Title: PReS-endorsed International Childhood Lupus T2T Task Force definition of Childhood Lupus Low Disease Activity State (cLLDAS).

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ABSTRACT

Objectives: The Childhood-onset Systemic Lupus Erythematosus (cSLE) International treat-to-target (T2T) Task Force sought to achieve a consensus-based cSLE specific definition of Low Disease Activity (LDA) for use in future T2T trials.

Methods: The Task Force, comprising of specialists in paediatric rheumatology/nephrology, and adult rheumatology undertook a series of Delphi surveys, exploring paediatric perspectives on adult-onset SLE LDA targets. Two virtual consensus meetings were held, employing a modified nominal group technique to discuss, refine, and vote upon matters underpinning the cSLE LDA target, and its individual criteria. Agreement of >80% was considered consensus.

Results: The Task Force agreed that the target should encompass cSLE as a whole and be based upon the adult-SLE Lupus Low Disease Activity State definition (LLDAS), with modifications to make it applicable to cSLE (cLLDAS). They agreed upon five cLLDAS criteria: (1) SLE Disease Activity Index (SLEDAI)-2K ≤4, with no activity in major organ systems (renal, central nervous system, cardiopulmonary, vasculitis, fever); (2) no new features of lupus disease activity compared with the last assessment; (3) Physician Global Assessment score of ≤1 (0-3 scale); (4) current prednisolone dose of ≤0.15mg/kg/day, 7.5mg/day/maximum; while on (5) stable antimalarials, immunosuppressives, and biologics. Maintenance treatment was considered stable if changes are not due to disease activity, but made due to side-effects, adherence, changes in weight and/or when building up to target dose.

Conclusions: A cSLE, age-appropriate definition of cLLDAS has been generated, maintaining sufficient alignment with the adult-SLE LLDAS definition to promote life-course research, including children, adolescent and adult-SLE patients together.

KEY MESSAGES

- LLDAS has been extensively investigated in SLE, but to date, a cSLE definition has been lacking.
- The cSLE International T2T Task Force have derived a cSLE appropriate definition; childhood LLDAS (cLLDAS).
- The cLLDAS definition will facilitate the development of T2T approaches in observational studies and trials.

INTRODUCTION

Childhood-onset Systemic Lupus Erythematosus (cSLE, also known as Juvenile-onset Systemic Lupus Erythematosus, JSLE) is a chronic autoimmune/inflammatory disease. When compared to patients with adult-onset SLE disease (aSLE), children and adolescents have higher disease activity, a greater medication burden and more severe organ manifestations, in-particular higher incidence of renal, cardiovascular and neuropsychiatric involvement than aSLE[1-4]. Standardised mortality rates remain higher in cSLE despite 10-year survival having improved[5, 6].

Treat-to-target (T2T) approaches improve short and longer term outcomes across a range of chronic medical conditions, including rheumatoid arthritis, psoriatic arthritis, hypertension, and diabetes mellitus[7-11]. In both in cSLE[12-17]and aSLE[18-23], international interest in T2T strategies is increasing. Although validation of T2T endpoints as associated with improved outcomes has been achieved in aSLE[21-32], formal randomised trials to test the value of intervening to attain these targets have not been performed. T2T may facilitate more effective use of treatments in a more structured way, with the aim of swiftly controlling disease activity, preventing organ damage, and improving health-related quality of life[33]. The **TARGET LUPUS©** research programme: '**T**argeting disease, **A**greeing **R**ecommendations and reducing **G**lucocorticoids through **E**ffective **T**reatment, in **LUPUS**' aims to develop T2T for cSLE[12, 13].

The first step in development of a T2T approach is the selection of an appropriate target. Remission is considered the ultimate target, but it is not attainable for all patients, for some low disease activity (LDA) may be more appropriate. In aSLE, several LDA definitions have been proposed, based on the principle of "tolerable" disease activity on stable treatment, with low glucocorticoid dosage, reducing the likelihood of adverse outcomes. In particular, the Lupus Low Disease Activity State (LLDAS) has been investigated extensively, with LLDAS attainment associated with reduced organ damage[23, 26-29, 34], fewer flares[25], glucocorticoid sparing[25, 28], improved HRQOL[30], and reduced healthcare costs[32]. Failure to achieve LLDAS within six months of diagnosis has been associated with early damage[27]. Most recently, LLDAS attainment has been shown in aSLE to be protective from mortality[35].

The **TARGET LUPUS©** group has convened an International T2T Task Force, to develop T2T overarching principles and points to consider (endorsed by the Paediatric Rheumatology European Society, PReS, *manuscript in press, Ann Rheum Dis, Dec 2022*)[36], cSLE appropriate T2T targets, and guidance to inform development of cSLE T2T trials. The existing validated definitions of LDA have been developed in the context of aSLE only, to date. The professional groups involved in their derivation did not include paediatric rheumatologists or nephrologists, and they were not devised with the intension for use in cSLE from the outset. An example of how the existing criteria are insufficient / inappropriate as they stand for use in cSLE relates to the glucocorticoid-related criteria which do not include a weight based cut-off for glucocorticoid dosing. Use of the existing aSLE-derived remission target could therefore allow treatment with a (relatively) high dose of glucocorticoid for younger children with cSLE. Here, the international cSLE T2T Task Force derives a cSLE-appropriate definition of LDA, building upon existing aSLE definitions, by including important modifications to improve the

applicability to cSLE patients while maintaining sufficient alignment to ensure that future T2T studies including both adolescents and adults are possible.

METHODS

International Task Force

The cSLE T2T International Task Force was established in July 2021, as previously described *manuscript in press, Ann Rheum Dis, Dec 2022*)[36]. In brief, it included three patient/parent representatives, 20 paediatric sub-specialists with extensive cSLE clinical and research expertise (including paediatric rheumatologists (n=14), combined paediatric/adult rheumatologists (n=2), nephrologists (n=4, including collaborators), an adult rheumatologist with extensive experience of aSLE LLDAS definition development[21-23], and two cSLE T2T International Task Force Steering Committee representatives (ES, MWB).

Experts were invited to self-nominate to become part of the Task Force through the Paediatric Rheumatology European Society (PReS), the Childhood Arthritis and Rheumatology Research Alliance (CARRA), the UK JSLE Study Group, and the UK British Association for Paediatric Nephrology (BAPN). Task Force members were selected according to pre-defined criteria (Supplementary Table S1). The final committee was selected based on the applicants' expertise, balancing representation of the different professional networks, distribution across all five continents, and the availability of the expert to participate in all steps of the consensus exercise.

Review of evidence

Literature searches were undertaken in MEDLINE, EMBASE and CINAHL databases to identify any initiatives deriving cSLE specific LDA targets, or providing cSLE specific evidence relating to existing aSLE T2T LDA targets. Studies were considered if they were written in English, published between 01/01/70 - 01/08/21, focused on paediatric patients (including at least 3 or more cSLE patients <18 years of age). The search terms comprised of three elements: a) paediatric, b) T2T, and c) cSLE related terms (see Supplementary Table S2 for full details). Papers were excluded if they were: reviews, conference abstracts, did not focus on cSLE or T2T, adult studies not fulfilling the specified age criteria, or non-human studies. A manual grey literature search was also undertaken, reviewing the reference lists of all the included studies**.**

Delphi surveys

Four Delphi surveys (1a/1b, 2a/2b) were sent to Task Force members in advance of two meetings to establish consensus on: (a) whether there should be a combined overall LDA target, or if Lupus Nephritis should be targeted separately from all other manifestations of lupus, (b) a conceptual definition for LDA for use in cSLE, (c) components of existing aSLE LDA targets that required modification for use in cSLE, (d) operationalisation of components of a LDA definition in cSLE. Existing evidence relating to each survey question was shared as relevant. Delphi 1a/2a results were shared with the experts in Delphi 1b/2b respectively, together with any provisional proposals from the Steering Committee based on the results of the previous survey. The results of the Delphi surveys were used to inform discussions during the consensus meetings.

Consensus meetings

Two virtual meetings were held in November 2021 and January 2022 to establish consensus on a cSLE LDA definition. The meetings were attended by 17 cSLE T2T Task Force voting members, with representation from West/East Europe, Africa, Australia, Asia, North and South America. The meetings were chaired by MWB, facilitated by ES (both non-voting members). Two patients (NM and LB) and one parent (JA) attended, actively participating in the discussions and representing the views of patients/families (non-voting members).

Modified nominal group technique (NGT)[37] was used during both consensus meetings to ensure equal participation amongst Task Force members. The chair (MWB) and facilitator (ES) framed each topic for discussion, sharing results from Delphi surveys alongside any relevant literature/unpublished data from the UK JSLE Cohort Study. Task Force members had the opportunity to share opinions without interruption (one minute each). After the discussion, participants voted anonymously on each item using an online poll. A threshold of ≥80% of attendees was set a priori as 'consensus achieved'. When <80% consensus was yielded, items were re-discussed and modified, with further voting rounds until consensus was achieved (wherever possible). The final LDA definition for children with SLE was endorsed by the PReS Executive Council and PReS cSLE Working Party Chair, on behalf of all members of PReS.

A summary of the process used to reach a consensus on the definition of LDA for use in cSLE is shown in Figure 1.

RESULTS

Structured literature review

The literature review revealed that no paediatric-specific LDA definitions for SLE have previously been derived. Two studies were identified that assessed the attainability, impact and predictors of attaining three different definitions of LDA in cSLE (Table 1)[12, 14]. A study including 430 UK JSLE Cohort Study patients, monitored between 2006-20, across 22 sites demonstrated that LLDAS, LA and Toronto-LDA definitions of LDA (see Table 1 for definitions) were attainable in 67%, 73% and 32% of patients respectively, in patients treated as per routine care, with achievement of these targets drastically reducing their risk for severe flare. LLDAS target attainment led to the greatest reduction in hazards of severe flare followed by Toronto-LDA, and LA respectively. The risk of severe flare progressively reduced as cumulative time in each LDA target increased, in keeping with results from aSLE studies[22, 23]. Achievement of all LDA targets also reduced the risk of subsequent organ damage accrual as defined using the Systemic Lupus International Collaborating Clinic Standardised Damage Index (SLICC-SDI)[12]. In a single centre study from the Netherlands (n=51), all cSLE patients reached LLDAS by a median of 6 months, with 72.5% remaining in LLDAS for >50% of follow-up time (LLDAS-50) and 53% achieving remission on treatment. Prednisolone dosage at three months, and treatment with mycophenolate mofetil (MMF; within three months), independently predicted LLDAS attainment[14]. A recent multi-centre Turkish cohort study (n=122), published since the consensus meeting, has shown 82% of patients reach LLDAS, with 68.9% achieving LLDAS-50. Attainment of LLDAS-50 was significantly associated with shorter time on high-dose glucocorticoid treatment, absence of proteinuria or subacute cutaneous manifestations of cSLE[15]. No other relevant papers were identifie

Key principles underpinning development of a cSLE Low Disease Activity state definition
Table 2 summarises the key statements underpinning the agreed 'cSLE Low Disease Activity state' definition.

Given the heterogeneity of cSLE, the Task Force discussed whether a cSLE LDA target should capture the status of the patient's cSLE condition as a whole or whether LN and other manifestations of cSLE should be targeted separately. Although LN was recognised as a major and particularly severe form of visceral organ involvement, it is frequently accompanied by other clinical/laboratory abnormalities present concurrently; therefore, it was agreed that the target should encompass cSLE as a whole (Table 2). There were concerns that separating out one organ system could lead to potential undertreatment of other organs. It was also noted that patients presenting solely with LN may develop other manifestations along the disease course, which may be missed if the target solely focuses on renal outcomes. A combined overall target was therefore agreed, as it also stresses the need for multidisciplinary management.

Considering (a) the attainability of aSLE LLDAS in cSLE[12, 14, 15], and (b) that reaching aSLE LLDAS is associated with greatest protection from severe flare and new damage compared to two other definitions of LDA[12] (Table 1), the Task Force agreed that the cSLE definition of LDA should be based upon the aSLE LLDAS definition[21, 23], with modifications to make it more applicable to cSLE. The Task Force therefore agreed that the cSLE specific LLDAS definition should be called the 'childhood Lupus Low Disease Activity State' (cLLDAS, Table 2).

The original conceptual definition of LLDAS, namely *'a state, which if sustained, is associated with a low likelihood of adverse outcome, considering disease activity and medication safety'*[23] was discussed extensively. The Task Force debated adding further details relating to growth, well-being, social participation, glucocorticoid toxicity, and damage. Noting that this is a conceptual definition, and not an operational definition, some important but subtle changes were made to the wording to reflect elements pertinent especially to the management of cSLE, further defining the term 'adverse outcome' (Table 2).
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Consensus definition of cLLDAS (Table 3)
Table 3 summarises the consensus agreed criteria for the cLLDAS definition.

Criterion 1 - Disease activity: The original disease activity item of the aSLE LLDAS definition[23] included a '*SLEDAI-2K≤4, with no activity in major organ systems (renal, CNS, cardiopulmonary, vasculitis, fever) and no haemolytic anaemia or gastrointestinal activity'[23]*. Haemolytic anaemia and gastrointestinal (GI) activity were mentioned specifically as these areas are absent from the SLEDAI-2K instrument[40]. The updated 2019 version of LLDAS, amended after a prospective validation study, removed haemolytic anaemia and GI items, as sensitivity analysis revealed that effects of these manifestations on the association of LLDAS with reductions in flare or damage were captured by the Physician Global Assessment (PGA). The revised disease activity criterion is easier to operationalise, with disease activity entirely discernible from the SLEDAI-2K score, and has the advantage of having been validated in a multinational prospective study in aSLE[21].

To inform the Task Force discussions, we re-examined data that were previously used to assess LLDAS attainment in cSLE from the UK JSLE Cohort Study[12]. LLDAS was not attained solely due to GI involvement in 4/4,738 visits, or due to haemolysis in a further 4/4,738 visits (0.002% of all follow-up visits). On balance, and in light of these data, 100% consensus was achieved that the cLLDAS definition should be consistent with the revised aSLE LLDAS disease activity criterion[21]. It should be operationally determined by the SLEDAI-2K (as in aSLE), with written guidance provided that the presence of haemolytic anaemia and/or GI involvement should be considered when scoring the PGA component of cLLDAS.

Criterion 2 - New features: 100% of the Task Force members agreed with aSLE LLDAS item 2, that there should be '*No new features of lupus disease activity compared with the previous assessment*', operationally defined by SLEDAI-2K. This was also supported by the Task Force patient representatives and the TARGET LUPUS qualitative study, where families stated that patients should not be considered to be 'in target' if they had new symptoms[13].

Criterion 3 - Physician global assessment (PGA) scale: Although members of the Task Force were more familiar with use of a 0-10 PGA scale, they agreed that where possible the cLLDAS definition should be consistent with the aSLE definition. This uses the 0-3 scale that was also recently affirmed by a global task force evaluating the use of PGA in SLE research[41].

Criterion 4 - Prednisolone (or equivalent) dosage: The Task Force extensively discussed the maximum ceiling dose of 7.5mg/day included within the aSLE LLDAS definition[21], noting that this would be a relatively high dose for young children. The group voted upon options to reduce the ceiling dose to 5mg/day or introduce a weight-based cut-off. There was consensus (88% of the Task Force) for the ceiling prednisolone dosage in cLLDAS target to be 0.15mg/kg/day, maximum of 7.5mg, aiming for whichever dose was lowest.

Criterion 5 - Immunosuppression: The aSLE LLDAS definition states that the patient must be on *'Well tolerated standard maintenance doses of immunosuppressive drugs and approved biological agents, excluding investigational drugs',* operationally interpreted to mean any standard immunosuppression is allowed. Again, the PGA and SLEDAI-2K are used to identify changes in disease activity that would reflect a significant change in immunosuppression[21]. In paediatrics, drug doses are frequently altered with weight changes, or where the formulation is not acceptable to the child, or due to associated side effects. To make the concept of '*Well tolerated standard maintenance doses'* clearer, the Task Force added further details to the aSLE definition, qualifying what maintenance treatment includes (Table 3).

DISCUSSION

An International Task Force of paediatric/adult rheumatologists, nephrologists, patients/caregivers, including representation from all major paediatric rheumatology networks, geographically distributed across all five continents, have achieved high levels of consensus on a cSLE-appropriate, PReS-endorsed definition of LDA, entitled cLLDAS. The cLLDAS is built upon the aSLE LLDAS definition with important modifications to improve applicability to cSLE, whilst maintaining sufficient alignment with the aSLE definition to promote life-course collaborative studies between the paediatric and adult rheumatology communities.

T2T targets for SLE are composite measures which consider disease activity, medication status, and supplement the SLEDAI-2K index with the PGA, mitigating against the inherent flaws of any one measure. For example, the SLEDAI-2K does not measure severity of disease activity within a given domain and omits GI involvement/haemolytic anaemia[40]. However, if these items are considered in the PGA scoring, disease activity in these areas is also captured. Inclusion of medication status within targets assessing immunosuppression and glucocorticoid dosage precludes attainment of LDA due to high-dose glucocorticoid treatment, or immunosuppressants with unacceptable side effects.

Criterion 1 of the cLLDAS aligns closely with the 2019 revised version of aSLE LLDAS[21]. The Task Force unanimously agreed with the SLEDAI-2K cut-off of ≤4, with the stipulation that disease activity in the major organ systems measured by the SLEDAI-2K is excluded (Table 3). Within a future prospective cLLDAS validation study, data on haemolytic anaemia and GI activity should be specifically collected, in-order to assess whether these items (specified in the original LLDAS definition[23]) are identified by other cLLDAS criteria (e.g. the PGA), and/or whether inclusion/exclusion of these items has a significant association with flare/damage reduction.

Criterion 2 remains the same as in aSLE[21, 23], as the Task Force agreed that detection of new disease activity features, not present at the previous visit (even in a permitted organ system), would suggest a worsening of disease and not be in-keeping with the concept of cLLDAS. Criterion 3 also remains the same as in aSLE[21], with the Task Force suggesting future initiatives to improve standardization of 0-3 scale PGA scoring prior to a cSLE T2T trial. Of note, similar initiatives are in progress for aSLE[41, 42].

The cLLDAS prednisolone ceiling dose was debated extensively. In aSLE, there is a clear dose-related association between glucocorticoid exposure and damage accrual[43], with accumulation of damage independently associated with time-adjusted mean prednisolone dose even in patients who have reached remission, emphasising that there is no 'safe low-dose' of glucocorticoid[24]. This has not been investigated in cSLE to date, although cSLE patients are known to be at increased risk of glucocorticoid-related damage than aSLE patients with longer exposure time over their lifetime as they have earlier onset of disease[44]. The Task Force members were cognisant that although remission, and the lowest possible prednisolone dose should ultimately be targeted, cLLDAS represents a state which is 'good rather than perfect', and therefore an 'acceptable' prednisolone dose should be included. Previous cSLE studies applying the 7.5mg prednisolone/day ceiling dose have demonstrated significant reductions in the risk of severe flare and new damage[12]. Overall, the Task Force agreed that it is appropriate to maintain the aSLE cut-off, as long as the patient does not receive more than 0.15mg/kg/day, aiming for lowest dose of the two options to prevent young children from receiving relatively high doses for their age/size. This will facilitate life-course studies. However, different prednisolone dose cut-offs should also be investigated within prospectively validation studies.

The essence of Criterion 5 is similar to the aSLE LLDAS definition, but cLLDAS includes an additional statement explaining what 'maintenance treatment' comprises, leaving this less open to interpretation. It makes it clearer that any treatment change in response to an

increase in disease activity is not consistent with 'stable antimalarials, immunosuppressives, and biologics,' but that treatment changes due to side-effects, adherence issues, increase in weight due to growth, or when building up to target dose (eg. for MMF), are consistent with meeting cLLDAS criterion 5.

This study is limited by the nature of the paediatric data currently available to date to inform development of the new cLLDAS definition, namely from three cohort studies[12, 14, 15]. In aSLE, the initial derivation of targets was followed by considerable work testing different target definitions in a range of settings (observational cohorts, registries and clinical trial data sets), arriving at data-driven conclusions relating to targets, anchored in clinical data and leading to the final recommendations for target definitions[33]. Going forward, cLLDAS should be validated, evaluating the association between cLLDAS achievement and outcomes, informing further refinement of the definition if necessary. Key areas to be explored within future studies include the (a) attainability of cLLDAS; (b) impact of cLLDAS attainment on flare and damage accrual; (c) minimum period of time required in cLLDAS to improve outcomes; (d) effect of different durations of cLLDAS (continuous and discontinuous) on outcome; (e) sensitivity analysis of the current cLLDAS definition, altering the SLEDAI-2K cut off, inclusion/exclusion of GI involvement and haemolytic anaemia, and PGA and prednisolone dosage cut offs. The current cLLDAS definition does not include a patient reported outcome measure (PROM) for health-related quality of life or fatigue, in-keeping with the aSLE definition[21, 23]. The association between cLLDAS attainment and PROMs should be explored, assessing whether cLLDAS attainment is associated with improvements in HRQOL and fatigue.

CONCLUSION

A cSLE-appropriate cLLDAS definition has been developed based upon data from existing cohorts[12, 14, 15] and expert cSLE International T2T Task Force consensus, endorsed by PReS. The development and validation of targets has been a key enabler for T2T trials in other diseases[45-47]. This therefore represents a significant step forward towards the development of T2T for cSLE, with potential for substantial clinical and research impact. The paediatric cSLE community, guided by the International cSLE T2T Task Force, will now work towards validation of cLLDAS and also develop remission definitions for cSLE.

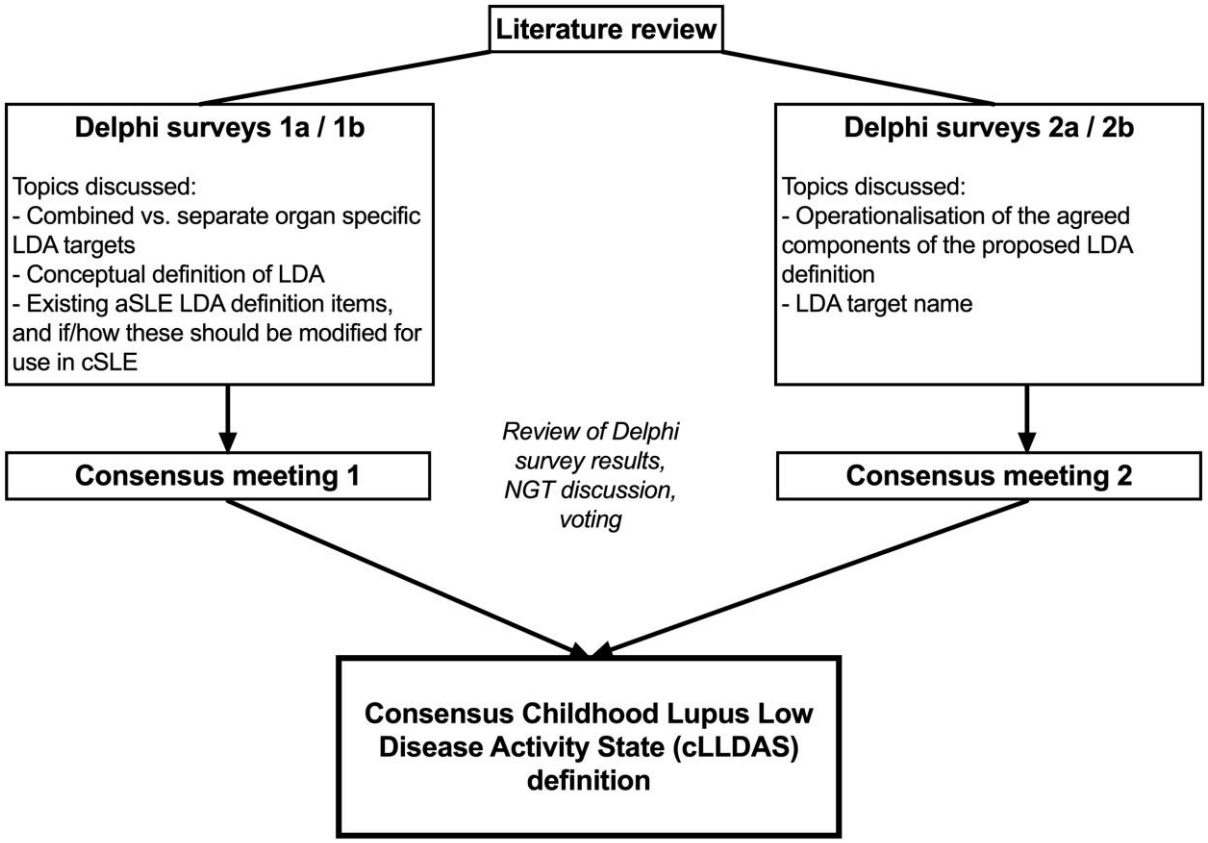

Figure 1 – Summary of the process used to reach a consensus definition of cLLDAS.
LDA = Low Disease Activity. NGT = Nominal Group Technique. cLLDAS = Childhood Lupus Low Disease Activity State. Eighteen core Task Force members and four collaborators participated in the Delphi surveys. Seventeen voting Task Force members included in the consensus meetings.

Definition of LDA with associated reference	N	LDA reached during follow-up	LLDAS-50 achieved	Predictors of LDA attainment	Impact of LDA attainment on 'severe flare' during follow-up (HR, 95% CI)	Impact of LDA on subsequent 'new damage' accrual (HR, 95% CI)	Cohort
LLDAS[23]	430	67%	NA	NA	0.14 (0.11, 0.19), p<0.001	0.24 (0.12, 0.48), p<0.001	UK JSLE Cohort[12]
LA[31, 38]		73%	NA	NA	0.31 (0.26, 0.37), p<0.001	0.44 (0.29, 0.67), p<0.001	
Toronto-LDA[39]		32%	NA	NA	0.17 (0.12, 0.25), p<0.001	0.35 (0.15, 0.83), p=0.017	
LLDAS[23]	51	100%	72.5%	Predictors of attaining LLDAS at 6 months: • Lower prednisone dose (p=0.041) • Receiving MMF treatment (p=0.018)	NA	NA	Rotterdam cSLE Cohort[14]
LLDAS[23]*	122	82%	68.9%	Predictors of attaining LLDAS-50: • Absence of proteinuria (p<0.02)	NA	NA	Turkish PeRA-RG group[15]

Table 1 – Attainability, associations and predictors of adult Low Disease Activity Target attainment within cSLE cohorts

LLDAS = Lupus Low Disease Activity State (definition (i) SLEDAI-2K≤4, 'no major active organ involvement' (renal, central nervous system, cardiopulmonary, vasculitis, fever), haemolytic anaemia or gastrointestinal involvement; (ii) no new features of lupus activity compared with previous assessment; (iii) physician global assessment ≤1 (0–3 scale); (iv) prednisolone dose ≤7.5 mg/day, no intravenous methylprednisolone pulses; and (v) tolerated standard maintenance immunosuppressive drugs/biological agents, excluding investigational drugs[23]. LA = as per the LLDAS definition[38] with criterion (i) limited to SLEDAI-2K ≤4, and exclusion of criterion (ii)[31, 38]. Toronto-LDA = (i) cSLEDAI- 2K score <3 (with or without high dsDNA-antibody levels, or low C3 or C4), only one manifestation of rash, alopecia, mucosal ulcers, pleurisy, pericarditis, fever, thrombocytopenia and leukopenia; (ii) no corticosteroids; and (iii) no immunomodulators (antimalarials were permitted)[39]. LDA = Low Disease Activity. N = number. LLDAS-50 = being in LLDAS for at least 50% of the observation time. HR = hazards ratio. CI = confidence interval.

NA = not available. MMF = mycophenolate mofetil. PeRA-RG = Pediatric Rheumatology Academy-Research Group. *Evidence published following the consensus meeting but data included within this table for completeness.

Table 2 - Statements underpinning the cSLE Low Disease Activity state definition

Item	Agreement
Combined vs organ specific targets • cSLE Low Disease Activity should encompass a combined overall target*	100%
Basis for the cSLE Low Disease Activity target • cSLE definition of Low Disease Activity should be based upon the aSLE LLDAS definition[21, 23], but will require minor modifications to make it more applicable for use in cSLE	100%
Name for the cSLE Low Disease Activity Target • Childhood Lupus Low Disease Activity State (cLLDAS)	100%
cSLE LLDAS conceptual definition • *'A state, which if sustained, is associated with a low likelihood of adverse outcome (considering disease activity, damage, and medication toxicity)'*	100%

LN = Lupus Nephritis. LLDAS = Lupus Low Disease Activity State. cLLDAS = Childhood Lupus Low Disease Activity State. 2 or 3 participants were absent from aspects of the on-line meeting, and not available to vote on these items due to urgent commitments. *Rather than targeting of LN and other manifestations of cSLE separately.

Table 3 - Consensus cLLDAS definition

cSLE Lupus Low Disease Activity (cLLDAS) criteria		Agreement
1. Disease activity	SLEDAI-2K ≤4, no activity in major organ systems (renal, central nervous system, cardiopulmonary, vasculitis, fever)[1]	100%
2. New features	No new features of lupus disease activity compared with the last assessment	100%
3. Physician global assessment score	PGA ≤1 (on a 0-3 scale)[2]	100%
4. Prednisolone dosage	≤0.15mg/kg/day or a maximum of 7.5mg/day (whichever is lower)[3]	88%
5. Immunosuppression	Stable antimalarials, immunosuppressives, and biologics (maintenance treatment is considered stable if changes are not due to disease activity, but made due to side-effects, adherence, changes in weight and/or when building up to target dose).	94%

cLLDAS = Childhood Lupus Low Disease Activity State. SLEDAI = Systemic Lupus Erythematosus Disease Activity Index. PGA = Physicians Global Assessment. NA = absent from the on-line meeting and not available to vote on this item due to urgent commitments. [1]The presence of haemolytic anaemia or GI involvement should be considered when scoring the PGA component of cLLDAS as these area are not captured by the SLEDAI-2K score. [2]0 = no activity; >0-1 = mild activity; >1-2 = moderate activity; >2-3 = severe activity. [3]Lowest dose of the two options required for cLLDAS to be attained. 1 to 3 participants were absent from aspects of the on-line meeting, and not available to vote on these items due to urgent commitments.

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