly asked to indicate how frequently they used different immunosuppressive treatments.

Respondents were categorized into four regions (North America, Europe, Latin America, and Asia and Africa), considering factors such as physical proximity, language, cultural similarities, and practice patterns of their country of origin. Asia and Africa were grouped together due to a small sample size. Additionally, respondents were classified into three levels of country income: low = < $20,000 international dollars (INT), mid = $20,000–49,000 INT, and high = > $50,000 INT] based on their country's Gross Domestic Product (GDP) per capita, using the same categories as were used in a study on lupus [18]. The GDP per capita was defined as the value of all final goods and services produced within a country divided by the average number of people in its population based upon the data from the 2021 International Monetary Fund [19].

Statistical analysis

Descriptive statistics were used to summarize each variable as mean and standard deviation for normally distributed continuous variables, median and interquartile range (IQR) for non-normally distributed continuous variables, and frequencies and percentages for categorical variables. To investigate factors contributing to practice variation among respondents, we explored bivariate associations between the frequency of use and the types of assessments and treatments stratified by region, GDP per capita, years of practice, and the number of patients followed. Fellows and other practitioners were excluded from these analyses. After checking assumptions of all statistical tests, non-parametric testing was performed using the Kruskal Wallis test for continuous independent variables and the Fisher's exact test for categorical independent variables. Two-tailed alpha of 0.05 was used to determine statistical significance. Statistical analysis was performed using Stata/IC software, version 15.1.

Scoping review searching strategy

In accordance with the Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) guidelines [20], we conducted a scoping LR to examine the extent, range, and nature of available data in outcome measures for organ system assessment in pediatric- and adult-onset SSc.

The specific research questions for the scoping review were:

1. What outcome measures or instruments have been used to assess disease status, with a focus on disease activity, in SSc?
2. How many of these measures/instruments have been used to evaluate JSSc?
3. If used in JSSc, do these instruments or outcome measures use 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?

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. All searches were conducted in June 2021 and covered the literature published in English, between 1994 and 2021. A search hedge from the Cochrane Highly Sensitive Search Strategy for identifying randomized trials was adapted to include observational and cohort studies. General search terms included scleroderma, systemic scleroderma, systemic sclerosis, juvenile scleroderma, treatment, therapy, randomized control trial, cross-sectional studies, case control studies, and observational studies. The specific search terms for the 4 databases are further detailed in the appendix (Additional file 2).

Scoping review screening strategy

After the initial search, references were imported to Covidence software to facilitate managing and tracking the LR. 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 multidisciplinary team of pediatric specialists conducted a rigorous LR process. The team included pediatric rheumatologists, fellows, and pediatric subspecialists in various fields (pulmonology, cardiology and gastroenterology), and articles were screened in multiple stages ensuring reliability through a voting system and conflict resolution process.

Scoping review eligibility criteria

Original peer-reviewed articles related to pediatric and/or adult SSc that included a measure from 1 of the 6 domains of interest were selected. Inclusion criteria included that the article was in English, published after 1993, had an abstract, included patients with SSc, included at least one SSc outcome measure, and if a case series, had a minimum of 3 pediatric or 10 adult SSc

cases. The following types of studies were allowed: observational cross-sectional or longitudinal studies, case–control studies, prospective cohort studies, randomized control trials (RCTs), non-RCTs, pragmatic treatment studies, and pre- and post (treatment) observational studies. Exclusion criteria included case series that had fewer than the minimum number of SSc patients, narrative reviews, conference abstracts, comments, editorials, lectures, non-Human (animal or lab), non-clinical (basic science), or those mainly focused on SSc-associated complications such as malignancy, cardiovascular risk, infection, osteoporosis, or sexual dysfunction.

Eligibility criteria was furthered refined in the 2nd and 3rd steps of the LR to include original studies only (no systematic reviews or meta-analysis), studies with detailed information on outcome measures relevant to each of the organ-focused groups, and for most groups, that the measure was assessed at 2 or more time points to enable evaluation of change over time. A study could be included in more than one group if it involved an outcome measure relevant to multiple organ-systems. Studies focused on identifying novel biomarkers that were not commercially available were excluded as we were focused on identifying feasible outcome measures for an international JSSc treatment trial. Measures for renal and neurological involvement were also excluded because of the rarity of these manifestations in the pediatric population [6].

Plan for data extraction

Following guidelines outlined by the Joanna Briggs Institute [21], members of the advisory group in collaboration with the respective pediatric subspecialists, developed data extraction forms for each domain group. A virtual meeting was conducted with the entire IJOG group to solicit feedback on the forms. Multiple rounds of beta testing were conducted on the pilot forms to ensure their feasibility and ability to capture relevant information for each domain and article.

The IJOG study was approved by the Albert Einstein College of Medicine Institutional Review Board.

Results

Preliminary survey results

Respondent characteristics

The survey was completed by 141 members from 26 countries with a response rate of 25% and 35% for CARRA and PRES members, respectively. Respondents were from North America (60.3%), Europe (22%), South America (6.4%), Asia (6.4%), Central America (3.5%), and Africa (1.4%). Most respondents were pediatric rheumatology physicians (79.4%), followed by fellows in training (11.4%) and other healthcare providers (9.2%). The latter group comprised full-time researchers, retired pediatric rheumatologists, professors, physicians in both pediatric and adult rheumatology, and advanced practice registered nurses (Table 1).

A total of 649 JSSc patients were reported to be followed internationally, with median 3.5 (IQR 2; 7) patients followed per center, and 3 (IQR 2; 6) per respondent over the past 5 years. A significant difference was observed in the median number of patients followed per respondent in the last 5 years based on region ($p=0.005$) and GDP per capita ($p<0.001$). The median number of patients per respondent was higher in Africa and Asia, and in low-income countries, compared to other regions and higher-income nations.

Cardiopulmonary assessment tools

Diffusing capacity of the lungs for carbon monoxide (DLCO) was rated the most important pulmonary function test (PFT) assessment for evaluating lung status/progression by 75% of respondents, followed by forced vital capacity (FVC), and total lung capacity (TLC) in 27% and 20% of respondents, respectively. Echocardiogram was rated the most important tool for evaluating cardiac status/progression in JSSc by 77% of respondents, followed by electrocardiogram (EKG), cardiac magnetic resonance imaging (MRI), and cardiac Holter monitoring in 29%, 9%, and 5% of respondents, respectively. Most respondents indicated they always use chest X-ray (67.7%), chest high-resolution computed tomography [HRCT] (54%), full PFTs [including spirometry, lung volumes and DLCO] (76.8%), EKG (62.7%), and echocardiogram (81.8%) for cardiopulmonary assessment of their JSSc patients. Tools that were never used or not available for respondents included cardiac MRI (37%), cardiac magnetic resonance angiography [MRA] (55%), and cardiac catheterization (56.5%) (Additional file 3).

Significant differences were observed in the use of different cardiopulmonary assessment tools for monitoring JSSc patients both by region and GDP per capita (Fig. 2 & Additional file 3). Respondents in North America and Europe consistently reported a higher proportion of "always using" full PFTs compared to their counterparts in Latin America, or Asia/Africa (89% and 80% vs. 22% and 45%, respectively; $p<0.001$). The 6-min walk test (6MWT) was used less frequently by respondents in North America than other regions ($p=0.004$), while cardiac MRA showed an overall low frequency of use among all respondents, with even less usage in North America, and Africa/Asia ($p=0.01$).

Significant differences were noted in the frequency of using full PFTs ($p<0.001$), 6MWT ($p=0.05$), Holter monitoring ($p=0.001$), and cardiac stress tests ($p=0.003$) based on GDP per capita (Fig. 2 & Additional file 3).

Table 1 Characteristics of respondents by region and GDP Per Capita

		Region				GDP Per Capita ($INT)		
	Overall (*n* = 141) n (%)	**Asia & Africa (*n* = 11)**	**Latin America (*n* = 14)**	**Europe (*n* = 31)**	**North America (*n* = 85)**	**< 20 k (*n* = 28)**	**20 k-49 k (*n* = 22)**	**> 50 k (*n* = 99)**
Professional Background								
Pediatric Rheumatologist	112 (79.4)	11 (100)	11 (78.6)	26 (83.9)	64 (75.3)	23 (82.1)	19 (86.4)	70 (76.9)
Fellow in training	16 (11.4)	0 (0)	0 (0)	3 (9.7)	13 (15.3)	2 (7.1)	1 (4.5)	13 (14.3)
Other[a]	13 (9.2)	0 (0)	3 (21.4)	2 (6.4)	8 (9.4)	3 (10.8)	2 (9.1)	8 (8.8)
Years in Practice (*n* = 109) [b]								
1–5	18 (16.5)	1 (10)	0 (0)	1 (3.8)	16 (25.4)	1 (4.8)	1 (5.3)	16 (23.2)
6–10	22 (20.2)	1 (10)	3 (30)	4 (15.4)	14 (22.2)	4 (19)	4 (21.1)	14 (20.3)
11–15	19 (17.4)	1 (10)	1 (10)	8 (30.8)	9 (14.3)	2 (9.5)	7 (36.8)	10 (14.5)
> 15	50 (45.9)	7 (70)	6 (60)	13 (50)	24 (38.1)	14 (66.7)	7 (36.8)	29 (42)
Patients Followed [b]								
Per center, current (*n* = 106)	3.5 [2; 7]	5 [2;15]	3.5 [1;10]	4 [3; 6]	3 [1; 5]	6.5 [2; 20]	4 [3; 5]	3 [1;5]
Per provider, last 5 years (*n* = 111)	3 [2; 6]	5 [2;20]	4.5 [2;15]	4 [3; 8]	2.5 [1;5] *	7 [4; 15]	4 [3; 5]	2.5 [1;5] **

Abbreviations: *GDP* gross domestic product, *INT* international dollars

* $p < 0.01$

** $p < 0.001$

[a] Full-time researchers, retired pediatric rheumatologists, professors, physicians in both pediatric and adult rheumatology, and advanced practice registered nurses

[b] Analysis excludes "Fellow in training" and "Other"

Respondents in mid- and high-income countries consistently reported a higher proportion of using full PFTs for monitoring JSSc patients compared to their counterparts in low-income countries. The 6MWT and Holter monitoring were used less frequently overall, but respondents in low-income countries reported using these tools in higher proportions compared to other income-level nations.

Immunosuppressive treatments

The most frequent immunosuppressive medications respondents reported "always using" included oral steroids (46.7%), methotrexate (MTX) (37%), and mycophenolate mofetil (MMF) (29.3%) (Additional file 4). When stratified by patient volume (number of patients followed per respondent) and GDP per capita, statistically significant differences were seen in the frequency of using different immunosuppressive medications (Fig. 2 & Additional file 4). Respondents with a patient volume of 11 or more reported "always using" MTX more frequently than those with a lower patient volume ($p = 0.04$). Conventional disease modifying anti-rheumatic drugs (cDMARDs) and corticosteroids were used more frequently across all groups compared to biologics. While no significant difference was observed for the frequency of using rituximab and abatacept, tocilizumab was used more frequently by respondents following ≥ 11 patients compared to those following fewer patients ($p = 0.02$).

Significant differences were also found in the frequency of oral corticosteroids ($p < 0.001$) and cyclophosphamide ($p = 0.008$) treatments based on GDP per capita. Respondents in low- and mid-income countries reported a higher proportion of 'always using' oral corticosteroids compared to those in high-income countries. Respondents in low-income countries also reported using cyclophosphamide more frequently than those in other income-level nations for the treatment of their JSSc patients.

Scoping review results

The search term list was finalized in June 2021, and 31,825 records were uploaded to Covidence (Fig. 3). After removing duplicates, 24,849 references remained for initial screening. From title and abstract screening by 34 investigators, 3,285 records were retained for screening by each of the six domain groups. From this screening by 39 investigators, between 239 to 620 references were identified for full-text screening and the subsequent groups identified between 36 to 156 articles for data extraction.

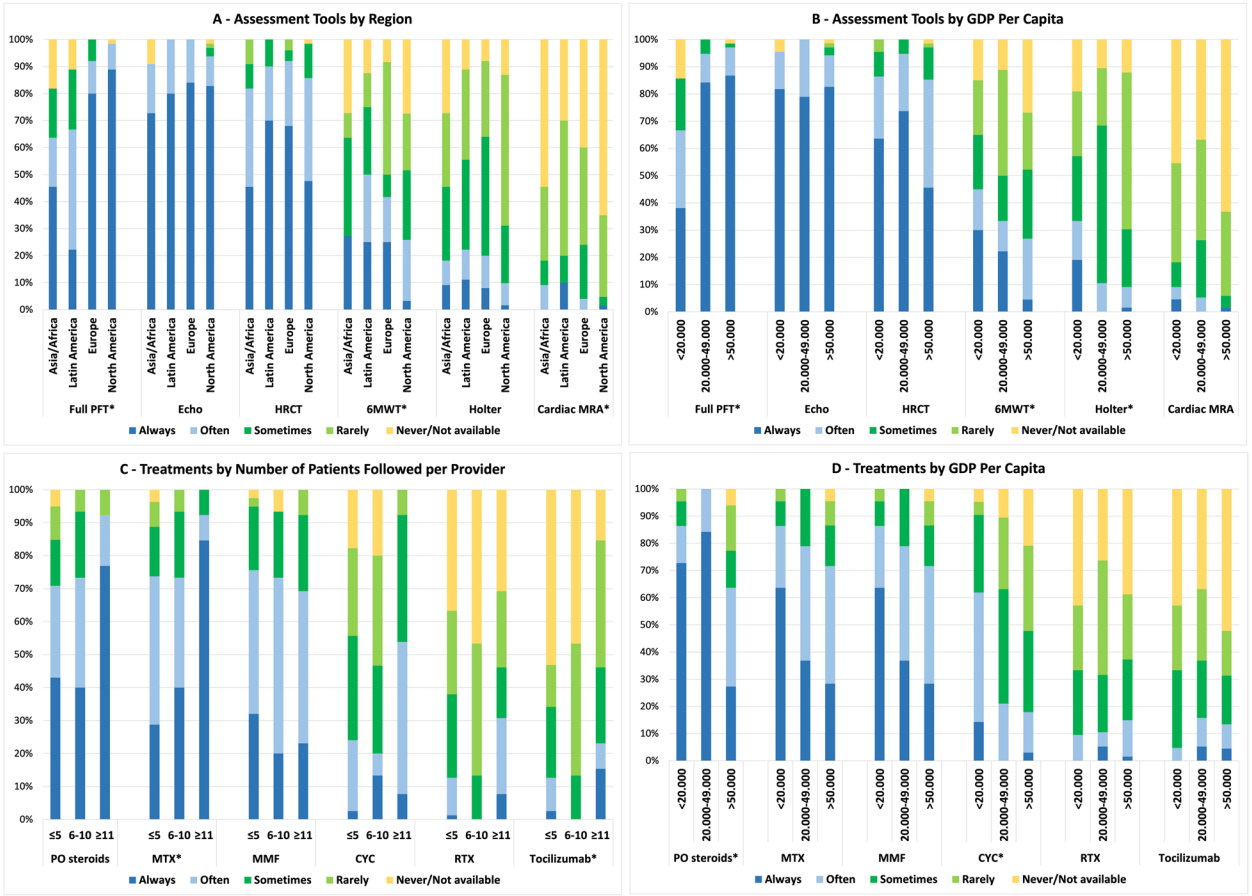

Fig. 2 Frequency Distribution of Cardiopulmonary Assessment Tools and Treatment Use by Pediatric Rheumatologists in Juvenile Systemic Sclerosis. Cells A-D display the frequency of assessment tools and treatments used in juvenile systemic sclerosis by region, Gross Domestic Product (GDP) per capita expressed in international dollars, and patient volume. Each bar plot compares assessment tool/treatment use across groups. Full PFT includes spirometry, lung volumes, and diffusion capacity. Statistical significance ($p < 0.05$) is indicated by an asterisk (*). Abbreviations: CYC = cyclophosphamide, Echo = echocardiogram, HRCT = high-resolution computed tomography, MMF = mycophenolate mofetil, MRA = magnetic resonance angiography, MTX = methotrexate, PO = by mouth, PFT = pulmonary function test, RTX = rituximab, 6MWT = six-minute walk test

Discussion

Using a combined data-driven and consensus methodology approach, the IJOG is working to develop consensus outcome measures feasible to use in diverse geographic and demographic populations for the assessment of JSSc in treatment trials. We present the results of a preliminary survey gaining insights into current assessment of cardiopulmonary involvement and treatment practices among pediatric rheumatologists worldwide, together with our strategy for a scoping LR to identify outcome measures for the most common disease domains of both adult and juvenile SSc. Our findings provide important insights into the worldwide management practices for JSSc and support the need for international collaboration.

We observed variations in the use of various clinical assessment tools and immunosuppressive treatments among pediatric rheumatologists influenced by geographical location, GDP per capita, and patient volume. Pediatric rheumatologists in North America, Europe, and mid- to high-income countries exhibited a higher frequency of advanced diagnostic tool utilization compared to their counterparts in Latin America, Asia/Africa, and low-income regions. Physicians in lower-income countries were more likely to prescribe cDMARDs and oral steroids over biologics. Additionally, pediatric rheumatologists from Asia/Africa, and lower-income regions tended to have a lower provider-to-patient ratio. These findings highlight possible disparities in healthcare resources, funding, and access to services and medications.

Our survey findings suggest that disparities in the utilization of clinical assessment tools and different immunosuppressive medications for monitoring and treating JSSc patients exist both regionally and economically. A

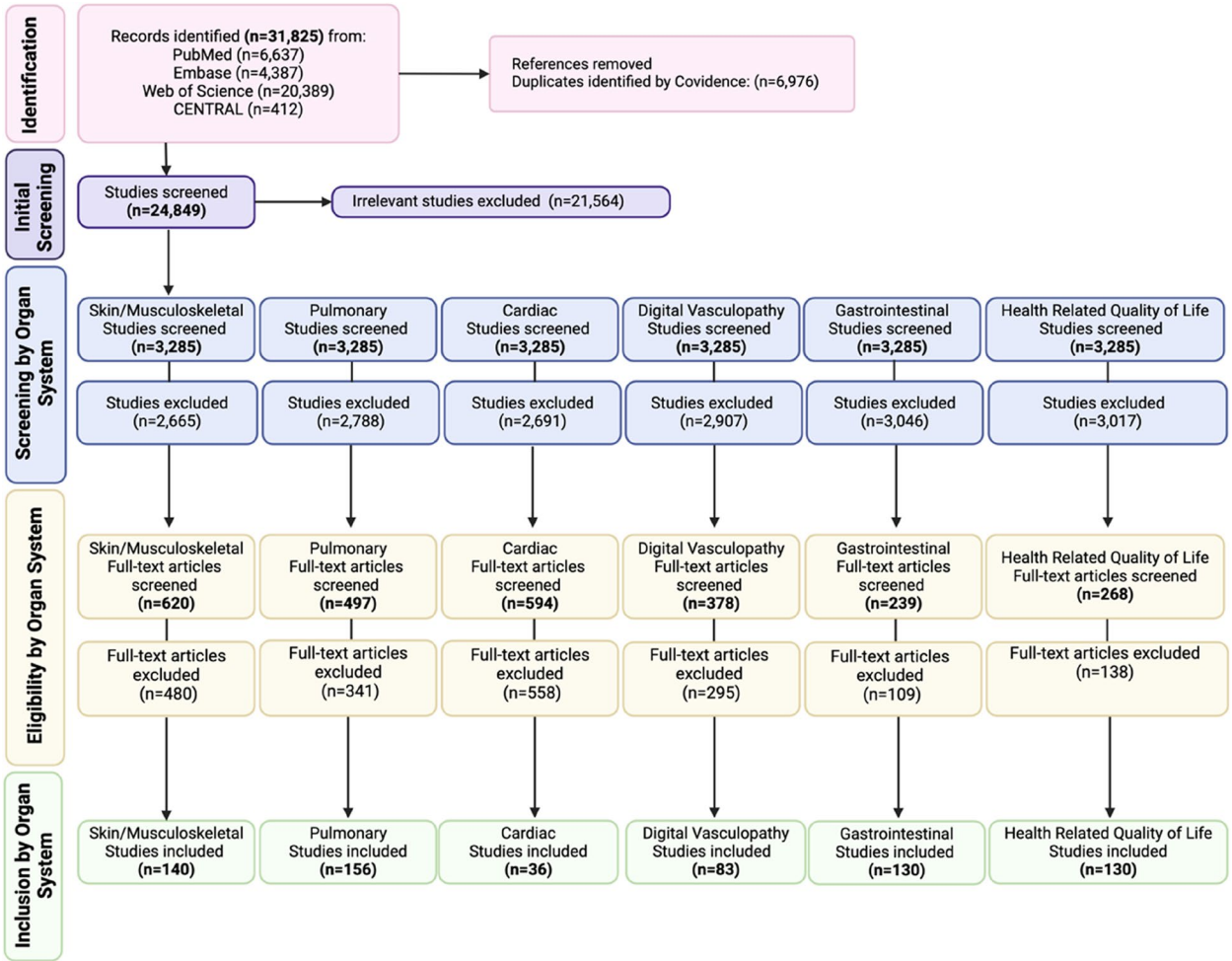

Fig. 3 Flow diagram of the scoping review process. The diagram presents the study selection process, starting with the initial search and ending with the included studies. Numbers represent the number of records at each stage of the review. The main reasons for exclusion from data extraction included conference abstracts, wrong outcome measure/irrelevance for the disease domain group, outcome measure not assessed on at least 2 time points, and wrong study design. Created in BioRender. Vasquez, N. [22] https://BioRender.com/i56e421

caveat is that we were not able to distinguish whether respondents never used or did not have access to the different tools or treatments because of how the answer choices were designed, and we did not control for factors such as type of medical training and education, personal biases and cultural beliefs, disease subtype, range of disease severity, type of insurance coverage, or patient preferences and their involvement in medical decision-making. However, we did not find differences based upon years of practice (Additional files 5 & 6), nor have clear regional differences been identified in JSSc patients to date. Importantly, the possible disparities identified may lead to variations in the quality of care and patient outcomes, highlighting the need for interventions to ensure equitable access to healthcare resources and standardize clinical practice guidelines.

The recently proposed response parameters for a 12-month trial [15] represent a significant step towards standardizing outcome measures in JSSc clinical trials, aligning with the goals of the IJOG study. While both the Hamburg Consensus [15] and the IJOG study aim to improve the consistency of outcome measures in JSSc, our study places a distinct emphasis on the feasibility and usability of these measures across diverse geographic and demographic settings. This emphasis is crucial, as our survey findings revealed significant disparities in resource availability and clinical practice patterns. By considering feasibility and usability across diverse settings, we ensure that these measures can be effectively implemented in global clinical trials, enhancing the generalizability of research findings and ultimately improving the care of JSSc patients worldwide.

The SHARE recommendations emphasize the importance of employing PFTs and HRCT in JSSc, considering them to be the most sensitive tools to detect the presence and severity of interstitial lung disease (ILD) [16]. While these tools are commonly utilized by pediatric rheumatologists, regional and economic disparities are evident, with lower-income countries employing them less frequently. Even in high-income countries where usage is more prevalent, 5–10% of pediatric rheumatologists do not utilize these tools, indicating a lack of adherence to the current recommendations. SHARE also recommends that JSSc patients have an assessment for organ involvement with cardiac echocardiogram, renal function, and modified Rodnan skin score at least every 6 months. In our preliminary survey, we found discrepancies between pediatric rheumatologists' choices for cardiopulmonary assessment tools and the current guidelines. While most pediatric rheumatologists surveyed considered DLCO and echocardiogram as the most important tools to assess cardiopulmonary disease status/progression in their patients, about a third of respondents still considered other tools more relevant. In addition, only about half of international pediatric rheumatologists reported always using HRCT for assessing pulmonary disease status in their patients, despite current evidence supporting its use in all pediatric and adult-onset SSc patients for ILD screening [23, 24].

The scoping LR identified a large number of manuscripts containing data on outcome measures for organ system assessment in SSc, which will guide the future steps of the IJOG study and ensure a more robust evidence base for the development of consensus outcome measures and standards for the assessment of JSSc. The substantial number of papers identified for each domain however has also made evaluation of outcome measures challenging. To address this, the scoping LR's inclusion criteria focused on extracting measures that assessed disease aspects that were considered likely to change in a 1-year clinical trial (e.g., those related to activity). Results of the scoping review for each of the six disease domain groups will be presented separately, and an update of the literature review search since 2021 is currently underway.

Our study has several strengths: it benefits from broadly international collaboration among pediatric rheumatologists and specialists with expertise or interest in JSSc, ensuring a diverse range of perspectives and expertise. Data extraction forms for the scoping LR were developed with input from specialists, ensuring the relevance and accuracy of data extraction, and maintaining consistency in the process. There were also limitations to our study. The survey had a low response rate, especially from some geographic areas, so findings may not fully reflect global patterns. The low rate is likely at least partly related to the rarity of JSSc, one of the rarest pediatric rheumatic diseases, limiting the number of respondents with sufficient experience to answer the survey. Choosing a scoping LR over a systematic LR may potentially affect the overall rigor and comprehensiveness of the review process as it does not involve assessing bias or conducting a quality appraisal of the included studies. However, our focus was to understand the extent, range, and nature of available data on SSc outcome to guide future steps of the IJOG study. Only a minority of studies have been conducted in JSSc, so more work is needed to evaluate the suitability of many measures for JSSc assessment. Lastly, excluding articles in other languages could have potentially overlooked relevant studies published in languages other than English.

Conclusions

The IJOG study represents an international collaborative effort to address existing gaps in the assessment and management of JSSc. We have completed the initial stages of a comprehensive scoping review of outcome measures for assessing six domains involved in SSc, including HRQoL measures. This process involved screening 24,849 unique articles, narrowing down to 36 to 156 articles for full-text extraction per domain. Our preliminary survey identified significant variability in preferences for assessments and treatments among pediatric rheumatologists. These variations underscore the need for standardized approaches in the assessment and management of JSSc. The lack of consensus and the range of opinions/strategies identified in the survey highlight the urgent need for a collaborative effort to improve the standardization of assessment and, subsequently, care of patients with JSSc. Moreover, the survey suggests variability in access to healthcare and limited adherence to SHARE recommendations [16], emphasizing the need for international collaboration.

Abbreviations

JSSc	Juvenile systemic sclerosis
SSc	Systemic Sclerosis
SHARE	Single Hub and Access point for Pediatric Rheumatology in Europe
LR	Literature review
IJOG	International Juvenile systemic sclerosis Outcome Group
CARRA	Childhood Arthritis and Rheumatology Alliance
PRES	Pediatric Rheumatology European Society
MSK	Musculoskeletal
GI	Gastrointestinal
HRQoL	Health related quality of life
INT	International dollars
GDP	Gross Domestic Product
IQR	Interquartile range
PRISMA-ScR	Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews
RCTs	Randomized control trials
DLCO	Diffusing capacity of the lungs for carbon monoxide
PFT	Pulmonary function test
FVC	Forced vital capacity

TLC	Total lung capacity
EKG	Electrocardiogram
MRI	Magnetic resonance imaging
HRCT	High-resolution computed tomography
MRA	Magnetic resonance angiography
6MWT	Six-minute walk test
MTX	Methotrexate
cDMARDs	Conventional disease modifying anti-rheumatic drugs
ILD	Interstitial lung disease
REDCap	Research Electronic Data Capture
CYC	Cyclophosphamide
Echo	Echocardiogram
MMF	Mycophenolate mofetil
PO	By mouth
RTX	Rituximab

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12969-025-01100-8.

Additional file 1. Peliminary survey to international pediatric rheumatologists. This data shows the specific questions and answer options for the preliminary survey distributed to international pediatric rheumatologists.

Additional file 2. Scoping review search terms. This data shows the search terms used in each database for the scoping literature review.

Additional file 3. Use of juvenile systemic sclerosis cardiopulmonary assessment tools by international pediatric rheumatologists stratified by region and GDP per capita. The table presents data on the use of various cardiopulmonary assessment tools by pediatric rheumatologists across different regions and Gross Domestic Product (GDP) per capita levels. Numbers in parentheses represent the number of respondents and the percentage of respondents who selected each response option. Statistical significance is indicated by asterisks, with more asterisks indicating a greater level of significance.

Additional file 4. Use of different juvenile systemic sclerosis treatments by international pediatric rheumatologists stratified by number of patients followed and GDP per capita. the table presents data on the use of various treatments in juvenile systemic sclerosis by pediatric rheumatologists across different regions and Gross Domestic Product (GDP) per capita levels. Numbers in parentheses represent the number of respondents and the percentage of respondents who selected each response option. Statistical significance is indicated by asterisks, with more asterisks indicating a greater level of significance.

Additional file 5. Use of juvenile systemic sclerosis cardiopulmonary assessment tools by international pediatric rheumatologists stratified by years of practice. The table presents data on the use of various cardiopulmonary assessment tools by pediatric rheumatologists stratified by years of practice. Numbers in parentheses represent the number of respondents and the percentage of respondents who selected each response option.

Additional file 6. Use of different juvenile systemic sclerosis treatments by international pediatric rheumatologists stratified by years of practice. The table presents data on the use of various treatments in juvenile systemic sclerosis by pediatric rheumatologists stratified by years of practice. Numbers in parentheses represent the number of respondents and the percentage of respondents who selected each response option. Statistical significance is indicated by an asterisk.

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Not applicable.

Authors' contributions
• NVC, CP, FZ, SL, and MT contributed equally to this study and were involved in all stages including conceptualization and design, data acquisition and analysis, writing and editing, and supervision and project management. • AM contributed with the scoping literature review strategy, search terms, and database searches. • MT provided the Covidence software for the scoping literature review, assisted with uploading references from the database searches, and guided all authors on the software utilization. • NVC, CP, FZ, AAY, SA, EM, EDG, AP, FT, GS, MÇ, MC, PRJ, KT, RK, OK, LR, EAA, AG, ML, HL, AR, BS, SS, EW, KC, RZ, BC, VL, VM, LS, LA, FR, PD, SL and MT contributed in different steps of the literature review screening process and acquisition of full text articles for data extraction. • NVC, CP, FZ, AAY, SA, EM, EDG, AP, FT, GS, MÇ, MC, PRJ, KT, RK, OK, LR, EAA, AG, ML, HL, AR, BS, SS, EW, KC, RZ, BC, VL, VM, LS, LA, FR, PD, AM, SL and MT read and approved the final manuscript.

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Data availability
The data generated or analysed during this study are included in this published article [and its supplementary information files]. The datasets used and/or analysed during the current study are also available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
The study was approved by the Albert Einstein College of Medicine Institutional Review Board (# 2020–12326) under Exempt 2: Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior. HIPAA does not apply to this study.

Consent for publication
Not applicable.

Competing interests

• NVC received grant funds from the Childhood Arthritis and Rheumatology Research Alliance and the Arthritis Foundation for the development and implementation of this project. Consulting services were paid to CP, FZ and SL using these funds. • NVC, SL, and KT have received consulting payments from Boehringer Ingelheim for their involvement in planning and designing clinical trials in Juvenile Systemic Sclerosis. • SL and FZ receive royalty payments from Wolters Kluwer for educational material Published in UpToDate related to Juvenile Scleroderma.

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