Gap Analysis of Patient-Reported Outcome Measures for Systemic Lupus Erythematosus

PCR205

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Plain Language Summary

- People with systemic lupus erythematosus experience symptoms that can be disabling and even life-threatening
- Patient-reported outcome measures are questionnaires that ask patients about disease-related symptoms and their impact on their lives
- Regulators responsible for approving new medications (such as the US Food and Drug Administration) recommend that studies testing new treatments for systemic lupus erythematosus include these measures to assess how well a treatment works
- In this study, we found 72 patient-reported outcome measures that have been used in studies testing new treatments for systemic lupus erythematosus; none were found to cover all the symptoms and impacts. Of the five measures that were found to cover the most symptoms and impacts, all were found to require further testing

Conclusions

- Existing PRO measures were found to assess symptom and impact concepts relevant to patients with SLE; however, none comprehensively captured all relevant concepts
- All five analysed PRO measures were found to have psychometric evidence gaps
- Balancing coverage with validation evidence, a combination of the SLAQ for capturing symptoms and the Lupus PRO or LupusQoL for capturing impacts may be the best available option for use in SLE clinical trials based on current available PRO measures

Introduction

- Systemic lupus erythematosus (SLE) is a heterogenous, multisystemic autoimmune disease[1] 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 system[2]
- The US Food and Drug Administration (FDA) and European Medicines Agency recommend incorporating patient-reported outcomes (PRO) measures as secondary endpoints in SLE clinical trials to evaluate relevant disease-related symptoms and impacts[3,4]
- The FDA further recommends using a conceptual disease model (CDM) to determine whether existing PRO measures capture the entirety of a concept of interest,[5] and to ensure that PRO measures for key trial endpoints are well defined and supported by evidence of reliability in the SLE trial population[3]

Objective

- To examine validation evidence of PRO measures covering the most concepts in a SLE CDM

Methods

Identification of PRO Measures

- SLE PRO measures were identified from:
  - a targeted literature review in Embase and MEDLINE (English full-text; 2018–2023). Publications were screened and selected for eligibility using predefined inclusion criteria based on population, intervention/comparator, outcomes, and study design (for details see the Supplemental Table available via the QR code)
  - the US clinical trials database (2018–2023)
  - health technology assessment (HTA) submissions (no search limits)
  - regulatory label claims (no search limits)
- The selection of PRO measures for conceptual analysis was based on the extent of disease specificity and use across the information sources

Conceptual Analysis and Mapping

- Concepts assessed by the selected PRO measures were mapped against an SLE CDM of the patient experience (poster presenting the CDM [PCR268] is available via the QR code), which comprised 82 symptom and 41 impact concepts (13 impacts proximal to SLE and 28 distal impacts)

Gap Analysis

- Disease-specific PRO measures covering the most concepts were assessed for gaps in psychometric properties using FDA guidance and consensus-based standards for the selection of health measurement instruments (COSMIN) criteria[6–10]

Results

PRO Measures

- In total, 72 PRO measures were identified from the targeted literature review, US clinical trial database, and HTA and label reviews

Conceptual Analysis and Mapping

- The following eight PRO measures were selected for conceptual analysis based on the extent of their disease specificity and use across the information sources:
  - Functional Assessment of Chronic Illness Therapy – Fatigue (FACIT-F)
  - Lupus Impact Tracker (LIT)
  - Lupus PRO
  - Lupus-Specific Quality of Life (LupusQoL)
  - Quality of Life in SLE (L-QoL)
  - 36-Item Short Form Health Survey (SF-36)
  - SLE Quality of Life (SLEQoL)
  - Systemic Lupus Activity Questionnaire (SLAQ)
- **Table 1** lists the number of symptom concepts, and proximal and distal impact concepts covered by the eight selected PRO measures
  - The SLEQoL provided the most comprehensive coverage overall, covering 20 of the 123 concepts included in the CDM
  - Symptoms were most comprehensively covered by the SLAQ (16/82)
  - Impacts were most comprehensively covered by the SLEQoL (6/13 proximal, 9/28 distal) followed by the Lupus PRO (5/13 proximal, 8/28 distal)

Gap Analysis

- The five disease-specific PRO measures covering the most concepts in the CDM (L-QoL, Lupus PRO, LupusQoL, SLAQ, SLEQoL) were included for gap analysis of their content validity and psychometric properties to assess whether the measures could be considered fit for purpose
- **Table 2** summarizes the results of the gap analysis
  - All measures had strong support for internal consistency, three had strong support for test-retest reliability (LupusQoL, Lupus PRO, L-QoL), four had strong support for content validity (LupusQoL, Lupus PRO, SLEQoL, L-QoL), and four had strong support for convergent validity (LupusQoL, Lupus PRO, SLAQ, L-QoL); only the L-QoL had strong evidence for known-groups validity
  - Evidence on responsiveness was missing for the L-QoL and limited for remaining measures
  - Overall, the LupusQoL had the fewest gaps regarding its psychometric properties

Table 1. Conceptual Mapping of Selected PRO Measures Against the CDM for SLE

CDM concepts	FACIT-F	LIT	L-QoL	Lupus PRO	LupusQoL	SF-36	SLEQoL	SLAQ
Symptoms (n = 82)	5	2	1	5	4	3	5	16
Proximal impacts (n = 13)	5	3	2	5	6	6	6	1
Distal impacts (n = 28)	6	3	2	8	6	5	9	1
All (n = 123)	16	8	5	18	16	14	20	18

CDM, conceptual disease model; FACIT-F, Functional Assessment of Chronic Illness Therapy – Fatigue; LIT, Lupus Impact Tracker; L-QoL, Quality of Life in Systemic Lupus Erythematosus; LupusQoL, Lupus-Specific Quality of Life; PRO, patient-reported outcome; SF-36, 36-Item Short Form Health Survey; SLAQ, Systemic Lupus Activity Questionnaire; SLE, systemic lupus erythematosus; SLEQoL, Systemic Lupus Erythematosus Quality of Life.

Table 2. Gap Analysis of Selected PRO Measures Covering the Most Concepts When Mapped Against the CDM

Psychometric properties	L-QOL	Lupus PRO	LupusQoL	SLAQ	SLEQoL
Conceptual framework	Ø	+	+	Ø	+
Item and scale refinement	++	++	+++	+	++
Reliability					
Internal consistency	+++	+++	+++	+++	+++
Test-retest	+++	+++	+++	+	+
Validity					
Content	+++	+++	+++	+	+++
Known-groups	+++	+	+	++	Ø
Convergent, discriminant	+++	+++	+++	+++	+
Factor analysis	Ø	++	+++	++	+++
Ability to detect change over time (responsiveness)	Ø	+	++	+	+
Meaningful threshold analysis	Ø	Ø	++	+	+
Interpretation of score	Ø	+	+	Ø	+
Linguistic equivalence	+++	Ø	Ø	+	+++

Assessment using FDA guidance and COSMIN criteria: +++, fully meets criteria; ++, partially meets criteria; +, significant concerns about meeting criteria; ø, no evidence that process, method, or test was completed.
CDM, conceptual disease model; COSMIN, consensus-based standards for the selection of health measurement instruments; FDA, Food and Drug Administration; L-QoL, Quality of Life in Systemic Lupus Erythematosus; LupusQoL, Lupus-Specific Quality of Life; PRO, patient-reported outcome; SLAQ, Systemic Lupus Activity Questionnaire; SLEQoL, Systemic Lupus Erythematosus Quality of Life.

References: 1. Hoi A, *et al. Lancet*. 2024;403:2326–38; **2.** Vaillant AAJ, *et al. StatPearls*. Updated 2023. Available from: https://www.ncbi.nlm.nih.gov/books/NBK535405/ (Accessed 5 September 2024); **3.** FDA. 2010. Available from: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/systemic-lupus-erythematosus-developing-medical-products-treatment (Accessed 5 September 2024); **4.** EMA. 2015. https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-clinical-investigation-medicinal-products-treatment-systemic-lupus-erythematosus-and-lupus-nephritis_en.pdf (Accessed 5 September 2024); **5.** FDA. *Health Qual Life Outcomes*. 2006;4:79; **6.** FDA. 2009. Available from: https://www.fda.gov/media/77832/download (Accessed 12 September 2024); **7.** Mokkink LB, *et al. Qual Life Res*. 2010;19:539–49; **8.** Mokkink LB, *et al. J Clin Epidemiol*. 2010;63:737–45; **9.** Terwee CB, *et al. Qual Life Res*. 2012;21:651–7; **10.** Terwee CB, *et al. Qual Life Res*. 2018;27:1159–70.

Acknowledgements: This study was funded by Gilead Sciences, Inc. Medical writing support was provided by Tamsyn Stanborough PhD of Oxford PharmaGenesis, Melbourne, Australia, and funded by Gilead Sciences, 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.

Presented at ISPOR Europe 2024, 17–20 November 2024, in Barcelona, Spain.