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Development of CARRA/PReS-endorsed consensus Core and Expanded Datasets in childhood-onset systemic lupus erythematosus for international registry-based research

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Contributors

AB, EMDS, JCC, LBL and RS developed the Delphi surveys, organised and facilitated the consensus meeting and wrote the first version of the manuscript. AAggarwal, AH, AMK, AM, AR, CC, CMH, CS, CS-M, DL, DAI, EvS, GT, HIB, KM, LB, LTH, LL, LES, MWB, MBS, NM, SA, SK, SM, SO, SA, SW and TA participated as voting members of the consensus meetings, contributing to decisions regarding items to be included in the Core and Expanded datasets. AD, Akinsete, AW, BE, BBR, CF, ERW, JC, RR-G and TBR participated in a task force meeting, making intellectual contributions to the decisions regarding which PROs to incorporate. All authors reviewed and approved the final draft of the manuscript. EMDS is the guarantor. RS, JCC, AB, are Co-first authors. EMDS and LBL are Co-last authors.

Competing interests

None declared.

Patient and public involvement statement

Patients and parents from the USA and Europe actively participated in the design and conduct of this research. The cSLE Patient/Caregiver committee included two parents and three young adults with childhood-onset SLE, now over 18 years old, providing patient-centred perspectives. They attended all virtual consensus meetings with full, equal voting rights. They joined a focus group to identify key domains and assess the patient experience using PRO measures, voting on the most important domains to be captured and participated in a PRO expert focus group with cSLE consensus group experts and additional PRO researchers. Additionally, they were involved in discussions on efficiently capturing cSLE patients' experiences with discrimination. Patients and parents reviewed the manuscript reporting the Core and Expanded cSLE datasets and are appropriately included as named authors.

Ethics approval

This study was reviewed and declared exempt from IRB review by the Duke University IRB (Pro #00110693).

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Abstract

Objectives: Childhood-onset systemic lupus erythematosus (cSLE), representing 15%–20% of individuals with SLE, has been difficult to study globally due to differences between registries. This initiative, supported by Childhood Arthritis Rheumatology Research Alliance (CARRA) and Paediatric Rheumatology European Society (PREs), aims to create Core and Expanded cSLE Datasets to standardise and enhance research worldwide.

Methods: 21 international cSLE experts and 4 patients participated in a Delphi process (questionnaires, 2 topic-specific focus groups and 3 virtual consensus meetings) to create 2 standardised cSLE datasets. The Core cSLE Dataset was designed to include data essential to meaningful clinical research across many settings. The Expanded cSLE Dataset was designed for centres able to consistently collect data to address broader research questions. Final data items for the Core and Expanded datasets were determined by consensus defined as >80% agreement) using an adapted nominal group technique and voting.

Results: The resulting Core cSLE Dataset contains 46 items, including demographics, clinical features, laboratory results, medications and significant adverse events. The Expanded cSLE Dataset adds 26 additional items and includes patient-reported outcomes. Consensus was also achieved regarding the frequency and time points for data collection: baseline, quarterly follow-up visits, annually and flare visits.

Conclusion: Standardised Core and Expanded cSLE Datasets for registry-based international cSLE research were defined through the consensus of global experts and patient/caregiver representatives, endorsed by CARRA and PReS. These datasets incorporate disease-specific and patient-specific features, optimised for diverse settings to facilitate international collaborative research for children and adolescents with SLE worldwide.

Keywords

Child; Lupus Erythematosus; Systemic; Lupus Nephritis; Outcome Assessment; Health Care; Patient Reported Outcome Measures

INTRODUCTION

Children and adolescents with childhood-onset systemic lupus erythematosus (cSLE) generally experience more severe disease manifestations when compared with people with adult-onset SLE (aSLE) [1-3]. Patients with cSLE experience more active and aggressive disease, greater medication burden and more frequent involvement of internal organs, such as renal, haematological and neuropsychiatric manifestations [4-7]. Children with cSLE have a higher standardised mortality rate when compared with people who develop lupus in adulthood (aSLE) [8,9].

Several cSLE registries exist worldwide, each intended to enhance our understanding of the epidemiology, phenotypes and prognosis of cSLE while also providing the opportunity to capture real-world data on medication response rates and toxicities [2,10,11]. Due to the rarity of cSLE, however, the study of specific disease manifestations remains underpowered using existing individual registries. Treatment paradigms for cSLE are currently based predominantly on adult lupus trial data, supplemented with data from relatively small paediatric clinical trials and observational studies [11,12]. It remains unclear in which instances children with cSLE have similar treatment responses to individuals with aSLE, and many cSLE manifestations, such as neuropsychiatric disease, are still understudied. Furthermore, there is regional variability in the manifestations of cSLE that likely influences diagnosis, surveillance, treatment response and prognosis of the disease [13]. These challenges highlight the need for international clinical research that focuses specifically on cSLE [2,14,15]. Importantly, registry data from large cohorts serve as a powerful tool for unifying data collection for this rare and clinically heterogeneous disease to establish prognosis and determine optimal treatment and long-term safety.

The three largest existing cSLE registries are (1) the Childhood Arthritis and Rheumatology Research Alliance (CARRA) Registry, which has enrolled approximately 1500 cSLE patients from the USA and Canada, (2) the UK JSLE Cohort Study and Repository, which has enrolled over 850 patients from across the United Kingdom [2,11,14] and (3) the Juvenile Inflammatory Rheumatism (JIR) Lupus Cohort (Pedialup), which includes more than 600 cSLE patients from 96 centres across 11 countries in and around Europe [10]. These three registries are independent inception cohorts, and while they share similar goals, they differ in several aspects, including inclusion and exclusion criteria, data items, and data collection time points. Although data from each registry have been useful in characterising

the regional cohorts, data collection differences between the registries have hindered the combination of data for inter-registry analyses.

For this study, we assembled an international group of clinicians and researchers with extensive expertise in cSLE research, alongside patient and caregiver representatives, to reach consensus on common data items for cSLE.

METHODS

Background and development

cSLE Expert Committee: A committee of international cSLE experts from CARRA, the Paediatric Rheumatology European Society (PReS), the UK JSLE Cohort Study, the JIR Cohort, the Paediatric Society of the African League Against Rheumatism, the Asia-Pacific League Against Rheumatism and the Pan American League Against Rheumatism along with patient/caregiver partners, developed a prototype Core and Expanded cSLE dataset. This cSLE Expert Committee was composed of 21 practising clinicians with extensive clinical and/or research experience of cSLE (15 paediatric rheumatologists, 4 combined adult medicine/paediatric trained or adult-trained rheumatologists, and 2 paediatric nephrologists who specialise in lupus nephritis, representing 10 countries across 5 continents). Although SLE is a systemic autoimmune disease that can affect any organ system, treatment is often determined by severe lupus nephritis, which led to the selection of rheumatologists and nephrologists in the consensus expert panel. The cSLE Patient/Caregiver members of the committee included two parents of patients with cSLE and three young adults with cSLE, now over 18 years old, who provided valuable patient-centred perspectives.

The cSLE Expert Committee was tasked with reaching consensus on the data items to include in a Core cSLE Dataset that would have sufficient detail to support meaningful clinical research across a broad array of research aims but also be streamlined enough to remain feasible for use at centres with limited research infrastructure. Experts were asked to reach consensus on additional data items to include in an Expanded cSLE dataset that would allow centres with sufficient research infrastructure to collect data needed to answer more expansive research questions. In both the Core and the Expanded datasets, emphasis was placed on defining each data item for a broad array of participating centres, considering countries beyond those currently participating in cSLE registry work to include regions of the world not yet represented.

To identify potential data items for inclusion, the CARRA/PReS Co-PI Committee (RS, JCC, EMDS, AB and LBL) compiled all data items used by current registries in North America and Europe, namely CARRA, the UK JSLE Cohort Study and the JIR Cohort; these data items were then supplemented by a literature review. From these items, the CARRA/PReS Co-PI Committee curated a list of potential data items as a starting point for the Delphi process. The cSLE Expert Committee was tasked with considering which items should be included in either 'Core' or 'Expanded' datasets. We defined 'Core' data items as the essential components for registry-based research on cSLE, aiming to streamline data entry to a maximum of approximately 15 min per patient visit. 'Expanded' dataset items refer to those that could significantly enhance the understanding of cSLE but are not

essential for effectiveness research—and due to the additional time and effort required for their entry, the inclusion of these data would likely be feasible primarily at centres with a more robust research infrastructure.

cSLE expert Delphi process

Premeeting Delphi surveys: The cSLE Expert Committee participated in two initial rounds of Delphi surveys to identify areas of agreement and disagreement ahead of the first virtual consensus meeting. The first Delphi survey was completed by 20 out of 21 experts and was administered through a piloted, custom-made, online Qualtrics questionnaire. Participants reviewed all variables currently collected in the existing CARRA, UK JSLE Cohort Study and JIR registries. For each data item, participants were asked whether to include the item in the Core or Expanded datasets, or in neither; they were also asked to determine the appropriate frequency for collecting each data item. Experts were encouraged to provide free text comments explaining their reasoning. Experts were also given the opportunity to suggest additional data items for consideration. The results of the first Delphi survey informed a second Delphi survey, which was also administered through Qualtrics and was completed by all 21 experts. This survey presented the summary scores from the first survey, along with key free-text comments (anonymised). In the second Delphi survey, experts were asked to reflect on the results from the first Delphi survey for each item and indicate whether they could agree with the majority response for that item.

Consensus meeting 1

The first virtual consensus meeting was conducted over 8 hours on two consecutive days. An adapted nominal group technique (NGT) methodology was used, led by a non-voting facilitator, to discuss and vote on data items to be included in the Core cSLE Dataset. Consensus was defined prior to the start of the meeting as >80% agreement. All 21 experts who participated in the Delphi survey were invited, and 20 were able to attend. In addition, four patients/caregivers attended the virtual consensus meeting and had full, equal voting rights. cSLE Expert Committee members were sent premeeting materials to review, including a summary of the Delphi results, a summary of relevant literature and a voting guide that summarised the results of the second Delphi survey. All items were reviewed during the meeting using NGT. For items that did not reach consensus for inclusion or exclusion after the first vote, we proceeded with discussion, statement refinement, and ultimately a re-vote until consensus was attained or it was clear that consensus would not be achieved.

The group voted to create focus groups to consider two especially complex topics: (1) how to best capture discrimination experienced by patients with cSLE and (2) what patient-reported outcomes (PROs) to include in the Expanded cSLE Dataset. The focus groups provided an opportunity to discuss existing literature in depth and get input from specialists in the relevant fields. These two topics, alongside items that did not reach a consensus at meeting 1 (including which laboratory values should be captured in a continuous fashion vs as categorical data), we sought additional input from specialists before reconvening for another consensus meeting. A third round of Delphi surveys was subsequently carried out to gauge opinions on these topics. Specialists' insights and recommendations, along with the

results of third-round voting, were presented to the cSLE Expert Committee members at consensus meeting 2.

Focus groups

PROs: Two separate focus groups were convened to examine the optimal utilisation of PROs in cSLE. The first group included five individuals diagnosed with cSLE and only four members of the CARRA-PReS Co-PI committee members; this smaller group of physicians aimed to help patients feel comfortable speaking freely and sharing their experiences without intimidation from a large group of cSLE experts. A summary of the discussion from this focus group was presented at a subsequent larger focus group, which included CARRA-PReS Co-PI committee members, one adult and eight paediatric rheumatologists with expertise in using PROs in SLE, two PRO methodology experts and two patients. At the conclusion of this 2-hour session, a consensus recommendation statement on PROs was drafted to be reported to the full cSLE Expert Committee at the second consensus meeting.

Capturing perceived discrimination: The initial consensus group identified racism and discrimination as important influences on health outcomes in cSLE. Racism can happen on many levels: systemic, institutional and individual [16]. While racism has a vast impact on health, it can be difficult to measure at the individual level. Minoritised individuals can experience discrimination based on many factors, such as race, gender identity or age [17]. Discrimination describes individual mistreatment and the perception of unjust treatment without specific cause. A focus group consisting of nine individuals with expertise in understanding the health effects of racism and other forms of discrimination, including one adult rheumatologist, eight paediatric rheumatologists, a social work professor and one patient was convened to discuss ways to efficiently capture the experiences of patients with cSLE regarding discrimination. The nine voting focus group members, along with CARRA-PReS Co-PI committee members, patients and caregivers, met to review existing tools for assessing patient experiences with racism and discrimination, ultimately developing a consensus recommendation statement that was reported to the full cSLE Expert Committee at the consensus meeting 2.

Consensus meeting 2

A second consensus meeting was held virtually over 1 day to finalise laboratory data collection units and to review the results of the aforementioned focus groups in order to select PRO measures for inclusion in the Expanded dataset. All cSLE experts, patients and caregivers who participated in the first meeting were invited, with 20 out of 21 experts and all 4 patients/caregivers participating in the second meeting. In addition, a non-voting PRO expert (BBR), not present during the first consensus meeting, joined the second meeting to offer technical input on PRO measures. Consensus was achieved on all remaining items during consensus meeting 2 (figure 1).

Patient and public involvement

Patients and parents from the USA and Europe actively participated in the design, conduct and dissemination of this research. The cSLE Patient/Caregiver committee included two parents and three young adults with cSLE, each now older than 18 years old, providing

patient-centred perspectives. They attended all virtual consensus meetings with full, equal voting rights. They also joined a focus group to identify key domains for capturing the patient experience using PRO measures, and participated as voting members in a PRO expert focus group. Additionally, they joined a focus group to discuss PROs for efficiently capturing cSLE patients' experiences with discrimination. Finally, patients and parents reviewed this manuscript. For all of these important efforts and contributions, they are included in this paper as named authors.

RESULTS

Core cSLE Dataset

Voting members of the consensus meetings achieved >80% agreement on the minimal core data items that were deemed crucial for collection in all international cSLE registries. Tables 1 and 2 summarise the data items voted into the Core cSLE Dataset and the recommended frequency for data collection.

Demographics: Demographic data items that can be consistently collected between international cohorts are shown in table 1. Following extensive discussion relating to whether race, ethnicity or ancestry should be collected, self-reported ancestry was deemed to be most appropriate for inter-registry research, using the specific question, 'What region(s) of the world do your ancestors come from?' and respondents can select all that apply. However, individual cohorts may choose to collect these data in an additional way, as appropriate for their country or region.

Initial presentation, classification criteria and family history: The SLICC 2012 [18] and EULAR/American College of Rheumatology (EULAR/ACR) 2019 classification criteria [19] were both voted into for collection at the initial visit and annual update, to capture cSLE features experienced over time. Data on the patient's initial presentation and family history of SLE in a first-degree relative should also be collected at baseline and annually, to capture the evolution of the disease and new family history (see table 1).

Baseline, routine follow-up visits (every 3 months) and unscheduled/emergency disease flare visits: There was consensus to collect blood pressure, height, weight, menarche and menstrual cycle status, disease activity (Systemic Lupus Erythematosus Disease Activity Index 2000, SLEDAI-2K) [20], medication information and significant adverse events at each visit. The experts agreed that the SLICC Standardised Damage Index (SDI) [21] should be collected annually (see table 1).

Laboratory tests: Haematology, biochemistry, immunology and pathology laboratory investigations that reached consensus for inclusion in the Core cSLE Dataset are listed in table 1, with the frequency and format of data varying according to the specific test, as summarised in table 2.

Data collection time points: There was a 100% consensus that registry data collection time points should include the time of diagnosis, follow-up visits at least every 3 months and urgent visits due to a flare or significant adverse event.

Expanded cSLE Dataset

Additional data items that reached consensus for inclusion in the Expanded cSLE Dataset are shown in table 3, and notable additions are discussed below.

Disease activity and damage: Disease activity assessment for the Expanded dataset should include a BILAG-2004, to enable a more detailed and comprehensive assessment of disease activity than the SLEDAI-2K [22]. UK-based experts shared their experience using the BILAG-2004 in clinical practice, and ease of use and the now available ‘Easy BILAG’ tool, which includes a colour-coded scoring system [23]. As in the Core cSLE Dataset, annual reporting of the SLICC-SDI was supported, including parental height to allow for the assessment of growth failure as a potential damage item.

Kidney biopsy data: In addition to ISN-RPS classification [24], the Expanded dataset should collect key histopathological features associated with renal outcomes, including the presence of thrombotic microangiopathy, percent cellular crescents, percent glomerulosclerosis, presence of interstitial fibrosis and/or tubular atrophy, and the modified NIH disease activity and chronicity indices [25], when available.

Genetic testing results: With increasing recognition of lupus caused by single gene mutations or a combination of two (or more) high-impact alleles [26-28] underlying primary immune dysregulation in cSLE, and given wider availability of genetic testing, the expert panel voted to include whether or not a patient had genetic testing relevant to SLE, and if they had a known or suspected pathologic variant.

Laboratory tests: Laboratory tests for the Expanded dataset include additional investigations for haemolytic anaemia, CH50, anti-C1q antibodies, and yearly assessment of routine screening investigations for thyroid disease, diabetes, cholesterol and vitamin D.

Comorbidities: The experts reached a consensus on the collection of data on additional autoimmune conditions and primary immunodeficiency. Both tuberculosis and HIV status were deemed important, due to significant implications for patient care and outcomes worldwide. Additionally, a diagnosis of depression was highlighted as an important comorbidity to incorporate into the Expanded cSLE Dataset.

PRO measures: During the first PRO focus group, which consisted entirely of patients, patients prioritised the collection of patient-reported symptoms of fatigue, depression and anxiety. Regarding PRO administration, patient-participants recommended that PRO assessments performed within routine clinical visits should take no more than 5–10 min to complete. During the second PRO focus group, in which patient perspectives were presented to a group of clinician cSLE experts, recommendations were developed, as described in online supplemental file 1. In brief, the PRO expert group and patient representatives agreed that fatigue (100%), depression (92%), anxiety (82%) and a global health (82%) measures should all be collected. To achieve this, they recommended the use of the corresponding Patient-Reported Outcomes Measurement Information System (PROMIS) Paediatric short-forms, which exist in multiple languages and have been validated extensively, including in

cSLE, with the existence of normative data and the ability to link scores from paediatric to adult-versions of PROMIS [29-31]. Patients raised some concerns about the ability of the PROMIS fatigue short-form to fully capture the mental and cognitive fatigue described by SLE patients. Despite this, they voiced that it was the best available instrument, preferring its brief recall period (past 7 days), question clarity, brevity, evidence for its validity and ability to link scores to those from adult versions of PROMIS fatigue measures, as compared with other fatigue PRO measures. During the second consensus meeting, the experts agreed with the recommendations from the PRO focus groups that PROMIS Paediatric short-forms for fatigue, depression, anxiety and global health should be collected within the Expanded dataset (all $\geq 80\%$ consensus), with the expectations that these would take no more than 10 min to complete. Children aged >8 years are expected to be able to complete PROMIS paediatric measures, with parent proxy measures available for younger patients.

Importantly, all cSLE experts agreed that the depression and anxiety PRO measures should only be implemented at sites that already have mental health screening and support as part of their clinical protocol, or sites where the PROMIS depression and anxiety scores could be reviewed in real time, during the clinical visit, by members of the clinical team. It was recommended that future work should focus on enhancing registry workflows to enable all PRO results to be available to clinicians during patient encounters, enabling conversations about information disclosed about patients' symptoms.

Discrimination: Following extensive discussion and review of existing tools, the expert panel voted to use the Everyday Discrimination Scale short-form [32,33] (online supplemental file 2), which is validated for individuals ages 14 years and older in multiple languages and cultural settings [34]. The Everyday Discrimination Scale short-form consists of five questions assessing day-to-day discrimination experiences. Affirmative responses lead to inquiries about frequency and perceived discrimination reasons (eg, ancestry or national origin, gender, race, age, religion, sexual orientation, height, weight, other aspects of physical appearance, education or income level), which may vary by geography (eg, in some locations, tribe, shade of skin colour or refugee status may be relevant).

Consensus was achieved to include the Everyday Discrimination Scale short-form within the Expanded dataset for patients aged ≥ 14 years (88% agreement). It was recommended that in the future, an additional question about healthcare discrimination should be considered. Of note, socioeconomic status indicators, such as household income, postal code and parent/caregiver occupation, were considered for inclusion in the Expanded dataset but did not reach consensus due to concerns about intrusiveness and potential discomfort for families.

Items not reaching consensus: Multiple items did not reach consensus for inclusion in the consensus datasets, and therefore, were not recommended for inclusion (online supplemental file 3).

DISCUSSION

cSLE represents one of the most challenging paediatric rheumatic diseases globally [3,9,35]. In this international initiative, recognised experts in cSLE achieved consensus on data

items essential for cSLE registries. This achievement is a significant advancement in the standardisation of cSLE data collection and will enhance our ability to perform cross-registry research. Funded by a collaborative grant from PReS and CARRA, there is a strong commitment to this initiative among the international paediatric rheumatology community. The standardised datasets are designed to facilitate future collaborative international cSLE research that is patient-centred, reflecting the diverse experiences and needs of children with SLE across the globe. It is crucial to emphasise that while the development of a similar dataset for aSLE is underway, the cSLE work provides valuable insights and will serve as a foundation to inform ongoing efforts.

The development a Core cSLE Dataset, which can be completed in 15 min in all settings, as well as a more comprehensive Expanded cSLE Dataset for centres able to collect additional data, allows for research that is both wide-ranging and inclusive of diverse settings. The broader scope of the Expanded cSLE Dataset incorporates more detailed family history, comorbidities, in-depth kidney biopsy and laboratory data, and genetic findings; it adds depth to the data, through the inclusion of the BILAG-2004 [22], alongside SLEDAI-2K [36] for disease activity, and it includes the 2019 EULAR/ACR classification criteria [19], to enable broad validation of these criteria in cSLE. These enhancements are expected to deepen our understanding of the impact of cSLE while creating avenues for addressing more complex research questions.

The involvement of patient and caregiver advocates had a substantial impact at every phase of this initiative, significantly influencing the composition of the final datasets. Patients and family members are the experts in the lived experience of cSLE, and they provided invaluable input to this effort [37]. Patient insights led to the adaptation of content, shaped the data administration methods and led the group to set a goal for a maximum amount of time (10 min) that is acceptable for patients to complete all PROs, given that patients recounted negative, even distressing experiences while completing PROs. In addition, direct patient input resulted in the omission of certain data items that patient representatives felt to be intrusive and upsetting.

Expert consensus among researchers, clinicians, patients and caregivers underscored the importance of PROs in understanding the full impact of cSLE on individuals. While PROMIS measures are publicly available for noncommercial use by researchers without charge in paper format, there is a fee for electronic integration into data collection. Fatigue was prioritised as a critical area for assessment within the Expanded cSLE Dataset, in recognition of its profound influence on quality of life and the limited scope with which it is currently evaluated. Patients and caregivers suggested that a future goal should be the development of a cSLE-specific PROMIS Fatigue short-form, drawing from the PROMIS Pediatric Fatigue item bank but tailored to fully capture the physical as well as the cognitive fatigue experience by cSLE patients.

The quality of life domains of depression and anxiety were prioritised by all, reflecting their prevalence in cSLE, as well as their impact on SLE outcomes. Of note, there was unanimous agreement on the need for immediate communication of severe depressive symptoms reported in PRO measures to the clinical team, thereby ensuring urgent clinical

intervention alongside registry data collection. Importantly, all patients who participated in the PRO focus group believed their PRO measure responses were being used for clinical purposes in addition to research, and the patients believed their healthcare providers were actively monitoring PRO responses in real time. This feedback emphasised the need for brief, clear and repeated explanations of the use of PROs, alongside a robust plan for a timely response to psychological distress.

Patients, caregivers and clinician cSLE experts from across the world agreed that racism and discrimination significantly affect health outcomes [38,39], emphasising the need for the expanded dataset to incorporate a measure of perceived discrimination. Informed by a systemic racism and discrimination focus group, the consensus voting panel agreed that the five-item Everyday Discrimination Scale [34] short-form for adolescents 14 years or older was the most time-efficient way to capture experiences of discrimination. Broad utilisation of the Everyday Discrimination Scale would allow for multinational validation in cSLE.

We acknowledge several study limitations. First, all meetings and focus groups were conducted exclusively in English, necessitating English language proficiency for participation. The dataset was constructed based on three current cSLE registries, which have all been developed in high-resource nations. In addition, it is important to note that while multiple subspecialties and five continents were represented among the experts, patients and caregivers, the majority of contributors were paediatric and adult rheumatologists and nephrologists from Europe and North America. Some of the rheumatologists in the consensus groups have expertise in neuropsychiatric SLE or cardiovascular disease in SLE. Future consensus groups to oversee revisions of this dataset could include other specialties involved in caring for cSLE, such as dermatology or neurology. Furthermore, while the Core cSLE Dataset was crafted to be practical for all clinicians or researchers, clinical environments lacking research support may find even the 15 min time frame burdensome. Currently, existing registries capture most of the Core cSLE Dataset and a significant proportion of the Expanded cSLE Dataset. Existing registries will need to develop a plan to implement the collection of the Core and Extended cSLE Dataset Items, which will require funding and alterations to existing registry infrastructure, including a plan for electronic integration of PROMIS measures, which are only available without a fee when used in paper format, which may be suboptimal in some settings. It is important to note that the Core and Expanded cSLE Datasets are intended to be iteratively refined to remain contemporary as they are integrated into established registries and implemented within new registries across diverse settings. Researchers will need to develop methods to compare historic data to the updated unified methods.

CONCLUSION

We present the first standardised Core and Expanded datasets for cSLE research, established by an international consensus process that included cSLE researchers, clinicians, patients and caregivers and was endorsed by CARRA and PreS. The integration of standardised cSLE datasets will mark a significant advancement in enabling the expansion of research to achieve robust global collaborations. The relatively low prevalence and high phenotypic heterogeneity of cSLE have thus far been an obstacle to clinical research. Now, through

unified data collection efforts, we can collaboratively pursue a broad range of clinical research questions with greater statistical power to advance cSLE care. Although defining guidance for standardising translational biosample collection is beyond the scope of this project, the proposed datasets will also facilitate contemporary lines of cSLE research, including the investigation of the underlying mechanisms of cSLE, the genetic basis of disease susceptibility, long-term patient outcomes, prognostic factors, cSLE treat-to-target initiatives [40], real-world comparative effectiveness and long-term safety, and a fuller understanding of the impact on health-related quality of life in affected children and adolescents. The development of these consensus-derived datasets represents a major strategic step towards the advancement of cSLE research, facilitating international collaboration and patient-centred studies designed to improve outcomes for children worldwide. Through consensus and standardisation of data collection globally, this initiative sets a new standard for cSLE registries in the field of paediatric rheumatology.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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REFERENCES

- [1]. Bader-Meunier B, Armengaud JB, Haddad E, et al. Initial presentation of childhood-onset systemic lupus erythematosus: a French multicenter study. *J Pediatr* 2005;146:648–53. doi: 10.1016/j.jpeds.2004.12.045. [PubMed: 15870669]
- [2]. Smitherman EA, Chahine RA, Beukelman T, et al. Childhood-Onset Lupus Nephritis in the Childhood Arthritis and Rheumatology Research Alliance Registry: Short-Term Kidney Status and Variation in Care. *Arthritis Care Res (Hoboken)* 2023;75:1553–62. doi: 10.1002/acr.25002. [PubMed: 36775844]
- [3]. Watson L, Leone V, Pilkington C, et al. Disease activity, severity, and damage in the UK juvenile-onset systemic lupus erythematosus cohort. *Arthritis & Rheumatism* 2012;64:2356–65. doi: 10.1002/art.34410. [PubMed: 22294381]
- [4]. Brunner HI, Gladman DD, Ibañez D, et al. Difference in disease features between childhood-onset and adult-onset systemic lupus erythematosus. *Arthritis Rheum* 2008;58:556–62. doi: 10.1002/art.23204. [PubMed: 18240232]
- [5]. Hersh AO, von Scheven E, Yazdany J, et al. Differences in long-term disease activity and treatment of adult patients with childhood- and adult-onset systemic lupus erythematosus. *Arthritis Rheum* 2009;61:13–20. doi: 10.1002/art.24091. [PubMed: 19116979]

- [6]. Mina R, Brunner HI. Pediatric lupus—are there differences in presentation, genetics, response to therapy, and damage accrual compared with adult lupus? *Rheum Dis Clin North Am* 2010;36:53–80. doi: 10.1016/j.rdc.2009.12.012. [PubMed: 20202591]
- [7]. Massias JS, Smith EMD, Al-Abadi E, et al. Clinical and laboratory characteristics in juvenile-onset systemic lupus erythematosus across age groups. *Lupus (Los Angel)* 2020;29:474–81. doi: 10.1177/0961203320909156.
- [8]. Chiche L, Jourde-Chiche N, Bader-Meunier B, et al. Acute pancreatitis as a cause of mortality in pediatric systemic lupus erythematosus: Results of a multiple cause-of-death analysis in France. *Semin Arthritis Rheum* 2016;46:e6–7. doi: 10.1016/j.semarthrit.2016.03.009. [PubMed: 27079760]
- [9]. Ambrose N, Morgan TA, Galloway J, et al. Differences in disease phenotype and severity in SLE across age groups. *Lupus (Los Angel)* 2016;25:1542–50. doi: 10.1177/0961203316644333.
- [10]. Cabrera N, Lega J-C, Kassai B, et al. Safety of biological agents in paediatric rheumatic diseases: A real-life multicenter retrospective study using the JIR-cohort database. *Joint Bone Spine* 2019;86:343–50. doi: 10.1016/j.jbspin.2018.08.003. [PubMed: 30201476]
- [11]. Smith EMD, Egbivwie N, Jorgensen AL, et al. Real world treatment of juvenile-onset systemic lupus erythematosus: Data from the UK JSLE cohort study. *Clin Immunol* 2022;239:109028. doi: 10.1016/j.clim.2022.109028. [PubMed: 35513304]
- [12]. Smith E, Al-Abadi E, Armon K, et al. Outcomes following mycophenolate mofetil versus cyclophosphamide induction treatment for proliferative juvenile-onset lupus nephritis. *Lupus (Los Angel)* 2019;28:613–20. doi: 10.1177/0961203319836712.
- [13]. Massias JS, Smith EM, Al-Abadi E, et al. Clinical and laboratory phenotypes in juvenile-onset Systemic Lupus Erythematosus across ethnicities in the UK. *Lupus (Los Angel)* 2021;30:597–607. doi: 10.1177/0961203320984251.
- [14]. Vazzana KM, Daga A, Goilav B, et al. Principles of pediatric lupus nephritis in a prospective contemporary multi-center cohort. *Lupus (Los Angel)* 2021;30:1660–70. doi: 10.1177/09612033211028658.
- [15]. Weill O, Decramer S, Malcus C, et al. Familial and syndromic lupus share the same phenotype as other early-onset forms of lupus. *Joint Bone Spine* 2017;84:589–93. doi: 10.1016/j.jbspin.2016.12.008. [PubMed: 28039062]
- [16]. Abubakar I, Gram L, Lasoye S, et al. Confronting the consequences of racism, xenophobia, and discrimination on health and health-care systems. *Lancet* 2022;400:2137–46. doi: 10.1016/S0140-6736(22)01989-4. [PubMed: 36502851]
- [17]. Potter L, Zawadzki MJ, Eccleston CP, et al. The Intersections of Race, Gender, Age, and Socioeconomic Status: Implications for Reporting Discrimination and Attributions to Discrimination. *Stigma Health* 2019;4:264–81. doi: 10.1037/sah0000099. [PubMed: 31517056]
- [18]. Petri M, Orbai A, Alarcón GS, et al. Derivation and validation of the Systemic Lupus International Collaborating Clinics classification criteria for systemic lupus erythematosus. *Arthritis & Rheumatism* 2012;64:2677–86. doi: 10.1002/art.34473. [PubMed: 22553077]
- [19]. Aringer M, Costenbader K, Daikh D, et al. 2019 European League Against Rheumatism/American College of Rheumatology classification criteria for systemic lupus erythematosus. *Ann Rheum Dis* 2019;78:1151–9. doi: 10.1136/annrheumdis-2018-214819. [PubMed: 31383717]
- [20]. Bombardier C, Gladman DD, Urowitz MB, et al. Derivation of the SLEDAI. A disease activity index for lupus patients. The Committee on Prognosis Studies in SLE. *Arthritis Rheum* 1992;35:630–40. doi: 10.1002/art.1780350606. [PubMed: 1599520]
- [21]. Gladman D, Ginzler E, Goldsmith C, et al. The development and initial validation of the Systemic Lupus International Collaborating Clinics/American College of Rheumatology damage index for systemic lupus erythematosus. *Arthritis Rheum* 1996;39:363–9. doi: 10.1002/art.1780390303. [PubMed: 8607884]
- [22]. Isenberg DA, Rahman A, Allen E, et al. BILAG 2004. Development and initial validation of an updated version of the British Isles Lupus Assessment Group's disease activity index for patients with systemic lupus erythematosus. *Rheumatology (Oxford)* 2005;44:902–6. doi: 10.1093/rheumatology/keh624. [PubMed: 15814577]

- [23]. Carter LM, Gordon C, Yee C-S, et al. Easy-BILAG: a new tool for simplified recording of SLE disease activity using BILAG-2004 index. *Rheumatology (Oxford)* 2022;61:4006–15. doi: 10.1093/rheumatology/keab883. [PubMed: 35077529]
- [24]. Weening JJ, D'Agati VD, Schwartz MM, et al. The classification of glomerulonephritis in systemic lupus erythematosus revisited. *Kidney Int* 2004;65:521–30. doi: 10.1111/j.1523-1755.2004.00443.x. [PubMed: 14717922]
- [25]. Bajema IM, Wilhelmus S, Alpers CE, et al. Revision of the International Society of Nephrology/Renal Pathology Society classification for lupus nephritis: clarification of definitions, and modified National Institutes of Health activity and chronicity indices. *Kidney Int* 2018;93:789–96. doi: 10.1016/j.kint.2017.11.023. [PubMed: 29459092]
- [26]. Belot A, Rice GI, Omarjee SO, et al. Contribution of rare and predicted pathogenic gene variants to childhood-onset lupus: a large, genetic panel analysis of British and French cohorts. *Lancet Rheumatol* 2020;2:e99–109. doi: 10.1016/S2665-9913(19)30142-0. [PubMed: 38263665]
- [27]. Almlöf JC, Nystedt S, Leonard D, et al. Whole-genome sequencing identifies complex contributions to genetic risk by variants in genes causing monogenic systemic lupus erythematosus. *Hum Genet* 2019;138:141–50. doi: 10.1007/s00439-018-01966-7. [PubMed: 30707351]
- [28]. Charras A, Haldenby S, Smith EMD, et al. Panel sequencing links rare, likely damaging gene variants with distinct clinical phenotypes and outcomes in juvenile-onset SLE. *Rheumatology (Oxford)* 2023;62:SI210–25. doi: 10.1093/rheumatology/keac275. [PubMed: 35532072]
- [29]. Jones JT, Carle AC, Wootton J, et al. Validation of Patient-Reported Outcomes Measurement Information System Short Forms for Use in Childhood-Onset Systemic Lupus Erythematosus. *Arthritis Care Res (Hoboken)* 2017;69:133–42. doi: 10.1002/acr.22927. [PubMed: 27111350]
- [30]. Weitzman ER, Gaultney A, von Scheven E, et al. Construct validity of Patient-Reported Outcomes Measurement Information System Paediatric measures in juvenile idiopathic arthritis and systemic lupus erythematosus: cross-sectional evaluation. *BMJ Open* 2023;13:e063675. doi: 10.1136/bmjopen-2022-063675.
- [31]. Translations promiss. Available: <https://www.healthmeasures.net/explore-measurement-systems/promis/intro-to-promis/available-translations/117-available-translations>; 2023.
- [32]. Williams DR, Yan Y, Jackson JS, et al. Racial Differences in Physical and Mental Health: Socio-economic Status, Stress and Discrimination. *J Health Psychol* 1997;2:335–51. doi: 10.1177/135910539700200305. [PubMed: 22013026]
- [33]. Sternthal MJ, Slopen N, Williams DR. RACIAL DISPARITIES IN HEALTH: How Much Does Stress Really Matter? *Du Bois Rev* 2011;8:95–113. doi: 10.1017/S1742058X11000087. [PubMed: 29887911]
- [34]. Kim G, Sellbom M, Ford K-L. Race/ethnicity and measurement equivalence of the Everyday Discrimination Scale. *Psychol Assess* 2014;26:892–900. doi: 10.1037/a0036431. [PubMed: 24708076]
- [35]. Tamirou F, Costedoat-Chalumeau N, Medkouri G, et al. Disease severity of proliferative lupus nephritis in Maghrebians. *Lupus (Los Angel)* 2018;27:1387–92. doi: 10.1177/0961203318772016.
- [36]. Gladman DD, Ibañez D, Urowitz MB. Systemic lupus erythematosus disease activity index 2000. *J Rheumatol* 2002;29:288–91. [PubMed: 11838846]
- [37]. Kennedy I. Patients are experts in their own field. *BMJ* 2003;326:1276–7. doi: 10.1136/bmj.326.7402.1276. [PubMed: 12805126]
- [38]. Kolasinski SL, Neogi T, Hochberg MC, et al. 2019 American College of Rheumatology/Arthritis Foundation Guideline for the Management of Osteoarthritis of the Hand, Hip, and Knee. *Arthritis Care & Research* 2020;72:149–62. doi: 10.1002/acr.24131. [PubMed: 31908149]
- [39]. Drenkard C, Bao G, Dennis G, et al. Burden of Systemic Lupus Erythematosus on Employment and Work Productivity: Data From a Large Cohort in the Southeastern United States. *Arthritis Care & Research* 2014;66:878–87. doi: 10.1002/acr.22245. [PubMed: 24339382]
- [40]. Smith EMD, Aggarwal A, Ainsworth J, et al. Towards development of treat to target (T2T) in childhood-onset systemic lupus erythematosus: PReS-endorsed overarching principles and

points-to-consider from an international task force. *Ann Rheum Dis* 2023;82:788–98. doi: 10.1136/ard-2022-223328. [PubMed: 36627168]

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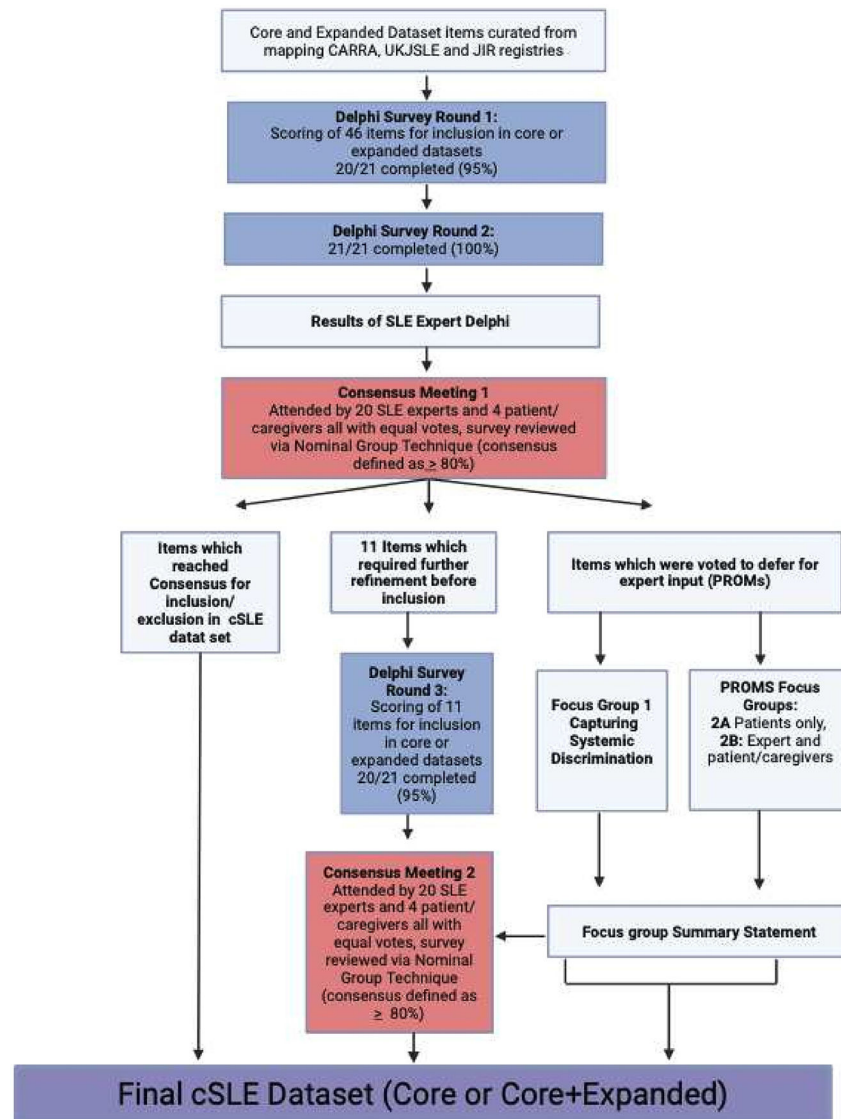


Figure 1. Methods used to create Core and expanded cSLE datasets. CARRA, Childhood Arthritis Rheumatology Research Alliance; cSLE, childhood-onset systemic lupus erythematosus; JIR, Juvenile Inflammatory Rheumatism; PROMS, Patient-Reported Outcomes Measurement System.

Table 1

Core cSLE dataset: data items

Section	Frequency of data collection			
	Baseline	Follow-up	Annually	Flare/AE
Demographics: DOB, country of residence, sex assigned at birth, gender identity, ancestry *	*			
Family history: SLE in a first-degree relative	*		*	
SLE onset: Date of SLE symptoms and date of SLE diagnosis	*		*	
SLE vs evolving/incomplete SLE vs other rheumatic or CTD	*		*	
SLE classification criteria: SLICC 2012 + EULAR/ACR 2019	*		*	
Basic observations: blood pressure, height, weight	*	*	*	*
Menarche status (age of menarche) and menstrual cycle status (currently menstruating, yes/no)	*	*	*	*
Disease activity: SLEDAI-2K, PGA, patient/parent global assessment of disease activity	*	*	*	*
SLICC Damage Index			*	
Investigations: CBC, CRP, ESR, Cr, Alb, IgG, ANA, ENA, dsDNA, APLs, C3/C4, UPC, urine dip/microscopy, kidney biopsy (ISN/RPS class, biopsy date)	*			
Medications				(frequency and format of data shown in table 2)
Corticosteroids				
Total daily dose of oral prednisolone (or equivalent)				
Number or intravenous corticosteroid pulses since last visit				
Immunomodulators/biologics (detailed data collection)				
Mycophenolate mofetil (dose, frequency, stop/start dates)				
Cyclophosphamide (dose of each infusion, route, infusion dates, stop/start dates)				
Rituximab (dose (mg) of each infusion, date of each infusion, stop/start dates)				
Belimumab (dose, route, frequency, stop/start dates)				
Other immunosuppressants/biologics (used Y/N, stop/start dates)				
Chloroquine, hydroxychloroquine, azathioprine, ciclosporin A, methotrexate, tacrolimus, voclosporin, anifrolumab, ofatumumab, ocrelizumab, obinutuzumab, JAKi, IVIG, other immunosuppressant (free text)				
Other medications				
Antihypertensives (ACEi, AT2 RB, Ca2 + channel blocker, blocker, diuretic), lipid-lowering agents, aspirin, anticoagulants (warfarin, other oral anticoagulant, subcutaneous LMWH), contraceptives (oestrogen containing, progesterone only, implantable/intrauterine), antidepressants, antiepileptics, bisphosphonates				
Significant adverse events	*	*	*	*

Section	Frequency of data collection		
	Baseline	Follow-up	Annually
Hospitalisation (reason, level of care), ESRD, dialysis (start/stop date, indication: acute kidney injury or chronic dialysis >3 months), kidney transplant, death (cause), pregnancy (date, outcome), malignancy (type)			Flare/AE
Minimum of 80% consensus for inclusion of each data item.			
ACEI, ACE inhibitors; ACR, American College of Rheumatology; Alb, serum albumin; ANA, antinuclear antibody; APLs, antiphospholipid antibodies; AT2 RB, angiotensin 2 receptor blocker; Ca ²⁺ , calcium; CBC, complete blood count; C3/C4, complement factor 3 or 4; Cr, serum creatinine; CRP, C reactive protein; cSLE, childhood-onset SLE; CTD, connective tissue disease; DOB, date of birth; DsDNA, anti-double stranded DNA; ENA, extractable nuclear antigens; ESR, erythrocyte sedimentation rate; ESRD, end stage renal disease; ISN/RPS, International Society of Nephrology/Renal Pathology Society; IV, intravenous; JAKi, Janus Kinase inhibitor; LMWH, low-molecular-weight heparin; PGA, Physicians Global Activity; SLE, systemic lupus erythematosus; SLEDAI-2K, Systemic Lupus Erythematosus Disease Activity Index 2000; SLICC 2012, Systemic Lupus International Collaborating Clinics SLE Classification Criteria; SLICC, Systemic Lupus International Collaborating Clinics; UPC, urine protein creatinine ratio; Urine dip, urine dipstick; Y/N, yes/no.			
*Self-identified ancestry, including a multiple-choice question with responses including Africa, East Asia, South Asia, Southeast Asia, Caribbean, Europe, Middle East/North Africa, South America, Indigenous/Native Population.			

Table 2
Core cSLE dataset investigations—data format and frequency of collection

Investigations	Data format	Frequency of data collection			
		Baseline	Follow-up	Annually	Flare/AE
Laboratory tests					
Complete blood cell counts WCC, Hgb, Plts, ANC, ALC	Continuous value+low vs normal vs elevated	*	*	*	*
C reactive protein	Continuous value+normal/low versus elevated	*	*	*	*
Erythrocyte sedimentation rate	Continuous value+normal/low vs elevated	*	*	*	*
Serum creatinine	Continuous value+normal/low vs elevated	*	*	*	*
Serum albumin	Continuous value+low vs normal/elevated	*	*	*	*
Total IgG	Continuous value+low vs normal/elevated				
Complements C3 and C4	Continuous value+low vs normal/elevated	*	*	*	*
Serologies					
ANA ≥1:80	Positive vs negative	*			
ENA (anti-Smith, anti-SSA, anti-SSB, anti-RNP)	Positive vs negative	*			
Anti-dsDNA titre	Continuous value+normal/low vs elevated	*	*	*	*
Lupus anticoagulant	Positive vs negative	*			
Anti-cardiolipin IgG, IgM	Continuous value+elevated vs negative/normal	*		*	
Anti-Beta-2-glycoprotein IgG, IgM	Continuous value+elevated vs negative/normal	*		*	
Urine studies					
Urine dipstick protein	Categorical (6 categories)	*	*	*	*
Urine dipstick specific gravity	Categorical (7 categories)	*	*	*	*
Urine dipstick leucocytes and blood	Categorical (5 categories each)	*	*	*	*
Urine microscopy red blood cells	Categorical (0–5 or >5 cells per hpf)	*	*	*	*
Urine microscopy white blood cells	Categorical (0–5 or >5 cells per hpf)	*	*	*	*
Urine microscopy red blood cell casts	Present vs absent	*	*	*	*
Urine protein to creatinine ratio	Continuous value for each+continuous for ratio w/ ratio reporting of normal/low vs elevated	*	*	*	*
Kidney biopsy data					
ISN/RPS Classification	ISN/RPS class (1–6), date(s) of biopsy(ies)	*	*	*	*

* denotes the frequency of data collection for each investigation.

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ALC, absolute lymphocyte count; ANA, antinuclear antibody; ANC, absolute neutrophil count; CBC, complete blood count; C3/C4, complement factor three or 4; cSLE, childhood-onset systemic lupus erythematosus; ENAs, extractable nuclear antigens; ESR, erythrocyte sedimentation rate; Hgb, haemoglobin; Hpf, high powered field; ISN/RPS, International Society of Nephrology/Renal Pathological Society; SSB, Sjögren Syndrome B.

Table 3

Expanded cSLE dataset—data items, format and frequency of collection

Data item	Data format	Frequency of data collection		
		Baseline	Follow-up	Annually
Family history (first-degree relatives)				
Primary Sjögren syndrome	Yes or no	*		*
Rheumatoid arthritis	Yes or no	*		*
Antiphospholipid syndrome	Yes or no	*		*
Other autoimmune disease	Yes or no, options+free text if yes	*		*
Disease activity				
BILAG-2004 Index	Domain and total scores	*	*	*
SLE-related damage				
Parental height (for final adult height estimate)	Continuous value	*		
Significant adverse events				
Hydroxychloroquine maculopathy	Yes or no, date if yes	*	*	*
Laboratory investigations				
Anti-C1q antibody	Positive or negative	*	*	*
Ferritin	Continuous value	*	*	*
Direct coombs	Positive or negative	*	*	*
Lactate dehydrogenase	Low/normal versus elevated	*	*	*
Haptoglobin	Low versus normal/elevated	*	*	*
Total complement activity (CH50)	Continuous value	*	*	*
Thyroid stimulating hormone	Continuous value	*	*	*
Haemoglobin A1c	Continuous values	*	*	*
Cholesterol panel (TC, TG, LDL, HDL)	Low versus normal/elevated	*	*	*
25-hydroxy vitamin D				
Genetic testing				
Confirmed or suspected monogenic lupus	Yes or no	*		*
DNA collected/sequenced	Yes or no	*		*
Known or suspected mutation/variant	Yes or no, free text if yes	*		*
Kidney biopsy data (initial/subsequent biopsies)				
Modified NIH disease activity index	0–24 scale	*	*	*

Data item	Data format	Frequency of data collection			
		Baseline	Follow-up	Annually	Flare/AE
Modified NIH disease chronicity index	0–12 scale	*	*	*	*
Cellular crescents	Percentage of glomeruli	*	*	*	*
Sclerosis	Percentage of glomeruli	*	*	*	*
Thrombotic microangiopathy present	Yes or no	*	*	*	*
Interstitial fibrosis present	Yes or no	*	*	*	*
Tubular atrophy present	Yes or no	*	*	*	*
Comorbidities					
Sjögren syndrome	Yes or no	*		*	
Autoimmune thyroid disease	Yes or no	*		*	
Other autoimmune disease	Yes or no, options+free text if yes	*		*	
Primary immunodeficiency	Yes or no	*		*	
Tuberculosis	Yes (latent/active) or no	*		*	
HIV	Yes or no	*		*	
Depression	Yes or no	*		*	
Patient-reported outcome measures					
Recommended to be available in real time to treating clinician					
Everyday Discrimination Scale Short-Form Ages 14+ years	5 questions	*		*	
PROMIS Paediatric Fatigue Short-Form Ages 8–17 years	10 questions	*	*	*	*
PROMIS Paediatric Global Health Ages 8–17 years	7 questions	*	*	*	*
PROMIS Paediatric Anxiety Short-Form* Ages 8–17 years	8 questions	*	*	*	*
PROMIS Paediatric Depressive Symptoms Short-Form* Ages 8–17 years	8 questions	*	*	*	*

Minimum of ≥80% consensus is required for inclusion of each data item.

* PROMIS Pediatric measures should not replace standard mental health screening.

BILAG, British Isles Lupus Assessment Group; cSLE, childhood-onset systemic lupus erythematosus; HDL, high-density lipoprotein; LDL, low-density lipoprotein; NIH, National Institutes of Health; PROMIS, Patient-Reported Outcomes Measurement Information Systems; TC, total cholesterol; TG, triglycerides.