Disease-Specific Patient Reported Outcome Tools for Systemic Lupus Erythematosus

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Purpose: Systemic lupus erythematosus (SLE) can significantly affect both health and non-health-related quality of life (HRQOL and non-HRQOL). However, of the existent published patient-reported outcome (PRO) tools, none were developed from US patients, an ethnically diverse population. Furthermore, these tools do not address men with SLE or assess non-HRQOL issues. Herein, we present the development and validation of the Lupus Patient-Reported Outcome tool (LupusPRO) and discuss its clinical utility and research value compared with other PRO tools currently available for SLE.

Methods: Beginning with a conceptual framework, items for LupusPRO were generated using feedback from women and men with SLE. The tool underwent iterations based on patient feedback and clinimetric and psychometric analyses. Validity (content, construct, and criterion) and reliability (internal consistency and test-retest) for the 44-item LupusPRO tool are presented.

Results: Consistent with the conceptual framework, items were identified that were related to HRQOL and non-HRQOL constructs. HRQOL domains included (1) lupus symptoms; (2) physical health (physical function, role physical); (3) pain–vitality; (4) emotional health (emotional function and role emotional); (5) body image; (6) cognition; (7) procreation; and (8) lupus medications. Non-HRQOL domains were (1) available social support and coping; (2) desires–goals; and (3) satisfaction with medical care. Internal consistency reliability (0.68-0.94), test-retest reliability (0.55-0.92), content, construct ($r > 0.50$ with SF-36), and criterion ($r > -0.35$ with disease activity) validity were fair to good.

Conclusions: LupusPRO is a valid and reliable disease-targeted patient-reported health outcome tool that is generalizable to SLE patients in the United States of varied ethnic backgrounds and either gender.

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Systemic lupus erythematosus (SLE) is a chronic multisystem autoimmune disease that primarily affects young women and has a significant impact on physical, social, and psychological health. With improvement in the survival rates of patients with SLE, increasing attention has been focused on the effects of SLE on quality of life (QOL) (1,2). QOL is 1 of the most important types of patient-reported outcomes, or outcomes where the patient is the primary informant. Inclusion of patient-reported outcome (PRO) as an endpoint is pivotal for patient care and research as it provides valuable information about the impact of SLE and treatment effectiveness not captured by clinical evaluation or by interview. QOL is a multidimensional construct that reflects an individual's responses to the physical, mental, and social factors contributing to daily living (3). Health-related QOL (HRQOL) refers to the components of QOL that relate directly to an individual's health (4). Although it is clearly important to understand disease effects on HRQOL from a physician's and clinical trials' perspective (5-7), understanding the broader impact of disease on components of QOL that are not directly related to health (non-HRQOL) are equally useful (8-13).

Non-HRQOL domains include features of both the natural and the created environment (ie, economic resources, communal resources) and personal resources (capacity to form friendships, social support, and religion) (14). Many factors, both internal and external, to an individual may affect health perceptions, functioning, and well-being (14). For example, patient-specific characteristics (eg, motivation and personality) may have important influences on HRQOL. Social networks, including family and friends, may help coping and adapting to a serious chronic disease, resulting in improved emotional well-being. Non-HRQOL factors may affect HRQOL, but unlike HRQOL domains, are less likely to improve with appropriate medical care. HRQOL may also affect non-HRQOL. Most medical literature focuses on HRQOL; however, measuring both HRQOL and non-HRQOL also provides an opportune insight into larger groups of patients and to larger geographical units, especially in epidemiological and observational studies.

Currently available SLE-specific PRO tools include "Systemic Lupus Erythematosus Quality of Life: SLE-QOL" (12), "Quality of Life in SLE: L-QoL" (15), and "Lupus Quality of Life tool: LupusQoL" (16). Because there are limitations to these tools that restrict their generalizability to US patients with SLE (17), we have developed a disease-targeted PRO measure for SLE (LupusPRO). Reported herein are its psychometric properties and a review of the alternately published SLE PRO tools.

METHODS

Our goal was to develop a SLE PRO tool for descriptive, discriminative, evaluative, and predictive purposes derived from an ethnically heterogeneous group of SLE patients in the United States to include issues pertinent to men with SLE and providing an assessment of non-HRQOL.

Psychometric properties studied included the following: internal consistency and reliability for each domain evaluated using Cronbach's α, where $\alpha > 0.70$ is considered acceptable (18). Test-retest reliability was tested by evaluating agreement between the patient responses to each domain at 2 time points. Content validity was evaluated by patient clinometric feedback on relative "importance" and "burden" of each item. Construct validity was evaluated based on the strength of correlation of LupusPRO with related domains on SF-36 using Spearman's correlation coefficient. Correlations were classified as strong ($r > 0.5$), moderate ($0.3 \leq r < 0.5$), weak ($0.1 \leq r < 0.3$), or absent ($r < 0.1$). Criterion validity of the LupusPRO was judged based on its correlation with either health status, measures of disease activity, or damage. The tool was considered to be responsive if changes in its domain or summary scores correlated with changes in health status and/or disease activity and in the expected direction.

The PRO measure was conceptualized based on frameworks used by the World Health Organization Quality of Life tool (19), as well as the PRO measurement information system (PROMIS). The research was conducted in stages. All participants were ≥18 years of age and met the American College of Rheumatology criteria for the classification of SLE (20).

Stages of design included item derivation, generation of a draft tool, and item reduction. At each stage the tool was revised based on either patient, expert, or data analysis feedback. Item reduction was achieved using clinometric and psychometric methods. The latter included exploratory factor and Rasch and internal consistency reliability analyses. LupusPRO tool underwent 6 iterations; psychometric properties of the final iteration of LupusPRO are presented.

Item pool for LupusPRO was derived from patient interviews. Eighteen SLE patients (16 women) from the outpatient clinic setting were interviewed individually using a semi-structured approach (21) (same investigator) inquiring their perceptions on how SLE and/or its treatment affected their health and QOL. The interviews and item pool generation were guided by a medical literature review on SLE and HRQOL/QOL, psychosocial literature in SLE, existing HRQOL/QOL tools, and input from clinicians with backgrounds in lupus/rheumatology and psychology. Interviews lasted from 15 to 45 minutes (median, 35 minutes), were audiotaped, and transcribed verbatim.

One hundred ninety-seven "issues" identified by the patients were noted on manual review of the interview transcripts pertaining to the impact of the disease or its treatment on patients' health and QOL. After screening for redundancy, reviewing for emergent themes and commonalities in themes, 93 unique "issues" remained and