Cross-cultural Validation of a Disease-specific Patient-reported Outcome Measure for Systemic Lupus Erythematosus in Canada

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ABSTRACT. ***Objective.*** The LupusPRO, a disease-targeted patient-reported outcome measure, was developed and validated in US patients with systemic lupus erythematosus (SLE). We report the results of the cross-cultural validation study of the English version of the LupusPRO among patients in Canada with SLE.

Method. The LupusPRO was administered to English-speaking Canadian patients with SLE. Demographic, clinical, and serological characteristics were obtained, and the Medical Outcomes Study Short Form-36 (SF-36) and LupusPRO were administered. Disease activity was ascertained using the Safety of Estrogens in Lupus Erythematosus National Assessment-Systemic Lupus Erythematosus Disease Activity Index (SELENA-SLEDAI) and the Lupus Foundation of America definition of flare (Yes/No). Damage was assessed using the Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index (SDI). Physician disease activity and damage assessments were also ascertained using visual analog scales. A mail-back LupusPRO form was completed within 2–3 days of the index visit. Items tested were internal consistency reliability (ICR), test-retest reliability (TRT), convergent and discriminant validity (against corresponding domains of the SF-36), criterion validity (against disease activity or health status), and known-groups validity.

Results. Participants were 123 Canadian patients with SLE (94% women); mean age was 47.7 (SD 14.8) years. The median (interquartile range) SELENA-SLEDAI and SDI were 4 (6) and 1 (3), respectively. The ICR of the LupusPRO domains ranged from 0.60 to 0.93, while the TRT range was 0.62–0.95. Measures observed were convergent and discriminant validity with corresponding domains of SF-36, criterion validity, and known-groups validity against disease activity, damage, and health status. Confirmatory factor analysis showed a good fit.

Conclusion. The LupusPRO has fair psychometric properties among Canadian patients with SLE, and prospective studies to establish minimally important difference are continuing. (J Rheumatol First Release June 15 2013; doi:10.3899/jrheum.121129)

Key Indexing Terms:
SYSTEMIC LUPUS ERYTHEMATOSUS QUALITY OF LIFE SELF-ASSESSMENT

Systemic lupus erythematosus (SLE) is associated with a poor quality of life[1,2], and patients with SLE have a poorer quality of life than patients with common chronic diseases[3]. Considering that the age at onset of SLE is much younger than in most other chronic diseases, and that SLE occurs most often in women, the potential for a cumulative effect of SLE on the patients and their families is immense[4]. Patient-reported outcomes (PRO) therefore constitute an important facet of overall health outcomes for the management of SLE. The US Food and Drug Administration recommends cross-cultural adaptation and validation of existing PRO tools, to improve their accessibility and applicability to patients and research universally[5]. The LupusPRO is a disease-targeted PRO measure that was developed and validated in patients with SLE (women and men) of heterogeneous ethnicity within the United States[6]. It includes both health-related and non-health-related quality of life domains (HRQOL, non-HRQOL), allowing an understanding of the broader burden of the disease. Its

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clinical utility and research value, compared with other PRO instruments currently available, have already been demonstrated[6,7]. We report the results of the cross-cultural validation study of the English version of the LupusPRO among Canadian patients with SLE (text of the questionnaire and scoring details available from the author on request).

MATERIALS AND METHODS

LupusPRO. The LupusPRO has 2 constructs: HRQOL and non-HRQOL. The HRQOL domains are SLE symptoms, cognition, SLE medications, physical health (themes: physical function and role physical), pain-vitality (fatigue, sleep), body image, emotional health (emotional function and role emotional), and procreation (sexual health and reproduction). The non-HRQOL domains are desires/goals, relationship/social support, coping, and satisfaction with medical care. In total, the LupusPRO comprises 43 items (30 for HRQOL construct, 13 for non-HRQOL construct) related to the past 4 weeks in the patient's life. Each item has 5 options ranging from "none of the time" to "all of the time." The survey takes between 5 and 7 minutes to complete. Individual domain scores, total HRQOL, and total non-HRQOL scores range from 0 to 100, where higher score signifies better QOL. The tool has excellent psychometric properties in US patients[6]. Our study was approved by the Institutional Ethics Board of the Montreal General Hospital and written consent was obtained according to the Declaration of Helsinki. The tool was pretested in 5 English Canadian individuals and no language modifications were indicated based on the feedback[8].

Patients. The McGill University Health Center SLE cohort enrolls and prospectively follows patients meeting the American College of Rheumatology (ACR) classification criteria for SLE[9]. The LupusPRO was administered to consenting adult patients (age ≥ 18 yrs) who were able to read and understand English. Participants were consecutive English-speaking outpatients coming for their annual research visit between August 2010 and April 2012. Data on demographic information and clinical and serological characteristics were collected at the baseline visit. The LupusPRO and Medical Outcomes Study Short Form-36 (SF-36)[10] were self-administered. Higher scores on the SF-36 denote better health. Disease activity was ascertained using the Safety of Estrogens in Lupus Erythematosus National Assessment–Systemic Lupus Erythematosus Disease Activity Index (SELENA-SLEDAI)[11], the SELENA Flare Index (SFI), and the Lupus Foundation of America (LFA) definition of flare (Yes/No)[12]. Damage was assessed using the Systemic Lupus International Collaborating Clinics/ACR Damage Index (SDI)[13]. In addition, physician assessments of disease activity and damage were ascertained using visual analog scales (MD activity VAS and MD damage VAS). These VAS scores ranged from 0 to 10, where a higher score indicated worse disease status. Patients were given 2 LupusPRO questionnaires. One had to be filled out at baseline (T1), and another had to be completed (along with a patient-reported change in health status that ranged from –7 to +7) within 2–3 days after baseline (T2) and mailed back to the study site.

Psychometric properties. The psychometric properties studied included reliability and validity. Reliability reflects the extent to which (1) different questions that are assumed to address the same underlying concept are correlated; and (2) the same question yields consistent results at different points in time if health remained unchanged[14]. The former is referred to as internal consistency reliability (ICR) and the latter as test retest reliability (TRT). Validity is the degree to which the measure reflects what it is supposed to measure rather than something else. There are many different types of validity that can be established using a variety of methods. Construct validity is considered to be an overarching concept that encompasses convergent, discriminant, criterion, and known-groups validity. Evidence for convergent validity is provided if the new instrument scores correlate with other measures of the same construct, and evidence of discriminant validity is established if scale scores do not correlate with measures of unrelated constructs. Criterion validity refers to the assessment of the new instrument against an external reference representing more "objective" results. In known-groups validity, the validity is determined by the degree to which an instrument can demonstrate different scores for groups known to vary on the items being measured[14]. Sensitivity to change (responsiveness) was not assessed in our study.

Statistical analyses. The ICR and TRT for each domain was evaluated using Cronbach's alpha coefficient, where alpha > 0.70 is considered acceptable[15]. TRT was tested by evaluating agreement between the patient responses to each domain at 2 timepoints, 2–3 days apart. Intraclass correlation coefficients were computed using a split half model. Convergent validity was evaluated using Spearman's correlation coefficient based on the strength of correlation of the LupusPRO with related domains on the SF-36 (physical health domain of LupusPRO against physical function, role physical, and physical component summary score of SF-36; emotional health of LupusPRO against mental health, role emotional, and mental component summary score of SF-36; and pain-vitality of LupusPRO against bodily pain and vitality of the SF-36). However, assessment of the convergent validity for the lupus symptoms domain was performed against disease activity assessments (SELENA-SLEDAI, MD activity VAS, SFI, LFA), because they measure the same concepts. Discriminant validity of LupusPRO domains using correlational analysis against nonrelated domains of the SF-36 was assessed. Criterion validity was judged using correlation between LupusPRO domains and physician-based measures of disease activity and damage (SELENA-SLEDAI descriptors and total scores, MD activity VAS, SFI, LFA flare, SDI descriptors and total scores, MD damage VAS). Correlations were classified as strong ($r \geq 0.5$), moderate ($0.3 \leq r < 0.5$), weak ($0.1 \leq r < 0.3$), or absent ($r < 0.1$). Known-group validity was judged against flares (SFI or LFA), MD activity VAS, and patient-reported health status (SF-36 item 1). ANOVA, with assumption of unequal variance between groups, was used to compare LupusPRO domain scores stratified by known groups. The conceptual framework (hypothesized item to scale relationships) of the LupusPRO was evaluated using confirmatory factor analysis (CFA) appropriate for categorical data. CFA was conducted with the LupusPRO item responses using a robust weighted least-squares estimator and the Mplus software (version 2)[16]. The latter uses a multistep method for ordinal outcome variables that analyzes a matrix of polychoric correlations rather than covariances. The goodness-of-fit of the hypothesized item-to-scale relationships (multifactor) was evaluated with the Comparative Fit Index (CFI) and the Tucker-Lewis Index (TLI). The CFI and TLI are comparative fit indices that quantify the amount of difference between the examined model and the independence model (i.e., a standard comparison model that asserts that none of the components in the model are related), with higher scores indicating larger differences. It is recommended that these 2 indices be 0.9 or greater as evidence of acceptable model fit[17]. All reported p values are 2-tailed.

RESULTS

One hundred twenty-three Canadian patients with SLE (94% women) participated (Table 1). For TRT assessment, 104 patients returned the T2 questionnaire (84.5% response rate) and data were complete for 103 patients. The mean (SD) age was 47.7 (14.8) years. Sixty percent were white, 23% Asian, and 9% African-Caribbean. Fifty-two percent were currently married and the median years of education was 14 [interquartile range (IQR) 3, minimum 4, maximum 17]. The median (IQR) SELENA-SLEDAI was 4.0 (6.0). Flare, as defined by the SFI and LFA criteria, was present among 19% (21 with mild/moderate and 2 with severe) and

Table 1. Description of the study cohort.

Characteristics	
Age, yrs (mean, SD)	47.7 (14.8)
Female (%)	94
Ethnicity (%)	
White	60.0
Asian	23.0
African-Caribbean	9.0
Other	8.0
Marital status (%)	
Never married	36.4
Currently married	52.1
Divorced	6.6
Separated	1.7
Widowed	3.3
Education, yrs (%)	
4–10	7
11–17	93
MD activity VAS, median (IQR)	0.2 (0.95)
SELENA-SLEDAI, median (IQR)	4.0 (6.0)
SFI flare present (%)	19
LFA flare present (%)	17
MD damage VAS, median (IQR)	0.3 (2.8)
SDI, median (IQR)	1.0 (3.0)

MD: physician assessments of disease; VAS: visual analog scale; IQR: interquartile range; SELENA-SLEDAI: Safety of Estrogens in Lupus Erythematosus National Assessment-Systemic Lupus Erythematosus Disease Activity Index; SFI: SELENA Flare Index; LFA: Lupus Foundation of America; SDI: Systemic Lupus International Collaborating Clinics/ACR Damage Index.

17% of participants at the time of the study. The median (IQR) SDI was 1.0 (3.0). The median (IQR) MD activity VAS and MD damage VAS scores were 0.2 (0.95) and 0.3 (3.0), respectively.

The median scores on the LupusPRO domains, floor and ceiling effects, and missing responses are shown in Table 2. Floor and ceiling effects for the SF-36 domains were as follows: physical function (0%, 26.8%), role physical (25.2%, 43.9%), bodily pain (0.8%, 20.3%), general health (0%, 0.8%), vitality (1.6%, 1.6%), social functioning (0.8%, 34.1%), role emotional (17.1%, 65.9%), and mental health (0%, 2.4%).

The ICR of the LupusPRO domains ranged from 0.60–0.93, while the TRT ranged from 0.62–0.96 for the 103 patients with complete LupusPRO at T2 and from 0.74–0.96 for patients who remained stable on the change in health status score (n = 63). Convergent validity with corresponding domains of SF-36 was observed (Table 3). Discriminant validity was evident from poor correlation between unrelated domains of LupusPRO and SF-36 [e.g., correlation coefficients of (a) lupus medication domain with SF-36 physical function and role physical were 0.18 and 0.16, respectively; and (b) procreation domain with SF-36 bodily pain was –0.06]. Criterion validity against disease activity measures (MD activity VAS, SELENA-SLEDAI, SFI, and LFA flare) was observed for all the HRQOL domains of the LupusPRO. These correlations were modest for the LupusPRO domains of lupus symptoms, physical health, pain-vitality, and body image (Table 3). Concerning damage, modest correlations with LupusPRO domains (lupus symptoms, physical health) were noted, while the other domains had weak correlations (Table 3). Known-groups validity of LupusPRO domains against flares (SFI, LFA), VAS activity MD, and health status (SF-36 item 1) were also noted (Table 4).

Results of confirmatory factor analysis lent empirical support for the conceptual framework of the LupusPRO (Table 5). The model fit for the hypothesized item-to-scale relationships were excellent (CFI = 0.98, TLI = 0.99). In addition, item-to-factor loadings representing the hypothesized item-to-scale relationships were also satisfactory. In general, items loaded > 0.6 with their respective factor.

Table 2. Descriptive scores of the LupusPRO (patient-reported outcome) domains in Canadian patients with systemic lupus erythematosus (SLE).

LupusPRO Domain	Median (IQR)	Floor Effect (% min score of 0)	Ceiling Effect (% max score of 100)	Missing Responses (%)
SLE symptoms	83.3 (33.3)	0	29	2.4
Cognition	75.0 (50.0)	0.8	32.5	0
Lupus medications	100.0 (25.0)	1.6	54.5	0.8
Physical health	95.0 (15.0)	0	47.2	0
Pain-vitality	80.0 (40.0)	0	21.1	0.8
Body image	90.0 (30.0)	0	39.8	0.8
Emotional health	79.2 (29.2)	0.8	15.4	3.3
Procreation	100.0 (0.0)	0.8	75.6	0.8
Desires-goals	87.5 (37.5)	0.8	32.5	0
Social support	75.0 (62.5)	14.6	27.6	0
Coping	66.7 (33.3)	1.6	14.6	1.6
Satisfaction with medical care	75.0 (75.0)	22	25.2	0.8

IQR: interquartile range; min: minimum; max: maximum.

Table 3. Psychometric properties of LupusPRO. Items in italic type represent moderate correlation. Items in bold type represent strong correlation.

Domain	ICR	TRT, n = 103	TRT, n = 63	Convergent Validity (correlation coefficient r, p value)	Criterion Validity (correlation coefficient r, p value)
Lupus symptoms	0.62	0.92	0.90	S-SLEDAI-arthritis (–0.23, 0.01) *S-SLEDAI-rash (–0.32, 0.001)* *S-SLEDAI-alopecia (–0.34, 0.0001)*	*LFA flare (–0.34, 0.001); SFI (–0.31, 0.001)* *MD activity VAS (–0.48, 0.0001)* MD damage VAS (–0.26, 0.01) *SDI chronic scarring alopecia (–0.33, 0.002)* SDI extensive scarring and panniculum (–0.20, 0.03)
Cognition	0.89	0.89	0.89		LFA flare (–0.21, 0.02) MD activity VAS (–0.29, 0.001)
Lupus medications	0.64	0.92	0.89		MD activity VAS (–0.26, 0.01)
Physical health	0.83	0.73	0.87	**PF (0.60, 0.0001)** **RP (0.51, 0.0001)** **PCS (0.58, 0.0001)**	*S-SLEDAI-arthritis (–0.36, 0.0001)* LFA Flare (–0.26, 0.004); SFI (–0.22, 0.02) MD activity VAS (–0.34, 0.0001) MD damage VAS (–0.20, 0.03) SDI diabetes (–0.20, 0.03) SDI valvular heart disease (–0.20, 0.03) SDI shrinking lung (–0.19, 0.04) *SDI ESRD (–0.34, 0.04)*
Pain-vitality	0.90	0.93	0.93	**BP (0.76, 0.0001)** **VT (0.81, 0.0001)**	*S-SLEDAI-arthritis (–0.30, 0.001)* LFA Flare (–0.27, 0.003), SFI (–0.23, 0.01) *MD activity VAS (–0.41, 0.0001)* MD damage VAS (–0.23, 0.01) SDI total (–0.19, 0.03) SDI pulmonary fibrosis (–0.22, 0.05) SDI angina (–0.18, 0.05) SDI estimated GFR (–0.22, 0.02)
Body image	0.93	0.92	0.92		S-SLEDAI-arthritis (–0.21, 0.02) S-SLEDAI-rash (–0.20, 0.03) *S-SLEDAI-alopecia (–0.30, 0.001)* Total S-SLEDAI (–0.19, 0.03) LFA Flare (–0.25, 0.006), SFI (–0.20, 0.03) *MD activity VAS (–0.37, 0.0001)* SDI extensive scarring/panniculum (–0.19, 0.03)
Emotional health	0.93	0.95	0.96	**MH (0.62, 0.0001)** **RE (0.50, 0.0001)** *MCS (0.38, 0.0001)*	LFA flare (–0.23, 0.01) SFI (–0.21, 0.02) MD activity VAS (–0.26, 0.005)
Procreation	0.78	0.96	0.95		SDI scarring chronic alopecia (–0.23, 0.01) Total SLICC-ACR/SDI (–0.22, 0.01) MD damage VAS (–0.18, 0.04)
Desires-goals	0.88	0.62	0.74		S-SLEDAI-arthritis (–0.23, 0.01) LFA flare (–0.21, 0.02) MD activity VAS (–0.28, 0.002) MD damage VAS (–0.24, 0.008) SDI AVN (–0.18, 0.05) SDI pericarditis (–0.18, 0.05)
Social support	0.84	0.85	0.85	—	—
Coping	0.60	0.80	0.79	—	S-SLEDAI-rash (–0.23, 0.01) SDI extensive scarring/panniculum (–0.20, 0.03)
Satisfaction medical care	0.93	0.87	0.90	—	—

For S-SLEDAI, no patients had seizures, psychosis, organic brain syndrome, cranial nerve disorder, headache, stroke, vasculitis, pericarditis, or fever. Of all the other S-SLEDAI descriptors tested for correlation with the Lupus Symptom domain, significant correlations were noted against arthritis, rash, and alopecia. Correlation with total S-SLEDAI score was not significant (r = –0.16, p = 0.09). AVN: avascular necrosis; BP: bodily pain; ESRD: endstage renal disease; GFR: glomerular filtration rate; ICR: internal consistency reliability; LFA: Lupus Foundation of America; MCS: mental component summary score; MH: mental health; PCS: physical component summary score; PF: physical function; PGA: physician global assessment; RE: role emotional; RP: role physical; SDI: SLICC/ACR Damage Index; SFI: SELENA Flare Index; S-SLEDAI: SELENA SLEDAI: Safety of Estrogens in Lupus Erythematous National Assessment-SLE Disease Activity Index; TRT: test retest reliability [TRT (n = 103): all patients (with complete LupusPRO at T2); TRT (n = 63): patients stable on the change in health status score]; VAS: visual analog scale; VT: vitality.

Table 4. Known-groups validity of LupusPRO against flare and disease activity (4A) and patient-reported health status (SF-36 Item 1; 4B). Except for p values, data are mean (SD).

4A.	SFI Flare			LFA Flare			MD Activity VAS		
Domain	Yes	No	p	Yes	No	p	< 1	≥ 1	p
Lupus symptoms	83.9 (18.7)	68.9 (20.6)	0.007	84.0 (18.5)	66.2 (19.5)	0.001	85.3 (18.0)	68.4 (20.2)	0.0001
Cognition	73.5 (27.5)	64.9 (24.6)	0.16	74.0 (27.3)	61.9 (21.8)	0.03	73.5 (27.6)	66.7 (24.4)	0.121
Lupus medications	84.3 (24.5)	81.0 (24.9)	0.57	84.7 (24.2)	75.0 (28.5)	0.16	86.8 (22.0)	70.4 (30.5)	0.002
Procreation	89.4 (22.7)	95.8 (13.3)	0.21	89.7 (22.5)	93.5 (16.6)	0.39	90.0 (22.3)	90.8 (19.9)	0.856
Physical health	90.0 (16.2)	84.3 (16.7)	0.16	90.2 (16.0)	81.0 (16.7)	0.03	89.8 (16.4)	84.7 (16.7)	0.048
Pain-vitality	76.8 (21.7)	63.6 (26.2)	0.04	77.1 (21.5)	59.0 (25.1)	0.005	77.1 (21.4)	63.5 (25.4)	0.005
Emotional health	76.0 (23.7)	65.0 (28.8)	0.07	76.2 (23.5)	58.3 (30.8)	0.004	75.3 (24.7)	65.6 (28.2)	0.084
Body image	85.4 (18.9)	74.5 (27.3)	0.03	85.5 (18.7)	66.8 (30.2)	0.0001	87.4 (16.6)	66.2 (29.1)	0.0001
Desires-goals	79.7 (23.9)	74.7 (23.2)	0.38	80.1 (23.7)	68.5 (25.3)	0.04	79.4 (24.1)	72.9 (24.6)	0.207
Social support	61.2 (36.5)	66.7 (32.4)	0.53	62.4 (36.6)	63.1 (31.5)	0.93	58.7 (37.4)	72.9 (28.1)	0.058
Cope	65.0 (25.0)	60.7 (21.1)	0.46	65.8 (25.1)	57.5 (19.9)	0.16	64.5 (25.1)	63.1 (22.3)	0.778
Satisfaction medical care	61.5 (39.9)	62.2 (33.1)	0.94	61.9 (39.9)	65.5 (32.6)	0.70	62.0 (39.7)	65.0 (34.9)	0.714

4B.						
Domain	Excellent, n = 7	Very Good, n = 34	Good, n = 43	Fair, n = 30	Poor, n = 5	p
Lupus symptoms	96.4 (6.6)	91.1 (8.7)	79.7 (20.7)	68.3 (21.7)	76.7 (18.1)	0.0001
Cognition	91.1 (11.9)	82.4 (25.0)	70.1 (26.7)	60.1 (24.2)	57.5 (33.8)	0.002
Lupus medications	96.4 (9.4)	91.9 (12.6)	80.1 (28.0)	75.8 (30.1)	65.0 (28.5)	0.016
Procreation	98.2 (4.7)	91.5 (15.6)	90.8 (25.3)	88.3 (23.7)	80.0 (28.8)	0.66
Physical health	100.0 (0.0)	96.0 (7.3)	84.4 (21.2)	83.9 (15.0)	81.0 (13.9)	0.002
Pain-vitality	97.1 (5.7)	88.1 (14.7)	74.3 (19.9)	56.3 (21.0)	44.0 (17.8)	0.0001
Emotional health	94.0 (5.8)	87.7 (12.1)	71.6 (21.8)	56.9 (29.8)	39.6 (33.1)	0.0001
Body image	94.3 (13.0)	89.6 (14.6)	85.5 (18.3)	67.0 (28.4)	74.0 (20.7)	0.0001
Desires-goals	97.3 (7.1)	89.2 (17.0)	74.1 (26.5)	66.1 (24.4)	73.8 (20.4)	0.0001
Social support	67.9 (39.4)	52.9 (42.4)	68.9 (31.6)	62.9 (32.8)	75.0 (26.5)	0.34
Cope	73.6 (22.6)	65.0 (26.8)	65.7 (25.5)	56.2 (20.1)	80.0 (20.1)	0.17
Satisfaction medical care	53.6 (44.3)	51.5 (43.1)	70.5 (36.7)	67.5 (30.6)	73.8 (42.5)	0.20

SFI: SELENA Flare Index; SELENA: Safety of Estrogens in Lupus Erythematosus National Assessment; LFA: Lupus Foundation of America; MD activity VAS: physician assessment of disease activity on visual analog scale; SF-36: Medical Outcomes Study Short Form-36.

DISCUSSION

Our study assessed the psychometric properties of the LupusPRO in Canada and supports the reliability and validity of this instrument in this population. The demographic and ethnic distribution of our cohort was representative of the patients seen in SLE clinics throughout Canada[18]. Because all the forms were checked to ensure their completion before patients were discharged, missing responses were few. We also had a high returned rate, suggesting that the LupusPRO is acceptable.

First, LupusPRO demonstrated good reliability. It is noteworthy that the ICR for LupusPRO domains with 2 or 3 items was lower than ICR for domains with > 3 items. ICR improves with a greater number of items forming the domain. For the coping domain, deletion of the item on spirituality/religious improved the ICR to 0.68, suggesting also some cultural differences in the study group. TRT, defined as giving the same result when an individual is retested while remaining in a clinical steady state, is another critical measurement property for HRQOL instruments that was demonstrated in our study. However, TRT for the desires and goals domain was low in our study. The reason for this is unclear. One hypothesis could be that when patients complete the LupusPRO at home versus at the clinic, they may more carefully consider both the immediate and longer-term effects of SLE on their desires and goals. Patients scored lower on this domain by an average of 13.5 points at T2 as compared to T1. However, the length of time between the 2 test administrations may affect this result. A very short time interval makes the carryover effects due to, for example, memory or practice, more likely, whereas a longer interval increases the probability that a change in status could occur. Studies of TRT for HRQOL instruments have used varying intervals between test administrations. The interval of 2 to 3 days was selected here because it is believed to be a reasonable compromise between recollection bias and unwanted clinical change. In a study comparing TRT at 2 days and 2 weeks, there were no statistically significant differences for the 2 time intervals[19].

Domains of the LupusPRO performed well against corresponding domains of the generic PRO tool for HRQOL (SF-36; convergent validity); did not correlate with noncorresponding SF-36 domains (discriminant validity); and correlated with measures of disease activity and/or damage

Table 5. Confirmatory analysis of HRQOL and non-HRQOL items of LupusPRO.

Factor			Factor Loadings
1	Symptoms	Loss of hair	0.666
		New flare	0.678
		SLE flare	0.752
2	Cognitive	Poor memory	0.968
		Lack of concentration	0.916
3	Medication	Meds cause side effects	0.813
		Concerned over number of medications	0.808
4	Procreation	Ability to have baby	0.852
		Ability to prevent pregnancy	0.817
5	Physical	Taking care of personal needs	0.781
		Getting in and out of bed	0.770
		Fulfilling family responsibilities	0.859
		Taking care of dependents	0.840
		Burden to family	0.860
6	Pain/vitality	Woke up feeling worn out	0.729
		Felt pain	0.806
		Unable to do usual activities	0.863
		Performing activities takes long	0.946
		Limited in kinds of activity	0.938
7	Emotional	Worried about SLE effects	0.889
		Worried about losing income	0.777
		Anxious	0.887
		Depressed	0.914
		Concerned SLE leads to more health problems	0.932
		Concerned SLE lasts a long time	0.960
8	Body image	Dislike my appearance	0.904
		Thought less of myself	0.906
		Lacked control over appearance	0.910
		Self-conscious about appearance	0.948
		Embarrassed about how others perceived me	0.906
9	Goals	Ability to plan	0.912
		Overall life satisfaction	0.943
		Enjoyment of life	0.914
		Fulfill career goals	0.750
10	Support	Receive support from friends	0.853
		Receive support from family	0.964
11	Coping	Focus on making situation better	0.646
		Learned to live with lupus	0.930
		Comfort/strength from religion	0.517
12	Satisfaction	Doctor accessible	0.847
		Doctor understood	0.905
		Doctor provided information	0.988
		Doctor discussed/monitored side effects	0.911
Tests of model fit		CFI	0.983
		TLI	0.988

HRQOL: health-related quality of life; SLE: systemic lupus erythematosus; CFI: Comparative Fit Index; TLI: Tucker-Lewis Index.

or health status (criterion and known-groups validity). Confirmatory factor analysis showed a good fit. Previous studies have failed to identify a significant relationship between SLE disease activity and patient-reported health status[19]. In our study, weak to modest correlations were noted between disease activity measures and LupusPRO domains. Poor relationship between PRO and disease activity or damage are well known[20,21]. This indicates that PRO measures provide uniquely valuable information about the effect of SLE and treatment effectiveness that is not captured by the disease activity or damage indices. It is also possible that the differing timeframes between disease activity (10 days), damage (6 months), and LupusPRO (4 weeks) assessments may contribute to the poor relationship between the 3 measures.

We did find significant ceiling effects with both LupusPRO and SF-36. This likely reflects the apparently well controlled or inactive or mildly active disease that is often encountered in the outpatient clinics, particularly among patients who are willing to participate in noninterventional

research. To accurately gauge ceiling and floor effects, the tool would need to be tested in a larger heterogeneous patient group with varied disease activity and manifestations.

Generic tools such as the SF-36 have been more widely used in SLE research than disease-specific tools. The SF-36 has been found to be responsive to changes in disease in some studies, while in others the responsiveness has been to changes in fibromyalgia in patients with SLE and not to changes in the disease[22]. It has been used in some clinical trials and it is not clear whether sensitivity to change was observed[23]. We used the SF-36 to evaluate the concurrent validity of the LupusPRO because of its widespread use and acceptability as a multipurpose generic measure of HRQOL in SLE. However, it may not identify all HRQOL domains that are significant to patients with SLE, such as sexual functioning, body image, and sleep.

Disease-specific patient-reported outcome tools provide for inclusion of all pertinent domains, and therefore increased sensitivity[24]. Patient-reported outcome measures specifically designed for patients with SLE have been developed, and each has its strengths and limitations[7]. An SLE-specific QOL instrument developed in Singapore was derived from input by physicians and nurse clinicians[25]. The L-QoL is a needs-based QOL model based on cognitive interviews of patients with SLE[26]. LupusQoL was derived from mostly white women in the United Kingdom and contains only HRQOL domains[27].

The LupusPRO has fair psychometric properties among Canadian patients with SLE. Before the LupusPRO can be recommended for use in clinical trials, prospective studies to establish sensitivity to change and minimally important differences are required.

REFERENCES

1. Jolly M, Utset TO. Health related quality of life among outpatient systemic lupus erythematosus University of Chicago cohort [abstract]. Arthritis Rheum 2003;48 Suppl:3642.
2. Jolly M, Pickard SA, Mikolaitis RA, Rodby RA, Sequeira W, Block JA. LupusQoL-US benchmarks for US patients with systemic lupus erythematosus. J Rheumatol 2010;37:1828-33.
3. Jolly M. How does quality of life of patients with systemic lupus erythematosus compare with that of other common chronic illnesses? J Rheumatol 2005;32:1706-8.
4. Thakkar A, Mikolaitis RA, Block JA, Jolly M. Caregiver burden is associated with worse dyadic relationship and health outcomes in lupus [abstract]. Arthritis Rheum 2011;63 Suppl:S557.
5. Guidance for industry. Systemic lupus erythematosus — Developing medical products for treatment. 2010. Washington, DC: U.S. Department of Health and Human Services. [Internet. Accessed April 30, 2013.] Available from: www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072063.pdf
6. Jolly M, Pickard AS, Block JA, Kumar RB, Mikolaitis RA, Wilke CT, et al. Disease specific patient reported outcome tools for systemic lupus erythematosus. Semin Arthritis Rheum 2012; 42:56-65.
7. Toloza SM, Jolly M, Alarcon GS. Quality-of-life measurements in multiethnic patients with systemic lupus erythematosus: Cross-cultural issues. Curr Rheumatol Rep 2010;12:237-49.
8. Guillemin F, Bombardier C, Beaton D. Cross-cultural adaptation of health-related quality of life measures: Literature review and proposed guidelines. J Clin Epidemiol 1993;46:1417-32.
9. Hochberg MC. Updating the American College of Rheumatology revised criteria for the classification of systemic lupus erythematosus. Arthritis Rheum 1997;40:1725.
10. Ware JE. The SF-36 health survey. In: Spiker B, editor. Quality of life and pharmacoeconomics in clinical trials. Philadelphia: Lippincott-Raven; 1996:337-45.
11. Petri M, Kim MY, Kalunian KC, Grossman J, Hahn BH, Sammaritano LR, et al. Combined oral contraceptives in women with systemic lupus erythematosus. N Engl J Med 2005; 353:2550-8.
12. Ruperto N, Hanrahan LM, Alarcon GS, Belmont HM, Brey RL, Brunetta P, et al. International consensus for a definition of disease flare in lupus. Lupus 2011;20:453-62.
13. Gladman D, Ginzler E, Goldsmith C, Fortin P, Liang M, Urowitz M, et al. The development and initial validation of the Systemic Lupus International Collaborating Clinics/American College of Rheumatology damage index for systemic lupus erythematosus. Arthritis Rheum 1996;39:363-9.
14. Aday LA. Designing and conducting health surveys. 2nd ed. San Francisco: Jossey-Bass Inc.; 1996.
15. Hu L, Bentler PM. Cutoff criteria for fit indexes in covariance structure analysis: Conventional criteria versus new alternatives. Struct Equ Modeling 1999;6:1-55.
16. Mplus user's guide [computer program]. Los Angeles: Muthén & Muthén; 2001.
17. Hays RD, Anderson R, Revicki D. Psychometric considerations in evaluating health-related quality of life measures. Qual Life Res 1993;2:441-9.
18. Peschken CA, Katz SJ, Silverman E, Pope JE, Fortin PR, Pineau C, et al. The 1000 Canadian faces of lupus: Determinants of disease outcome in a large multiethnic cohort. J Rheumatol 2009; 36:1200-8.
19. Marx RG, Menezesb A, Horovitz L, Jones EC, Warren RF. A comparison of two time intervals for test-retest reliability of health status instruments. J Clin Epidemiol 2003;56:730-5.
20. Jolly M, Utset TO. Can disease specific measures for systemic lupus erythematosus predict patients health related quality of life? Lupus 2004;13:924-6.
21. Jolly M, Pickard AS, Wilke C, Mikolaitis RA, Teh LS, McElhone K, et al. Lupus-specific health outcome measure for US patients: The LupusQoL-US version. Ann Rheum Dis 2010;69:29-33.
22. Kuriya B, Gladman DD, Ibanez D, Urowitz MB. Quality of life over time in patients with systemic lupus erythematosus. Arthritis Rheum 2008;59:181-5.
23. McElhone K, Abbott J, Teh SL. A review of health related quality of life in systemic lupus erythematosus. Lupus 2006;15:633-43.
24. Juniper EF, Guyatt GH, Jaeschke R. How to develop and validate a new health related quality of life instrument. In: Spiker B, editor. Quality of life and pharmacoeconomics in clinical trials. Philadelphia: Lippincott-Raven; 1996:49-55.
25. Leong KP, Kong KO, Thong BY, Koh ET, Lian TY, Teh CL, et al. Development and preliminary validation of a systemic lupus erythematosus-specific quality-of-life instrument (SLEQOL). Rheumatology 2005;44:1267-76.
26. Doward LS, McKenna SP, Whalley D, Tennant A, Griffiths B, Emery P, et al. The development of the L-QoL: A quality of life instrument specific to systemic lupus erythematosus. Ann Rheum Dis 2008;59:84-8.
27. McElhone K, Abbott J, Shelmerdine J, Bruce IN, Ahmad Y, Gordon C, et al. Development and validation of a disease-specific health-related quality of life measure, the LupusQol, for adults with systemic lupus erythematosus. Arthritis Rheum 2007:57:972-9.