

Scoping literature review to identify candidate domains for the OMERACT Systemic Lupus Erythematosus core outcome set

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ABSTRACT

Objective: To identify candidate Systemic Lupus Erythematosus (SLE) domains from the literature for consideration towards the development of the SLE Core Outcome Set.**Methods:** This was a comprehensive scoping literature review of SLE clinical trials and systematic reviews published since 2010. Studies were identified from 5 databases and were screened for eligibility. Candidate domains were extracted from the included studies. Candidate domains were winnowed and binned by the Outcome Measures in Rheumatology (OMERACT) SLE Advisory Group.**Results:** Of the 4063 studies identified, 507 met inclusion criteria and proceeded to data extraction. Multiple domains and items were extracted, which winnowing and binning reduced to 25 candidate domains.**Conclusion:** The 25 candidate domains cover the important aspects of SLE and the 4 core areas of disease impact according to OMERACT framework. The 25 candidate domains constitute a feasible and manageable number of domains to proceed with to the core domain consensus stage that covers the wide range of impact of SLE. The candidate domains will be supplemented by ongoing qualitative research with patients living with SLE to identify additional domains before proceeding to the consensus stage.

Background

Systemic Lupus Erythematosus (SLE) is a heterogeneous autoimmune disease with unique and complex clinical presentations [1–3]. The multisystemic nature of SLE can involve multiple organ systems [3,4] resulting in a wide range of symptoms which can significantly influence

the patient's quality of life [5]. The impact of a disease, especially a multisystemic heterogeneous disease such as SLE, can occur through many different facets beyond symptomology of disease activity.

Outcome Measures in Rheumatology (OMERACT) has defined 4 core areas that assess the impact of an intervention on health or a health condition, which are manifestations and abnormalities, life impact,

death and lifespan, and lastly societal and resource use [6]. The individual concepts or constructs that define single areas of disease impact are referred to as domains [7]. To capture the true impact of a disease, the most important domains should be measured in all clinical trials and research studies. Standardizing the capturing and measuring of domains can be achieved with a core outcome set (COS) [7].

In 2018, the OMERACT SLE Working Group was re-established to update the OMERACT SLE COS [8]. The COS consists of a Core Domain Set (CDS) and the measurement instruments to capture the domains. The first phase of the COS update is developing a new CDS, which begins with candidate domain generation where multiple projects are undertaken to identify domains from various sources. To identify candidate SLE domains from the literature, we conducted this scoping literature review.

The decision to conduct a scoping literature review in place of another type of review was due to the nature of our topic. Identifying all the different domains of SLE is a very broad concept, and having a strict concept and selection criteria as required with a systematic review could risk missing important domains or require many reviewers and a long time to complete [9]. To ensure strong methodological quality, the Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) Checklist [10] was followed and the scoping literature review was registered with Open Science Framework [11].

Methods

Literature search

Keywords targeting the 4 core areas to capture the broad range of domains were prepared in conjunction with an experienced librarian and search terms were individualized for the five databases searched: Medline, Embase, Cochrane, CINALH, and PsycINFO (Appendix A). The inclusion criteria were SLE clinical trials and systematic reviews, written in English, and published since 2010. The rationale for this decision was that the clinical trials would capture all domains that have been highly developed and researched, while the systematic reviews would capture more novel and important domains still being developed and researched without yielding an unmanageable number of articles.

Study selection

Study requirements included being in English language and meeting the PICOC; population: Adults (18+) living with SLE, intervention: all interventions pharmacological and non-pharmacological, control: standard of care therapy and placebo as per trial design, outcome: SLE preliminary domains, context: controlled and non-controlled trials, systematic reviews, and meta-analyses. Study selection was not restricted to specific types of clinical trials as to prevent omitting domains not typically captured in current controlled trials.

Study screening

Study screening was performed using Covidence software [12]. Duplicate studies were removed before screening. The first round of screening of titles and abstracts was performed by 3 reviewers (WN, CMJ, AT) with 1 reviewer per article due to the large number of articles identified. An agreement test was performed on the first 100 articles with the 3 reviewers, which yielded a 98 % agreement, and the 2 disagreements were resolved with discussion. Full-text screening was performed by 2 reviewers (WN, FK) with 2 reviewers per article. Any disagreement was resolved through discussion.

Data extraction

Data extraction was performed by 2 reviewers (WN, FK) with 2 reviewers per article. Data was collected in custom-made collection forms. Data collected included standard study information (first author, year of publication, type of study), SLE domains and outcomes and their

definitions, and method of assessment or measurement tools.

Data synthesis

The items generated by the scoping review were preliminarily sorted by the 2 reviewers performing data extraction into domains. The resulting domains and the items forming them were reviewed by the OMERACT SLE Advisory Group, which includes 2 patient research partners (MD, YE) and clinician researchers, at 10 bi-weekly meetings [13]. A winnowing and binning of domains and items was conducted to eliminate any domains that were too broad, specific, or contextual and to combine any like-terms.

Domain definition

Definitions collected in the scoping literature review were supplemented with definitions identified from an additional literature search. The OMERACT SLE Advisory Group met monthly for 5 months to discuss, remove, and modify identified definitions until agreed upon definitions were established.

Results

Study selection

The results of the study selection are demonstrated in Fig. 1. After duplicates were removed, 4063 articles were identified. Title and abstract screening removed 1429 articles, 47 full-text articles could not be retrieved, and full-text screening removed 817 articles leaving 507 for inclusion.

Data synthesis

An extensive list of items was identified, and then winnowed and binned into 25 domains as shown in Table 1. Items that were not deemed to form domains on their own and were not winnowed out for being too specific, contextual, or broad were binned into the 25 domains either as sub-domains or examples to assist in the understanding of the domain as shown in Table 1. The 25 domains identified are: Adverse Events; Anxiety; Cognition Impact; Cognitive Function; Depression; Economic Cost Impact; Emotional Health (living with and managing SLE); Fatigue; Flares; Frailty, Health-Related Quality of Life, Pain Intensity; Pain Interference; Participation in all aspects of life (family, social, educational, work, and leisure activities); Patient Global Assessment of Disease Activity; Physical Function; Physician Global Assessment of Disease Activity; Reproductive Health; Sexuality; SLE Disease Activity; Sleep; Stress; Tissue/Organ Damage; Treatment Satisfaction; Use of Glucocorticoids Including Tapering. The items forming each domain in Table 1 are not the entire list of all items but rather examples to better explain the domain.

The 25 domains were then sorted into the core areas of OMERACT (Economic Cost, Adverse Events, Life Impact, and Pathophysiological Manifestations) to which they belonged (Fig. 2). Of the 25 domains, 9 domains were deemed to belong solely to a single core area, 11 domains were deemed to belong to 2 core areas, and 5 domains were deemed to belong to 3 core areas. The relative placement of the domains that belonged to >1 core area was intentional to demonstrate a corresponding proportion of how related the domain is to its respective core areas as illustrated in Fig. 2. The placement of domains in the core areas is not definite nor their limiting sole impact, but rather an interpretation of the main areas of impact of each domain and the complexities the domains can have with regards to their definition and classification.

Candidate domain definition

Definitions for the 25 candidate domains generated were captured in the scoping literature review and from an additional literature search. Definitions were reviewed by the OMERACT SLE Advisory Group,

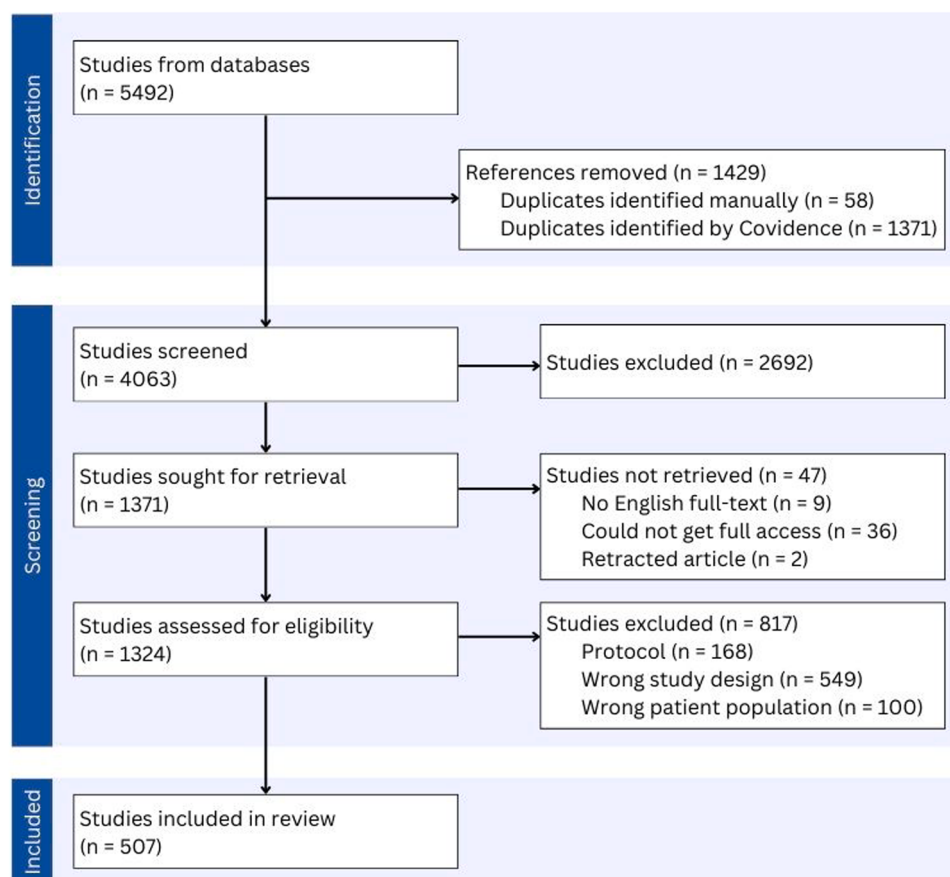


Fig. 1. PRISMA flow diagram of study selection.

modified in certain circumstances, and agreed upon. The agreed-upon definitions are shown in Table 2.

Conclusion

A comprehensive list of candidate domains has been identified through the scoping literature review. The 25 candidate domains capture the most impactful domains of SLE on patients. The candidate domains cover the 4 core areas that assess the impact of an intervention on health or a health condition, ensuring a broad coverage of the areas of impact is captured. Definitions for the candidate domains were identified in the literature, reviewed, and agreed upon. The definitions will establish common interpretations of each domain among collaborators (patients, clinicians, researchers, and more), which is necessary for the next stage of domain consensus to occur.

The 25 candidate domains identified include a number of life impact domains, of which several provide a subjective assessment (such as fatigue, cognition impact, pain interference, and stress) and capture the patient experience that is often under-represented in treatment outcomes [14]. These life-impact domains which capture the patient experience are essential for a holistic evaluation of patient's health. Our domain generation efforts identified discrepancies in domain prioritization between patients and other collaborators [15] that has been further reported in the literature [16]. The CDS will acknowledge the differing values of the many collaborators, especially that of patients, and ensure domains important to both patients and other collaborators are considered and included.

Potential limitations and controversies of the candidate domains are the levels at which the lines are drawn to classify and define the domains. Domains could be deconstructed and have their sub-items classified as domains; however, this would result in an extensive list of

highly specific candidate domains. An extensive list would make the following consensus stage to decide the CDS arduous and laborious, and require the CDS to contain numerous domains and consequently measurement instruments to capture the important aspects of SLE. Conversely, the further binning of domains to combine related ones would result in domains that consist of multiple concepts only capturable by extensive composite nonfeasible measurement instruments that target multiple domains. The 25 candidate domains presented have been deemed to be adequately classified with only necessitated like-items binned together.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: **Vibeke Strand** is a founding member of the executive committee of Outcome Measures in Rheumatology (OMERACT) [1992 – present], an international consensus organization that develops and validates outcome measures in rheumatology randomized controlled trials and longitudinal observational studies and has received arms-length funding from as many as 36 sponsors.

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Table 1

Candidate domains and example sub-items.

Domain	Example Sub-Domains	Examples to Facilitate Understanding
Adverse Events	Adverse drug reactions Infection-related AEs	Infusion-related AEs Bacterial Fungal Parasitic Viral
Anxiety	Mortality Severity of AEs Anxiety disorders Anxious misery Fear Hyperarousal	Mild, moderate, severe Dread Worry Fearfulness Panic Nervousness Restlessness Tension Dizziness Racing heart Application of cognitive abilities Difficulties in cognitive abilities Patient's perceived cognitive ability Support network perceived cognitive impairment Attention
Cognition Impact	Cognitive impairment	Complex Simple
Cognitive Function	Executive skills Fluid cognition Language/verbal fluency Memory Psychomotor speed Reasoning/problem solving Social processing	Learning Recall Basic social processing Complex social cognition
Depression	Visual-spatial processing Decreased engagement Decreased positive affect Depression severity Depressive symptoms Depressive/negative mood Negative views of self Social cognition	Loss of meaning, interest, purpose Sadness Self-criticism Worthlessness Interpersonal alienation Loneliness Drug costs Healthcare products Healthcare resource utilization (HCRU) Laboratory test costs Self-care/non medical costs Work time missed Suffering
Economic Cost Impact	Direct costs Indirect costs	
Emotional Health (living with and managing SLE)	Intangible costs Body image Coping Guilt Mental/emotional well-being Mood disorders Mood disturbances Shame Stigma	

Table 1 (continued)

Domain	Example Sub-Domains	Examples to Facilitate Understanding
Fatigue	Drained Exhaustion Severity of fatigue Tiredness	
Flares	Flare rate/frequency Mild, Moderate, Severe flare Relapse Time to flare	
Frailty	Capacity of body Fitness	
Health-Related Quality of Life	Impact of health on daily functioning Perceived health Perception of well-being	Physical Mental Social Emotional
Pain Intensity	Quality of life Pain reduction Pain severity	
Pain Interference	Interference with daily life Limitations in life tasks	Familial Leisure Social Education Work
Participation in all aspects of life (family, social, educational, work, and leisure activities)	Performing daily activities Performing leisure activities Role participation Social function Work productivity	Absenteeism Presenteeism Unemployment Work disability Work impairment
Patient Global Assessment of Disease Activity		
Physical Function	Functional ability Physical activity Physical capability Physical fitness Self-reported physical activity	Aerobic capacity
Physician Global Assessment of Disease Activity		
Reproductive Health	Fertility	Amenorrhea Aspermia Azoospermia Impaired sperm quality Infertility Ovarian failure Sterility
	Fetal outcomes	Still birth Congenital malformation Preterm birth
	Pregnancy outcomes	Bleeding during pregnancy Caesarean operation Eclampsia Ectopic pregnancy Intrauterine distress Maternal outcomes Miscarriage Postpartum hemorrhage Pre-eclampsia
Sexuality	Intimate relationships Libido Sexual esteem	

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Table 1 (continued)

Domain	Example Sub-Domains	Examples to Facilitate Understanding
SLE Disease Activity (Global as well as Organ Specific)	Sexual experience Sexual functioning Cardiovascular	Coronary disease, acute coronary syndrome Arterial stiffness Cardiovascular disease Carotid disease Endocarditis Endothelial function Hypertension Myocardial infarction Myocarditis Pericardial effusion Pericarditis Peripheral edema Stroke and transient ischemic attack Thromboembolic event Valvopathies
	Constitutional Gastrointestinal	Fever Weight loss Ascites Colitis Duodenitis Enteritis Gastritis Hepatitis Intestinal ischemia Intestinal lesions Pancreatitis Peritonitis Protein losing enteropathy Chronic anemia Hemolytic anemia Leukopenia Thrombocytopenia Thromboembolic events
	Hematological	Immune related tests Non-immune related test
	Immunological / Laboratory Tests	Alopecia Livedo reticularis Lupus rash Mucosal ulcers Sicca syndrome Skin lesions
	Mucocutaneous	Arthralgia Arthritis Arthropathy Myalgia Myositis Swollen joints Tender joints
	Musculoskeletal	Diffuse syndromes Focal syndromes (CNS and PNS)
	Neuropsychiatric	Optic neuritis Retinal disease Scleritis
	Ophthalmic	Complete Organ-Specific Overall Partial Time to remission
	Remission	Lupus nephritis Renal flare Renal function Sclerosis
	Renal	Pleural effusion Pneumonitis Pulmonary embolism Pulmonary hypertension
	Respiratory	

Table 1 (continued)

Domain	Example Sub-Domains	Examples to Facilitate Understanding
		Shrinking lung syndrome Sinusitis Neurogenic bladder Urinary tract dysfunction Small, medium, large vessels
	Urinary Tract	
	Vasculitis	
Sleep	Insomnia Interference with daily life Sleep disorders Sleep disturbance Sleep efficiency Sleep latency Sleep quality	
Stress	Daily stressful events Degrees of stress from events Perceived stress	
Tissue/Organ Damage	Chronic damage Cumulative damage Endocrine organ damage Neuropsychiatric damage Non-renal damage Renal damage	Diabetes Chronic kidney disease End stage renal disease
Treatment Satisfaction	Time to initial damage Satisfaction with information on treatment Satisfaction with treatment outcomes	
Use of Glucocorticoids Including Tapering	Reduction of glucocorticoids dose Use of glucocorticoids	

TIA: transient ischemic attack, PNS: peripheral nervous system, CNS: central nervous system,.

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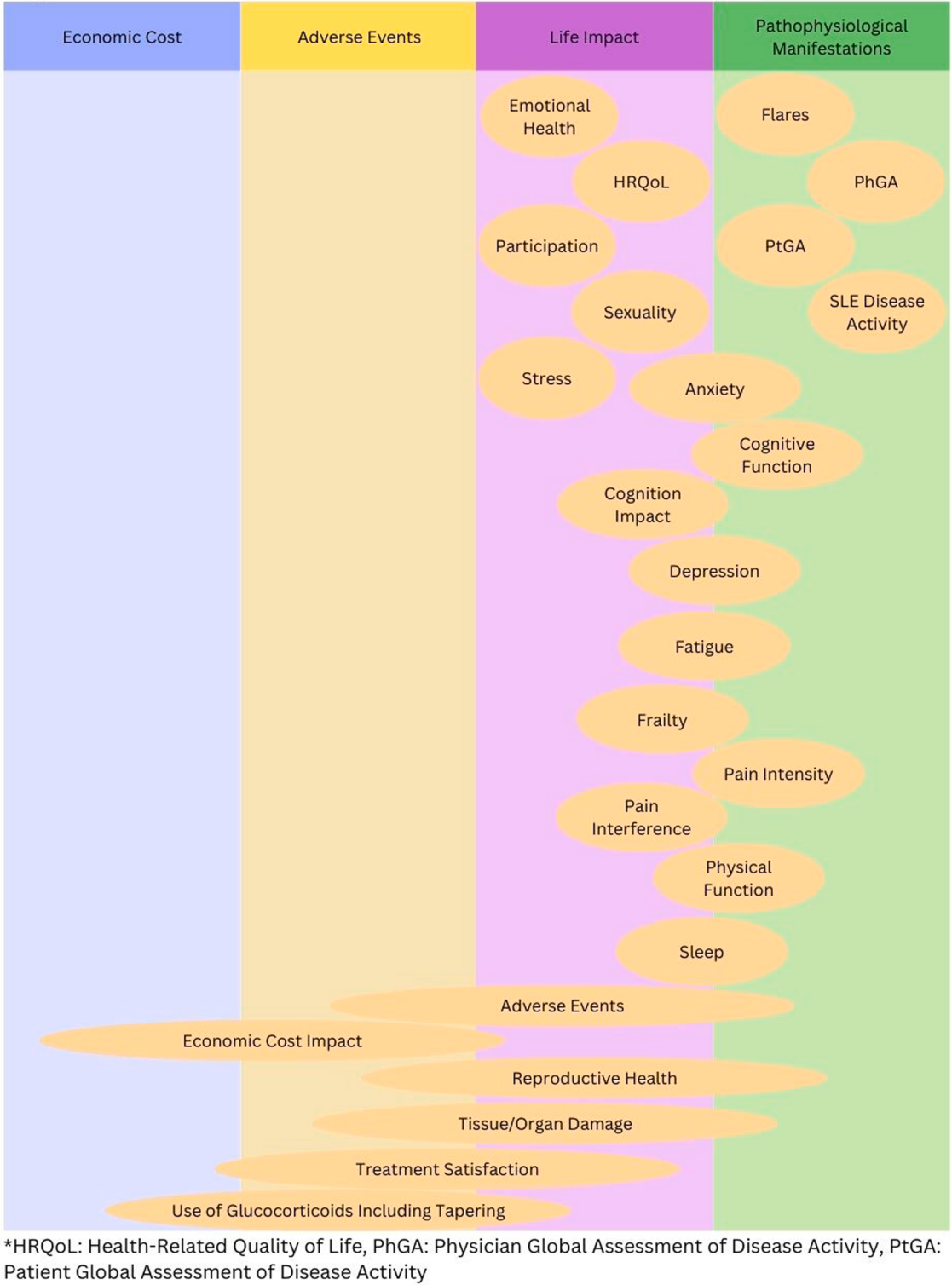


Fig. 2. Candidate domains and core area placement

*HRQoL: health-related quality of life, PhGA: physician global assessment of disease activity, PtGA: patient global assessment of disease activity.

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Table 2
Candidate domains and definitions.

Domain	Definition
Adverse Events	Any untoward medical occurrence in a participant, which does not necessarily have a causal relationship with the trial intervention.
Anxiety	Fear (fearfulness, panic), anxious misery (worry, dread), hyperarousal (tension, nervousness, restlessness), and somatic symptoms related to arousal (racing heart, dizziness).
Cognition Impact	The extent to which cognitive function is perceived (by the patient and their support network and immediate circle, as well as the healthcare team) to interfere with daily functioning and a patient's life.
Cognitive Function	Mental acuity, concentration, verbal and nonverbal memory, verbal fluency, and other cognitive domains and their noted changes (this includes subjective and objective assessments).
Depression	Negative mood (sadness, guilt), views of self (self-criticism, worthlessness), and social cognition (loneliness, interpersonal alienation), as well as decreased positive affect and engagement (loss of interest, meaning, and purpose).
Economic Cost Impact	The resources that is expended or forgone as a result of a health problem. It includes health sector costs (direct costs), the value of decreased or lost productivity by the patient (indirect costs), and the cost of pain and suffering (intangible costs).
Emotional Health (living with and managing SLE)	A construct consisting of multiple domains that describes one's expression, perception, and conceptualization of emotions which includes knowledge, reactivity, and regulation of emotions. It is your ability to cope with both positive and negative emotions
Fatigue	Range of symptoms from mild subjective feelings of tiredness to an overwhelming, debilitating, and sustained sense of exhaustion that likely decreases one's ability to execute daily activities and function normally in family or social roles.
Flares	An increase in disease activity in one or more organ systems involving new or worse clinical signs and symptoms and/or lab measurements. The increase must be considered clinically significant and in most cases, should prompt the consideration of a change or an increase in treatment.
Frailty	A clinically recognizable state in which the ability of people to cope with everyday or acute stressors is compromised by an increased vulnerability brought by declines in physiological reserve and function across multiple organ systems.
Health-Related Quality of Life	A term referring to the health aspects of quality of life, generally considered to reflect the impact of disease and treatment on disability and daily functioning. It has also been considered to reflect the impact of perceived health on an individual's ability to live a fulfilling life.
Pain Intensity	The intensity of the sensation of pain, encompassing the entire spectrum from a complete absence of pain to the most extreme levels of discomfort.
Pain Interference	Consequences of pain on relevant aspects of one's life. This includes the extent to

Table 2 (continued)

Domain	Definition
Participation in all aspects of life (family, social, educational, work, and leisure activities)	which pain hinders engagement with social, cognitive, emotional, physical and recreational activities. The involvement of people in all areas of life, and the participation restrictions they experience (functioning of a person as a member of society).
Patient Global Assessment of Disease Activity	A patient's self-perception of the degree of SLE disease activity.
Physical Function	One's ability to carry out various activities that require physical capability, ranging from self-care (activities of daily living) to more vigorous activities that require increasing degrees of mobility, strength or endurance.
Physician Global Assessment of Disease Activity	The physician's judgement of the degree of SLE disease activity.
Reproductive Health	Refers to the state of complete physical, mental, and social well-being in all matters relating to the reproductive system and implies that people can have a satisfying and safe sex life and that they have the capability to reproduce and the freedom to decide if, when, and how often to do so.
Sexuality	A person's behaviors, desires, and attitudes related to sex and intimacy.
SLE Disease Activity	Reversible manifestations (global as well as organ specific) of the underlying inflammatory process and is a reflection of the type and severity of organ involvement at each point in time.
Sleep	Perceptions of sleep quality, sleep depth, and restoration associated with sleep.
Stress	A state of worry or mental tension caused by a difficult situation.
Tissue/Organ Damage	Damage is a health state related to tissue/organ structure and function. The degree of reduced tissue/organ function relates to physiologic impairment. Damage can occur before a diagnosis of SLE but should be attributable to SLE. Damage to a tissue/organ is irreversible, but the functional consequences on that tissue/organ may improve over time through physiological adaptation or treatment.
Treatment Satisfaction	The individual's rating of attributes of the process and outcomes of their therapeutic plan.
Use of Glucocorticoids Including Tapering	The use of any form of administration of glucocorticoids including tapering and stopping.

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Future Directions

Qualitative research of focus groups with patients living with SLE from around the world has been conducted and is in the data extraction stage further identifying candidate SLE domains important to patients. Domains identified from the focus groups will supplement this list if needed and further validate the identified candidate domains.

Once all domain generation research is complete, the consensus

stage consisting of a 4-round Delphi consensus exercise will be held in 2025 to agree on the most important domains according to collaborators (patients, physicians, pharmaceutical representatives, and more). The Delphi will determine the most important domains that will form the core domain set. The first-round of the Delphi offers collaborators the opportunity to suggest additional domains to be considered for the CDS, and introduce any domains which may have been missed.

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References

- [1] 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(9):1151–9. <https://doi.org/10.1136/annrheumdis-2018-214819>.
- [2] Touma Z, McGhie TK, Beaton D, et al. Chapter 1 introduction: metrics and domains measured in SLE. In: *Outcome Measures and Metrics in Systemic Lupus Erythematosus*. Springer; 2021. p. 1–28.
- [3] Kaul A, Gordon C, Crow MK, et al. Systemic lupus erythematosus. *Nat Rev Dis Primers* 2016;2(1):16039. <https://doi.org/10.1038/nrdp.2016.39>.
- [4] Tian J, Zhang D, Yao X, Huang Y, Lu Q. Global epidemiology of systemic lupus erythematosus: a comprehensive systematic analysis and modelling study. *Ann Rheum Dis* 2023;82(3):351–6. <https://doi.org/10.1136/ard-2022-223035>.
- [5] Elera-Fitzcarrald C, Fuentes A, González LA, Burgos PI, Alarcón GS, MF Ugarte-Gil. Factors affecting quality of life in patients with systemic lupus erythematosus: important considerations and potential interventions. *Expert Rev Clin Immunol* 2018;14(11):915–31. <https://doi.org/10.1080/1744666X.2018.1529566>.
- [6] Boers M, Beaton DE, Shea BJ, et al. OMERACT filter 2.1: elaboration of the Conceptual framework for outcome measurement in Health intervention studies. *J Rheumatol* 2019;46(8):1021–7. <https://doi.org/10.3899/jrheum.181096>.
- [7] Maxwell LJ, Beaton DE, Boers M, et al. The evolution of instrument selection for inclusion in core outcome sets at OMERACT: filter 2.2. *Semin Arthritis Rheumatism* 2021;51(6):1320–30. <https://doi.org/10.1016/j.semarthrit.2021.08.011>.
- [8] Nielsen W, Strand V, Simon LS, et al. Updating the core domains set in Systemic Lupus Erythematosus: work planned by the Systemic Lupus Erythematosus OMERACT working group. *Lupus* 2023;32(4):586–8. <https://doi.org/10.1177/09612033231162769>.
- [9] Bouck Z, Straus SE, Tricco AC. Systematic versus rapid versus scoping reviews. *Methods Mol Biol* 2022;2345:103–19. https://doi.org/10.1007/978-1-0716-1566-9_6.
- [10] Tricco AC, Lillie E, Zarin, et al. PRISMA extension for scoping reviews (PRISMA-ScR): checklist and explanation. *Ann Intern Med* 2018;169(7):467–73. <https://doi.org/10.7326/M18-0850>.
- [11] Nielsen W. Scoping literature review of the measurement domains of systemic Lupus Erythematosus. *Open Sci Framework* 2023. osf.io/n594j.
- [12] Covidence systematic review software, Veritas Health Innovation, Melbourne, Australia. Available at www.covidence.org.
- [13] Nielsen W, Strand V, Simon LS, et al. OMERACT 2023 Systemic Lupus Erythematosus Special Interest Group: winnowing and binning preliminary candidate domains for the core outcome set. *Semin Arthritis Rheum* 2024;65:152380. <https://doi.org/10.1016/j.semarthrit.2024.152380>.
- [14] Kernder A, Elefante E, Chehab G, Tani C, Mosca M, Schneider M. The patient's perspective: are quality of life and disease burden a possible treatment target in systemic lupus erythematosus? *Rheumatology* 2020;59(5). <https://doi.org/10.1093/rheumatology/keaa427>. 63–v68.
- [15] Nielsen W, Strand V, Simon L, et al. OMERACT systemic lupus erythematosus domain survey. *Semin Arthritis Rheum* 2024;68:152520. <https://doi.org/10.1016/j.semarthrit.2024.152520>.
- [16] Askanase AD, Daly RP, Okado M, Neville K, Pong A, Hanrahan LM, Merrill JT. Development and content validity of the Lupus Foundation of America rapid evaluation of activity in lupus (LFA-REAL™): a patient-reported outcome measure

for lupus disease activity. Health Qual Life Outcomes 2019;17(1):99. <https://doi.org/10.1186/s12955-019-1151-8>.