Development of a Conceptual Disease Model of the Patient Experience of Systemic Lupus Erythematosus

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Plain Language Summary

- People with systemic lupus erythematosus experience symptoms that can be disabling and even life-threatening
- Regulators responsible for approving new medications (such as the US Food and Drug Administration) recommend that studies testing new treatments for the disease include suitable questionnaires that ask patients about relevant diseaserelated symptoms and their impact on their lives
- We looked at recently published studies where adults with systemic lupus erythematosus talked about their symptoms and the impact of the disease on their lives, and found 82 different symptoms (most commonly tiredness, joint and muscle pain, and skin rash) and 41 different impacts on patients' lives (most commonly how well they can move around, how they feel emotionally, and their relationships with others)
- We used this information to create a model of the patient experience of systemic lupus erythematosus, which will be used to test the suitability of questionnaires for use in clinical studies

Conclusions

- A CDM of the patient experience of SLE that includes 14 symptom dimensions, three proximal impact dimensions, and seven distal impact dimensions was developed based on a literature review
- This CDM is being used to evaluate the suitability of PROs for supporting, in combination with clinical outcomes, the approval of new SLE therapies, as per FDA guidance on patient-focused drug development (poster presenting these data [PCR205] is available via the QR code)

Introduction

- Systemic lupus erythematosus (SLE) is a heterogenous, multisystemic autoimmune disease¹ characterized by symptoms such as fatigue, fever, weight loss, rashes, and joint and muscle pain, as well as life-threatening complications that affect the kidneys, heart, lungs, and central nervous system²
- The importance of incorporating patient-reported outcome (PRO) measures in SLE clinical trials is recognized,^{3,4} with the US Food and Drug Administration (FDA) recommending the use of a conceptual disease model (CDM) to determine whether existing PRO measures capture the entirety of a concept of interest⁵

Objective

To develop a CDM of the symptoms and impacts of SLE

Methods

Identification of Patient-Reported Symptoms and Impacts

- A targeted literature review (TLR) was conducted in Embase and Medline to identify English-language full-text publications (published 2018–2023) detailing patient-reported symptoms and the impacts experienced by adults with SLE
- Publications were screened for eligibility using predefined inclusion criteria based on population, intervention/comparator, outcomes, and study design (Table)
- Data on patient characteristics, and symptoms and impacts of SLE were extracted from selected qualitative and quantitative publications

CDM Development

- A CDM of SLE symptoms and impacts was developed based on the concepts identified from the TLR
- Thematic analysis was used to group health concepts by common themes into dimensions capturing symptoms and impacts
- Impacts were categorized as 'proximal' if they were directly related to SLE or 'distal' if they occurred because of a proximal impact

Results

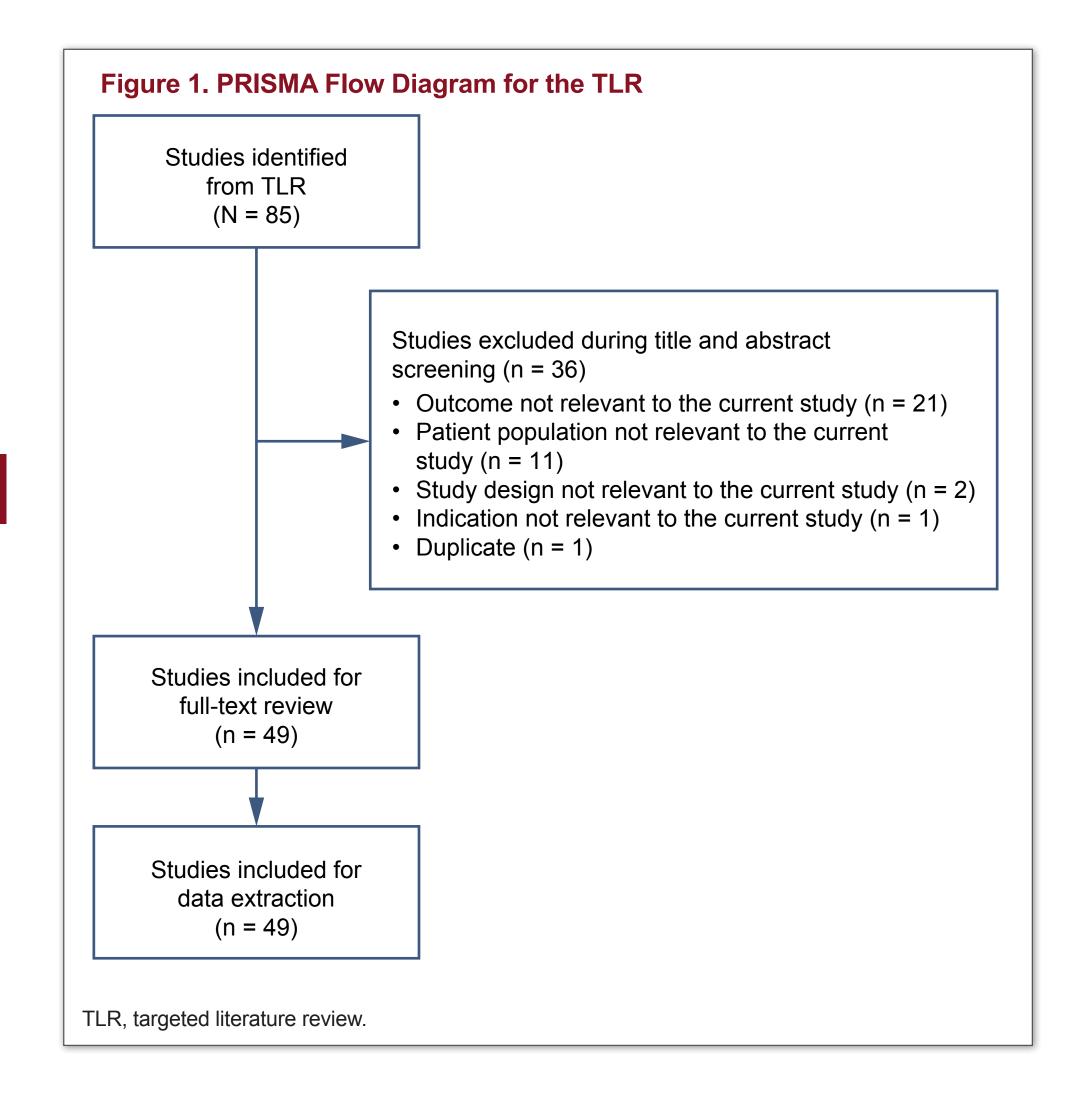
Patient-Reported Symptoms and Impacts

- The TLR identified 49 publications for data extraction (Figure 1) describing experiences of patients from the USA (n = 19), the UK (n = 6), Italy (n = 3), France (n = 3), China (n = 2), and Singapore (n = 2)
- In total, 82 symptoms and 41 impacts of SLE were identified
 - The most frequently reported symptoms (in ≥ 10 publications) were fatigue (n = 76), joint pain (n = 38), muscle pain (n = 36), rash (n = 36), and bodily pain (n = 30)
 - The most frequently reported impacts (in ≥ 10 publications) were physical functioning (n = 20), emotional health (n = 16), intimate relationships (n = 11), and cognitive impairment/ dysfunction (n = 10)

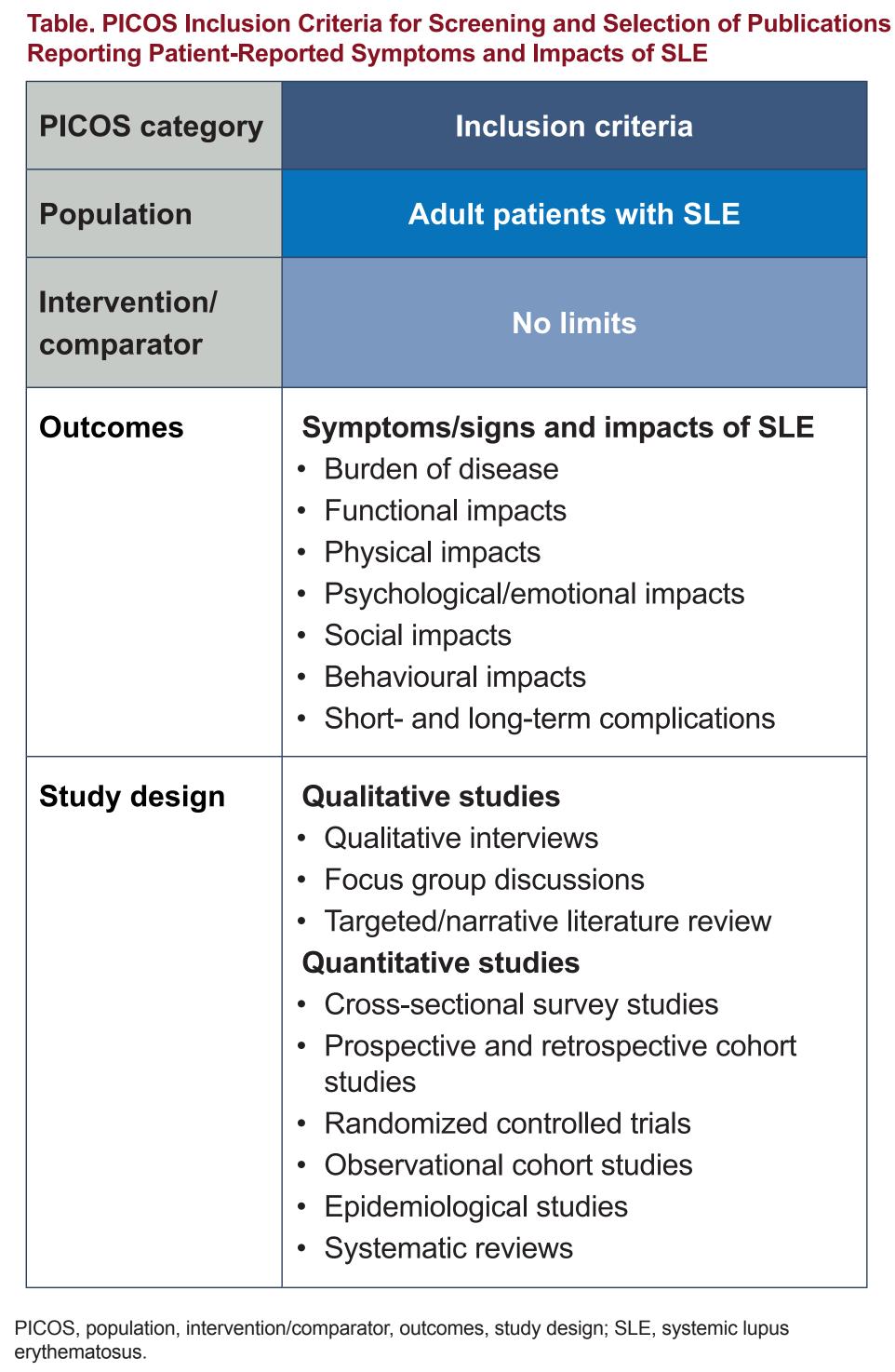
CDM of SLE

 A CDM of the patient experience of SLE was developed (Figure 2)

Figure 2. Conceptual Model of SLE



 The CDM grouped the 82 identified symptoms into 14 dimensions, the 13 impacts proximal to SLE into three dimensions, and the 28 impacts distal to SLE into seven dimensions



Systemic lupus erythematosus Bold coloured font: most frequently reported concepts in three or more Italicized font: concepts identified in **Symptoms** previously published models Energy-related **Weakness** Skin-related Joint-related **Kidney Heamatological** Flu-like **Inflammation** Mouth/ Hair-related Other Pain and **Smell** problems abnormalities taste-related discomfort Muscle Fatigue; Rash; Alopecia/ Joint swelling; Serositis; Fever, cough Anosmia: vitality; cutaneous hair loss foot/ankle pleurisy; diarrhoea; sensation involvement Joint pain/ Kidney Oral ulcer Cytopenia; involvement; vasculitis photosensitivity of bad smell oedema; dizziness; arthralgia; muscle involvement Raynaud's ageusia; pain; pain; chest tiredness; bleeding; articular vomit; nausea difficulty phenomenon; xerostomia; pain; headache: mental and mucocutaneous involvement/ chills; colds fissured tongue; breathing; haemolysis Bladderarthritis; stiff cognitive fatigue skin lesions; vitamin D fibromyalgia; dysgeusia; related joints; myalgia deficiency itch; finger stomatodynia foot pain; discoloration locked jaw; deformity; stomach pain; sore Bubbly or skin lupus; dark infection/lump throat; lip cheilitis foamy urine; grooves; clicking; spot; pallor; hyposalivation pyuria; erythema; haematuria; crepitation; bruxism bladder pain; petechiae; weight gain; restricted proteinuria ulcers swollen glands dry eyes numbness; earache **Proximal impacts Daily Physical** Psychological/emotional Physical functioning; physical health; usual activities; Daily activities/daily functioning; inability to drive Depression; anxiety; mood disorder; emotional health; fear; mental difficulty walking; physical disability health problems (anxiety disorder; bipolar disorder; ADHD; schizophrenia) **Distal impacts** Sleep Social Relationship Cognitive **Economic** Independence **Appearance** Intimate relationships: Financial struggle/strain; Sleep disturbance/ Feeling a burden to others Cognitive **Body image**; Social functioning: impairment/dysfunction; social withdrawal/isolation overweight or support from others impact on career/ obese/weight gain/ brain fog; difficulty thinking educational endeavours; clearly; lack of weight loss; self-image being uninsured; productivity loss; negative effects on concentration; worsening employment; reduced income; of cognitive abilities; absenteeism; lack of support neurological involvement; from work; changing patterns forgetfulness; to dynamics; limited financial psychological impact freedom; stress of losing work

Concepts described in the literature were characterized as: symptoms (e.g. 'joint pain', 'muscle pain'); proximal impacts if they were reported as being a direct result of SLE symptoms (e.g. 'physical functioning', 'physical health'); and distal impacts if they occurred because of a proximal impact (e.g. 'cognitive impairment', 'brain fog'). The most frequently reported concepts (in ≥3 publications) are shown in bold font. ADHD, attention deficit hyperactivity disorder; CNS, central nervous system; SLE, systemic lupus erythematosus.

Available from: https://www.ncbi.nlm.nih.gov/books/NBK535405/ (Accessed 5 September 2024); 3. FDA. 2010. Tamsyn Stanborough PhD of Oxford PharmaGenesis, Melbourne, Australia, and funded by Gilead Sciences, Available from: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/systemic-lupus-Inc. in accordance with Good Publication Practice 2022 (GPP2022) guidelines (https://www.ismpp.org/gpp-2022).

Disclosures: MA and **TF** are employees of Evidera, which received funding from Gilead to conduct the study. **MR** and **CK** are employees and shareholders of Gilead Sciences, Inc.

References: 1. Hoi A, et al. Lancet 2024;403:2326–38; 2. Vaillant AAJ, et al. StatPearls. Updated 2023.

Acknowledgements: This study was funded by Gilead Sciences, Inc. Medical writing support was provided by